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INVITATION

Dear Colleagues,

Our 57th ERA-EDTA Congress will continue as planned on the originally scheduled dates of June 6-9, 2020 in a fully virtual manner.

As every year, it will be the time to celebrate goals and achievements as well as explore new paths and be fascinated by innovations and developments which influence the world of nephrology in a fully virtual, but still highly interactive, manner.

The Scientific Committee, chaired by Prof. Peter J. Blankestijn, has worked very hard to guarantee an outstanding scientific programme that could meet the expectations of virtual attendees and satisfy the nephrology community.

We are looking forward to sharing with all of you the experience of this extraordinary and unique virtual edition of the 2020 ERA-EDTA Congress.



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The authors of the abstracts below will receive a diploma.

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Nephrology Dialysis Transplantation 35 (Supplement 3): iii1–iii2, 2020
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ADPKD – TOLVAPTAN AND BEYOND

SO001

BOTH HYDROCHLOROTHIAZIDE AND METFORMIN AMELIORATE AQUARETIC SIDE-EFFECTS IN ADPKD PATIENTS THAT ARE TREATED WITH TOLVAPTAN

Bart Kramers[1], Iris Koorevaar[1], Sophie Aapkes[1], Claire Dekkers[2], Hiddo Lambers Heerspink[2], Ronald Gansevoort[1], Esther Meijer[1]

[1]University Medical Center Groningen, Department of Nephrology, Groningen, Netherlands and [2]University Medical Center Groningen, Department of Clinical Pharmacy and Pharmacology, Groningen, Netherlands

Background and Aims:

The vasopressin V2 receptor antagonist tolvaptan is the first drug that was proven to ameliorate kidney function decline in ADPKD. Blockade of the vasopressin V2 receptor, however, also results in nephrogenic diabetes insipidus (NDI), with an associated polyuria of on average 6 to 8 L/24h, limiting its clinical use. Hydrochlorothiazide (HCT) is an established treatment in NDI of other origins, but is unclear whether it is also efficacious in tolvaptan-caused NDI. Importantly, the combination of HCT and tolvaptan could cause electrolyte disturbances, and HCT treatment could theoretically increase vasopressin, which might accelerate ADPKD disease progression. Recently, metformin has been shown to ameliorate aquaresis in an animal model of NDI, but has never been investigated for this indication in humans. We aimed to investigate efficacy and safety of hydrochlorothiazide and metformin treatment to ameliorate the aquaretic side-effects of tolvaptan.

Method:

This is an investigator driven, double-blind, randomized, controlled cross-over trial. ADPKD patients (Ravine criteria) were eligible for inclusion if they were 18-55 years of age, had an eGFR $\geq$ 30 mL/min/1.73m^2 and were treated with a stable dose of tolvaptan. Patients were treated for three 2 week-periods with hydrochlorothiazide (HCT) 25 mg (12.5 mg in the first week), metformin 2000 mg (1000 mg in the first week) or placebo (half dose in the first week), in random order. Primary outcome was change in 24-hour urine volume (average of 2 collections) compared to baseline. Key secondary outcomes were measured GFR (mGFR), plasma copeptin (the stable precursor of vasopressin), quality of life and electrolytes.

Results:

All 13 patients that were included were able to complete every treatment period in the trial. Their mean age was 45±8 years, 54% was female and mGFR was 55±11 mL/min/1.73m^2 (Table). 85% of participants used the maximum tolvaptan dose (90/30 mg). At baseline urine volume was 6.9±1.4 L/24h. On HCT treatment urine volume decreased with -25±13% ($p<0.001$) and on metformin with -22±10% ($p<0.001$). Metformin treatment induced no change in mGFR and copeptin compared to baseline. During HCT treatment however, both mGFR and copeptin were lower ($p=0.002$ and $p=0.001$, respectively). There were no adverse events that required dose reductions. Quality of life was found to be equal on metformin and borderline better ($p=0.06$) on HCT treatment when compared to tolvaptan only. Plasma sodium was similar during all three treatment periods. Plasma potassium was significantly lower during HCT treatment ($p=0.01$), but in only three cases mild hypokalemia was noted (plasma potassium 3.0-3.5 mmol/L).

Conclusion:

This is the first study to show that metformin can ameliorate aquaresis in NDI, and that HCT improves tolvaptan-caused NDI. Both treatments were well tolerated and safe during short-term use. The fact that copeptin is not increased by metformin, and even decreased by HCT suggests that these treatments will not negatively impact renoprotection by tolvaptan. These data provide an evidence base to test metformin and especially HCT in a real life setting to improve aquaresis and tolerability in patients with tolvaptan induced NDI.

	Baseline	HCT	Placebo	Metformin
Absolute urine volume (L/24h)	6.9	5.1**	6.3	5.4**
Change in urine volume (%)	0	-25**	-8	-22**
Creatinine excretion (mmol/24h)	15.8	15.4	16.1	15.7
Osmolar excretion (mOsm/24h)	1044	1020	1013	947*
mGFR (mL/min/1.73m^2)	55	51**	55	54
SBP (mmHg)	125	117**	122	120
Plasma copeptin (pmol/L)	25	20**	26	28
Plasma sodium (mmol/L)	141	139	141	140
Plasma potassium (mmol/L)	3.8	3.6*	3.9	4.0
Plasma urea (mmol/L)	7.0	8.6**	6.9	7.2
QoL Improved	N/A	7 (58%)	2 (17%)	1 (8%)

Results in n=13 ADPKD patients on highest tolerated tolvaptan dose
*P<0.05 compared to placebo
** p<0.01 compared to placebo

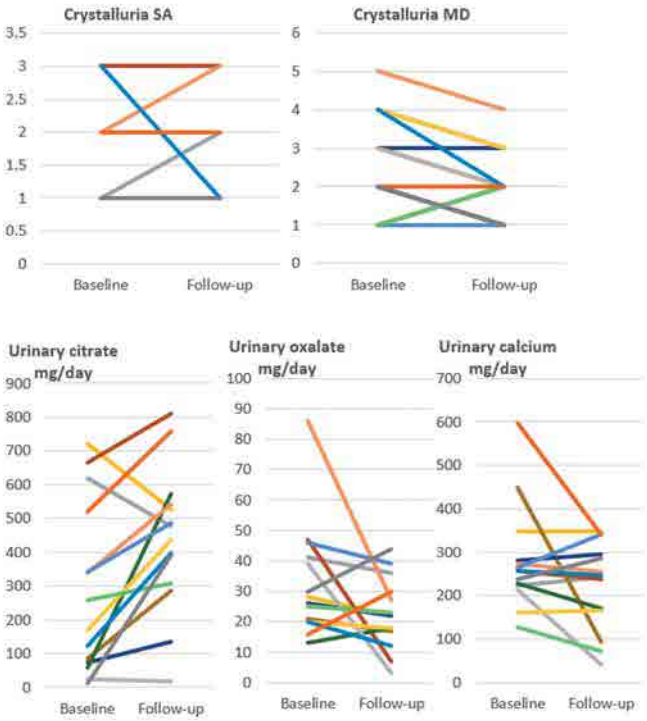


Figure:

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SO002

INTERIM RESULTS FROM ACQUIRE: A STUDY MEASURING QUALITY OF LIFE, TREATMENT PREFERENCE AND TREATMENT SATISFACTION OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE PATIENTS IN EUROPE

Dominique Joly[1], Madhusudan Kabra[2], Helen Doll[3], Anne De Jong-Laird[2]

[1]Necker Hospital, Nephrology Department, Paris, France, [2]Otsuka Pharmaceutical Europe Ltd., Wexham, United Kingdom and [3]Clinical Outcomes Solutions, Folkestone, United Kingdom

Background and Aims: Data suggest the health-related quality of life (HRQoL) of autosomal dominant polycystic kidney disease (ADPKD) patients (pts) may be lower than the general population [1,2]. In this 'real life' cohort of ADPKD pts with chronic kidney disease (CKD) stages 1–3 and rapidly progressing disease, we aimed to describe pt demographics, treatment patterns and pt reported outcome measures (PROMs).

Method: ACQUIRE (NCT02848521) is a prospective, non-interventional, real-world observational study ongoing in 7 European countries. Rapidly progressing ADPKD pts (CKD stages 1–3) completed validated PROMs at enrolment (baseline), Month 1, Month 3 and every 3 months to Month 18. This abstract reports results through 9 months. The primary objective was change in Physical Health Composite Scale (PCS) scores of the 12-item Short Form Health Survey (SF-12). Other objectives included changes in SF-12 Mental Health Composite Scale (MCS) scores, ADPKD-specific PROMs including the ADPKD-Impact Scale (IS), -Urinary Impact Scale (UIS) and -Pain & Discomfort Scale (PDS), and treatment satisfaction using the Treatment Satisfaction Questionnaire for Medication (TSQM-9). Treatment preferences will be measured using a discrete choice experiment on study completion.

Results: Pt demographics and changes from baseline in SF-12, ADPKD-IS and TSQM-9 at Month 9 are presented in **Table 1**; no changes were observed in ADPKD-UIS or ADPKD-PDS.

Conclusion: The study population is relatively young and in full-time employment. During this interim analysis, pts reported reduced scores in the PCS component of SF-12, increased ADPKD-IS scores and reduced treatment satisfaction. These data suggest that disease progression over 9 months negatively impacts pts with early stages of ADPKD. The final analyses will further investigate the contribution of different factors on PROMs and treatment satisfaction.

Table 1. Patient demographics and changes in SF-12, ADPKD-IS and TSQM-9 at Month 9 by CKD stage

				CKD stage			Total (N=402)		
Parameter, mean (SD)*				1 (n=79)	2 (n=123)	3 (n=200)			
Patient demographics and disease characteristics									
Sex, female, n (%)				49 (62.0)	56 (45.5)	89 (44.5)	194 (48.3)		
Age, years				34.0 (10.2)	40.7 (8.4)	47.8 (9.2)	42.9 (10.6)		
Any chronic condition, n (%)				31 (39.2)	40 (32.5)	95 (47.5)	166 (41.3)		
Hypertension, n (%)				41 (51.9)	92 (74.8)	169 (84.5)	302 (75.1)		
Age of ADPKD symptom onset				24.0 (12.2)	28.6 (9.3)	32.5 (12.7)	29.6 (12.1)		
Employed full-time, n (%)				48 (66.7)	90 (78.3)	137 (73.3)	275 (73.5)		
Prescribed tolvaptan, n (%)				33 (41.8)	70 (56.9)	137 (68.5)	240 (59.7)		
Changes from Baseline at Month 9									
SF-12 (range: 1–100)	N			22	39	64	125		
		PCS	BL		53.9 (7.3)	55.8 (5.3)	51.4 (8.3)	53.3 (7.5)	
				Mth 9 CfB		-2.4 (8.06)	-0.9 (5.13)	-2.2 (5.61)	-1.8 (5.96)
			p value#		0.180	0.302	**0.002**	**0.001**	
		MCS	BL		46.1 (10.9)	50.0 (6.9)	47.2 (9.2)	47.8 (9.1)	
		Mth 9 CfB		0.8 (7.48)	0.0 (8.73)	2.5 (8.76)	1.4 (8.55)		
ADPKD-IS (range: 1–5)	N			19	37	63	119		
		Physical		BL	1.50 (0.65)	1.37 (0.59)	1.70 (0.75)	1.56 (0.70)	
				Mth 9 CfB	0.33 (0.64)	-0.04 (0.56)	0.06 (0.48)	0.07 (0.54)	
		Emotional		BL	2.08 (0.83)	1.94 (0.75)	2.16 (0.81)	2.08 (0.80)	
				Mth 9 CfB	-0.22 (0.38)	-0.27 (0.62)	-0.04 (0.66)	-0.14 (0.61)	
		Fatigue		BL	1.92 (1.01)	1.64 (0.79)	2.00 (0.92)	1.87 (0.91)	
			Mth 9 CfB		0.29 (0.56)	0.10 (0.59)	0.05 (0.65)	0.11 (0.62)	
TSQM-9 (range: 1–100)	N			17	33	61	111		
		Global satisfaction		BL	57.7 (23.1)	67.2 (19.7)	67.1 (23.2)	65.4 (22.4)	
			Mth 9 CfB	-7.1 (16.4)	0.4 (17.4)	-3.4 (19.1)	-2.8 (18.2)		

Baseline demographics: Full Analysis Set (all patients fulfilling inclusion criteria); CfB: Primary Analysis Set (all patients providing a baseline SF-12 measurement; CKD1: n=63; CKD2: n=93; CKD3: n=149). *Unless otherwise stated. #paired t-test, reported for primary endpoint only. Where range is 1–100, 1 is lowest; 100 is highest. Where range is 1–5, 1 is not difficult/bothered; 5 is extremely difficult/bothered. BL: baseline; CfB: change from baseline; MCS: mental component score; Mth: month; PCS: physical component score; SD: standard deviation.

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THE INFLAMMATORY PATHWAY IN CKD: TREATMENTS AT LAST?

SO003 LIFE-LONG NLRP3 INFLAMMASOME-MEDIATED SYSTEMIC INFLAMMATION ASSOCIATES WITH CARDIOVASCULAR MORTALITY: A GENETIC ASSOCIATION STUDY OF >500,000 INDIVIDUALS

Stefan Schunk[1], Marcus E. Kleber[2], Winfried Maerz[2], Stephen Zewinger[1], Jaumann Isabella[1], David Schmit[1], Danilo Fliser[1], Laufs Ulrich[3], Thimoteus Speer[1]
[1]*Saarland University Hospital, Homburg, Germany,* [2]*Universitätsklinikum Mannheim, Mannheim, Germany and* [3]*University Hospital Leipzig, Leipzig, Germany*

Background and Aims: Chronic kidney disease (CKD) represents one of the strongest cardiovascular risk factors. Recently, we have shown that activation of the NOD-like receptor protein-3 (NLRP3) inflammasome mediates progression of kidney injury and CKD-associated vascular disease (Zewinger et al. Nat Immunol 2013). Components of the NLRP3 inflammasome pathway such as interleukin-1β (IL-1β) can therapeutically be targeted. Associations of genetically determined life-long inflammasome-mediated systemic inflammation with CVD and mortality in humans are unknown.

Method: We explored the association of genetic *NLRP3* variants with prevalent CVD and cardiovascular mortality in 3,061 patients enrolled in the LURIC study undergoing coronary angiography in a gene-centric approach. Functional relevance of the rs10754555 *NLRP3* variant was studied in freshly isolated human monocytes. Findings were validated in 39,755 participants from eight independent studies (CV risk populations) as well as in 483,258 participants of the UKBiobank study (general population).

Results: Genetic analyses identified the highly prevalent (MAF 39.9%) intronic *NLRP3* variant rs10754555 to affect *NLRP3* gene expression. rs10754555 carriers showed significantly higher C-reactive protein and serum amyloid A plasma levels. Expression of *NLRP3* mRNA and inflammasome-dependent effector responses of isolated human monocytes from rs10754555 carriers were significantly higher as compared to non-carriers. In homozygous rs10754555 carriers, the prevalence of coronary artery disease (CAD) was significantly higher as compared to non-carriers with a significant interaction between rs10754555 and age in LURIC and in UKBiobank. Importantly, in LURIC and in UKBiobank, homozygous rs10754555 carriers had significantly higher risk for cardiovascular mortality during follow-up (HR 1.37, 95%-CI 1.08-1.74 and HR 1.13, 95%-CI 1.02-1.25, respectively). Consistently, rs10754555 was associated with higher cardiovascular mortality (HR 1.11, 95%-CI 1.05-1.16; $P<0.001$) in an additive model in patients with prevalent CAD.

Conclusion: The *NLRP3* intronic variant rs10754555 is associated with increased systemic inflammation, inflammasome activation, prevalent CAD and mortality. This study provides evidence for a substantial role of life-long, genetically-driven systemic inflammation in cardiovascular disease and highlights the NLRP3 inflammasome as a therapeutic target in the general population and particular in patients with CKD.

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SO004

IDENTIFICATION OF HUB GENES, FOCUSED ON CHEMOKINES AND CHEMOKINE RECEPTORS, ASSOCIATED WITH THE DECLINE OF RENAL FUCTION OF DIABETIC KIDNEY DISEASE BY WEIGHTED GENE CO-EXPRESSION NETWORK ANALYSIS.

Songtao Feng[1], Bicheng Liu[1], Linli Lv[1], Gao Yueming[1], Di Yin[1], Cao Jingyuan[1]

[1]*Zhongda Hospital, Southeast University School of Medicine, Nephrology, Nanjing, P.R. China*

Background and Aims: The fact that activation of the innate immune system and chronic inflammation are closely involved in the pathogenesis of diabetic Kidney disease (DKD). Recent studies have suggested the inflammatory process plays a crucial role in the progression of DKD. Identifying novel inflammatory molecules closely related to the decline of renal function is of significance in diagnosing and predicting the progression of DKD. The weighted gene co-expression network analysis (WGCNA) algorithm represents a novel systems biology method that provide the approach of association between gene modules and clinical traits to find the genes involvement into the certain phenotypic trait. The goal of this study was to identify hub genes and their roles in DKD from the gene sets associated with the decline of renal function by WGCNA.

Method: The Gene Expression Omnibus (GEO) database and "Nephroseq" website were searched and transcriptome study from DN biopsies with well-established clinical phenotypic data were selected for analysis. Next, we constructed a weighted gene co-expression network and identified modules negatively correlated with eGFR by WGCNA in the data of glomerular tissue. Functional annotations of the genes in modules negatively correlated with eGFR were analyzed by Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses. Through protein-protein interaction (PPI) analysis and hub gene screening, the hub genes were obtained. Furthermore, we compared the expression level of hub genes between DKD and normal control and drew ROC curves to determine the diagnosis value to DKD of these genes.

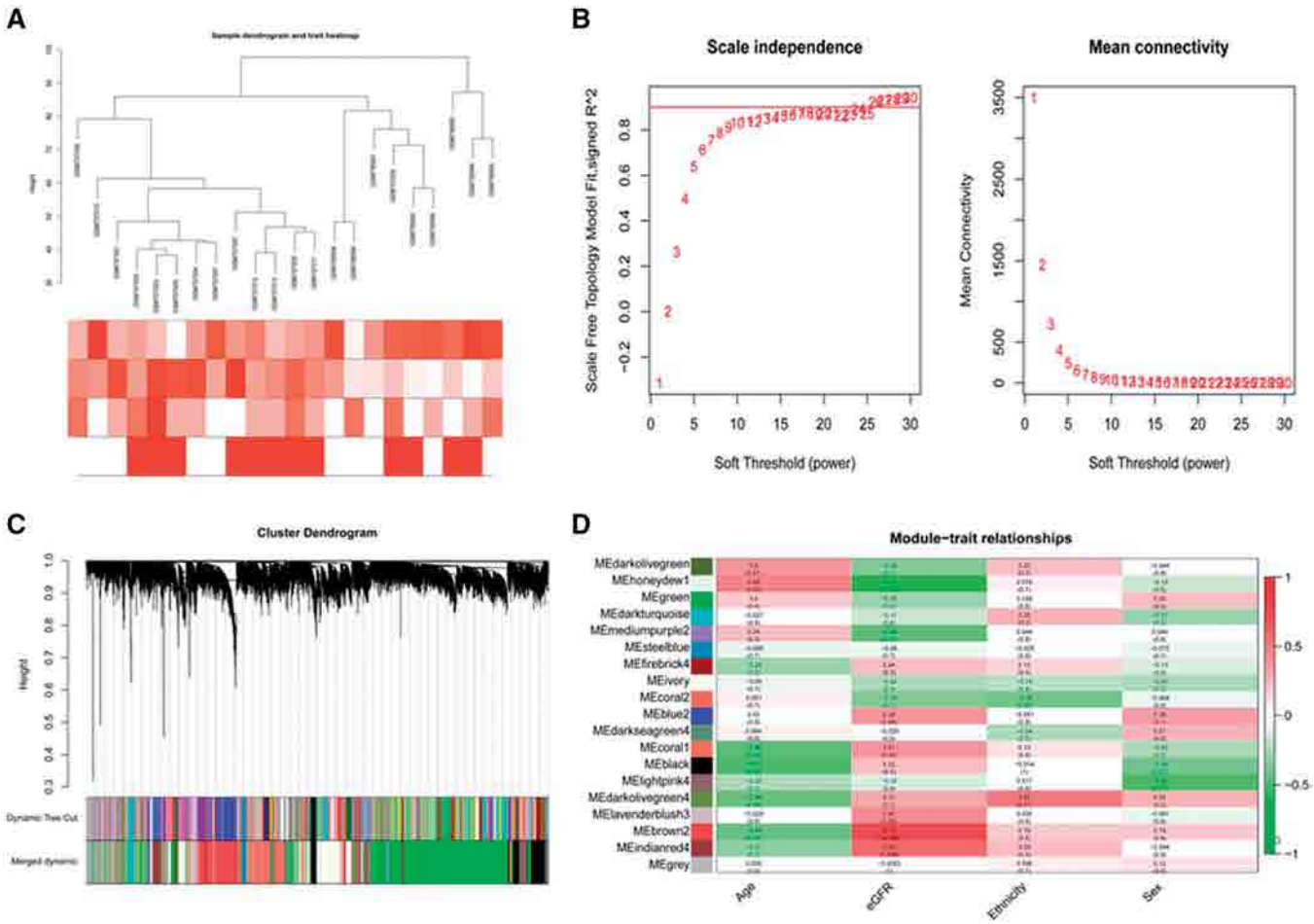


Figure:

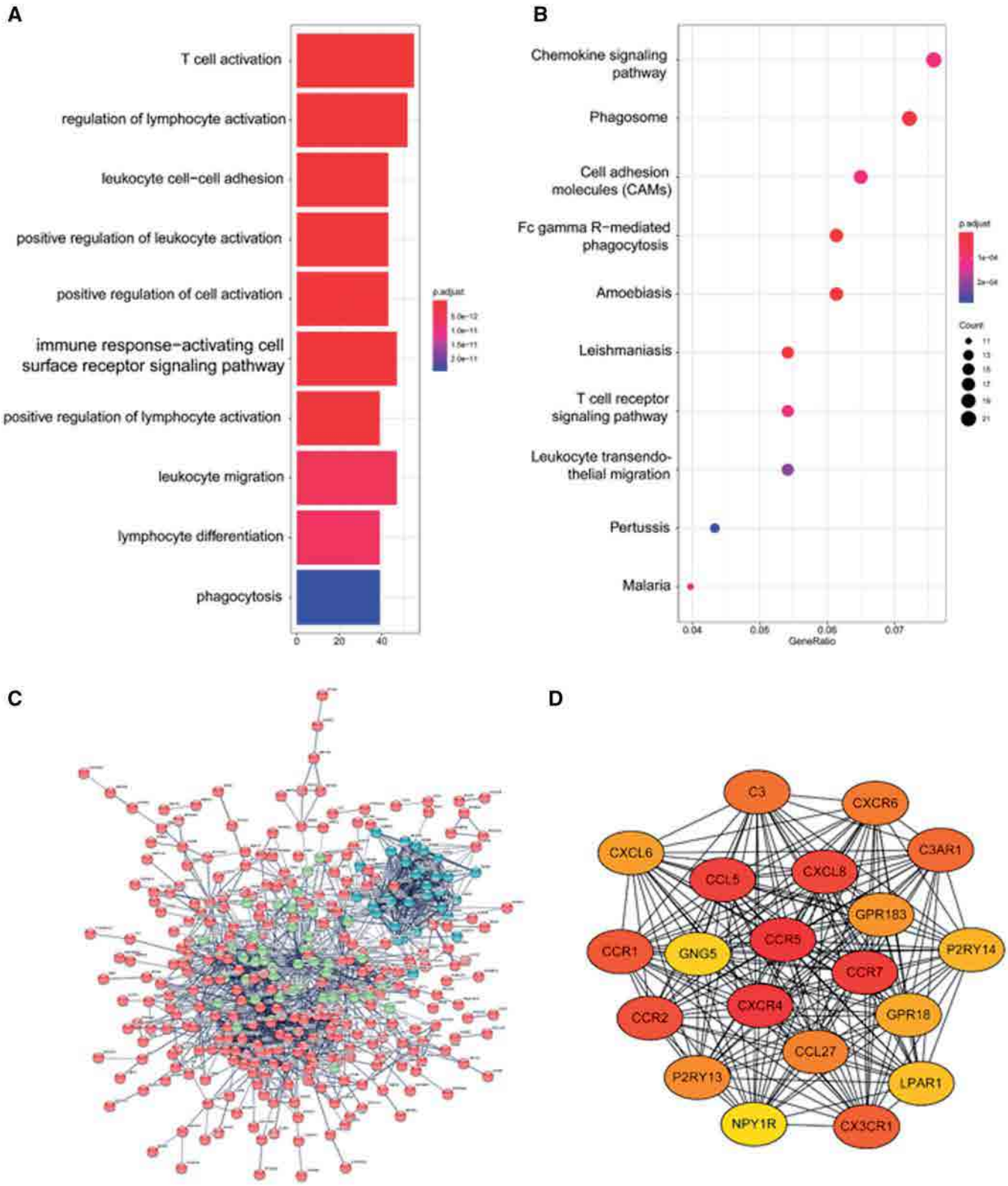

A
T cell activation
regulation of lymphocyte activation
leukocyte cell−cell adhesion
positive regulation of leukocyte activation
positive regulation of cell activation
immune response−activating cell surface receptor signaling pathway
positive regulation of lymphocyte activation
leukocyte migration
lymphocyte differentiation
phagocytosis
0
20
40
p.adjust
B
Chemokine signaling pathway
Phagosome
Cell adhesion molecules (CAMs)
Fc gamma R−mediated phagocytosis
Amoebiasis
Leishmaniasis
T cell receptor signaling pathway
Leukocyte transendothelial migration
Pertussis
Malaria
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0.07
GeneRatio
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Count
C
D
C3
CXCR6
CXCL6
C3AR1
CCL5
CXCL8
GPR183
CCR1
GNG5
CCR5
P2RY14
CCR7
CXCR4
CCR2
GPR18
CCL27
P2RY13
LPAR1
NPY1R
CX3CR1

Figure:

Results: The microarray-based expression datasets GSE30528 were screened out for analysis, which included glomeruli tissue of 9 cases of DKD and 13 cases of control. This microarray platform represented the transcriptome profile of 12411 well-characterized genes. Using WGCNA, a total of 19 gene modules were identified. Then module eigengene were analyzed for correlation with clinical traits of age, sex, ethnicity and eGFR and the "MEhoneydew1" module showed negative associated with eGFR (r=-0.58). GO functional annotation showed that these 551 genes in the "MEhoneydew1" module mainly enriched in the T cell activation. KEGG annotation showed mainly enriched in chemokine signaling pathway. Except for C3, top 10 hub genes, CCR5, CXCR4, CCR7, CCL5, CXCL8, CCR2, CCR1, CX3CR1, C3AR1 and C3, are all members of chemokines or chemokine receptors. Furthermore, we compared the expression level of these 9 genes between DKD and control, and found that all of these 9 genes increased in the DKD group, and the differences of 6 genes, CCR5, CCR7, CCL5, CCR2, CCR1, C3AR1, were of statistical significance. Linear correlation analysis showed that the expression of these 6 genes was negatively correlated with eGFR, and the ROC curve showed that the area under the curve could reach 0.812∼1.0.

Conclusion: We identified a panel of 6 hub genes focused on chemokines and chemokine receptors critical for decline of renal function of DKD using WGCNA. These genes may serve as biomarkers for diagnosis/prognosis and as putative novel therapeutic targets for DKD.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii7–iii11, 2020

HOME DIALYSIS

SO005

BARRIERS TO PERITONEAL DIALYSIS IN SASKATCHEWAN CANADA: RESULTS FROM A PROVINCE WIDE SURVEY

Bhanu Prasad[1], Lucas Diebel[2], Maryam Jafari[3], Sachin Shah[4]

[1]Regina General Hospital, Saskatchewan Health Authority, Medicine, Regina, Canada, [2]College of Medicine, University of Saskatchewan, Medicine, Saskatoon, Canada, [3]Dr. T Bhanu Prasad Medical Prof Corp, Regina, Canada and [4]St. Paul's Hospital, Saskatchewan Health Authority, Medicine, Saskatoon, Canada

Background and Aims: Peritoneal dialysis (PD) offers similar clinical outcomes to hemodialysis (HD) at a fraction of the cost. PD remains underutilized as remote HD patients in the province of Saskatchewan often relocate or travel hundreds of kilometers weekly in order to receive dialysis related care. Many barriers to patient uptake of PD have been described, but the scale of their impact on our patient population have not been quantified. To improve uptake of peritoneal dialysis in Saskatchewan, we need to address the most prominent barriers to patient access to PD to ensure that they truly have a choice in determining the modality with which they choose to dialyze. The purpose of this study was to determine the barriers to receiving PD in Saskatchewan

Method: We conducted a cross sectional survey of in-center HD patients across the province of Saskatchewan, Canada. A total of 740 in-center HD patients at two academic sites and 7 satellite units were approached by study coordinators. 421 patients (n=268 in the main units and n=153 in the satellite units) agreed to participate in the study. A questionnaire using a five-point Likert scale was created to identify barriers to PD with questions addressing PD awareness and knowledge, accessibility, and risks, fears, beliefs surrounding PD. Responses were anonymous and tabulated using a data collection tool. Survey data were summarized using descriptive statistics.

Results: 45.9% of participants had more than 12 years of formal education. 11% lived on farm, 19% on reserve, and 71% in town/city. The median (interquartile range=IQR) distance of home to in-center dialysis units was 10 (5-70) kilometers. Only 82% of patients were aware of PD as a treatment option. 35% of patients felt they had no understanding of the benefits or risks of PD. Despite only 13% of patients being told they were unsuitable for PD by their nephrologist, approximately half (47%) had ever considered it as a treatment option. Prominent barriers to PD that we identified were: excellent care in the HD unit (62%), proximity to dialysis unit (41%), unwilling to dialyze daily (36%), and unwilling to learn a new technique (34%). Beliefs held by patients that figured prominently in their decision to choose HD over PD included not wanting to take their disease home (32%), fear of being a burden on family (32%), lack of space (28%), risk of infection, issues with self-image while on PD, and PD being an inferior modality to HD (all approximately 24%).

Conclusion: Several barriers to PD were identified with a few consistent themes being identified, including deficiencies in knowledge, patient specific beliefs, poor patient education, and perceived benefits of in-center care (satisfaction with current care). The most frequently reported knowledge barrier was a lack of understanding of benefits and risks of PD. These findings suggest that not enough patients are receiving formal education, or active involvement in deciding which modality they would be most suitable for them when initiating dialysis.

To improve uptake of PD in Saskatchewan, we will have to generate both increased awareness of PD as a treatment modality, alongside improved educational strategies to enable patients to make an informed choice about how they receive renal replacement therapy. While the study does not reflect the views of all patients, the information gained will be valuable in designing an educational program to improve adoption of PD within our province.

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SO006

DIPEPTIDYL PEPTIDASE-4 INHIBITOR PROTECTS FROM PERITONEAL FIBROSIS— A TRANSLATIONAL RESEARCH FROM CLINICAL OBSERVATION TO ANIMAL STUDY

Yi-Chen Li[1], Chihchao Yang[2], Pei-Hsun Sung[1], Hon-Kan Yip[1]

[1]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Division of Cardiology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C. and [2]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Division of Nephrology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C.

Background and Aims: The increasing prevalence rate of end-stage renal disease (ESRD) has emerged as a global health burden. Peritoneal dialysis (PD) possesses the survival and convenient advantage for ESRD during the first 2 years of dialysis treatment. However, long-term PD and hyperglycemia have been identified to frequently result in peritoneal fibrosis (PF) as subsequently to lead the failure of peritoneal function. Therefore, how to prevent PF is an important issue, especially in diabetic ESRD patients.

Method: To explore the effective protection in PD patients, Taiwan National Health Insurance Research Database was utilized to conduct the retrospective population-based cohort study from 1997 to 2013. A total of 19,828 diabetic ESRD patients with PD were analyzed the incidence of PD failure in the user and nonuser of dipeptidyl peptidase-4 (DPP4) inhibitors. On the other hand, the pathological role of DPP4 was further verified by cellular model and animal model of PF induced by chlorhexidine gluconate (CG).

Results: The rate of PD failure was significantly lower in diabetic ESRD patients with than without receiving DPP4 inhibitors ($p<0.0001$). Among all collected types of anti-diabetic drugs, diabetic ESRD patients with DPP4 inhibitors treatment had the lowest rate of PD failure. In cellular study, the high concentration of glucose induced the increase of DPP4 protein levels, accumulating with the epithelial–mesenchymal transition (EMT), inflammation and the generation of oxidative stress in the mesothelial cells. However, sitagliptin treatment remarkably suppressed high concentration of glucose-inducing cellular damage. Additionally, in vivo study, sitagliptin treatment significantly decreased DPP4 activity, reversed EMT process via attenuating TGF-β/ Smad3 axil, ameliorated angiogenesis, reduced oxidative stress generation and inflammation through inhibiting NF-κB/ MyD88 signaling, followed by protected peritoneal integrity and function against CG-inducing PF in rats.

Conclusion: DPP4 contributed to the peritoneal fibrosis and functional impairment, whereas DPP4 inhibitors were suggested as a clinical protective strategy for extending PD.

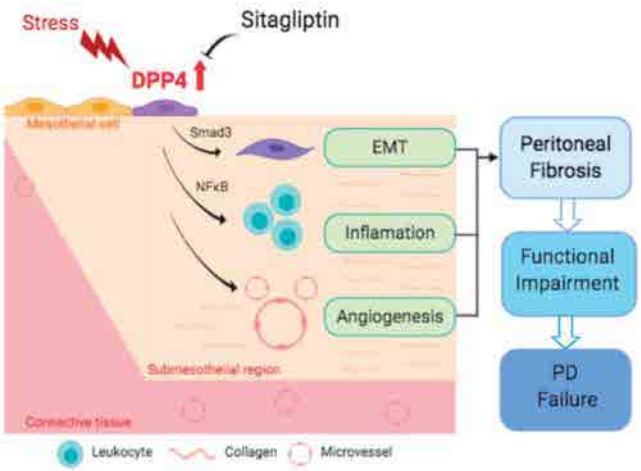


Figure:

SO007 **OVERHYDRATION TREATMENT WITH COMBINED CRYSTALLOID AND COLLOID PD SOLUTION**

CLAUDIA YUSTE[1], Paula Jara Caro Espada[1], LUCIA RODRIGUEZ GAYO[1], Begoña Aguado[1,1], Maria Jesus Aranda[1], Teresa Bada Bosch[1], Manuel Praga[1]

[1]*University Hospital 12 de Octubre, Nephrology, Madrid, Spain*

Background and Aims: Peritoneal dialysis (PD) fluids used colloid or crystalloid solutions to achieve ultrafiltration. Here we presented our clinical experience with the intraperitoneal (IP) use of mixed solutions (MS) (crystalloid plus colloid) to treat overhydration.

Method: We studied the kinetics of 4-hour single-dwell exchange using 2L MS in 3 different sessions. We analysed IP fluids and IP pressure at 0,30,60,120 and 240 min plus blood samples at 0, 120 and 240 min. MS kinetics were compared with standard 4-hour 3.86 % glucose (GS) exchange.

MS composition. We modified a single-dwell exchange of 2L Icodextrin (Extraneal, Baxter®) by adding a continuous 50% glucose infusion (50g Glucose per 100mL) in an aseptic technique through infusion pump (42 ml/h) over 4 hours.

Results: MS exchange induced a progressive increase in IP pressure with an inverse decrease in IP sodium, without significant changes in IP glucose or osmolarity. MS exchanges were well tolerated without side effects (total 25 sessions). We did not observe any remarkable change in bloods samples during the MS exchange. The combination fluid enhanced net ultrafiltration (mean 1030 ml) compared with GS (650 ml). Although the net glucose dispensed was slightly higher with MS (79 g MS vs 77.2 g GS), similar net glucose absorption was observed (49.8 g MS vs 49.9g GS) and smaller maximum intraperitoneal glucose levels (1739 mg/dL at 120 min with MS vs 2695 mg/dL with GS at 0 min). GS induced a faster initial reduction in dialysate sodium concentration while MS maintained the sodium sieving over 4-hour dwell enhancing net ultrafiltration due to sustained IP glucose concentration.

Conclusion: The combination fluid could be a new strategy to enhance ultrafiltration in PD patients, leaded by colloid osmosis at the beginning of PD exchange maintained by crystalloid osmosis.

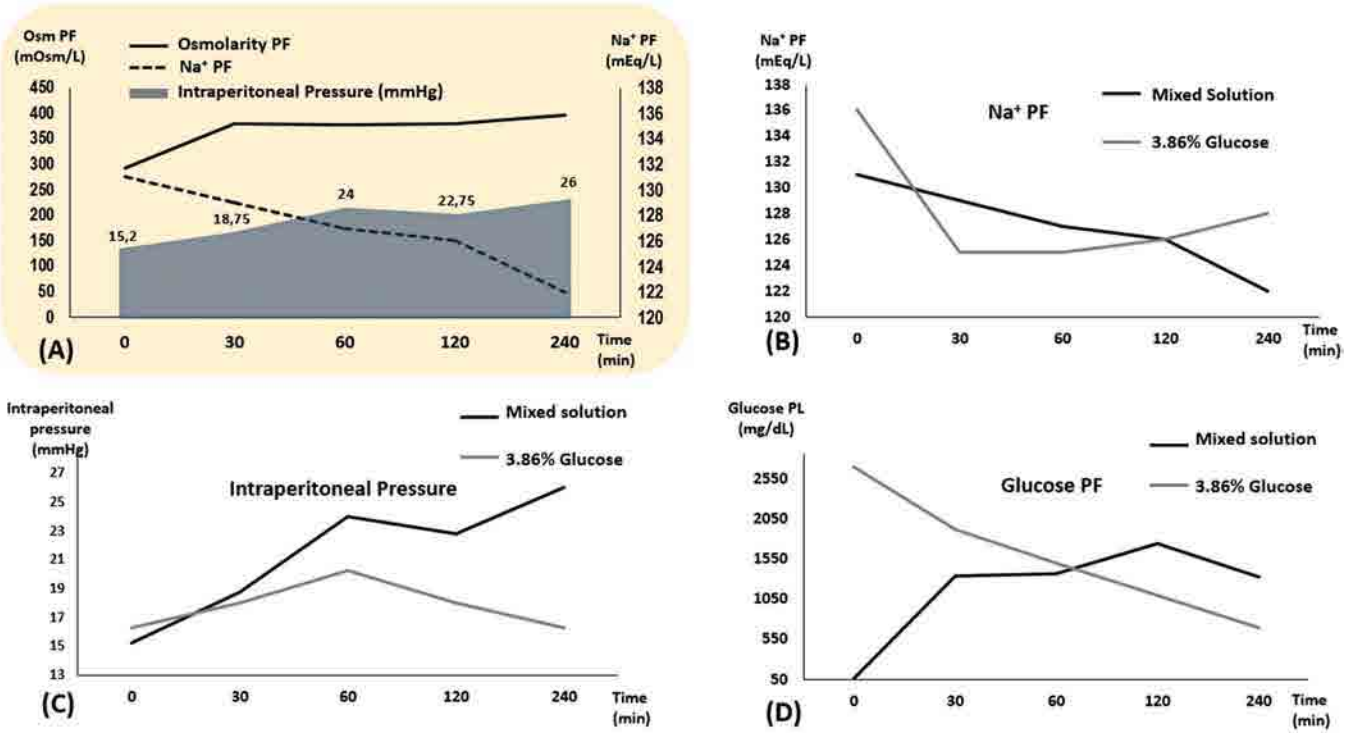


Figure: (A) Intraperitoneal kinetics of MIXED SOLUTION for IP sodium (Na^+ PF), Osmolarity PF and intraperitoneal pressure. (B, C, D) Comparison between MIXED SOLUTIONS (black line) vs Glucose solution 3,86 % (gray line) intraperitoneal kinetcs for sodium (B), intraperitoneal pressure (C) and glucose (D).

SO008

STREPTOCOCCI NOW DOMINATE THE CLINICAL SPECTRUM OF PERITONEAL DIALYSIS (PD)-RELATED PERITONEAL INFECTIONS. AN ANALYSIS OF TRENDS DURING 30 YEARS

Joana Margarida Eugénio Santos[1], Catuxa Rodriguez[2], Inês Coelho[3], Daniela Estefania[2], Letícia Garcia[2], Ana Rodriguez-Carmona[2], Miguel Perez Fontan[2]

[1]Hospital Espírito Santo de Évora, Nephrology, Évora, Portugal, [2]Universitary Hospital A Coruña, Nephrology, A Coruña, Spain and [3]Hospital Local de Saúde de Castelo Branco, Nephrology, Castelo Branco, Portugal

Background and Aims: Peritoneal infections remain as a significant source of morbidity and mortality in PD patients. A steady decline of their incidence has been accompanied by changes in the etiologic spectrum of these infections, during the last decades. We have undertaken a review of trends in the compared incidence of PD-related peritonitis in our centre during a 30-year period, with a particular interest in streptococcal infections.

Method: Following an observational, retrospective design, we analyzed trends in the incidence and outcomes of peritoneal infections diagnosed in our centre between January 1990 and October 2019. We mainly focused on the incidence, risk factors and outcomes of streptococcal peritonitis. We excluded fungal peritonitis (very low incidence), surgical enteric infections and non-infectious peritonitis. Treatment failure was defined by transfer to hemodialysis for at least 3 months after the infection or death related to peritonitis. We applied Cox's model to define clinical predictors of streptococcal infection, and stepwise logistic regression to investigate predictors of treatment failure.

Results: We recorded 1026 episodes of peritoneal infection in 878 patients, including 234 (22.8%) streptococcal infections, 57 (5.6%) infections by Staphylococcus aureus (SAu), 285 (27.8%) infections by coagulase-negative staphylococci (CNSt), 182 (17.7%) infections by gram-negative bacteria, 135 (13.2%) infections with 2 or more microorganisms and 133 (13.0%) culture-negative cases. Remarkably, streptococci were also main components in polimicrobial infections (present in 58.2% of cases). The incidence of peritonitis decreased during the observation period, from 0.91 (1990-94) to 0.47 episodes (2015-19) per patient and year This decline affected preferentially infections by SAu (0.068 to 0.006) and CNSt (0.361 to 0.067), while the incidence of infections by other etiologic agents remained essentially stable. As a consequence, the relative clinical spectrum moved to a predominance of streptococcal (10.7 to 23.3%), polimicrobial (8.0 to 15.7%) and culture-negative infections (4.7 to 16.2%). On multivariate analysis, patients suffering streptococcal infections were older (p=0.019), and presented lower albumin levels (p=0.004), than either patients suffering infections of other etiologies or presenting a peritonitis-free clinical course. After logistic regression analysis, older age, longer time on dialysis at the time of the infection, comorbidity, previous immunosuppression and plasma albumin were most consistent predictors of peritonitis-related mortality and treatment failure. Streptococcal peritonitis showed more benign outcomes than SAu (p<0,001) or gramnegative infections (p=0.032), with rates of treatment failure comparable to those observed for CNSt, non-enteric polimicrobial or culture-negative infections.

Conclusion: Streptococcal and polimicrobial (often including streptococci) infections have become dominant in the clinical spectrum of PD-related peritonitis, after the decline in the incidence of staphylococcal infections. The clinical aggressiveness of these infections appears intermediate between that observed in Staphylococcus aureus and CNSt infections.

SO009

MORTALITY AND HOSPITALIZATION IN A LARGE INTERNATIONAL PERITONEAL DIALYSIS INSTITUTION DURING 2018

Belén Marrón[1], Suzanne Pearce[2], Charlotta Wollheim[3], Carlos Lucas[4], Marietta Torok[5], Dan Munteanu[6], Michael Roesch[7], Janusz Ostrowski[8], Pawel Kochman[8], Attila Orosz[9], Daniel Pérez[10], Alejandro Pacheco[11], Fernando Macário[12]

[1]Diaverum Renal Services, Corporate Home Therapies & Patients Safety Director. Medical Office, Mälmo, Sweden, [2]Diaverum Renal Services, Corporate Nursing Director, Mälmo, Sweden, [3]Diaverum Renal Services, Corporate Data Management Director. Medical Office, Mälmo, Sweden, [4]Diaverum Renal Services, Corporate Medical Protocols & Standarization. Medical Office, Mälmo, Sweden, [5]Diaverum Renal Services, Corporate Integration Director. Medical Office, Mälmo, Sweden, [6]Diaverum Renal Services, Fundeni Clinic, Bucharest, Romania, [7]Diaverum Renal Services, Schlankreye Clinic, Hamburg, Germany, [8]Diaverum Renal Services, Wloclawek Clinic, Wloclawek, Poland, [9]Diaverum Renal Services, Bajcsy Clinic, Budapest, Hungary, [10]Diaverum Renal Services, SEINE Clinic, Montevideo, Uruguay, [11]Diaverum Renal Services, Chilean Medical Office, Santiago, Chile and [12]Diaverum Renal Services, VP Medical Office, Mälmo, Sweden

Background and Aims: With the exception of some national registries, data referred to mortality or hospitalization within a single large international peritoneal dialysis (PD) institution are seldom reported.

To study all-cause mortality, transplantation rate, hospitalizations and peritonitis rates in our large PD program during 2018.

Method: Observational, prospective registry in 8 countries. The following variables were tracked: crude mortality rate and causes, hospitalization variables (n° of hospitalization days per patient; n° of hospitalization episodes per patient; n° of days per hospitalization episode; causes of hospitalization), peritonitis rate (episodes/year at risk and patient months at risk to a peritonitis episode) and transplantation rate.

Results: By the end of December 2018, 1207 pt. were treated (11 countries) but only 8 countries submitted data. Evaluated population as "*patients treated at risk during the year*": AR (319.5), RO (173.5), DE (137), HU (103), PL (97), UR (69.5), CL (27), KZ (7). Crude mortality rate was 13.1%, same if first 90 days on therapy were excluded. Lowest mortality was seen in HU (9.9%) and highest in DE (19.3%). Causes of death: cardiac 32%, all type infections 22% [Sepsis 78%, PD related 11% (as 0.7% of total mortality), pulmonary 3.7%, others 7.4%], vascular 10%, gastrointestinal 3.3%, unknown 10.7% (highest in DE, 23%), other known causes 21.5%. Hospitalization rates: 0.55 episodes/per patient-year and 7.6 days of hospitalization per patient-year. N° of days per hospitalization episode was 13.7. Causes of hospitalization: PD related 38%, cardiovascular 17%, non-PD infection sepsis 10.7% (higher in LA, 16.6%), vascular access 2.1%, unknown 4.5%, others 23.3%. Global peritonitis rate was 0.18 episodes/pt-year at risk (1 episode every 66 m.). However, large differences were seen among countries. Transplantation rate was 6.5% (much higher in UR). PD was withdrawal in 35% of pt. Country specific data have been evaluated but are not shown here.

Conclusion: The use of a common registry in our institution increases quality and allows homogeneous comparisons across countries that if promptly addressed may increase patients' outcomes. Our series may bring light into the PD community as one of the ever largest tracked in a single institution.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii12–iii19, 2020

NOVEL ASPECTS OF NEPHROLITHIASIS

SO010

URINARY LITHOGENIC RISK PROFILE IN ADPKD PATIENTS TREATED WITH TOLVAPTAN

Matteo Bargagli[1], Nasser A. Dhayat[2], Manuel Anderegg[2], Mariam Semmo[2], Uyen Huynh-Do[2], Bruno Vogt[2], Pietro Manuel Ferraro[1,3], Daniel Guido Fuster[2]

[1]Università Cattolica del Sacro Cuore, Roma, Italy, [2]Inselspital, Bern University Hospital, University of Bern, Department of Nephrology and Hypertension, Bern, Switzerland and [3]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Nefrologia, Roma, Italy

Background and Aims: Nephrolithiasis is a common health problem in autosomal dominant polycystic kidney disease (ADPKD) and significantly contributes to patient morbidity. In observational studies, prevalence rates of up to 36% have been reported. Kidney stones of ADPKD patients are typically composed of uric acid (UA) or calcium oxalate (CaOx), and hypocitraturia and low urinary pH have been reported as the main prolithogenic abnormalities. Recently, Tolvaptan has been introduced for the treatment of ADPKD, but its impact on the lithogenic risk profile in ADPKD patients remains unknown.

Method: We conducted a retrospective analysis of patients enrolled in the Bern ADPKD registry, an observational cohort study. Inclusion criteria were age $\geq$ 18 years, clinical diagnosis of ADPKD, and informed consent. The main exclusion criterion was need for renal replacement therapy. 24-h urine analyses were performed at baseline and then at yearly follow-ups. Relative supersaturation ratios (RSS) for CaOx, calcium phoshate (CaP) and UA were calculated with EQUIL2. Univariate and multivariate mixed-effects linear regression models, adjusted for age, sex, BMI, eGFR and endogenous acid production, estimated by net acid excretion, were used to assess the impact of Tolvaptan treatment on urinary composition.

Results: 38 patients received Tolvaptan treatment (39.5% females) and were included in the analysis. Six patients (15.8%) had a history of symptomatic stone events. In multivariate analysis, Tolvaptan treatment was significantly associated with reductions of CaOx, CaP and UA RSS ($p < 0.01$) and increased urinary citrate ($p = 0.015$) and calcium ($p < 0.01$) excretion. In contrast, Tolvaptan treatment was not associated with alterations in urinary oxalate excretion or urinary pH.

Conclusion: Tolvaptan significantly reduces RSS for CaOx, CaP and UA. Future studies are needed to assess the impact of Tolvaptan treatment on stone recurrence in ADPKD patients.

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SO011

OXALATE-DEGRADING ACTIVITY IN FECAL MICROBIOTA ASSOCIATED WITH BLOOD LIPID PROFILE IN DIALYSIS PATIENTS

Natalia Stepanova[1], Ganna Tolstanova[2], Iryna Akulenko[2], Olena Savchenko[1], Larysa Lebid[1], Marharyta Skovorodka[2], Mykola Kolesnyk[1]

[1]State Institution «Institute of Nephrology of the National Academy of Medical Sciences», Nephrology & Dialysis, Kyiv, Ukraine and [2]Taras Shevchenko National University of Kyiv, Kyiv, Ukraine

Background and Aims: Cardiovascular disease (CVD) remains the leading cause of morbidity and death in end-stage renal disease (ESRD) patients. Thus, the accumulation of oxalate due to ESRD can increase the risk of CVD. Also, the ability of fecal oxalate-degrading activity (ODA) to reduce plasma oxalate levels has been discussed. On the other hand, despite a key role of atherogenic dyslipidemia *in the development of* CVD, only a few studies have shown a potential role of microbiota in the regulation of blood lipid profiles in the general population. However, at present, there is a general lack of research on this topic in dialysis patients.

The present study aimed to investigate the association between oxalate-degrading activity (ODA) in fecal microbiota and blood lipid profiles in ESRD patients.

Method: We represented the data of a cross-sectional pilot study examining ODA in fecal microbiota, plasma oxalate concentration (POx) and blood lipid profile markers in 32 ESRD patients. Among the patients, there were 21 hemodialysis (HD) patients and 11 peritoneal dialysis (PD) patients. The average age of the patients was 52.5 [39; 65] years.

The redoximetric titration with KMnO4 was adopted to evaluate total ODA in fecal microbiota. The results were expressed in % oxalate degradation per 0.01 g of feces. The blood lipid spectrum was determined in all patients: total cholesterol level (TC), high (HDL), low (LDL) and very low (VLDL) density cholesterol, triglycerides (TG) and atherogenic index of plasma (AIP).

The median (Me) and interquartile ranges [Q25; Q75] were calculated using the non-parametric Kruskal-Wallis test. The Spearman test was used for the correlation analysis. Chi-square tests were used for comparison of 2 proportions. All statistical analyses were performed using MedCalc.

Results: Dyslipidemia defined as an increase in atherogenic lipoprotein fractions and inhibition of HDL cholesterol was identified in 13/32 (40.6%) ESRD patients. Negative ODA in fecal microbiota ($\leq$ 0 % /0.01 g) was observed in 14/32 (43.7%) patients. Among them, there were 5/21 (23.8%) HD patients and 7/11 (63.6%) PD patients (χ^2=3.9, p=0.04).

Significantly lower ODA in fecal microbiota was observed in the patients with atherogenic dyslipidemia in comparison with dyslipidemia-free patients (-5.0 [-8.7; 3.7] vs 3.0 [0.5; 9] %/0.01 g of feces, p=0.02) (Fig. 1). Less ODA in fecal microbiota was, higher levels of TG (r=-0.5, p=0.004) (Fig. 2), VLDL (r=-0.34, p=0.05) (Fig. 3) and, accordingly, AIP (r=-0.38, p=0.03) (Fig. 4) occurred.

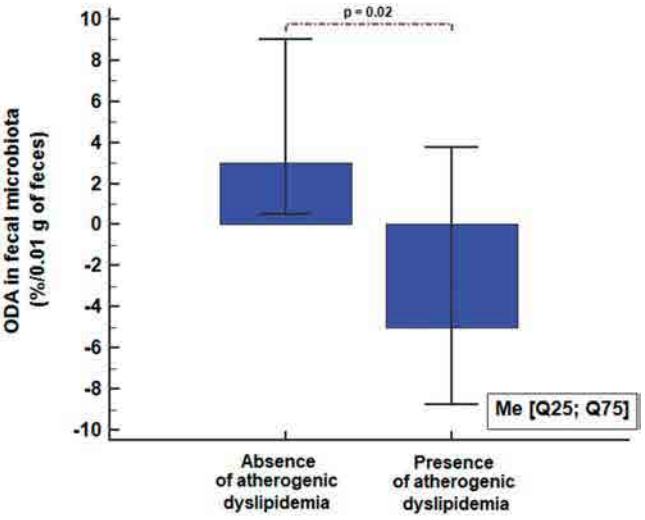


Figure 1: ODA in fecal microbiota in dialysis patients according to atherogenic dyslipidemia status.

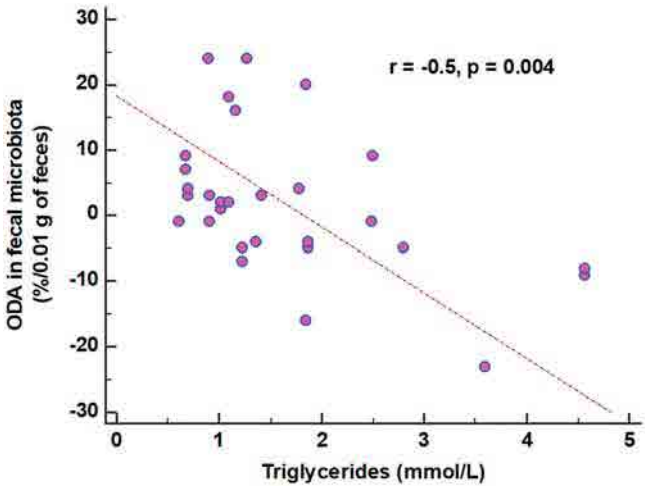


Figure 2: The association between ODA and triglycerides.

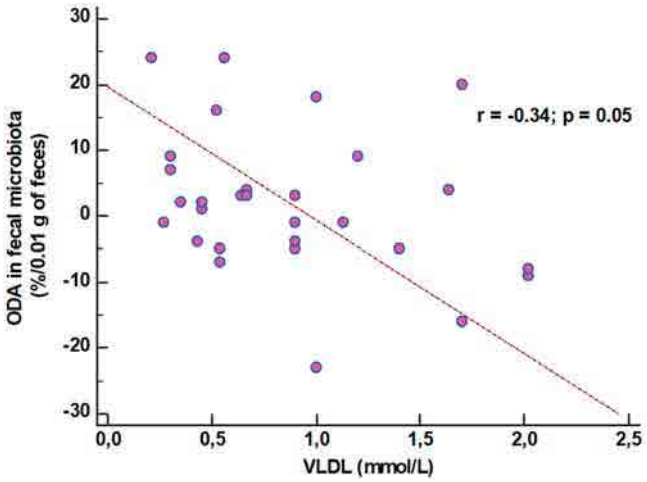


Figure 3: The association between ODA and very-low-density lipoproteins.

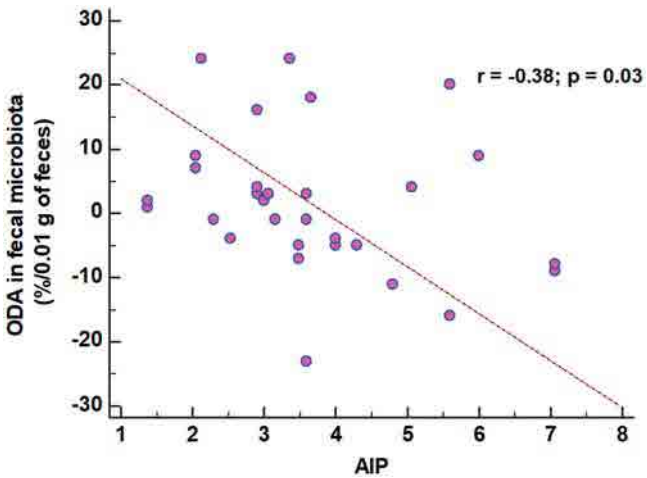


Figure 4: The association between ODA and the atherogenic index of plasma.

Conclusion: The results of our study have provided preliminary evidence on the fact that a decrease in total ODA in fecal microbiota is associated with atherogenic dyslipidemia. Further studies are needed to determine the role of fecal ODA in the formation of dyslipidemia.

SO012

RENOPROTECTIVE EFFECTS OF FEBUXOSTAT AND ALLOPURINOL IN PATIENTS WITH HYPERURICEMIA AND CHRONIC KIDNEY DISEASES: A META-ANALYSIS

Sherida Edding[1], Brian Michael Cabral[1], Monica Therese Cating-Cabral[1]

[1]*St. Luke's Medical Center - Global City, Taguig, Philippines, The*

Background and Aims: Hyperuricemia is associated with rapid deterioration of renal function in patients with chronic kidney disease (CKD). The two most common urate-lowering drugs available in the market are allopurinol and febuxostat. Randomized controlled trials (RTCs) have shown that the individual drugs have potential to slow down progression of renal function in patients with chronic kidney disease (CKD) and hyperuricemia. However, it is unclear which drug is more effective because of insufficient direct comparison between the two. Hence our study aims to perform a meta-analysis of RCTs to assess the renoprotective and urate-lowering effects between the two drugs in patients with CKD and hyperuricemia.

Method: A comprehensive literature search of randomized controlled trials using PubMed was performed with the following search terms: febuxostat, allopurinol, chronic kidney disease, renoprotection. Four prospective RCTs were selected and analyzed using Cochrane Revman v5.3. Outcomes assessed were change in serum creatinine, estimated glomerular filtration rate (eGFR), proteinuria and serum uric acid levels from baseline to 3 months post-initiation of therapy.

Results: Four relevant trials comprising of 486 patients were selected - 247 patients treated with febuxostat and 239 patients with allopurinol. No significant differences were found in the changes in serum creatinine (mean difference -0.04; CI -0.15, 0.07; P = 0.51) and eGFR (mean difference 1.57; CI -0.83, 3.97; P = 0.20) from baseline to 3 months between the febuxostat and allopurinol group. Decrease in proteinuria was significantly observed more in the febuxostat group (mean difference -50.13; CI -90.54; -9.71, P = 0.02). Similarly, serum uric acid levels were significantly more reduced in the febuxostat group (mean difference -1.11; CI -1.53, -0.68, $P < 0.00001$).

Conclusion: Our study showed that febuxostat is non-inferior in terms of delaying renal function decline (as measured by eGFR) but it offers a better anti-proteinuric as well as a urate-lowering effect. However, more studies are needed to assess the efficacy of febuxostat across the spectrum of chronic kidney disease, including those requiring hemodialysis.

SO013

CRUCIAL ROLE OF SERUM RESPONSE FACTOR IN EPITHELIAL-MESENCHYMAL TRANSITION OF RENAL TUBULAR EPITHELIAL CELLS IN HYPERURICEMIC NEPHROPATHY

Long Zhao[1], Yan Xu[1]

[1]*The Affiliated Hospital of Qingdao University, Nephrology, Qingdao, P.R. China*

Background and Aims: To investigate the role of serum response factor (SRF) in epithelial-mesenchymal transition (EMT) of renal tubular epithelial cells (TECs) in hyperuricemic nephropathy (HN).

Method: The expression of SRF, epithelial markers (E-cadherin and ZO-1) and mesenchymal markers (fibronectin, α-SMA, FSP-1) was examined in rat renal tubular epithelial cells (NRK-52E cells) or renal medulla tissues following uric acid (UA). SRF was upregulated by SRF plasmids and downregulated by CCG-1423(a small molecule inhibitor of SRF) to investigate how SRF influenced EMT in TECs of HN. Oxonic acid (OA) was used to generate HN in rats.

Results:

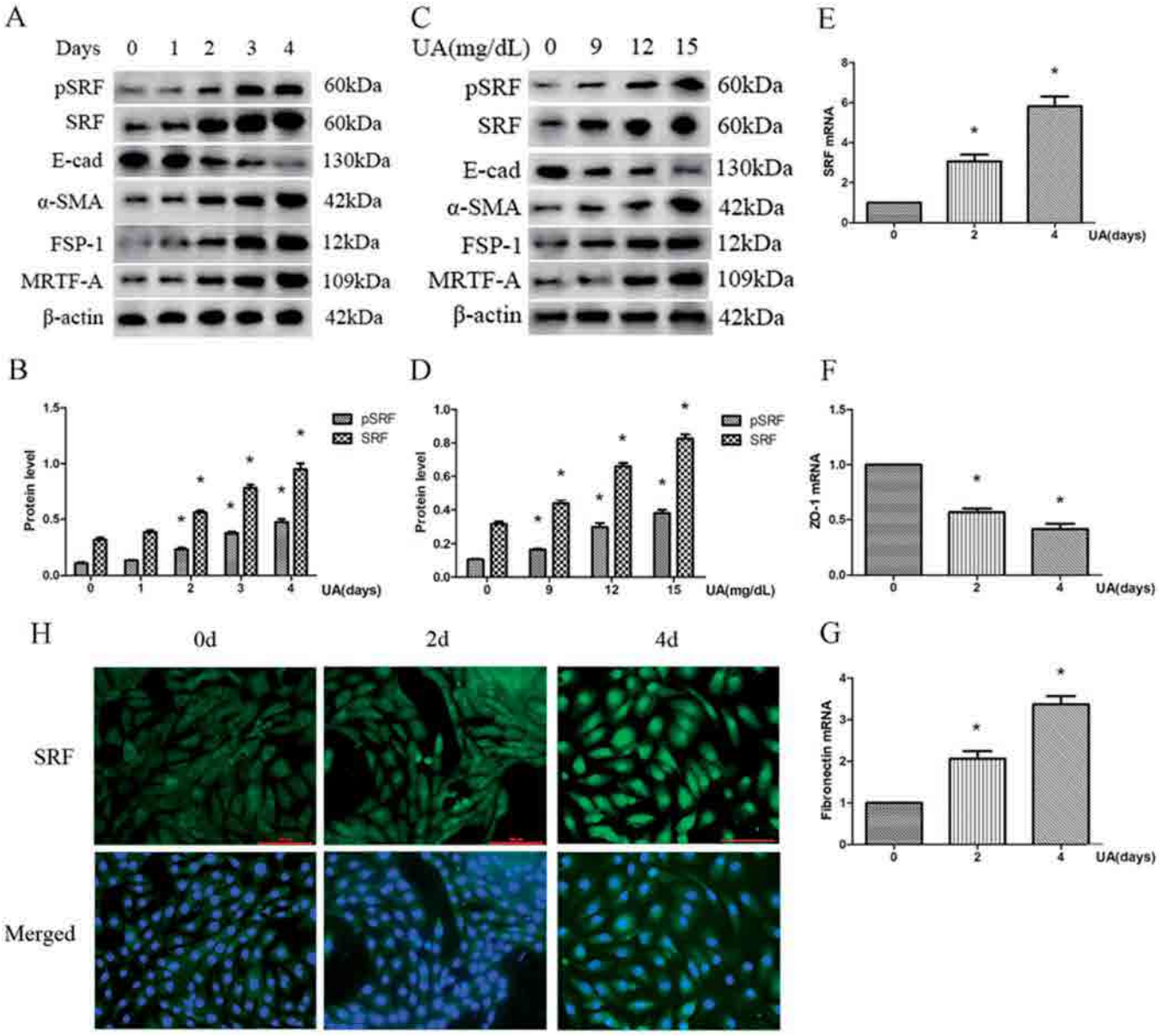


Figure 1. UA induced EMT and SRF upregulation in NRK-52E cells. (A) Western blot analysis showing that UA (15 mg/dL) mediated the upregulation of phosphorylated SRF (pSRF), SRF, α-smooth muscle actin (α-SMA), and Fibroblast specific protein-1 (FSP-1) expression and the downregulation of E-cadherin expression in a time-dependent manner. (C) Western blot analysis showing that UA mediated the upregulation of pSRF, SRF, α-SMA, and FSP-1 expression and the downregulation of E-cadherin expression in a dose-dependent manner at 48 h. (B, D) Quantitative determination of relative SRF levels. (E-G) Quantitative RT-PCR analysis of SRF, ZO-1 and fibronectin (FN) mRNA expression. (H) Immunofluorescence staining for SRF.

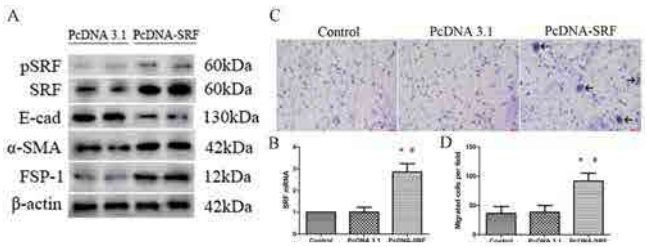


Figure 2: SRF overexpression mediated EMT and migration in NRK-52E cells. (A) Western blot analysis showing the induction of SRF, α-SMA, and FSP-1 expression and a reduction in E-cadherin expression. (B) Quantitative RT-PCR analysis of SRF mRNA expression. (C) Representative micrographs of the transwell chamber migration assay at an original magnification of 200×. Arrowheads indicate some of the migrated cells. Bar=50 μm. (D) Quantitative analysis of the number of migrated NRK-52E cells per field in three groups.

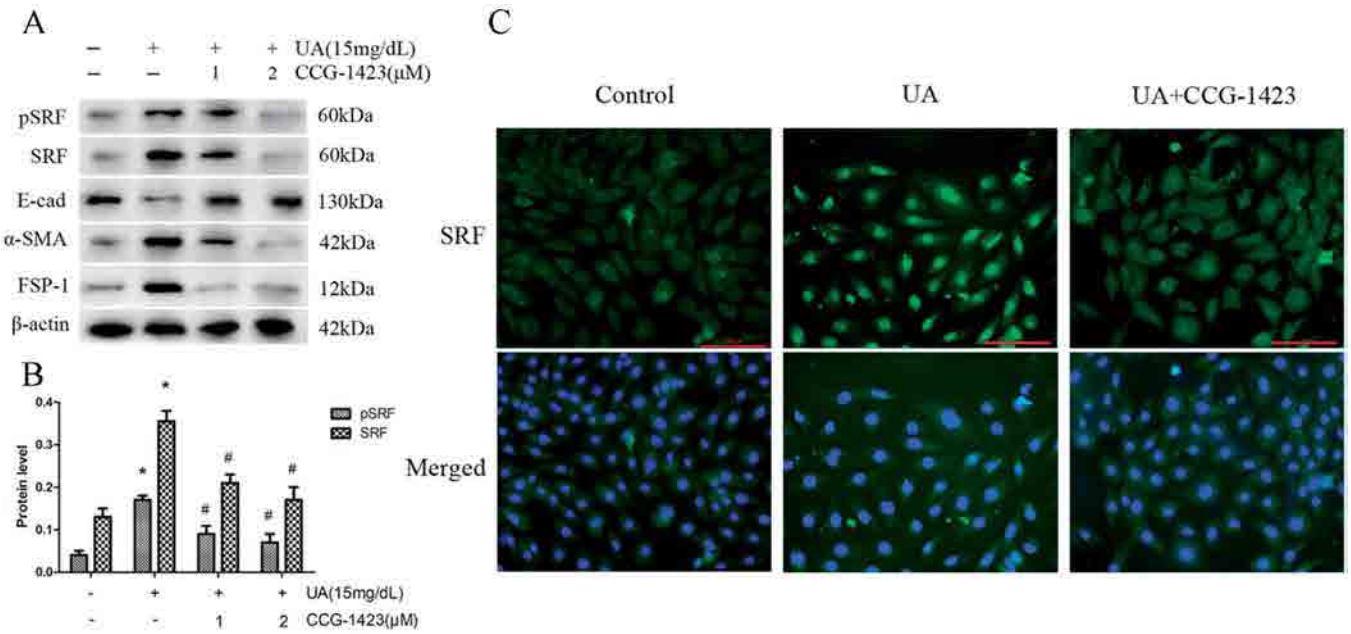


Figure 3: Inhibition of SRF preserved phenotypes of NRK-52E cells after UA stimulation in vitro. NRK-52E cells were pretreated with CCG-1423 (1 μM or 2 μM) or DMSO for 1 h, followed by treatment with UA (15 mg/dL) for 72 h. (A) Protein expression of pSRF, SRF, E-cadherin, α-SMA and FSP-1 measured by western blot analysis. (B) Quantitative determination of the pSRF and SRF protein levels. (C) Immunofluorescence staining for SRF.

Conclusion: Together, increased SRF activity promotes EMT and dysfunction of TECs in HN. Targeting SRF by small molecule inhibitor may be an attractive therapeutic strategy for HN.

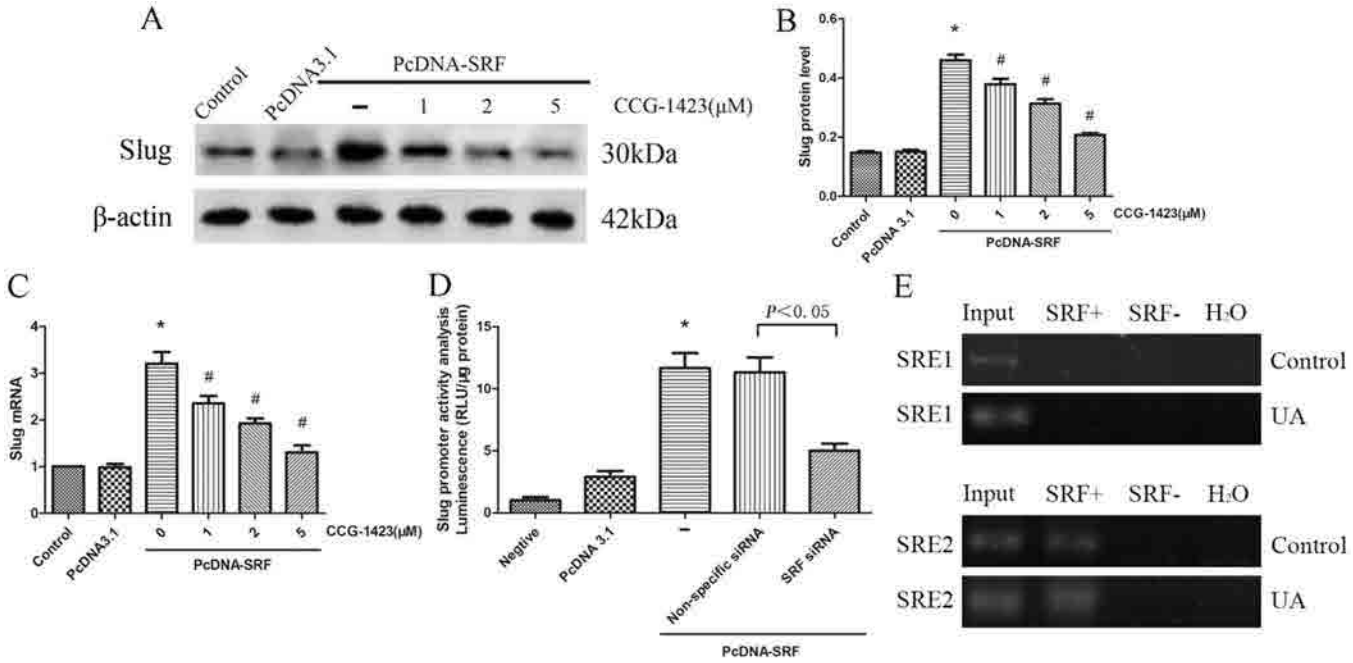


Figure 4: Inhibition of SRF suppressed slug upregulation in vitro. (A-C) NRK-52E cells were transfected with PcDNA3.1-SRF or empty pcDNA3.1 vectors. After 24 h, the cells were incubated with different doses of CCG-1423 for another 24 h. The protein and mRNA expression levels of slug were measured by western blot analysis and quantitative RT-PCR. (D) Slug promoter activity was analyzed by measuring luminescence. (E) Chromatin immunoprecipitation was used to examine SRF binding to the slug promoter in NRK-52E cells.

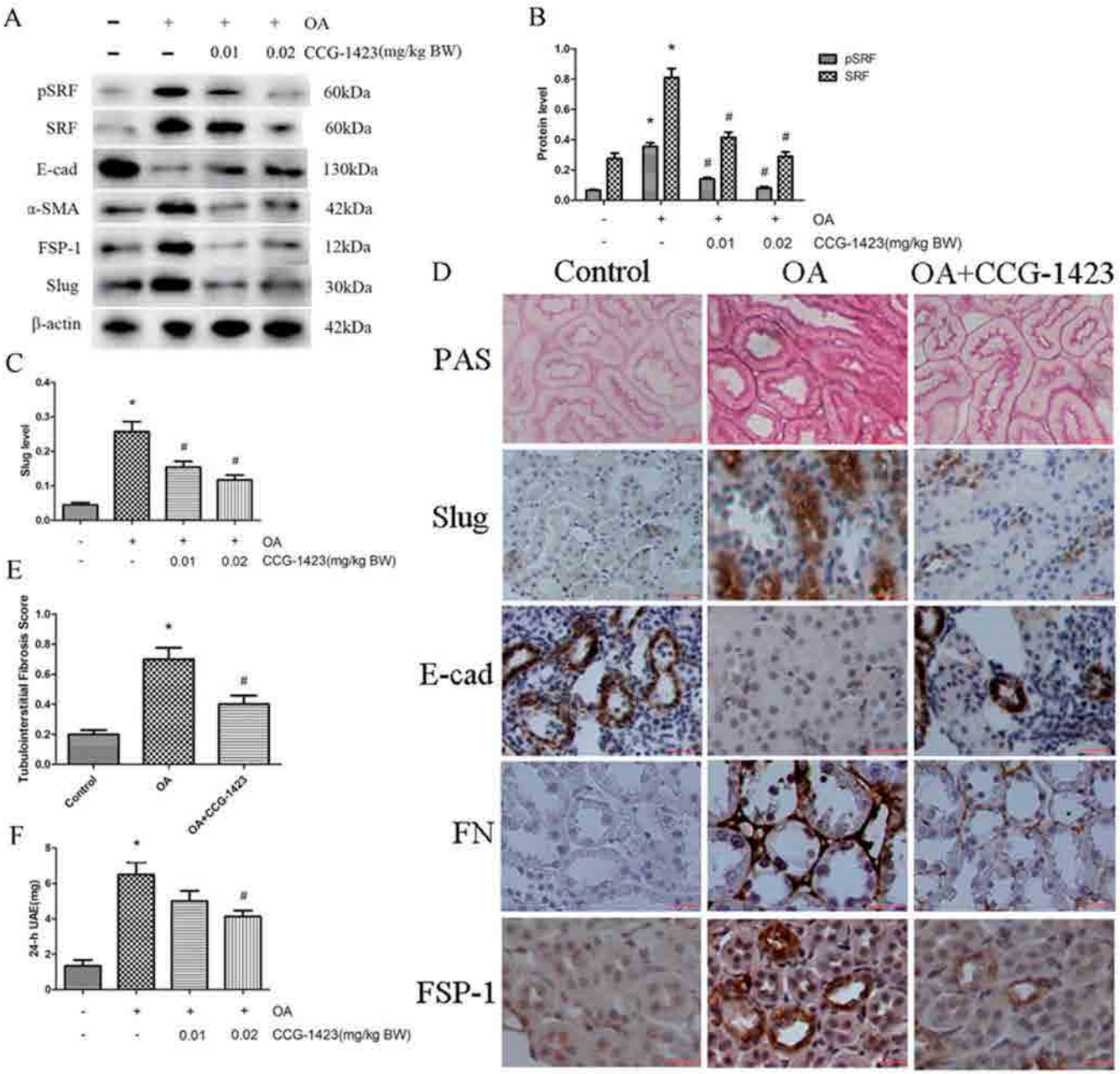


Figure 5: Inhibition of SRF improved epithelial phenotype of TECs, renal tubulointerstitial fibrosis and albuminuria in vivo. (A-C) Protein expression levels of pSRF, SRF, E-cadherin, α-SMA, FSP-1 and slug measured by western blot and quantitative analyses. (D) Renal tubulointerstitial fibrosis in the three groups measured by PAS staining. Immunohistochemical staining for slug, E-cadherin, FN and FSP-1 in the three groups. (E) Tubulointerstitial fibrosis scores of the three groups. (F) Dose-dependent reduction in 24-h UAE in HN rats induced by CCG-1423 treatment.

SO014 **CHANGES IN CHARACTERISTICS OF CRYSTALLURIA IN PATIENTS WITH RECURRENT NEPHROLITHIASIS**

Federica Di Maio[1], Silvia Barbarini[2], Rocco Baccaro[1,2], Giuseppe Grandaliano[1,2], Pietro Manuel Ferraro[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Nefrologia, Roma, Italy and [2]Università Cattolica del Sacro Cuore, Roma, Italy

Background and Aims: The study of crystals in the urinary sediment finds application in the diagnosis of hereditary or metabolic nephrolithiasis and in the identification of crystals from drugs.

Method: We conducted a thorough microscopic urine examination, focused on the determination of crystalluria, associated with the metabolic study at baseline and about 6 months after the start of a metaphylactic therapy, in 21 patients with recurrent nephrolithiasis, followed at the Metabolic Stone Clinic of our Institution. The analysis of the crystals was performed in parallel and blind through direct microscopic examination (MD) and automated instrumentation (SA) (SediMax analyzer - Menarini Diagnostics) of our institution. We used a semi-quantitative approach for both methods.

Results: We examined 42 sediments (21 at baseline and 21 after an average follow-up of 196±88 days) from 21 patients (8 females, 13 males), all of them showing calcium oxalate crystalluria. The analysis on baseline evaluation and follow-up on both Crystalluria MD and crystalluria SA through spaghetti plots showed a tendency to reduction of severity for the first one only. This trend is consistent with the data obtained from the metabolic studies: urinary oxalate and calcium excretions, the main drivers of calcium oxalate crystallization, which showed decreasing levels. The same examination for urinary citrate excretion showed a rising trend, again in accordance with the on-going changes in urine lithogenic profile.

Conclusion: The study of crystals in the urinary sediment, repeated over time, may represent a further indicator of the effectiveness of metaphylactic therapy and an indicator of patient adherence to the prescription in metabolic calcium oxalate nephrolithiasis.

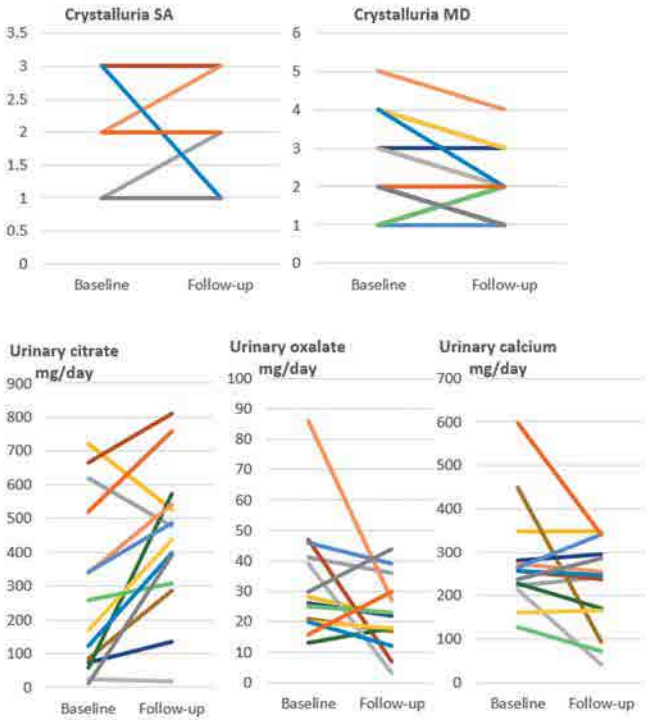


Figure:

PREVENTION OF AKI

SO015

URINE NMR-BASED METABOLOMICS FOR EARLY DETECTION OF POST-PROCEDURAL CONTRAST NEPHROPATHY

Nooshin Dalili[1], Shiva Kalantari[1], Mohsen Nafar[1]

[1]*Chronic Kidney Disease Research Center, Shahid Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Background and Aims: Contrast induced nephropathy (CIN) has been reported to be the third foremost cause of acute renal failure. Metabolomics is a robust technique that has been used to identify potential biomarkers for early detection of renal damage after procedures with using contrast media. We aim to analyze the serum and urine metabolites changes, after using contrast for coronary angiography, to determine if metabolomics can use as a tool for early detection of CIN.

Method: Sixty-six patients with positive primary non-invasive diagnostic tests for coronary artery disease (CAD) who were candidate of elective coronary angiography recruited. Spot urine samples collected in the morning before angiography and 4 hours after angiography. Patients with $>$ 0.5 mg/dL creatinine rise compared to baseline were considered as case (CIN group). Urine samples were centrifuged at 3000 rcf for 20 minutes at 4°C to remove the cell debris and after addition of sodium azide to prevent bacterial growth, were stored at -80 degree Celsius in aliquots until required. The mixtures were then transferred to a standard 5 mm NMR tube for analysis. ^{1}H-NMR spectra were acquired at 300 K on a Bruker DRX 500 MHz spectrometer by using Carr–Pucell–Meiboom–Gill (CPMG) technique. For each spectrum, 154 scans were collected into 32K data points using a spectral width of 8389.26 Hz during the relaxation time of 2.5 s.

Results: Structure and outliers of the dataset composed of patient with CIN (n = 10) before angiography and after angiography were evaluated by PCA. A model with two principal components (PC1 and PC2) with R2X = 0.775 and Q2(cum) = 0.487 was obtained .A supervised OPLS-DA model was built to identify discriminative variables between metabolite profiles before and after angiography in patients with CIN. The high level of AUC 0.95 that was obtained from 10-fold cross validation besides decreased R2 (0.0, 0.415) and Q2 (0.0, -0.454) intercepts of 999 random permutations reflects the good validity of this diagnostic model. According to this valid OPLS-DA model, 15 chemical shifts were significant based on VIP $>$ 1 and FC $>$ 1.2. To check these suggested chemical shifts if their changes are due to kidney injury and not caused by contrast agent, a decoy OPLS-DA model was built for non-CIN patients before and after angiography .Two common significant chemical shifts (2.42 and 2.78 ppm) were found in comparison of these two models (i.e. before vs. after angiography in CIN group in compared with before vs. after angiography in non-CIN group) and were excluded from the results. Metabolites corresponding with the remaining list of 12 significant chemical shifts were identified and suggested as early detection biomarker candidates for CIN (Fig 1). The AUC value of a panel of four biomarker candidates were higher than single biomarkers that reflects the value of simultaneous measurement of these four metabolite candidates than single candidates. Figure 2 shows the list of diagnostic metabolite candidates with $p < 0.05$. Pathway characterization was used to better understanding of pathophysiology of CIN. As the input data was small list of metabolites, only "*Histidine_ lysine_ phenylalanine, tyrosine, proline and tryptophan catabolism*" pathway ($p < 0.05$) was significant and suggested as the most important disturbed pathway in CIN.

Table 1: Early detection biomarker candidates for contrast nephropathy.

Metabolite name	Chemical shift (ppm)	Fold change (CIN after angiography vs. CIN before angiography)	Direction of change	VIP	Sensitivity	Specificity	AUC
Urocanic acid	7.26	1.7	↑	1.1	70 %	80 %	0.65
Unknown	1.38	1.2	↑	1.3	60 %	70 %	0.62
Epi-coprostanol	0.7, 0.78, 0.66, 0.58	2.3	↓	1.4	60 %	60 %	0.55
11α-Hydroxyprogesterone	0.54	2.1	↑	2.9	80 %	40 %	0.53
Tyrosine	7.18	1.2	↑	1.1	70 %	60 %	0.52
A + B	-	-	-	-	70 %	80 %	0.67
A+ B + C	-	-	-	-	70 %	60 %	0.72
A + B + C + D	-	-	-	-	80 %	50 %	0.74

Definition: A: Urocanic acid; B: Epi-coprostanol; C: 11α-Hydroxyprogesterone; D: Tyrosine

Conclusion: Early detection of CIN as early as only 4 hours after using contrast can help better management of these patients. In this study, only after 4 hours passed from using contrast a panel of metabolites could be found in urine of patients who develop CIN, which facilitates early detection of CIN. This is the first study to investigate urine metabolic profile using NMR-based metabolomics for early detection of CIN after coronary angiography. The use of this suggested panel might significantly improve clinical consequences of this harmful complication.

Figure 1:

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SO016 **SPREAD OF ACUTE KIDNEY INJURY IMPROVEMENT PROGAMME ACROSS A LARGE MULTI SITED NHS HOSPITAL**

Prasanna Hanumapura[1], Leonard Ebah[1], Deryn Waring[1], Robert Henney[1], Michelle Murphy[1], Rachael Challiner[1], Siobhan Halligan[1], Katherine Hayden[1], Charlotte O'Toole[1]

[1]*Manchester Foundation Trust, Renal Medicine, Manchester, United Kingdom*

Background and Aims: Acute kidney injury (AKI) is a widely recognised serious health care issue. Up to 25% of hospital patients can develop it, with worse outcomes compared non AKI. A UK–wide audit in 2009 and our local audit in 2014 showed consistently poor AKI care including delays in detection and inconsistent management of cases. The trust set up the AKI Team in 2014 to improve AKI detection, care and outcomes.

Successful implementation of a Multifaceted Quality Improvement (QI) Programme for AKI across the main hospital campus since 2015 saw significant improvement in AKI care and outcomes; recognition within 24hrs improved from 52% to 100% since 2016; there has been a 34% reduction in AKI incidence, 26% reduction in AKI length of stay (LoS) ,42% reduction in AKI days (time to recovery) and 10% less AKI associated mortality.

The Trust being one of the largest acute trusts in the UK (10 hospitals across 6 sites, over 2000 beds), the QI spread represented a formidable challenge.

We describe the methodology and outcomes of AKI QI spread across the trust.

Method:

Central Campus Hospitals: Improvement on this site involved setting a bespoke electronic alert coupled with education, key stake holder engagement, gradual culture change and AKI Priority Care Checklist (PCC) and use of change agent (AKI Clinical Nurse Specialist-CNS) visiting local teams and empowering them to manage AKI using Demming's Model for Improvement

A stepwise staggered similar approach was implemented first in the Women's and Eye Hospitals followed by Children's Hospital after a local adaptation and testing of algorithm, PCC and appointment of local change agent, a Paediatric AKI CNS.

West Campus Hospital: A DGH with 230 beds, 1-2 incident cases of AKI/day required a bespoke approach. The central AKI team runs an AKI alerts report and remotely alert the local multidisciplinary teams and empowering them to implement the PCC.

South Campus Hospitals: A large tertiary hospital merged in 2018 with an existing AKI CNS team. Detection algorithms, education material, PCC, reporting, and approach have been progressively harmonized using the Central Campus model.

Data is expressed using SPC charts and analysed by t-test.

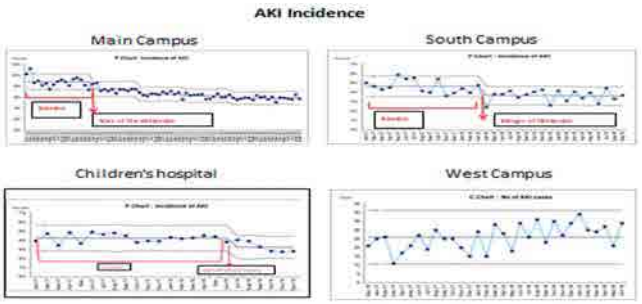
Results: Care process and outcome measures have seen a consistent improvement across all sites. As reported in the Central Campus, recognition of AKI within 24hrs has improved from 52% to 100% since 2016; there has been a 34% reduction in AKI incidence ($p<0.00001$), 26% reduction in AKI LoS and a 42% reduction in AKI days (time to recovery).

The Children's Hospital had 24% reduction ($p<0.0001$) in AKI incidence and a 34% reduction in hospital acquired AKI. Recognition of AKI has improved from 42% to 100%; 15% reduction in AKI LoS and 22% reduction in AKI days.

In the South Campus recognition of AKI has improved from 67% to 100% and 19% reduction ($p<0.0015$) in AKI incidence. LoS and AKI days data yet to be reported whilst IT systems are been harmonised.

In West Campus recognition is 100% but the small numbers prevent any meaningful analysis of other outcomes.

Conclusion: This study demonstrates how a cluster of simple interventions and approach to AKI detection and care were successfully rolled out across a multisite large complex acute care organization taking into account the local realities of each site/ Hospitals whilst maintaining the core interventions.



Figure

SO017

EFFECT OF HIGH-CUTOFF DIALYSIS FOR ACUTE KIDNEY INJURY SECONDARY TO CAST NEPHROPATHY IN PATIENTS WITH MULTIPLE MYELOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

Blanca Tarragon[1], Nan Ye[2], Martin Gallagher[2], Shaundeep Sen[3], Jose' M. Portoles[1], Amanda Wang[2]

[1]Hospital Puerta de Hierro-Majadahonda, Nephrology, Majadahonda, Spain, [2]The George Institute for Global Health, Renal, Newtown, Australia and [3]Concord Repatriation General Hospital, Renal, Concord, Australia

Background and Aims: The incidence of multiple myeloma (MM) is increasing. Abnormal secretion of serum free light chains (sFLC) can lead to cast nephropathy and severe acute kidney injury (AKI) requiring haemodialysis (HD), which is associated with increased morbidity and mortality. High cut-off (HCO) HD membranes demonstrate better sFLC clearance. However, their role in all-cause mortality and renal recovery remains uncertain.

Method: A systematic review and meta-analysis was performed examining all randomized controlled trials (RCTs) and observational studies assessing the effect of high cut-off HD compared to conventional HD on clinical outcomes of patients with MM complicated by cast nephropathy induced-severe AKI. Medline, EMBASE, and the Cochrane Central Register of Controlled Trials were searched until September 2019. The primary outcome was all-cause mortality at the end of the study. The secondary outcomes included all-cause mortality at 12 months, haemodialysis independence at 3, 6 and 12 months, biopsy-proven haematologic responses at 90 days and sFLC (kappa and lambda) reduction. Random effect models were used to pool relative risks (RR) with 95% confidence intervals (CIs) for individual studies.

Results: The search identified 5 studies including 276 patients with a mean follow-up of 18.7 months. There were 2 RCTs and 3 retrospective cohort studies. Compared with patients treated with conventional HD, patients on HCO dialysis did not show survival benefits at 12 months (4 studies, 186 patients, RR 0.79; 95% CI 0.46-1.36), or at the end of the study (5 studies, 276 patients, RR 0.86; 95% CI 0.60-1.25). Although survival benefits at the end of study (3 studies, 88 patients, RR 0.64; 95% CI 0.45-0.90) were seen in observational studies, no differences in all-cause mortality was seen in RCTs (2 studies, 188 patients, RR 1.31; 95% CI 0.50-3.46). Likewise, although the pooled data from the observational studies demonstrated significantly higher rates of HD independence at 90 days (2 trials, 78 patients, RR 2.23; 95% CI 1.09-4.55), this difference disappeared when the data from RCTs were included to the analysis (4 studies, 266 patients, RR 1.28; 95% CI 0.95-1.73). There was no difference in HD Independence at 6 months (2 studies, 188 patients, RR 1.19; 95% CI 0.68-2.06), and 12 months (2 studies, 188 patients, RR 1.14; 95% CI 0.58-2.26) between these two therapies. Patients receiving HCO dialysis, however, had significantly better biopsy-proven haematologic response at 90 days by 40% (3 studies, 176 patients, RR 1,40; 95% CI 1.13-1.74) and a significantly higher kappa light chain reduction (2 studies, 188 patients, standardized mean difference (SMD) 2.37; 95% CI 1.99-2.75; I2 = 0%). Overall, the majority of the studies were of suboptimal quality and underpowered.

Conclusion: Current evidence from RCTs and observational studies suggest HCO dialysis provides haematological benefits but makes no significant improvement in all-cause mortality and renal outcomes, compared to conventional HD for patients with multiple myeloma associated cast nephropathy. However, there is a trend towards better renal outcomes, therefore further large-scale RCTs are needed to assess the effect of HCO dialysis on clinical outcomes in patients with multiple myeloma complicated by cast-nephropathy.

SO018

NON-INVASIVE ASSESSMENT AND MONITORING OF SKELETAL MUSCLE MASS IN CRITICALLY ILL PATIENTS WITH AKI BY QUADRICEPS MUSCLE ULTRASOUND

Alice Sabatino[1,2], Giuseppe Regolisti[1,2], Chiara Cantarelli[1,2], Andrea Palladini[2], Tommaso Di motta[1,2], Umberto Maggiore[1,2], Enrico Fiaccadori[1,2]

[1]Parma University Medical School, Nephrology Unit, Department of Medicine and Surgery, Parma, Italy and [2]Parma University Medical School, Postgraduate School in Nephrology, Parma, Italy

Background and Aims: Critically ill patients undergo important muscle wasting during ICU stay, and a significant loss of muscle mass still occurs in the first few days of hospital stay. This may delay both functional recovery and weaning from mechanical ventilation, being also a well-known predictor of mortality. Quite often, muscle wasting is masked by fluid overload, increasing the risk for underestimating the presence of malnutrition, as frequently occurs in critically ill patients with AKI.

An important concern in this clinical setting is the lack of adequate tools for routine bedside evaluation of the skeletal muscle mass. Lately, the use of ultrasound (US) for the assessment of muscle mass has aroused considerable interest. It is a non-invasive technique, applicable at the bedside and even in non-collaborative patients, it is economically viable, safe and do not require specialized staff. Recently, its reliability and validity have been demonstrated in critically ill patients with AKI. On this premise, in the present study, we aimed to evaluate the clinical application of US for both evaluation and monitoring of quadriceps muscle thickness in critically ill patients with AKI.

Method: This is an observational study, conducted in the renal ICU of the Parma University Hospital. All adult patients with AKI, with no distinction regarding the severity of AKI, admitted in the renal ICU from 15/03/2017 to 15/03/2018, with previous hospital stay less than 72h, with a likely ICU stay of at least 5 days were eligible for entering the study. The diagnosis of AKI was made according to KDIGO. Quadriceps rectus femoris and vastus intermedius thickness (QRFT and QVIT) were measured at the midpoint and at the border between the upper third and lower two-thirds between the anterior superior iliac spine (ASIS) and the upper pole of the patella. US was performed twice during ICU stay, i.e., at baseline (within 72h from admission) and after 5 days since the first measurement.

Results: We enrolled 30 patients, 70% (n= 21/30) were male, mean age ± SD age 74±11 years, APACHE II mean ± SD, 22 ± 5. Ultrasonography took less than 10 minutes to set up and complete image acquisition and less than 10 minutes per image to complete measurement analysis in all patients. A total of 472 images were analyzed across the 30 subjects.

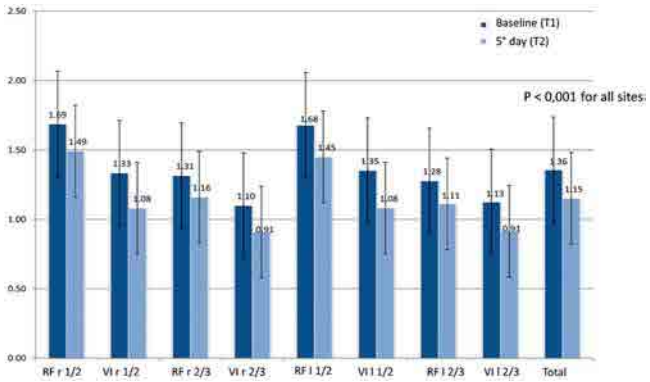


Figure 1: Average differences between T1 and T2.

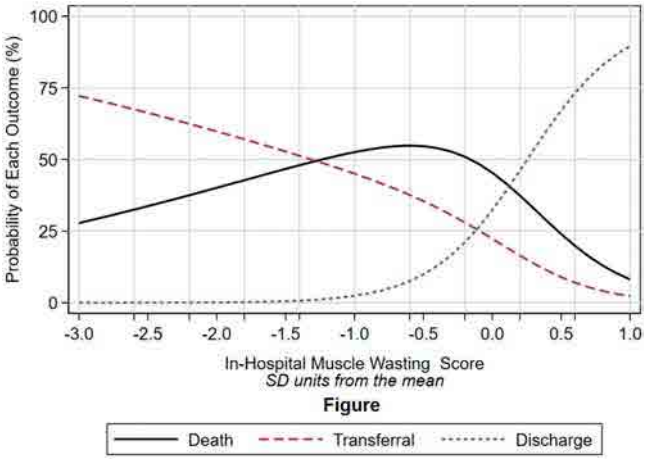


Figure 2: Probability of outcome based on the intensity of muscle wasting.

SO019

A PREDICTIVE MODEL OF MORTALITY IN ACUTE RENAL FAILURE IN THE CRITICAL PATIENT: USEFULNESS OF ARTIFICIAL INTELLIGENCE

Jose Ibeas[1], Elia Lleal[2], Edwar Macias[3], Carolina Rubiella[1], Antoni Morell[3], Javier Serrano[3], Jose Vicario[3]

[1]Parc Taulí University Hospital, Nephrology, Sabadell, Barcelona, Spain, [2]Pompeu Fabra University, Biomedical Engineering, Barcelona, Spain and [3]School of Engineering, Autonomous University Barcelona, Cerdanyola del Valles, Barcelona, Spain

Background and Aims: Patients with Acute Renal Failure (ARF) have a high risk of mortality, especially those who enter the Intensive Care Unit (ICU). In this population, predictive models of mortality on prognostic scales, such as SAPS-II (Simplified Acute Physiology Score II), linearly relate risk factors without taking into account the complex relationship's variables can have. There are models where Machine Learning (ML) techniques have been used, but there is still room for improvement. The implementation of deep artificial neural networks (DANN) can be challenging.

The literature models, using SAPS-II report an accuracy, f1 and ROC area (receiver operating curve) in ranges of 0.538-0.621, 0.333-0.377 and 0.781-0.809 respectively. The best results with ML are improved in neural networks of a hidden layer or random forest, being the best performance in the latter: accuracy 0.715-0.741, F1 0.449-0.470 and ROC between 0.862-0.870.

The aim is to evaluate and improve the predictive capacity of ML techniques for the prediction of mortality in patients with ARF admitted to the ICU, through the use of the open database MIMIC-III (Medical Information Martfor Intensive Care III).

Method: Design: Retrospective analysis of historical cooperation of 20,928 patients with ARF from Beth Israel Deaconess (Boston), from 2001 to 2012.

Method: ML algorithm based on DANN. Creation of a model to predict in-hospital mortality after discharge from the ICU with the variables of the first 24 hours after admission to the ICU.

To evaluate the robustness of the model has been performed cross-validation by separating the samples into different combinations of training and test data (k-folds). The unavailable variables haematological with means extracted from the training set of the respective fold. The DANN trained with the complex relationship's variables folds, two hidden layers of 75 and 40 neurons respectively.

Inclusion criteria: $>$ 16 years, AKI according to KDIGO criteria and predictive variables based on SAPS-II.

Variables: Age, sex, type of admission, number of admissions in ICU, heart rate, blood pressure, temperature, PaO2, FiO2, sodium, potassium, bilirubin, bicarbonate, urea, leukocytes, diuresis and diagnosis of ICD-9 (metastatic cancer, haematological malignancies).

Results: Accuracy: 76.7% 0 $\pm$ 1.7%, f1: 86.6% $\pm$ 1.9%, RO area: 0.859 $\pm$ 0.006, sensitivity: 75.7% $\pm$ 2.8%, specificity: 80.5% $\pm$ 2.9%.

Conclusion: The use of Machine Learning techniques based on deep artificial neural networks can improve the predictive ability of mortality in acute renal failure of the critically ill patient of traditional clinical risk scales and even current Machine Learning models.

SO020 NEPHROLOGY INTERVENTION IN PATIENTS AWAITING CARDIAC SURGERY: A RANDOMISED CONTROLLED TRIAL

Sergi Codina[1], Ana Coloma[1], Fabrizio Sbraga[1], Enric Boza[1], Jose Maria Vazquez-Reveron[1], Eva Ferreiro[1], Josep Cruzado[1], Nuria Montero[1]

[1]*Bellvitge University Hospital, Nephrology, L'Hospitalet de Llobregat, Spain*

Background and Aims: Acute kidney injury (AKI) is a frequent complication after cardiac surgery. Its incidence ranges from 19 to 44% depending on the study and which definition is used. There are some well-known risk factors associated with AKI, including baseline patient characteristics (age and comorbidities), need of perioperative blood transfusion or presence of previous chronic kidney disease. We wanted to evaluate if a nephrologist management and control of potential risk factors of renal disease can be used to prevent AKI, thereby minimizing the risk of need RRT, reducing costs and improving survival in these patients. It will be the first study focused on this intervention. The aim of this study is to assess if a nephrology intervention before cardiac surgery can reduce the postoperative incidence of AKI.

Method: Unicentric prospective randomized controlled trial of 298 participants from 2015 to 2019. The inclusion criteria was patients undergoing scheduled cardiac surgery of $>$ 18 years old. The exclusion criteria was a requirement for renal replacement therapy before surgery. Clinical Research Ethics Committee of Bellvitge has approved the study before initiation. All patients have given written informed consent. We have done an intention-to-treat analysis, continuous variables have been compared between groups using Student's *t* test and categorical variables using X^2.

Results: Nephrology intervention before surgery, included a preoperative study done minimum 1 month before the surgery to optimize the patient' s overall condition by optimization of hydration state, remove or minimize dose of drugs that potentially deteriorate kidney function and correct metabolic disorders. No differences in the characteristics of the patients between groups was found (Table 1). The number of patients with AKI were 49 without differences between groups (0.112), with most of them presenting a stage 1 AKI, only 3 patients present a stage 3 AKI, but none of them required renal replacement therapy (Table 2). We found 1.3% of mortality (1 participant in the intervention group and 3 in control group). Data at 1 year follow-up (n= 144) showed low incidence of kidney disease (creatinine in intervention arm 91.87±30.79μmol/L and in control arm 87.08±23.58, p=0.292) without differences in albuminuria.

Conclusion: In summary, we did not find any difference in acute kidney injury and death when a nephrology intervention is done to cardiac surgery patients, probably it would be necessary to increase the sample size to make conclusions. The results at 1 year follow-up showed no kidney disease in these patients.

Table 1. Characteristics of the included population

Characteristic	Nephrology Intervention Group n=174	Control n=124
Age (years, mean±SD)	64.52±15.85	67.26±31.44
Gender (M/F)	115/59	73/48
Hypertension (%)	73.6	70.2
Type 2 Diabetes (%)	24.7	25
Cerebrovascular accident (%)	7.5	7.3
Chronic Pulmonary Obstructive Disease	22.4	14.5
Chronic Kidney Disease (%)	17.8	12.9
Type of surgery (%)		
▪ Aneurism	2.3	1.6
▪ Coronary bypass	19.5	20.9
▪ Heart valve repair or replacement	58.1	62.1
▪ Combined	20.1	15.3
▪ Other	0	0.1

Figure:

Nephrology Dialysis Transplantation 35 (Supplement 3): iii000–iii000, 2020

BASIC SCIENCE IN DIABETES

SO021

EFFECTS OF SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITOR, CANAGLIFLOZIN ON GLOMERULAR HYPERFILTRATION AND OXIDATIVE STRESS IN MICE WITH TYPE 2 DIABETES

Megumi Kondo[1], KENGO KIDOKORO[1], Yoshihisa Wada[1], Atsuyuki Tokuyama[1], Hiroyuki Kadoya[1], Tamaki Sasaki[1], Naoki Kashihara[1]

[1]*Kawasaki medical school, Depertment of Nephrology and Hypertension, Kurashiki, Okayama, Japan*

Background and Aims: In most developed countries, diabetic kidney disease (DKD) is the most common cause of chronic kidney disease, which can lead to end-stage renal disease. In recent clinical trials, sodium–glucose cotransporter 2 inhibitors (SGLT2is) slowed the progression of kidney disease as compared with a placebo in patients with type 2 diabetes. One of the main mechanisms of the renoprotective effects of SCLT2is in DKD is considered the ability of these inhibitors to improve glomerular hyperfiltration. We previously demonstrated that the adenosine/adenosine A1 receptor pathway played a pivotal role in the tubuloglomerular feedback(TGF) system in a type 1 diabetic model, Akita mice (*Circulation,* 2019). We also reported that increased oxidative stress was involved in the pathogenesis of diabetic vascular complications. Uncoupling of endothelial nitric oxide (NO) synthase (eNOS) via oxidation of tetrahydrobiopterin (BH4), a cofactor required for NO production, played a major role in generation of oxidative stress (*AJPRP,* 2005; *JASN,* 2013). In the present study, we explored the renal protective effects of SGLT2 inhibition, with a focus on glomerular hemodynamics and glomerular oxidative stress.

Method: This study used type 2 diabetic db/db mice and db/m+ mice as a control (male, 8wk old). We developed a novel method to measure the glomerular filtration rate of single nephrons (SNGFRs) in mice using multiphoton laser microscopy. In the first experiment, we measured the SNGFRs in 12 wk-old db/db and db/m+ mice to confirm glomerular hyperfiltration. Next, we evaluated the SNGFRs change before and after the administration of a single dose of canagliflozin (CANA) (10 mg/kg). The SNGFRs, glomerular permeability of macromolecules, glomerular reactive oxygen species (ROS) and NO production, and tetrahydrobiopterin (BH4) level in serum and kidney were evaluated after the CANA treatment for 8 wk. Finally, human glomerular endothelial cells (hGECs) were exposed to normal glucose (5 mmol/L), high glucose (30 mmol/L of D-glucose), or a hyperosmotic control (5 mmol/L of D-glucose plus 25 mmol/L of L-glucose) in the presence or absence of CANA (10 μmol/L).

Results: The CANA treatment ameliorated glomerular hyperfiltration in the db/db mice. In the db/db mice, glomerulus ROS production increased, and NO production decreased as compared with the levels in the control mice. CANA improved the imbalance between ROS and NO production. The serum and kidney concentrations of BH4 declined in the non-treated db/db mice, whereas the CANA treatment preserved the BH4 level. Leakage of 70-kD FITC-labeled albumin into the urinary space was observed in the db/db mice. The CANA treatment reduced the amount of FITC-labeled albumin in the urinary space of the db/db mice. The CANA treatment also alleviated vascular endothelial damage in glomeruli. BH4 levels decreased in the hGECs exposed to high glucose. CANA did not improved BH4 level in the hGECs exposed to high glucose.

Conclusion: SGLT2i ameliorated glomerular hyperfiltration, preserving BH4 levels and improving the glomerular ROS/NO imbalance in type 2 diabetic mice.

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SO022

EVALUATION OF GLOMERULAR HEMODYNAMIC CHANGES BY SGLT2 INHIBITION IN TYPE 2 DIABETIC RATS USING IN VIVO IMAGING TECHNIQUES

Yoshihisa Wada[1], KENGO KIDOKORO[1], Atsuyuki Tokuyama[1], Megumi Kondo[1], Hiroyuki Kadoya[1], Hajime Nagasu[1], Tamaki Sasaki[1], Naoki Kashihara[1]

[1]*Kawasaki Medical School, Department of Nephrology and Hypertension, Kurashiki, Okayama, Japan*

Background and Aims: In recent clinical trials, the SGLT2 inhibitor (SGLT2i) slowed the progression of kidney disease compared with the placebo in patients with type 2 diabetes. Improvement of glomerular hyperfiltration via tubuloglomerular feedback (TGF) is considered to be one of the possible pathways for renal protection with SGLT2 inhibition (SGLT2i) in diabetic kidney disease (DKD). We have successfully developed the novel method to measure single-nephron GFR (SNGFR) in mice using multiphoton laser microscopy and demonstrated that the adenosine/adenosine A1 receptor (A1aR) pathway plays a pivotal role in the TGF mechanism in the type 1 diabetic model, Akita mice (Kengo Kidokoro, David Z. I. Cherney et al. Circulation. 2019). It has been suggested that the mechanism of improvement effects in glomerular hyperfiltration by SGLT2i is different in type 1 diabetes and type 2 diabetes. However, the detailed regulatory mechanism of GFR by SGLT2i is not fully understood in type 2 diabetes. This study aims to clarify the effects of SGLT2i on glomerular hemodynamics in type 2 diabetic rats.

Method: Zucker lean (ZL) rats and Zucker diabetic fatty (ZDF) rats were used. In the first experiment, SNGFR and diameters of glomerular afferent/efferent arterioles were measured in both groups. Next, we examined the change of SNGFR and diameters of glomerular afferent/efferent arterioles, as well as urinary excretions of glucose and sodium in ZDF after a single-dose administration of SGLT2i (luseogliflozin; 10mg/kg, gavage) for 120 minutes, which generated the following three groups: SGLT2i group, SGLT2i + adenosine A1 receptor (A1aR) antagonist (8-cyclopentyl-1,3-dipropylxanthine, 1mg/kg) group, and insulin group.

Results: SNGFR in the ZDF group was significantly higher than in the ZL group. The diameter of the afferent arteriole and efferent arteriole was also wider in ZDF rats than in ZL rats. The SNGFR and diameter of the afferent arteriole were significantly decreased after a single-dose administration of SGLT2i in ZDF. However, there was no significant diameter change in the efferent arteriole. Moreover, a decrease of SNGFR was not observed in the A1aR antagonist group after SGLT2i administration. Urinary excretions of glucose and sodium showed a similar pattern in the SGLT2i and SGLT2i+ A1aR antagonist groups.

Conclusion: The adenosine/A1aR pathway plays an important role in the regulation of the tonus of the afferent arteriole and is involved in the suppression of glomerular hyperfiltration by SGLT2 inhibition in type 2 diabetes.

SO023

HEPATOCYTE GROWTH FACTOR (HGF) PRECLUDE HIGH-FAT DIET-INDUCED OBESITY AND IMPROVED INSULIN RESISTANCE IN MICE

Jun Muratsu[1,2], Yoshiaki Taniyama[1], Fumihiro Sanada[1], Atsuyuki Morishima[2], Katsuhiko Sakaguchi[2], Hiromi Rakugi[3], Ryuichi Morishita[1]

[1]Osaka University Graduate School of Medicine, Department of Clinical Gene Therapy, Suita, Japan, [2]Sumitomo Hospital, Department of Nephrology and Hypertension, Osaka, Japan and [3]Osaka University Graduate School of Medicine, Department of Geriatric Medicine and Nephrology, Suita, Japan

Background and Aims: Obesity and its associated chronic inflammation in adipose tissue initiate insulin resistance, which is related to several pathologies including hypertension and atherosclerosis. Previous reports demonstrated that circulating hepatocyte growth factor (HGF) level was associated with obesity and type 2 diabetes. However, its precise role in obesity and related-pathology is unclear.

Method: In this experiment, cardiac-specific over-expression of human HGF in mice (HGF-Tg mice) which showed 4-5 times higher serum HGF levels than wild-type mice were used. We chose cardiac specific HGF overexpression, as other strain of HGF transgenic mice such as liver and kidney specific HGF overexpression mice develop cancer and cystic diseases, which are rare in the heart. In the present study, using HGF-Tg mice and anti-HGF neutralizing antibody (HGF-Ab), we explored the role of HGF in obese and insulin resistance induced by high fat diet (HFD) for 14 weeks (200 or 400ug/week).

Results: With normal chow diet (ND), there were no significant changes in body weight between WT and HGF-Tg mice. While body weight in wild-type mice fed with HFD for 14 weeks was significantly increased accompanied with insulin resistance, HGF-Tg mice prevented body weight gain and insulin resistance. Insulin resistance in obesity arises from the combination of altered functions of insulin target cells (e.g., liver, skeletal muscle, and adipose tissue) and the accumulation of macrophages that secrete pro-inflammatory mediators in adipose tissue. The accumulation of macrophages and elevated levels of inflammatory mediators in adipose tissue were significantly inhibited in HGF-Tg mice as compared to wild-type mice. In the gWAT, the mRNA levels of the mature macrophage marker F4/80, the chemoattractants, MCP-1 and CXCL2, and the inflammatory cytokines, such as TNF-α and iNOS, were significantly increased in WT mice fed with HFD. However, these levels were markedly reduced in HGF-Tg mice fed with HFD. Additionally, activation of Akt by insulin administration was significantly reduced in the gWAT SM, and liver by HFD; however, this activation was restored in HGF-Tg mice. Moreover, insulin-induced Akt signaling was decreased in HGF-Ab groups as compared to saline group under HFD condition. Importantly, HFD significantly increased the level of HGF mRNA by approximately 2 fold in gWAT, SM, and liver without changing cMet expression. All together, these data indicate that the HGF as one of the systemic gWAT, SM, and liver-derived growth factor plays a role in compensatory mechanism against insulin-resistance through the at least anti-inflammatory effect in adipose tissue. The HFD-induced obesity in wild-type mice treated with HGF-neutralizing antibody showed an exacerbated response to the glucose tolerance test.

Conclusion: HGF suppresses inflammation in adipose tissue induced by a high-fat diet, and as a result improves systemic insulin resistance. These gain-of-function and loss-of-function studies demonstrated that the elevated HGF level induced by HFD have protective role against obesity and insulin resistance.

SO024 THE GPR120 AGONIST TUG-891 AMELIORATES KIDNEY FIBROSIS AND INFLAMMATION IN DIABETIC NEPHROPATHY

Tiantian Wei[1], Liang Ma[1], Ping Fu[1]

[1]*West China Hospital, Sichuan University, Department of Nephrology, Chengdu, P.R. China*

Background and Aims: ω3-Fatty acids (ω3FAs) attenuated inflammation, glomerulosclerosis and albuminuria in most experimental studies of diabetic nephropathy (DN). GPR120 has been identified as a first receptor for ω3FAs. Compared to ω3FAs, TUG-891 is a highly potent and selective agonist for GPR120. In this study, we examined the protective effects of GPR120 agonist TUG-891 in DN and investigated the possible mechanisms.

Method: Expression of GPR120 was detected in human renal biopsy tissue obtained from patients with early or advanced DN and in normal renal tissues. Effects of TUG-891 on the development of DN were investigated in male C57BLKS/J db/db mice and murine podocytes (MPC5). Expression of collagen IV, fibronectin, αSMA, TGF-β/smad2/3, IL-6, GPR120/β-arrestin2/TAK1 binding protein-1 and downstream pathways were measured.

Results: The expression of GPR120 was negatively correlated with the progression of DN. IF stainings showed that GPR120 was mainly expressed in podocytes of the glomerulus by co-localization of a special marker nephrin. In db/db mice, oral administration of TUG-891 significantly reduced urinary albumin excretion, improved podocyte injury and reduced collagen deposition in glomerulus. Meanwhile, TUG-891 inhibited the expression of fibronectin, collagen IV, α-SMA, TGF-β1 and IL-6, as well as down-regulated phosphorylation of Smad3 and STAT3 to alleviate the glomerulosclerosis. Mechanistically, TUG-891 effectively up-regulated the GPR120 expression in kidneys of db/db mice and HG-stimulated podocytes. TUG-891 also suppressed TAB1 expression and the phosphorylation of TAK1, IKKβ, NF-κB, JNK and p38 MAPK signals.

Conclusion: In summary, our result highlighted that TUG-891 ameliorated kidney fibrosis and inflammation by activating the intracellular GPR120 signaling pathway.

SO025

DCR2 ACCELERATES RENAL FIBROSIS AND TUBULAR CELL SENESCENCE BY PHOSPHORYLATING TYR 194 OF PRDX1 IN DIABETIC NEPHROPATHY

Jia Chen[1], Yani He[1]

[1]*Daping Hospital, Army Medical University, Nephrology, Chongqing, P.R. China*

Background and Aims: Cell senescence of renal tubular epithelial cells (RTECs), which is involved in renal tubulointerstitial fibrosis (TIF), is a key event in the progression of diabetic nephropathy (DN). However, the underlying mechanism remains unclear. This study aims to investigate the role and mechanism of decoy receptor 2 (DcR2) in TIF and cell senescence of RTECs.

Method: Streptozotocin (STZ)-induced DN mice model and high glucose (HG)-induced cell senescent model were constructed. The expression of DcR2 were regulated by ultrasound-mediated gene transfer of DcR2-siRNA or DcR2-overexpression plasmid *in vivo*. The co-expression of DcR2 with senescent markers (p16, p21 and SA-β-gal) and fibrotic markers (FN, collagen I and α-SMA). The interaction of DcR2 and its ligand TRAIL and antagonistic receptor DR5 were detected by laser confocal and Co-IP. The DcR2-interaction proteins were screened in renal tissue of DN patients and HG-induced cells by Co-IP combining with LC-MS/MS. The interaction of DcR2 and PRDX1 was validated by Co-IP, pull down assay and immunofluorescence co-staining. Peroxidase activity of PRDX1 was assessed by the kits of reactive oxygen species (ROS) and specific 2-cys peroxidase activity. The level of PRDX1 phosphorylation was measured through WB and the phosphorylated site were studied by wild-type PRDX1 and mutant Tyr^{194} PRDX1.

Results: DcR2 was co-expressed with senescent markers and co-localization with fibrotic markers in DN patients and STZ-DN mice. Knockdown of DcR2 effectively decreased renal fibrosis and tubular cell senescence in STZ-induced DN mice. However, DcR2 overexpression showed the opposite effects. DcR2 didn't interacted with TRAIL or DR5 in vivo and vitro. The following study indicated that PRDX1 is a novel DcR2-interacting protein using quantitative proteomics, which have peroxidase and antioxidant activity in cytoplasm. The interaction of DcR2-PRDX1 mediated RTEC senescence in vitro. Knockdown of DcR2 inhibited the level of ROS and promoted the peroxidase activity of PRDX1, resulting in oxidative stress and cell senescence, and DcR2 overexpression presented the contrary results. DcR2 regulated the level of PRDX1 phosphorylation by interacting Tyr^{194} of PRDX1, and the mutant Tyr^{194} of PRDX1 can't be phosphorylated by DcR2.

Conclusion: DcR2 mediates renal fibrosis and RTEC senescence by phosphorylating with PRDX1, suggesting DcR2 could serve as a potential therapeutic target for the amelioration of DN progression.

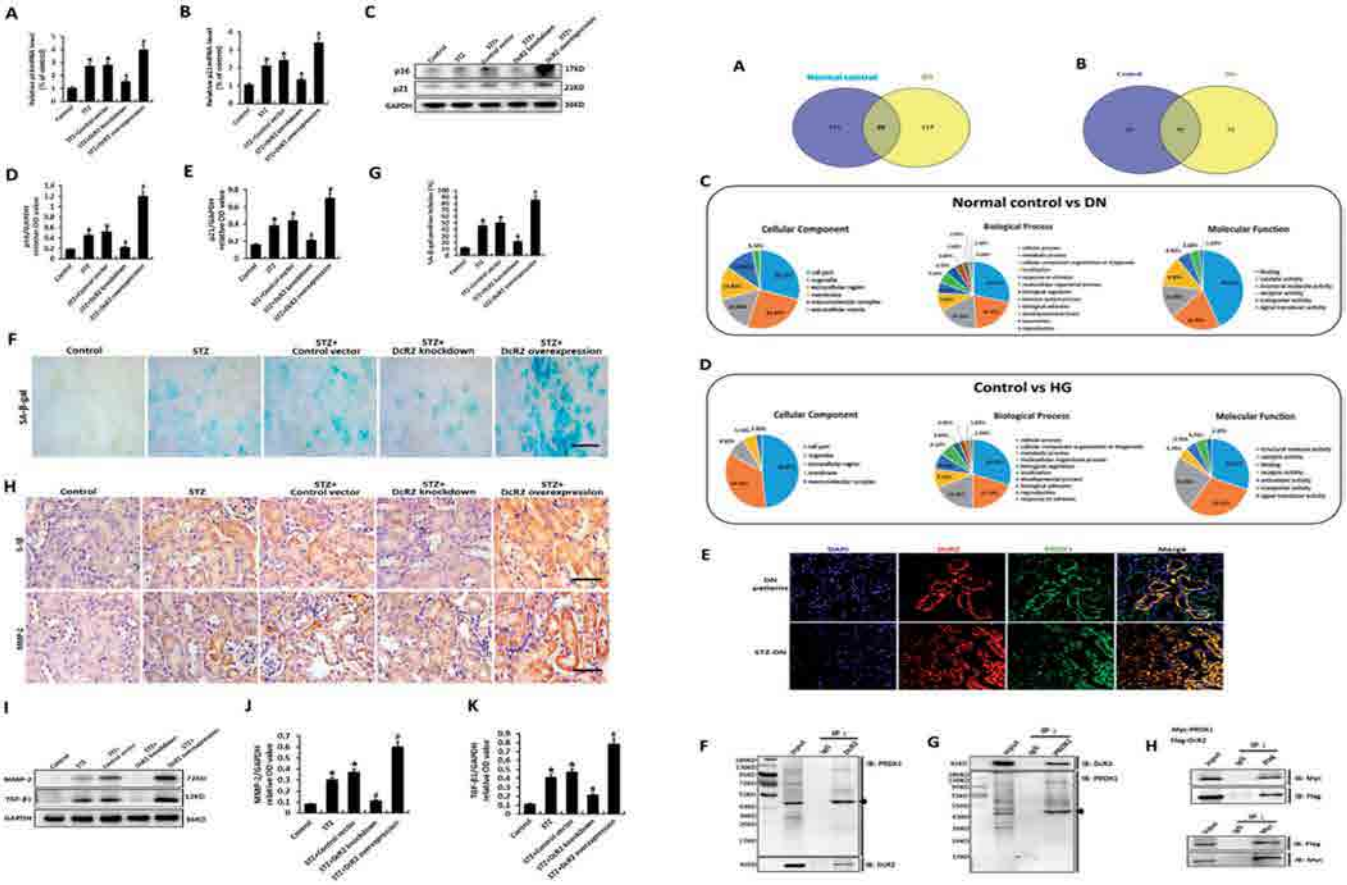


Figure:

SO026

HUMAN KIDNEY PROXIMAL TUBULAR 3D SPHEROIDS TO STUDY THE ROLE OF ADAM17 IN DIABETIC NEPHROPATHY

Vanesa Palau[1], Bramasta Nugraha[2], Maximilian Emmert[3], Simon Hoerstrup[3], Julio Pascual Santos[1], Maria Jose Soler Romeo[4], Marta Riera[1]

[1]IMIM, Nephrology, Barcelona, Spain, [2]Institut für Parasitologie Universität ZH, Zürich, Switzerland, [3]Institute for Regenerative Medicine - IREM, Schlieren, Switzerland and [4]VHIR - Vall d'Hebron Institut de Recerca, Nephrology, Barcelona, Spain

Background and Aims: ADAM17 is a disintegrin and metalloproteinase initially described to cleave the tumor necrosis factor α (TNFα). Currently, it is known that it can also release ectodomains of a diverse variety of molecules such as, transforming growth factor α (TGFα), L-selectin, and angiotensin-converting enzyme 2 (ACE2). It has been shown that ADAM17 protein expression increases in kidney mesangial cells after incubation with high glucose media mimicking what has been observed in diabetic patients and experimental models of diabetic nephropathy. We now studied the effect ADAM17 deletion on human kidney cells (HKC-8) in a 3D spheroids *in vitro* cell culture incubated with high glucose, low glucose and mannitol medium resembling the *in vivo* human kidney diabetic environment.

Method: ADAM17 deletion was performed using the CRISPR/Cas9 technology. HKC8 cells grew inside a RGD-functionalized dextran hydrogel to obtain 3D spheroids. 13 days post-seeding, the spheroids were incubated with 35mM of D-glucose (HG), 5mM of D-glucose (LG) or 35mM of mannitol as osmotic control for 6h, 24h or 72h. The quality of the established 3D cell culture of mature HKC-8 spheroids was assessed by Aquoporin-1 and Glut-1 staining. After incubations quantitative-PCR analyses were performed for fibrotic and inflammatory markers. Immunofluorescence for fibrotic markers was performed on HKC-8 spheroids incubated for 72h.

Results: High glucose (HG) medium induced CCL5 gene expression on wild-type HKC-8 spheroids after 6h and 24h of incubation in comparison with the control group. Interestingly, in the ADAM17-deleted spheroids, CCL5 gene expression maintained similar to control after 6h of incubation with HG medium and tended to decrease after 24h of incubation in comparison with the wild-type. Collagen IV gene expression was increased in the wild-type spheroids incubated with HG in comparison with the control group. In ADAM17-deleted spheroids, Collagen IV gene expression was significantly decreased in the cells incubated with HG in comparison with the wild-type cells incubated with HG. HG increased the expression of α-SMA, fibronectin and Collagen IV in wild-type spheroids. Adam17 deletion blocked the increase of α-SMA, fibronectin and Collagen IV expression compared with wild-type cells after 72h of incubation.

Conclusion: ADAM17 blockade protects against fibrosis and inflammation in human kidney tubular spheroids under high glucose.

Table 1

	CCL5		Collagen IV	
	6h	24h	6h	24h
LG-WT	1.47±0.77	1.23±0.39	1.00±0.22	1.10±0.26
HG-WT	4.70±2.19*	5.64±1.67*	1.44±0.61	13.97±1.54*
M-WT	1.21±0.67	1.15±0.75#	1.43±0.23	0.72±0.26#
LG-KO	1.96±0.93	1.44±0.41	0.62±0.12	2.20±0.44
HG-KO	1.04±0.28	2.73±0.24*	1.00±0.59	3.21±1.43$
M-KO	0.77±0.14	1.56±0.74	1.01±0.10	1.27±0.54

*p<0.05 HG vs. LG;
$p<0.05 KO vs. WT;
#p<0.05 M vs. HG

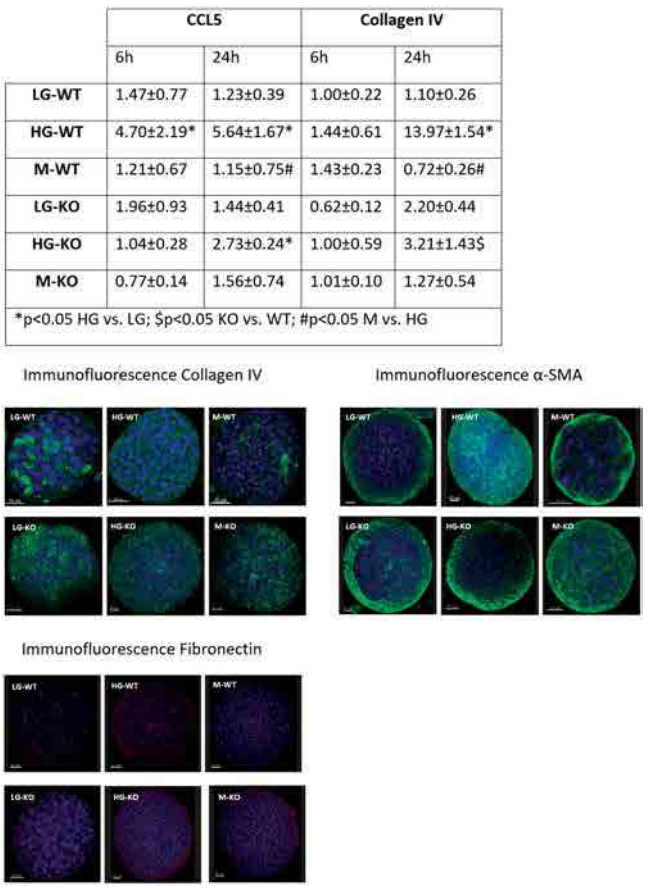


Figure:

Nephrology Dialysis Transplantation 35 (Supplement 3): iii32–iii32, 2020

ADVANCED RENAL MRI - THE NON-INVASIVE RENAL BIOPSY IN 2020

SO027 ASSOCIATIONS OF MUSCLE SODIUM DEPOSITION WITH SODIUM-23 MRI IN HEMODIALYSIS PATIENTS

Fabio Salerno[1,2], Alireza Akbari[1,3], Sandrine Lemoine[1], Justin Dorie[1], Tanya Tamasi[1], Christopher McIntyre[1,2]

[1]The Lilibeth Caberto Kidney Clinical Research Unit, Medicine - Nephrology, London, Canada, [2]Western University, Medical Biophysics, London, Canada and [3]Robarts Research Institute, London, Canada

Background and Aims:

The development of sodium-23 magnetic resonance imaging (^{23}Na MRI) allows the clinical quantification of tissue sodium. Recent studies have shown that hemodialysis (HD) patients have a tendency to retain tissue sodium due to impaired mechanisms in local tissue sodium clearance. However, the clinical significance of tissue sodium deposition in the HD patient population is unclear yet. The aim of this study was to investigate the association of tissue sodium deposition with well-established biomarkers of clinical outcomes.

Method:

Chronic, thrice weekly HD patients underwent ^{23}Na MRI of the leg on a non-dialysis day, during either the long or short interdialytic interval. Blood samples were also taken for the measurement of standard blood-based biomarkers. A multinuclear-capable 3.0-T MRI (GE Healthcare, Milwaukee WI) was used to acquire proton and sodium images. Maps of tissue ^{23}Na concentration were generated using an in-house software developed within MATLAB (Mathworks, Natick, USA, R2018a). ^{23}Na concentration maps were superimposed with the proton-anatomy images to delineate the regions of interest. Using the Horos (The Horos Project, Version 4.0.0) software, the soleus muscle was segmented (Figure, Panel A) and the sodium concentration in the region of interest was recorded for analysis.

Results:

28 HD patients completed both ^{23}Na MRI and bloodwork; 7/28 (25%) patients were females; mean$\pm$SD age was 66.1$\pm$8.3 years, mean body mass index was 30.9$\pm$6.5 kg/m^2, and mean HD vintage was 30.2$\pm$34.9 months. Soleus muscle sodium concentration showed a strong, negative correlation with serum albumin (Figure, Panel B; r=-0.66, $p<0.0001$). Furthermore, soleus muscle sodium concentration showed a minor association with plasma hemoglobin (r=-0.46, p=0.01).

Conclusion:

Serum albumin is a recognized, powerful predictor of mortality in the hemodialysis patient population. The strong relationship between muscle sodium concentration and serum albumin levels suggests that tissue sodium deposition may be a relevant biomarker of clinical outcomes. In addition, muscle sodium deposition may be involved in the development of anemia. These findings warrant further studies investigating the consequences of sodium removal on these biomarkers.

Figure: Panel A: sample ^{23}Na MRI image with soleus muscle region of interest (in green). Panel B: linear regression fit of soleus sodium concentration vs serum albumin (95% confidence interval bands).

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CLINICAL OUTCOMES IN TRANSPLANTATION 1

SO028

LONG-TERM OUTCOMES IN LIVE KIDNEY DONORS: PREVALENCE OF ISCHEMIC HEART DISEASE, DIABETES, CANCER AND CEREBROVASCULAR DISEASE AFTER DONATION COMPARED TO HEALTHY CONTROLS

Anders Haugen[1], Dag Olav Dahle[1], Stein I. Hallan[2], Karsten Midtvedt[1], Anna Varberg Reisater[1], Hallvard Holdaas[1], Geir Mjøen[1]

[1]Oslo University Hospital, Transplantation, Oslo, Norway and [2]St Olavs Hospital, Nephrology, Trondheim, Norway

Background and Aims: During long-term follow-up kidney donors are at increased risk of hypertension and end-stage renal disease after donation. Hypertension is a known risk factor for development of cardiovascular disease, but it is unknown whether kidney donors are at increased risk of cardiovascular disease.

We evaluated a large Norwegian kidney donor cohort and assessed prevalence of ischemic heart disease after donation compared to healthy controls. Prevalence of cancer, diabetes and cerebrovascular disease was also calculated.

Method: Follow-up data were retrospectively retrieved from past kidney donors. Healthy non-donor controls from a general population screening study were selected. Controls were selected according to standard donation criteria, assessed in similar time periods as the living donors. Stratified logistic regression was used to estimate associations with various disease outcomes. The diagnoses at follow-up were self-reported for the controls and registered by a physician for the donors.

A total of 1029 donors and 16084 controls were included.

Results: Mean observation time was eleven years after donation. Forty-four per cent of donors were male and mean age at follow-up was 56 years. Among the controls, 39 % were male and mean age at follow-up was 53 years.

At the time of follow up, 3.5 % of donors vs 1.7 % of controls had been diagnosed with ischemic heart disease, 3.7 % vs 4.4 % cancer, 1.8 % vs 1.4 % cerebrovascular disease and 4.1 % vs 1.9 % diabetes.

After adjusting for gender, age at follow up, smoking at baseline, BMI at baseline, systolic blood pressure at baseline and time since donation (time since participation in general population survey for controls), odds ratio for ischemic heart disease was 1.64 (CI 1.10-2.43; P=0.01) in previous kidney donors compared with healthy controls. Other outcomes did not differ significantly between donors and controls.

Conclusion: During long-term follow-up of kidney donors we find an increased risk of ischemic heart disease compared to healthy controls. This information may be important in the follow-up and selection process of living kidney donors.

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SO029

FIRST YEAR RENAL OUTCOME OF TRANSPLANTATIONS OF KIDNEYS FROM HEPATITIS C INFECTED DONORS TO HEPATITIS C NEGATIVE RECIPIENTS

Miklos Zsolt Molnar[1,2], Manish Talwar[1,2], Vasanthi Balaraman[1,2], Anshul Bhalla[1,2], Ambreen Azhar[1,2], Masahiko Yazawa[1,2,3], Makoto Tsujita[1,2,4], Pradeep Podila[5], Satheesh Nair[1,2], James Eason[1,2]

[1]Methodist University Hospital, James D Eason Transplant Institute, Memphis, United States of America, [2]University of Tennessee Health Science Center, Surgery, Memphis, United States of America, [3]St. Marianna University School of Medicine, Divison of Nephrology and Hypertension, Japan, [4]Nagoya Daini Red Cross Hospital, Division of Nephrology and Hypertension, Japan and [5]Methodist Le Bonheur Healthcare, Memphis, United States of America

Background and Aims: Transplant centers in US are increasingly willing to transplant kidneys from hepatitis C infected donors to hepatitis C negative recipients. Long-term renal outcome data from non-prophylactic treatment approach outside clinical trials is missing.

Method: We compared kidney graft function of 132 hepatitis C negative recipients, who received HCV infected (NAT+ and antibody+/-; HCV+) versus HCV negative (NAT- and antibody-; HCV-) in 2018, in a single center, retrospective, observational study. Categorical variables were compared using χ^2 tests and continuous variables were compared using t-tests or Mann–Whitney U-tests, as appropriate. Linear regression was applied to assess independent association between graft function and HCV viremic status.

Results: The mean±SD age of recipients was 52±11 years, 44% were female, 20% and 79% of recipients were Caucasian and African-American, respectively. Baseline characteristics were similar between HCV+ vs HCV- groups, except dialysis duration, donors race, KDPI and cold ischemic time (Table). The DGF rate, estimated GFRs at post-transplant 3, 6, 9 and 12 months was similar between HCV+ and HCV- groups (Table). HCV viremic status was not a predictor of 3, 6, 9 and 12 months eGFR in our unadjusted model and after adjustment for donor and recipient characteristics.

Conclusion: Recipients of HCV-viremic kidneys have similar renal allograft function in the first year after transplantation compared to those who received from HCV-non-viremic kidneys.

Table:

Parameter	Entire cohort	HCV+	HCV-	P-value
Observations (n)	132	73	59	
Recipient baseline characteristics				
Age (years), mean (SD)	52 (11)	52 (11)	52 (12)	0.86
Female gender, N, (%)	58 (44%)	30 (41%)	28 (47%)	0.46
Race, N, (%)				
Caucasian	27 (20%)	14 (19%)	13 (22%)	0.62
African American	104 (79%)	58 (80%)	46 (78%)	
Other	1 (1%)	1 (1%)	0 (0%)	
Dialysis duration (months), median (IQR)	60 (37-87)	49 (30-75)	71 (50-98)	<0.01
Comorbidity, N, (%)				
Diabetes	61 (46%)	36 (49%)	25 (42%)	0.43
Hypertension	128 (97%)	71 (97%)	57 (97%)	0.83
Peripheral vascular disease	9 (7%)	8 (11%)	1 (2%)	0.04
Coronary artery disease	21 (16%)	11 (15%)	10 (17%)	0.74
Chronic obstructive pulmonary disease	8 (6%)	5 (7%)	3 (5%)	0.67
Donor Characteristics				
Age (years), mean (SD)	33 (10)	32 (5)	34 (13)	0.17
Female gender, N, (%)	60 (45%)	37 (47%)	26 (44%)	0.77
DCD, N, (%)	18 (14%)	8 (11%)	10 (17%)	0.32
Comorbidity, N, (%)				
Diabetes	2 (2%)	1 (1%)	1 (2%)	0.88
Hypertension	12 (9%)	6 (8%)	6 (10%)	0.70
Race, N, (%)				
Caucasian	107 (82%)	70 (96%)	37 (64%)	<0.01
African American	21 (16%)	0 (0%)	21 (36%)	
Other	3 (2%)	3 (4%)	0 (0%)	
KDPI, mean (SD)	45 (19)	50 (16)	38 (21)	<0.01
Transplant characteristics				
Cold Ischemic Time (hours), median (IQR)	18.2 (12.7-21.8)	19.3 (16.2-23.2)	15.3 (9.1-20.3)	<0.01
ATG dose (mg/kg), mean (SD)	4.9 (0.9)	4.8 (0.8)	5.0 (1.3)	0.25
Renal Outcome Data				
Delayed Graft Function, N, (%)	13 (10%)	6 (8%)	7 (12%)	0.49
Estimated GFR at 3 months after transplantation (ml/min), mean (SD)	63 (19)	63 (17)	64 (21)	0.76
Estimated GFR at 6 months after transplantation (ml/min), mean (SD)	66 (19)	66 (17)	66 (21)	0.97
Estimated GFR at 9 months after transplantation (ml/min), mean (SD)	66 (17)	66 (15)	67 (20)	0.61
Estimated GFR at 12 months after transplantation (ml/min), mean (SD)	65 (19)	65 (16)	66 (22)	0.65

SO030

HISTOLOGICAL CHARACTERIZATION OF RENAL BIOPSIES FROM HCV-INFECTED DONORS: A VALUABLE SOURCE OF KIDNEY ALLOGRAFTS

Vincenzo L'Imperio[1], Mattia Rossi[2], Ruchi Naik[3], Beatrice Concepcion[3], Meghan Kapp[4]

[1]Unviersity of Milano Bicocca, Medicine and Surgery, Pathology, monza, Italy, [2]University and hospital of Verona, Renal Unit, department of Medicine, Verona, Italy, [3]Vanderbilt University Medical Center, Medicine, Division of Nephrology, Nashville, United States of America and [4]Vanderbilt University Medical Center, Pathology, Microbiology and Immunology, Nashville, United States of America

Background and Aims: The introduction of effective direct-acting antiviral agents (DAAs) has allowed safe transplantation of kidneys from HCV positive (HCV+) donors into HCV negative (HCV-) recipients. Some studies demonstrated an increased risk for rejection as well as polyomavirus infection in these situations (Molnar et al, Am J Transplant. 2019 Nov;19(11):3046-3057), possibly due to the development of an inflammatory milieu in the setting of HCV seroconversion and persistent viremia (Durand et al, Am J Transplant. 2019 Nov;19(11):2969-2970). With this concern for HCV-associated renal injury and increased risk for rejection, this retrospective study explores the histologic findings of allograft biopsies from HCV+ donors.

Method: Fifty renal allograft biopsies from 28 recipients of HCV+ donors evaluated at Vanderbilt University Medical Center between September 2018 and December 2019 were retrospectively reviewed with recording of clinical and histological features, and final diagnoses. All recipients were transplanted under a clinical protocol and were treated with DAA therapy. In the same period of time, 30 renal allograft biopsies from 24 recipients of HCV- donors were selected having the same post-transplant interval as the study cohort. Categorical variables are expressed in percentage and compared using Pearson's chi-squared test. Continuous variables are expressed as mean ± SD and compared used Student t-test. A p-value of <0.05 was considered as statistically significant.

Results: The complete results of the comparison between the two groups (HCV+ and HCV- donors) are demonstrated in Figure. The differences reaching statistical significance include higher frequency of males and tubulointerstitial fibrosis (IFTA) in the HCV+ group (p = 0.038 and 0.044, respectively) and the higher incidence of DSA positivity and acute tubular injury in the control group (p = 0.001 and 0.029). Notably, no significant differences were noted in terms of antibody-mediated events (microcirculation inflammation, transplant glomerulopathy, C4d positivity, or diagnostic ABMR), or T-cell mediated events including borderline or diagnostic T-cell mediated rejection (Banff 2013). The two groups also demonstrated the same incidence of polyomavirus nephropathy and de novo/recurrent glomerulonephritis. Interestingly, two of the HCV+ cases showed mesangial IgA deposits on immunofluorescence and electron microscopy on the first biopsy, of which one showed persistence of deposits, 18 and 44 days after transplant respectively. Once case demonstrated a de novo focal proliferative IgM-dominant glomerulonephritis on the 7th biopsy, 266 days after transplantation.

Conclusion: Kidneys from HCV+ donors represent a valuable resource in the era of DAA therapy. This reported experience demonstrates similar frequency of rejection and viral infection affecting allografts from HCV positive and negative donors. The presence of immune complex deposits and glomerulonephritis in some of these cases could represent either a donor-derived injury or an acquired post-seroconversion feature. In conclusion, HCV+ donors appear to be a safe resource for transplantation. Further studies with post-transplant intervals will provide additional characterization of their impact.

	HCV+	Controls	p values
N biopsies	50	30	
N patients	28	24	
Age	58 ± 11,49	52 ± 11,70	0,122
Males (N, %)	21 , 75%	12 , 50%	**0,038**
Etnicity			
African American (N, %)	15 , 54%	12 , 50%	
White (N, %)	13 , 46%	11 , 46%	
Interval of time (d)	106 ± 104,70	136 ± 85,47	0,205
DSA positivity	4 , 8%	11 , 37%	**0,001**
BK viremia	9 , 18%	4 , 13%	0,584
Serum Creatinine (mg/dl)	3,84 ± 2,77	2,74 ± 1,89	0,054
Hypertension (N, %)	25 , 89%	19 , 79%	0,341
Light Microscopy			
Total glomeruli	17 ± 9,74	15 ± 6,93	0,323
IFTA (N, %)	19 , 38%	5 , 17%	**0,044**
Microcirculation inflammation (N,%)			
Moderate	14 , 28%	9 , 30%	0,848
Any	22 , 44%	12 , 40%	0,726
Endothelialitis/arteritis (N,%)	5 , 10%	1 , 3%	0,273
Transplant glomerulopathy (N,%)	10 , 20%	4 , 13%	0,447
Peritubular capillary C4d+ (N, %)	8 , 16%	6 , 20%	0,649
Final diagnosis			
Acute tubular injury (N, %)	28 , 56%	24 , 80%	**0,029**
TCM events (N, %)			
Borderline	10 , 20%	6 , 20%	1
TCMR	12 , 43%	3 , 10%	0,120
Any	22 , 44%	9 , 30%	0,281
Any ABMR (N, %)	5 , 10%	6 , 20%	0,209
Any rejection (N,%)	16 , 32%	7 , 23%	0,407
De novo/recurrent GN (N,%)	7 , 14%	4 , 13%	0,933
Polyomavirus nephropathy (N,%)	4 , 8%	1 , 3%	0,404

Figure: Clinical and histological features of patients with HCV+ donor kidney transplant and controls. Significant p-values are reported in bold. DSA, donor specific antibodies; IFTA, interstitial fibrosis and tubular atrophy; TCMR, T-cell mediated rejection; ABMR, antibody mediated rejection; GN, glomerulonephritis

SO031

ANGIOTENSIN II TYPE 1 RECEPTOR (AT1R) EXPRESSION IN RENAL TRANSPLANT BIOPSIES AND ANTI-AT1R ANTIBODIES IN SERUM AS AN INDICATOR OF THE RISK OF TRANSPLANT LOSS

Agnieszka Sas-Strózik[1], Piotr Donizy[2], Katarzyna Kościelska-Kasprzak[3], Dorota Kamińska[1], Kamila Gawlik[1], Oktawia Mazanowska[1], Katarzyna Madziarska[1], Sławomir Zmonarski[1], Agnieszka Hałoń[2], Krajewska Magdalena[1], Mirosław Banasik[1]

[1]Wroclaw Medical University, Department of Nephrology and Transplantation Medicine, Wrocław, Poland, [2]Wroclaw Medical University, Department of Pathomorphology and Oncological Cytology, Wrocław, Poland and [3]Wroclaw Medical University, Research laboratory, Wrocław, Poland

Background and Aims: The manifestation of anti-angiotensin II type 1 receptor (AT1R) antibodies is considered a risk factor for transplant injury, however, the occurrence of AT1-Receptor expression in renal transplant biopsy may be an additional feature which can help to predict transplant loss.

The aim of our study was to evaluate the expression of AT1R together with their antibodies and assess the risk of transplant loss in patients who had a renal transplant indication biopsy.

Method: AT1-Receptor immunoreactivity was analyzed in renal transplant biopsies. Additionally, we analyzed the presence of anti-AT1R antibodies in these patients using ELISA method. The result of more than 10 was assessed as positive.

Immunohistochemical evaluation of AT1-Receptor expression was performed on 4 µm-thick paraffin sections mounted on silanized slides. AT1-Receptor expression was analyzed in five compartments: 1.tubular epithelium, 2.glomeruli, 3.peritubular capillaries, 4.interstitium and 5.renal blood vessels (small and intermediate arteries) based on a 3-step scale.

Results: We checked 156 samples of biopsies for the immunoreactivity of the AT1-Receptor. In all these patients we were able to access the presence of anti-AT1R antibodies.

A group of 67 patients had positive AT1-Receptor expression (R+) and 16 patients had positive anti-AT1R antibodies (R+Ab+) results. A group of 89 patients had no expression of AT1-Receptor (R-), among which 51 had also no anti-AT1R (R-Ab-). One-year post-biopsy graft loss in the R+Ab+ patients was 37% (6/16) compared to 10% (7/69) in the R-Ab- patients ($p = 0.006$). Two-year and three-year graft loss was 43% vs. 17% ($p=0.02$) and 50% vs. 21% ($p=0.02$) respectively.

Moreover, six patients had positive staining of AT1-Receptors in microcirculation (glomeruli and peritubular capillaries), which was associated with antibody mediated rejection.

Conclusion: The presence of anti-AT1R antibodies in serum together with the expression of AT1-Receptor in transplant biopsy was associated with a significantly higher graft loss. The relevance of AT1-Receptor expression analyzed together with anti-AT1R antibodies should be considered for better transplant immunological risk assessment.

SO032

THE DISCARD AND DECLINE OF HEPATITIS C VIRUS POSITIVE DONOR KIDNEYS IN THE UNITED STATES

Tarek Alhamad[1], Krista Lentine[2], David Axelrod[3], Sami Abdulnabi[1], Mark Schnitzler[2], Su-Hsin Chang[1]

[1]Washington University in St. Louis, [2]Saint Louis University and [3]University of Iowa

Background and Aims: With more transplant centers in the United States are accepting hepatitis C virus infected (HCV+) deceased donor kidneys (dHCV+), the trend of non-utilization and decline of these organs have not been re-examined.

Method: We used data from the national Organ Procurement and Transplantation Network on deceased donor kidneys between Jan 2000 and Dec 2018 in the United States. Kidney non-utilization for HCV+ was defined as a positive donor HCV status and positive hepatitis as the reason for non-utilization. dHCV+ kidney decline was defined as a donor HCV+ status among kidneys recovered for transplantation but not transplanted. We assessed associations of a dHCV+ status with kidney non-utilization or decline, adjusted for donor characteristics (age, race, sex, body mass index, diabetes, hypertension, kidney donor profile index), using multivariable logistic regression.

Results: A total of 274,570 deceased donor kidneys procured for transplantation between 2000 and 2018 were identified. Among these kidneys, 4.1% were from dHCV+. Proportion of dHCV+ non-utilization among all non-utilized kidneys increased from 2000-2005 (3.9%) and then subsequently declined. This proportion increased slightly to 1.1% in 2014 and decreased to 0.5, 0.8, 0.4, 0.6% in 2015-2018, respectively. Multivariable-adjusted odds ratios for dHCV+ non-utilization and decline by year demonstrate consistently an increasing trend from 2000-2006 followed by a decreasing trend from 2006-2011 (**Fig A-B**). Multivariable-adjusted odds ratios for dHCV+ (compared to dHCV-) non-utilization and decline increased to 6.56 (95% CI 5.30-8.12) and 6.66 (95% CI 5.39-8.24), respectively, in 2012, and decreased to 2.32 (95% CI 2.01-2.69) and 2.28 (95% CI 1.98-2.64), respectively, in 2018.

Conclusion: dHCV+ non-utilization and decline have decreased in the last few years, particularly after 2014. 2018 had a historic lowest odds ratio for non-utilization and decline of dHCV+ organs, which reflects the increased acceptability of transplant centers to these kidneys. Overall, since 2014, the odds ratios for dHCV+ non-utilization and decline decreased by half. Yet, there is more room for decreasing the non-utilization and decline for these potentially life-saving organs.

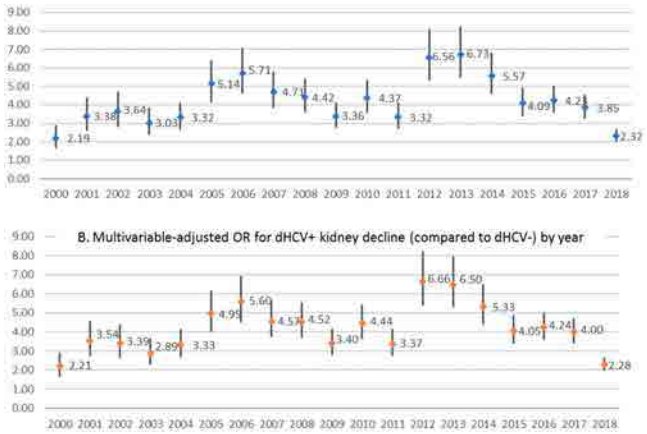


Figure:

HYPERTENSION AND CKD

SO033

PATIROMER TO ENABLE SPIRONOLACTONE IN PATIENTS WITH RESISTANT HYPERTENSION AND CHRONIC KIDNEY DISEASE (AMBER): PRESPECIFIED RESULTS BY BASELINE SERUM POTASSIUM

Patrick Rossignol[1], Susan Arthur[2], Ansgar Conrad[2], William B. White[3], Bryan Williams[4], Rajiv Agarwal[5]

[1]University of Lorraine and FCRIN INI-CRCT, Nancy, France, [2]Relypsa, Inc., a Vifor Pharma Group Company, Redwood City, United States of America, [3]University of Connecticut School of Medicine, Farmington, United States of America, [4]University College London (UCL), London, United Kingdom and [5]Indiana University School of Medicine, Indianapolis, United States of America

Background and Aims: Spironolactone (SPIRO) is effective at reducing blood pressure in patients with resistant hypertension (RHTN); however, its use in patients with advanced chronic kidney disease (CKD) is often limited by hyperkalaemia. In AMBER, patiromer (PAT) enabled more persistent use of SPIRO in patients with RHTN and eGFR 25 to ≤45 mL/min/1.73 m^2. Patients were required to be normokalaemic at baseline, with serum potassium (sK^+) 4.3 to 5.1 mmol/L. Since higher baseline sK^+ may increase the risk for developing hyperkalaemia on SPIRO, we evaluated AMBER results in prespecified subgroups by baseline sK^+.

Methods: This was a randomised, double-blind, placebo (PBO)-controlled trial in adults with eGFR 25 to ≤45 mL/min/1.73 m^2, uncontrolled RHTN, and sK^+ 4.3 to 5.1 mmol/L. Patients were assigned (1:1) to receive PBO or PAT, and SPIRO 25 mg QD, with dose titrations permitted after 1 week (PAT) and 3 weeks (SPIRO). The primary endpoint was the between-group difference at Week 12 in the percentage of patients on SPIRO. The secondary endpoint was the difference between treatment groups in the change in systolic automated office blood pressure (AOBP) from baseline to Week 12 (or to the last available measurement before the addition of any new antihypertensive medications or increase in any of the baseline antihypertensive medications). The primary and secondary endpoints were assessed in prespecified subgroups by baseline sK^+ stratum: 4.3 to <4.7 mmol/L and 4.7 to 5.1 mmol/L.

Results: 295 patients were randomised, 129 (44%) and 166 (56%) with baseline sK^+ 4.3 to <4.7 mmol/L and sK^+ 4.7 to 5.1 mmol/L, respectively. Baseline mean (SD) systolic AOBP (mmHg) was 144.0 (7.3) and 144.1 (6.4), and eGFR (mL/min/1.73 m^2) was 36.4 (7.6) and 35.2 (7.2), respectively. Significantly more patients treated with PAT than with PBO remained on SPIRO at Week 12 in both subgroups (between treatment difference of 16.2% [*P*=0.0167] for patients with sK^+ 4.3 to <4.7 mmol/L and 22.4% [*P*=0.0016] for patients with sK^+ 4.7 to 5.1 mmol/L) with *P*=0.45 for interaction between subgroups (**Figure**). In patients with sK^+ 4.3 to <4.7 mmol/L, LS mean (SE) systolic AOBP change from baseline was –10.7 (1.9) mmHg in patients receiving PBO and –13.0 (1.9) mmHg in patients receiving PAT; systolic AOBP change from baseline was –10.5 (1.6) (PBO) and –10.5 (1.6) mmHg (PAT) in patients with sK^+ 4.7 to 5.1 mmol/L (*P*<0.001 for all changes from baseline and *P*=NS for all differences between treatment groups). LS mean (SE) cumulative SPIRO dose was higher with PAT than PBO by 373.2 (157.0) mg and 392.3 (185.0) mg in patients with sK^+ 4.3 to <4.7 mmol/L and sK^+ 4.7 to 5.1 mmol/L, respectively. Adverse events occurred in 52% (PBO) and 56% (PAT) of patients with sK^+ 4.3 to <4.7 mmol/L and in 55% (PBO) and 56% (PAT) of patients with sK^+ 4.7 to 5.1 mmol/L. Adverse events of hyperkalaemia or blood K^+ increased occurred in 2 (PBO) and 4 (PAT) patients with sK^+ 4.3 to <4.7 mmol/L and in 12 (PBO) and 5 (PAT) patients with sK^+ 4.7 to 5.1 mmol/L. One PBO and 2 PAT patients (sK^+ 4.3 to <4.7 subgroup) and 1 PAT patient (sK^+ 4.7 to 5.1 subgroup) had serum Mg 0.49 to <0.58 mmol/L; none had serum Mg <0.49 mmol/L.

Conclusion: PAT enabled more patients with advanced CKD and RHTN to continue treatment with SPIRO, regardless of baseline sK^+ stratum.

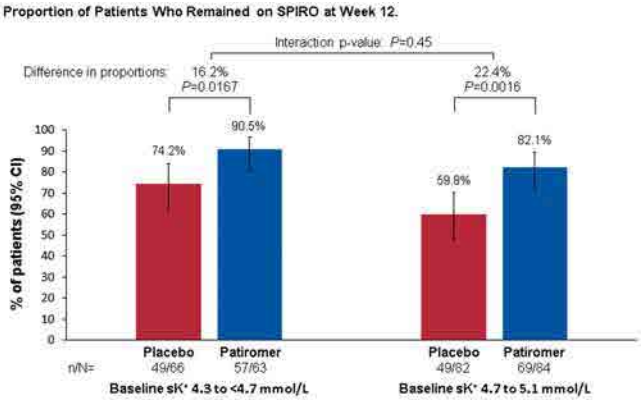


Figure:

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SO034 **A NEW MARKER OF RESISTANT HYPERTENSION IN CKD PATIENTS**

Guido Gembillo[1], Rossella Siligato[1], Valeria Cernaro[1], Ersilia Satta[2], Giovanni Conti[3], Antonino Salvo[1], Adolfo Romeo[1], Vincenzo Calabrese[1], Giovanna Sposito[4], Guido Ferlazzo[4], Domenico Santoro[1]

[1]Policlinic G. Martino, Department of Clinical and Experimental Medicine, Unit of Nephrology and Dialysis, ME, Italy, [2]Nefrocenter Research Network, Napoli, Italy, [3]Policlinic G. Martino, Pediatric Nephrology Unit, ME, Italy and [4]Policlinic G. Martino, Department Human Pathology, Laboratory of Immunology and Biotherapy, ME, Italy

Background and Aims: Monocytes -HDL ratio (MHR), has emerged as a possible marker of inflammation and oxidative stress (OS), demonstrating its possible use in the population with Chronic Kidney Disease (CKD). These effects seem to be modulated by an increased lipid production, by reduced cellular catabolism of fatty acids and by the alteration of the antioxidant, anti-inflammatory mechanisms and the reverse cholesterol transport of HDL. The latter to exert favorable effects on inflammatory and oxidative pathway. The purpose of our research is to evaluate the link between MHR and resistant hypertension (RH) which, together with inflammation, OS and atherosclerosis, represents a widespread feature in the population with CKD and carries a greater risk of premature death due to cardiovascular disease.

Method: A retrospective study has been performed on 251 hypertensive patients, admitted in the last 6 months to the Unit of Nephrology and Dialysis of the Policlinic G. Martino of Messina, Italy. 80 patients were diagnosed with RH, defined as blood pressure that remains above 140/90 mmHg despite use of three different classes of antihypertensive medications (one of which must be a diuretic) at the maximum tolerated doses.

We evaluated the distribution of data with Kolmogorov-Smirnov test and, considering that MHR had a non-normal distribution, we expressed the values as medians and interquartile ranges (IQR). Moreover, differences between groups with Mann-Whitney test, correlations with Rank Correlation and Spearman's Rho coefficient were also considered in the analysis. Finally, we assessed the differences of variables between the means of different groups with ANOVA test using multiple regression to valuate independent relations between variables.

Results: MHR appeared to be positively correlated with serum creatinine levels (ρ=0.24; P=0.0001) (Figure 1). MHR correlated with the number of antihypertensive drugs per patient in the entire cohort of patients (F = 18.23; P <0.001) (Figure 2). Patients with RH had a significantly higher MHR than patients without resistant hypertension (0.1493 [IQR 0.12 - 0.18] versus 0.11 [IQR 0.0 - 0.13], P <0.0001) (Figure 3).

Conclusion: MHR has proven to be an accurate tool in quantifying inflammatory status and OS, whose effectiveness lies in the close correlation that exists between HDL and monocytes. HDL prevent and reverse the recruitment of monocytes in the arterial wall and their activation through a decrease in their F-actin content, thereby reducing the expression of CD11b on monocytes, and modulating their adhesion to the endothelium. Our study showed that MHR could be a useful and immediate tool to evaluate OS and inflammatory status in order to select high-risk patients and identify earlier and appropriate treatment strategies.

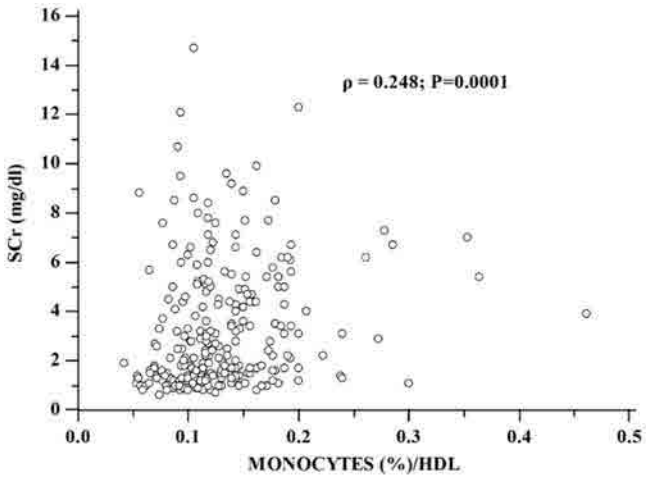


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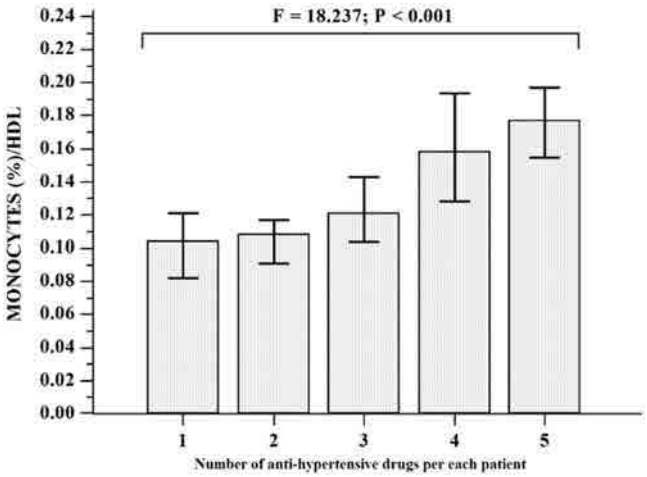


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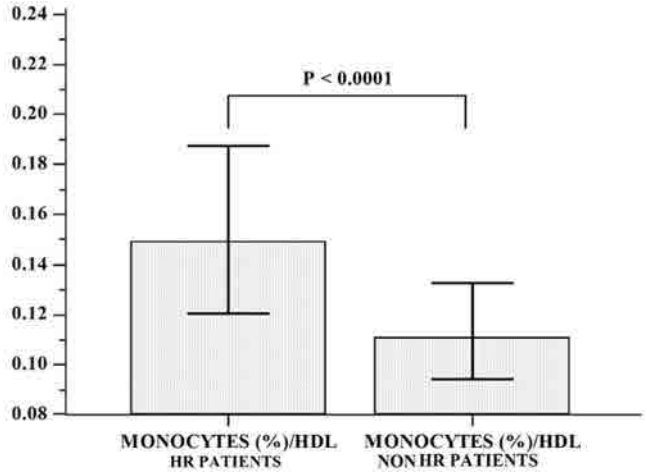


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SO035

EFFECT OF DIETARY SALT REDUCTION ON BLOOD PRESSURE IN KIDNEY TRANSPLANT PATIENTS: A RANDOMISED CONTROLLED TRIAL

Louise Ross[1], Rebecca Suckling[1], Fengjun He[2], Mark Dockrell[1], Thomas Bailey[3], Pauline Swift[1]

[1]St Helier Hospital, Sutton, United Kingdom, [2]Queen Mary University of London, London, United Kingdom and [3]University of Warwick, Coventry, United Kingdom

Background and Aims: Cardiovascular morbidity and mortality are increased in kidney transplant patients. High blood pressure (BP) contributes significantly to this risk and is associated with shortened allograft survival. Dietary salt reduction is widely recommended as a strategy to lower BP in the general population and in chronic kidney disease. Due to a lack of evidence there is currently no consensus on dietary salt restriction in kidney transplant patients. The primary aim of the study was to examine the impact of reduced dietary salt intake on BP in kidney transplant patients.

Method: Sixty stable kidney transplant patients, $\geq$ 6-months post-transplantation, with BP $\geq$120/80 mmHg, and sodium intake $\geq$80 mmol/24hrs, were randomised in this parallel-designed study to receive either a regular-salt diet (target 150 mmol/24hr) or a low-salt diet (target 80 mmol/24hr) for 8-weeks. The primary outcome measure was systolic and diastolic BP. Secondary outcome measures included 24-hour ambulatory BP (ABP) and proteinuria. Dietary salt intake was assessed by 48-hour urinary sodium excretion.

Results: At baseline, patients (72% men) were 56$\pm$11 years with estimated glomerular filtration rate (eGFR) 53$\pm$18 mL/min/1.73m2. Mean urinary sodium was 128$\pm$42 mmol/24hr, mean systolic BP was 132$\pm$12 mmHg, and mean diastolic BP was 77$\pm$10 mmHg. At the end of the intervention period sodium excretion was significantly lower in the low-salt group compared with the regular-salt group (90$\pm$37 vs. 132$\pm$51 mmol/24hr; adjusted mean difference, -36 [95% CI, -59 to -14] mmol/24hr; P=0.002). We found no difference in systolic BP (adjusted mean difference, -2 [95% CI, -12 to 9] mmHg; P=0.750), diastolic BP (adjusted mean difference, 0 [95% CI, -4 to 4] mmHg; P=0.887), 24-hour systolic ABP (adjusted mean difference, -3 [95% CI, -9 to 2] mmHg; P=0.213) or 24-hour diastolic ABP (adjusted mean difference, -2 [95% CI, -5 to 1] mmHg; P=0.267). There was no significant effect on proteinuria or eGFR.

Conclusion: In this study baseline urinary sodium was lower than expected and baseline BP was well controlled. Reducing dietary salt by 2g/day did not have a significant effect on office blood pressure readings.

SO036

THE EFFECT OF DAPAGLIFLOZIN ON AMBULATORY AORTIC BLOOD PRESSURE AND ARTERIAL STIFFNESS PARAMETERS IN PATIENTS WITH TYPE-2 DIABETES MELLITUS: A DOUBLE-BLIND RANDOMIZED CLINICAL TRIAL

Eirini Papadopoulou[1,2], Charalampos Loutradis[2], Kalliopi Kotsa[3], Spiros Karras[3], Christos Sambanis[1], Glyceria Tzatzagou[4], Anastasios Karakozoglou[4], Triantafillos Didangelos[5], Marieta Theodorakopoulou[2], Ioanna Minopoulou[2], Apostolos Tsapas[6], Asterios Karagiannis[1], Pantelis Sarafidis[2]

[1]Aristotle University of Thessaloniki, Second Propaedeutic Department of Internal Medicine, Thessaloniki, Greece, [2]Aristotle University of Thessaloniki, Department of Nephrology, Thessaloniki, Greece, [3]Aristotle University of Thessaloniki, First Department of Internal Medicine, Thessaloniki, Greece, [4]Papageorgiou Hospital, First Department of Internal Medicine, Thessaloniki, Greece, [5]Aristotle University of Thessaloniki, First Propaedeutic Department of Internal Medicine, Thessaloniki, Greece and [6]Aristotle University of Thessaloniki, Second Department of Internal Medicine, Thessaloniki, Greece

Background and Aims : Arterial stiffness is a prominent risk factor for heart failure and overall mortality in patients with type-2 diabetes mellitus (DM). Sodium-glucose co-transporter 2 (SGLT-2) inhibitors reduce the incidence of heart failure and death in these patients. The aim of this study is to evaluate the effects of dapagliflozin on ambulatory central blood pressure (BP) levels and arterial stiffness parameters in patients with type-2 DM.

Method : This is a double-blind, randomized, placebo-controlled clinical trial including 85 adult patients with type-2 DM on monotherapy or combination therapy with two of: metformin, sulphonylurea, DDP-4 inhibitor, or insulin. Patients were randomized in a 1:1 ratio to oral dapagliflozin 10 mg per day or placebo for 12 weeks. Study participants underwent 24-h ambulatory BP monitoring with the Mobil-O-Graph NG monitor at baseline and study-end.

Results : Baseline demographic, clinical and laboratory parameters were similar in the two groups (age 61.74±6.73 vs 60.64±9.35; p=0.534). During follow-up, 24-hour central SBP/DBP significantly decreased in dapagliflozin (117.41±10.52/78.88±7.25 vs 113.30±8.75/77.25±6.54; p=0.002/p=0.047), but not in the placebo group. Corresponding reductions of 24-hour central SBP (-4.12±8.00 vs -0.65±7.77; p=0.046) were greater with dapagliflozin than placebo. Aortic pulse pressure (PP) decreased only in the dapagliflozin group (38.53±7.44 vs 36.05±6.59 mmHg; p=0.004). 24-hour heart-rate adjusted augmentation-index significantly decreased with dapagliflozin. Importantly, there was a significant difference in the change of 24-hour PWV (-0.16±0.32 vs 0.02±0.27; p=0.007) favoring dapagliflozin.

Conclusion : Treatment with dapagliflozin significantly reduces ambulatory central BP and PWV levels in type-2 diabetics. Improvement in these parameters may substantially contribute to the cardiovascular benefits of SGLT-2 inhibitors.

SO037

AMBULATORY BLOOD PRESSURE IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE - IMPROVING DIAGNOSIS AND OPTIMIZING THERAPY

Magdalena Jankowska[1], Marek Aniserowicz[2], Piotr Nowak[2], Anna Szyndler[3], Michal Hoffmann[3], Krzysztof Narkiewicz[3], Alicja Debska-Slizien[1]

[1]Medical University of Gdansk, Department of Nephrology, Transplantology and Internal Medicine, Gdansk, Poland, [2]Medical University of Gdansk, Faculty of Medicine, Gdansk, Poland and [3]Medical University of Gdansk, Poland, Department of Arterial Hypertension and Diabetology, Gdansk, Poland

Background and Aims : Hypertension (AH) is an early complication of autosomal dominant polycystic kidney disease (ADPKD), which significantly increases the risk of decline of kidney function and impacts cardiovascular risk. The diagnosis of AH is often delayed and the optimal control of blood pressure (BP) is difficult to achieve in this group of patients. Of note, the optimal treatment of AH in ADPKD is yet to be established.

Aim of the study was to diagnose AH (including the prevalence of masked hypertension) and to evaluate the control of BP with the use of ABPM in a cohort of ADPKD patients.

Method : ABPMs were performed in 163 consecutive patients, with ADPKD according to Pei criteria, appointed for the first outpatient visit. Prior to the ABPM, the diagnosis based on office BP or current AH treatment was established as well as age, sex, medication intake, and eGFR (CKD-EPI formula) were recorded. The study had a cross-sectional design.

Results : Out of 163 performed ABPMs, 143 were eligible for further analysis. The study group consisted of 93 females and 50 males, median age was 40 (18-87) years and median eGFR was 79.5(13-90) ml/min/1.73m^2. 68% of patients had CKD G1 or 2. Median systolic blood pressure (SBP) was 127 (101-157) mmHg with blood pressure variability (BPV) 12 (7.8-23); median diastolic blood pressure (DBP) was 79 (58-98) mmHg, BPV 10.8 (6.2-17.4). 35% of patients were non-dippers, 2.7% extreme dippers and 4.9% reverse-dippers. In 31 (55%), out of 56 patients without previous diagnosis of AH, masked hypertension was found. Among 87 diagnosed with AH before the measurement, 49% were treated with 1 drug, and 29% with 2, 13% with 3, and 2% with 4. The most prevalent medication was ACE-inhibitor. Among treated, only 5.5% had all ABPM values within the target.

Conclusion : 55% of patients previously not diagnosed with AH on the basis of office BP proved to suffer from masked hypertension. The night DBP was the most suboptimally controlled value in ADPKD patients. Whether this is a consequence of nonadherence or suboptimal treatment, needs further investigation. ABPM is an indispensable tool in managing patients inflicted with ADPKD.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii43–iii47, 2020

MOLECULAR NEPHROLOGY

SO038

A TRANSLATIONAL KIDNEY ORGANOID SYSTEM BOLSTERS HUMAN RELEVANCE OF CLINICAL DEVELOPMENT CANDIDATE

Amy Westerling-Bui[1], Thomas Soare[2], Srinivasan Venkatachalan[1], Michael DeRan[3], Eva Fast[2], Alyssa Fanelli[1], Sergii Kyrychenko[1], Hien Hoang[1], Grinal Corriea[1], Wei Zhang[4], Maolin Yu[5], Goran Malojcic[6], Xin-Ru Pan-Zhou[7], Mark Ledeboer[5], Jean-Christophe Harmange[8], Maheswarareddy Emani[9], Thomas T. Tibbitts[2], John Reilly[1], Peter Mundel[1]

[1]Goldfinch Bio, Inc., Biology, Cambridge, United States of America, [2]Goldfinch Bio, Inc., Computational Biology & Statistical Genetics, Cambridge, United States of America, [3]Diamond Age Data Science, Somerville, United States of America, [4]Bristol-Myers Squib, San Diego, United States of America, [5]Goldfinch Bio, Inc., Chemistry, Cambridge, United States of America, [6]Goldfinch Bio, Inc., Lead Discovery, Cambridge, United States of America, [7]Goldfinch Bio, Inc., Pharmacology/Non-Clinical, Cambridge, United States of America, [8]Goldfinch Bio, Inc., Drug Discovery, Cambridge, United States of America and [9]Broad Institute, Cambridge, United States of America

Background and Aims: A major challenge in drug discovery is gaining confidence in the human relevance of pre-clinical animal studies. While human iPSC-derived organoids offer exciting opportunities to address this, concerns about applicability and scalability remain. Here, we report a high-throughput human organoid platform for assessment of kidney disease targeting compounds.

Method: *In vitro* & *in vivo* transplanted under athymic rat kidney capsule, differentiated organoids were characterized using single cell RNA sequencing (scRNA-Seq), NanoString, & immunofluorescence techniques. Immunofluorescence quantitative analysis of aggregated actin per *in vitro* organoid in a protamine sulfate (PS) podocyte injury model was used to evaluate efficacy of GFB-887, a sub-type selective, small molecule transient receptor potential canonical 5 (TRPC5) inhibitor. In pharmacokinetic studies, GFB-887 was orally administered into rats, then the presentation of GFB-887 was measured in rat plasma, rat kidney, & *in vivo* transplanted human organoids. In pharmacodynamic studies of transplanted human organoids, rats were co-perfused with GFB-887 & PS or orally dosed with GFB-887 prior to PS, then immunofluorescence quantitative analysis of mean synaptopodin intensity in podocytes of the *in vivo* transplanted organoids was used to evaluate efficacy of GFB-887.

Results: We confirmed platform reproducibility by scRNA-Seq and derived a NanoString panel for efficient quality control. Organoid transplantation in rats for 2 to 4 weeks promoted organoid maturation and vascularization. In functional studies, cyclosporine A (CsA), a calcineurin inhibitor clinically utilized for the treatment of nephrotic syndrome, and GFB-887, a novel sub-type selective TRPC5 inhibitor currently in clinical development, protected *in vitro* kidney organoids from injury. Pharmacodynamic studies with GFB-887 delivered orally to rats were also successfully performed in human transplanted organoids.

Conclusion: These data show how human organoids can deliver confidence in taking development candidate compounds to the clinic, fulfilling their promise to revolutionize drug discovery.

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SO039

BETA3-ADRENORECEPTOR AS A NEW PLAYER IN SYMPATHETIC REGULATION OF THE ACID-BASE HOMEOSTASIS IN THE KIDNEY.

Serena Milano[1], Andrea Gerbino[2], Monica Carmosino[3], Maria Svelto[1], Giuseppe Procino[1]

[1] University of Bari, Department of Biosciences, Biotechnologies and Biopharmaceutics, Bari, Italy, [2]CNR, Institute of biomembrane and bioenergetics (IBIOM), Bari, Italy and [3]University of Basilicata, Department of Sciences, Potenza, Italy

Background and Aims: Sympathetic nervous system has a key role in the regulation of renal function. We previously showed that, in mouse, the β_3-adrenoreceptor (β_3-AR) localizes in most of the nephron segments and its selective agonism promotes a potent antidiuretic effect. Here, we evaluate the expression of β_3-AR in kidney intercalated cells (ICs) which are associated with the regulation of acid-base homeostasis in distal segments of the kidney tubule. The aim of this study is to investigate whether the β_3-AR might play a role in the acid-base homeostasis operated by the kidney.

Method: The β_3-AR expression in mouse kidney ICs was investigated by confocal microscopy. Wild type (wt) and β_3-AR knock-out (ko) mice were used to study the role of β_3-AR in the renal acid-base homeostasis. Mouse urine were collected using metabolic cages and pH was measured. Immunofluorescence and Western blotting experiments were performed to evaluate the localization and the abundance of renal H^+-ATPase in wt and β_3-AR ko mice. Kidney cells expressing human β_3-AR (M1-β_3-AR) and endogenous H^+-ATPase were used to investigate the possible effects of β_3-AR stimulation on the activity/localization of H^+-ATPase. Live imaging experiments using the pH-sensitive dye BCECF were carried out to determine intracellular pH and assess H^+-ATPase activity. Immunofluorescence experiments were performed to reveal the effects of β_3-AR activation on H^+-ATPase localization.

Results: Co-localization study of β_3-AR with either H^+-ATPase or Cl^-/HCO_3^- exchanger pendrin in mouse kidney showed that β_3-AR is expressed in H^+-secreting type A, in HCO_3^- secreting type B, and in non-A non-B ICs. The urine pH of β_3-AR ko mice was significantly higher compared with wt mice. In line with these results, localization and expression analysis showed that renal H^+-ATPase significantly decreased in β_3-AR ko mice compared to wt mice, supporting the idea that H^+ secretion is partially blunted in these animals. Of note, exposure of M1-β_3-AR cells to a selective β_3-AR agonist induced a 2.5 fold increase of H^+-ATPase activity compared to resting cells and this effect was prevented by a selective β_3-AR antagonist or by the H^+-ATPase inhibitor bafilomycin. Moreover, β_3-AR agonism enhanced H^+-ATPase apical expression in M1-β_3-AR cells. In addition, the PKA inhibitor H89 abolished the stimulatory effect of β_3-AR agonism, demonstrating the involvement of the cAMP/PKA pathway.

Conclusion: The present data suggest that modulation of H^+-ATPase activity in renal ICs by endogenous β_3-AR agonists may play an addition physiological role in hormonal control of renal acid-base homeostasis.

SO040

ROLE OF INTRACELLULAR CA2+ IN THE REGULATION OF THE RENAL CHLORIDE CHANNEL CLC-KA

Andrea Gerbino[1], Roberta De Zio[2], Daniela Russo[3], Luigi Milella[3], Serena Milano[4], Giuseppe Procino[4], Michael Pusch[5], Maria Svelto[2], Monica Carmosino[3]

[1]CNR, Institute of Biomembranes, Bioenergetics and Biotechnologies, Bari, Italy, [2]University of Bari, Department of Biosciences, Biotechnologies and Biopharmaceutics, Bari, Italy, [3]University of Basilicata, Department of Sciences, Potenza, Italy, [4]University of Bari, Department of Biosciences, Biotechnologies and Biopharmaceutics, Bari, Italy and [5]CNR, Institute of Biophysics, Genova, Italy

Background and Aims: It has been recognized that the physiological role of ClC-Ka and its mouse homolog ClC-K1 in the nephron is to confer high Cl- permeability in the thin Ascending Limb of loop of Henle (tAL), which in turn is essential for establishing the high osmolarity of the renal medulla in the countercurrent system. Accordingly ClC-K1 KO mice display a severe polyuria resembling a Nephrogenic Diabetes Insipidus (NDI) phenotype. Thus, ClC-Ka in human nephron could be an interesting target for diuretic and anti-hypertensive drugs. Unfortunately the regulation of ClC-Ka in and its electrophysiological properties are still not completely known.

Method: We analyzed, by whole-cell voltage-clamp, Cl^- currents in HEK293 cells co-expressing GFP-ClC-Ka and the accessory m-Cherry-tagged barttin subunit, upon intracellular Ca^{2+} mobilization. The patch clamp protocol consists of a holding potential from 0 mV, which is stepped to various test potentials from -195 and +125 mV for 150 ms. Pulses ended with a tail pulse to -125 mV for 20 ms. Concomitantly we monitored by live confocal microscopy, the membrane expression of either GFP-ClC-Ka or barttin-mCherry.

Results: In control conditions we found a linear current/voltage relationship over a broad range of membrane voltages except of hyperpolarization below -100 mV, where the channel open probability was reduced, providing the well-known hook-shaped appearance of the *I-V* curve for ClC-Ka channel. Interestingly, both 100 μM ATP and 400 μg/ml of dandelion root extract (DRE), both increasing intracellular Ca^{2+} in HEK293, significantly inhibited Cl^- currents in a time dependent way. Pre-treatment of cells with either the Ca^{2+} chelator BAPTA-AM or the PCK inhibitor Calphostin C, reverted the inhibitory effects of both ATP and DRE. Interestingly, 1μM of phorbol meristate acetate (PMA), a specific PKC activator, mimicked the inhibitory effect of ATP and DRE on Cl^- currents. We finally demonstrated that 30 μM Heclin, an inhibitor of E3 ubiquitin ligase, did not revert the DRE- and ATP- induced Cl^- currents inhibition, thus suggesting that the ClC-Ka inhibition is independent of channel ubiquitination. Accordingly, live confocal analysis showed that all the Ca^{2+} mobilizing compounds tested did not induced neither ClC-Ka nor Barttin internalization. We hypothesized that phosphorylation in the putative PKC consensus sites present in ClC-Ka amino acidic sequence may be involved in the inhibition of channel activity.

Conclusion: In conclusion, we demonstrated for the first time that the activity of ClC-Ka in renal cells could by inhibited by either receptor agonists or natural molecules able to activate an intracellular Ca^{2+}/PKC pathway, thus opening venues for the development of new diuretic drugs.

SO041

THE EFFECT AND MECAHNISM OF THE LOX IN AT1R/B-ARRESTIN BIASED PATHWAY INDUCED RENAL INTERSTITIAL FIBROSIS

Xiaoqin Zhang[1], Chen Yu[2]

[1]Tongji Hospital, Tongji University School of Medicine,, Department of Nephrology,, Shanghai, P.R. China and [2]Tongji Hospital, Tongji University School of Medicine,, Department of nephrology, Shanghai, P.R. China

Background and Aims: We studied the downstream and mechanism of β-arrestins signaling in renal fibrosis process and the role of lysyl oxidase (LOX) in the AT1R-β-arrestins pathway.

Method: The mechanism of β-arrestins signaling was studied in normal rat kidney tubule epithelial cells (NRK-52E) treated with SII in vitro. BAPN or placebo was administered during ischemia reperfusion (IR)-induced fibrosis progression. Collagen crosslinking and fibrosis progression were assessed histologically and biochemically.

Results: The mRNA and protein levels of β-arrestin-1 and β-arrestin-2 were significantly upregulated in renal fibrosis model both in vitro and in vivo. SII activated the ERK-STAT3 PY705 but not STAT3-Try727 in nucleus of NRK-52E cells, which effects were abolished when transfection of siRNA targeting β-arrestin-1 and β-arrestin-2 or pretreated with PD98059 (MEK inhibitor). LOX was strongly induced in fibrotic kidney and NRK-52E cells treated with SII. Active LOX significantly increased collagen crosslinking. In established IR-28d renal fibrosis, LOX inhibition promoted fibrosis reversal and with a 25% decrease insoluble collagen. Gene silencing of β-arrestin-1 + 2 or STAT3 apparently inhibited SII-induced LOX expression in vitro. Besides, chromatin immunoprecipitation (ChIP) assay clearly demonstrating the interaction between STAT3 and the LOX promoter, which indicated LOX is a direct target gene of SII-β-arrestins-STAT3 signaling.

Conclusion: The ERK/STAT3 was downstream of AT1R-β-arrestins, ERK entered the nucleus and activated STAT3-PY705. LOX mediates collagen crosslinking and fibrotic matrix stabilization during renal fibrosis via the AT1R-β-arrestins-ERK-STAT3-PY705 signaling. By blocking this profibrotic pathway, therapeutic LOX inhibition attenuates the fibrosis and suggesting target the LOX has significant potency for the treatment of patients with fibrotic kidney disorders.

SO042

WHOLE GENOME SEQUENCING OF HUMAN KIDNEY PROGENITORS IDENTIFIES A MUTATION-PRONE CELL TYPE IN THE PROXIMAL TUBULE

Irene Franco[1], Hafdis Helgadottir[1], Aldo Moggio[2], Malin Larsson[3], Peter Vrtacnik[1], Anna Johansson[3], Nina Norgren[3], Pär Lundin[3], David Mas-Ponte[4], Johan Nordstrom[5], Torbjörn Lundgren[5], Peter Stenvinkel[6], Lars Wennberg[5], Fran Supek[4], Maria Eriksson[1]

[1]Karolinska Institute, Biosciences and Nutrition, Huddinge, Sweden, [2]Karolinska Institute, ICMC, Huddinge, Sweden, [3]Science for Life Laboratories, Sweden, [4]IRB Barcelona, Barcelona, Spain, [5]Karolinska University Hospital, Division of Transplantation Surgery, Huddinge, Sweden and [6]Karolinska University Hospital, Division of Renal Medicine, Huddinge, Sweden

Background and Aims: The genome of every cell accumulates somatic mutations while aging. Somatic mutation data can be used to track a cell's exposure to mutagens, thereby allowing the discovery of cell types that are more susceptible to mutate and become cancer and the underling mechanisms.

Method: To detect somatic mutations in healthy, human kidney, we set up a protocol for whole genome DNA sequencing of single non-cancer cells. The protocol requires in vitro clonal expansion prior to sequencing, a step that restricts the analysis to cells able to proliferate in vitro (progenitors), but allows a gene expression analysis in addition to genome sequencing. Cells were obtained from six living kidney donors undergoing surgery. In addition to the kidney cortex biopsy, multiple control tissues (skin, subcutaneous fata and visceral fat) were obtained from each donor, allowing a well-controlled comparison of mutation landscapes in different cell types. Donors´age spanned from 30 to 69.

Results: Somatic mutation and gene expression data showed that we were able to culture two different populations of CD133/CD24 positive, tubular cells. One population showed a low amount of somatic mutations and a mutation profile similar to progenitors from other tissues (fat, skeletal muscle and blood), consistent with a lack of exposure to mutagens. Conversely, the other population showed high mutation burden and a unique mutation landscape, characterized by mutation enrichment in active chromatin, regulatory, and transcribed regions. Accumulation of potential, cancer-driver mutations was 6-fold faster in these compared to control cells. The mutation profile was similar to that of the most common kidney cancer subtypes (clear cell- and papillary cell-carcinoma) and indicated that these cells originated from the proximal tubule, in agreement with gene expression data.

Conclusion: Our somatic mutation data from single genomes support the existence of two different populations of proliferating tubule cells in healthy, human kidney. One is protected from mutagen exposure, similar to stem cells from other organs. The other population is derived from damaged proximal tubule cells and shows a high mutation rate between 30 and 70 years of age. Mutations are enriched in transcribed genes and regulatory regions, thus enhancing the chances of tumorigenic transformation and suggesting conditions that predispose to cancer in the kidney proximal tubule.

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MALNUTRITION IN DIALYSIS

SO043

MALNUTRITION-INFLAMMATION IS A RISK FACTOR FOR BRAIN ATROPHY RELATIVE COGNITIVE IMPAIRMENT IN MAINTENANCE DIALYSIS PATIENTS

Yujun Qian[1], Ke Zheng[1], Tianye Lin[2], Feng Feng[2], Fei Han[3], Yicheng Zhu[3], Xuemei Li[1]

[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Nephrology, Beijing, P.R. China, [2]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Radiology, Beijing, P.R. China and [3]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Neurology, Beijing, P.R. China

Background and Aims: Cognitive impairment (CI) are prevalent and devastating in dialysis patients, whereas the pathophysiology is not very clear. Brain atrophy may involve in the process of CI. To explore the correlation between brain atrophy and cognitive impairment, as well as the risk factors of brain atrophy, we used the voxel based morphometry (VBM) method to evaluate the changes of brain multi-component volume in maintenance dialysis patients, and analyzed it relationship with detailed cognitive function.

Method: From July 2013 to July 2014, 181 maintenance dialysis patients in our hospital were enrolled for 3.0T MRI examination and cognitive function evaluation. The statistical parameter map (SPM) 8 software package was used for VBM analysis, and the Monte Carlo simulation method (alphasim method) in the functional neural image analysis software package (AFNI) was used for multiple comparison correction at the cluster level to extract the volume of brain multi-component. Cognitive function was evaluated with MMSE, MoCA, Philadelphia word learning test, Boston Naming Test, semantic fluency test and trial making test. The risk factors for brain volume were explored, and the correlation between brain volume and CI was investigated by regression analysis.

Results: This study enrolled 181 dialysis patients, including 119 cases of maintenance hemodialysis and 62 cases of peritoneal dialysis. According to MMSE and MoCA, the incidence of cognitive impairment was 22.7% and 66.3% respectively. The mean values gray matter volume and white matter volume were 575.4mm^3 and 457.8mm^3, respectively. The volume of gray matter, white matter, amygdala, caudate nucleus and hippocampus were positively correlated with the scores of specific cognitive functions such as total, memory, language and execution. Among them, amygdala volume atrophy was significantly related to the decrease of cognitive function such as MMSE ($\beta = 2.81$, $P = 0.005$), MoCA ($\beta = 6.26$, $P < 0.001$). Serum albumin is the risk factor of gray matter volume ($\beta = 5.0$, 95% CI = 3.1 to 6.9, $P < 0.001$) and white matter volume ($\beta = 3.6$, 95% CI = 1.7 to 5.5, $P < 0.001$); Serum Hypersensitive C-reactive protein is the risk factor of gray matter volume ($\beta = -0.9$, 95% CI = -1.7 to - 0.1, $P = 0.037$).

Conclusion: Brain atrophy in maintenance dialysis patients is closely related to multiple cognitive impairment, and malnutrition - microinflammation may be a risk factor for multi-component brain atrophy.

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SO044

ALPHA LIPOIC ACID COMPARED TO SELENIUM IN MITOCHONDRIAL RESUSCITATION AND MI RNA-126 EXPRESSION IN HEMODIALYSIS PATIENTS

Magdy ElSharkawy[1], Zainab Al Kasaby[2], Hosny A. Elewa[3], Maha Abdelrahman[2]

[1]Ain Shams University, Cairo, Egypt, [2]Al-Azhar University, Pharmacy, Cairo, Egypt and [3]Horus University In Egypt (HUE), Pharmacy, Cairo, Egypt

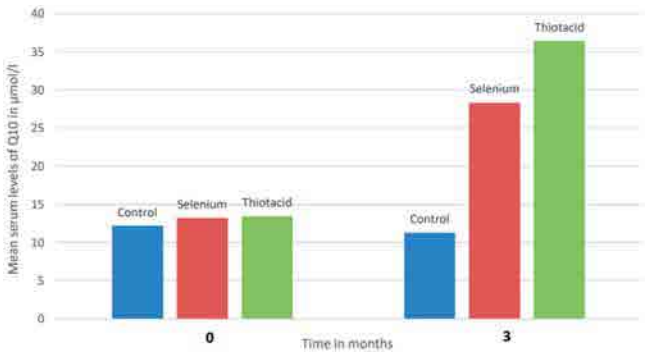
Background and Aims: anti-oxidants may decrease the risk of cardiovascular complications (CVC) in HD patients. We aimed to study antioxidant effect of Alpha lipoic acid and selenium on oxidative stress, endothelial repair, and mitochondrial functions in HD patients by evaluating the serum level of reactive oxygen species (ROS), miRNA-126, and CoQ10.

Method: 60 individuals were enrolled and randomized into 3 groups, G1; 22 HD patients as control, G2; 20 HD patients received Selenium, and G3;18 HD patients received. Serum levels of ROS, CoQ10, and miRNA-126 were assessed at base line and after three months treatment for all patients.

Results: At baseline, all groups were matched regarding their demographic data and target parameters.

After three months, in G1; the serum level of ROS increased significantly ($P < 0.05$), CoQ10 didn't change significantly ($P > 0.05$), while the fold expression of miRNA-126 decreased significantly ($P < 0.05$). In G2,3; there were statistical significant changes in target parameters after the treatment, ROS level decreased significantly by 34%, and by 79%, CoQ10 mean levels increased significantly from 13.21 to 28.35, and from 13.46 to 36.43 ng/ml, mean fold expression of miRNA126, increased significantly by 6.94, and 10.54 folds, in Selenium and, Thiotacid groups respectively. The results showed that Thiotacid was better than Selenium in ROS level reduction, and CoQ10 level improvement, while no statistical significant difference between two drugs regarding miRNA126 level ($P > 0.05$).

Conclusion: Selenium and, Thiotacid reduce oxidative stress and also they enhancing the endothelial repairing, and improve mitochondrial functions and thus may reduce risk of CVC.



SO045

DOES MALNUTRITION INFLAMMATION SCORE MAINTAINS ITS PREDICTIVE RISK ASSESSMENT IN THE MODERN HEMODIALYSIS ERA?

Vitor Sá Martins[1,2], Teresa Adragao[3,4], Leila Aguiar[3], Catarina Dias[3], Pedro Lourenço[3], Rita Figueiredo[3], Tania Pascoal[3], Juliana Pereira[3], Tatiana Pinheiro[3], Inês Ramião[3], Brígida Velez[3], Ana Luisa Papoila[5], Iola Pinto[6,7], Nuno Borges[2,8], Conceição Calhau[8,8,8,9,10], Fernando Macário[3]

[1]DIAVERUM Portugal, Medical Department, Sintra, Portugal, [2]Faculdade de Ciências da Nutrição e Alimentação de Universidade do Porto, Porto, Portugal, [3]DIAVERUM Portugal, Medical Department, Sintra, , [4]Hospital Santa Cruz, Serviço de Nefrologia, Carnaxide, Portugal, [5]Nova Medical School, CEAUL e CEDOC, Lisboa, Portugal, [6]Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, CMA, Caparica, Portugal, [7]Instituto Superior de Engenharia de Lisboa, Lisboa, Portugal, [8]CINTESIS - Centro de Investigação em Tecnologias e Serviços de Saúde, Porto, Portugal, [9]Nova Medical School, Lisboa, Portugal and [10]Nova Medical School, Unidade de Universitária de Lifestyle Medicine, Lisboa, Portugal

Background and Aims: Malnutrition Inflammation score (MIS) is a risk score published in 2001 (Kalantar-Zadeh, 2001) and validated in 2008 (Rambod, 2009). It is associated with a high mortality and morbidity risk in hemodialysis (HD) patients (pts).

Currently, HD pts population is composed of much older individuals, submitted to a high efficient treatment with access to pharmacological and nutritional therapy, assured by a bundled payment, when comparing with the validation study population.

The objective of this study is to evaluate if MIS maintain its predictive risk assessment.

Method: Cross sectional analysis of HD pts from 25 outpatient clinics. MIS was evaluated at the study baseline. Univariable and multivariable Cox additive regression models were used to analyze the data. C-index was estimated to assess the performance of the final model. A level of significance of $\alpha = 0.05$ was considered.

Results: A total of 2444 pts were analyzed (59.0% males; 32.0% diabetic) during a median period of 48 months (P_{25}=31; P_{75}=48), 875 patients registered MIS<5, corresponding to 35.8%. All-cause mortality was observed in 860 pts (35.2%). There were 202 (35.8%) events in the group of patients with MIS<5, while in the group with MIS≥5, the number of deaths was higher (658 pts, 41.9%).

In univariable analysis using Cox additive model, the main results were:

		95% CI		p-value
	Hazard ratio (HR) estimate	Lower limit	Upper limit	
MIS [a]	1.130	1.113	1.147	<0.001
Age [b]	1.054	1.047	1.061	<0.001
nPNA[c]	0.757	0.716	0.799	<0.001
IDWG [d]	0.932	0.880	0.988	0.018
Kt/V [e]	0.887	0.798	0.987	0.027
Diabetes	1.457	1.270	1.672	<0.001

[a]– MIS as a continuous score. HR for unit increment.

[b]– Patients age at the baseline.

[c]– nPNA - normalized Protein Nitrogen Appearance. HR for each 0.2 increment.

[d]– IDWG - Interdialytic Weight Gain. 3 months average (baseline, t-1 and t-2)

[e]- Kt/V – 3 months average. HR for each 0.5 increment.

In multivariable analysis, adjusting for age, nPNA, IDWG, Kt/V and diabetes, a MIS ≥ 5 and ≥ 7 showed, respectively, a HR of 1.761 (IC 95%, p<0.001) and 1.822 (IC 95%, p<0.001).

Conclusion: The findings of this analysis confirms that MIS maintains a discriminative power to identify higher risk of mortality. In this model, age and diabetes also correlate with mortality risk increase, while nPNA, IDWG and Kt/V have the opposite effect.

SO046

REGULATION OF GUT MICROBIOTA AND HOST CO-METABOLISM BY POTASSIUM HOMEOSTASIS IN PATIENTS ON HEMODIALYSIS

Dominic Raj[1], Bei Gao[2], Elizabeth Barrows[3], Muralidharan Jagadeesan[1], Richard Amdur[4], Ashte Collins[1], Renu Regunathan-Shenk[1], Danielle Kincaid[1], Badryah Omar[1], Muhammad Siddiqi[1]

[1]George Washington Medical Faculty Associates, Division of Renal Diseases and Hypertension, Washington D.C., United States of America, [2]University of California, Department of Medicine, United States of America, [3]Georgetown University, Department of Hematology and Oncology and [4]George Washington Medical Faculty Associates, Department of Surgery, Washington, United States of America

Background and Aims: Gut microbiota composition is dysregulated in hemodialysis patients. However, the impact of potassium homeostasis on the gut microbiota and their metabolites has not been studied. Patiromer is a potassium binding polymer that exchanges calcium for potassium in the gastrointestinal (GI) tract, thereby increasing fecal potassium excretion and reducing serum potassium levels.

Method: In this non-randomized, open label, 3-period crossover trial with repeated measures within each period, we investigated the effect of 12 weeks of treatment with patiromer on the microbiome profile and microbiota-related metabolites in 27 hemodialysis patients using multi-omics integration of data from shotgun metagenomic sequencing and untargeted and targeted metabolomic profiling. Data from hemodialysis patients at baseline was first compared with individuals without kidney disease (n=20).

Results: We found that 18 bacterial species and 49 plasma chemical clusters were significantly different between patients and controls. Serum potassium decreased significantly from baseline (5.62$\pm$0.65 mEq/L) with patiromer treatment (4.80$\pm$0.46 meq/L) and increased during the post-treatment phase (5.45 $\pm$ 0.67 meq/L), ($p<0.001$). Three bacterial species and one bacterial pathway were altered by patiromer. We identified 52 serum metabolites, which were significantly different in patients at baseline compared with controls, and were partially reversed with patiromer treatment. Specifically, the serum levels of polyphenols such as vanillic acid, gallic acid and benzoic acid, and other microbiota-related metabolites such as 2,6-diaminopimelic acid, 2-ketogluconic acid, indole-3-carboxaldehyde and 3-hydroxyphenylacetic acid were reduced by patiromer treatment.

Conclusion: Our study suggests that control of hyperkalemia by patiromer alters the gut microbial composition and host co-metabolism in hemodialysis patients.

SO047

HEMODIAFILTRATION DECREASES RISE OF LEPTIN AND RESISTIN IN PROTEIN ENERGY WASTING (PEW) WITHOUT HARMFULL EFFECT ON ALBUMIN CONCENTRATION

Bernard Hory[1], Christophe Robino[2]

[1]*Nephrology and Internal Medicine Center, Clinical Research, Avignon, France and*
[2]*Centre Hospitalier Princesse Grace, Nephrology, Monaco, France*

Background and Aims: The role of adipocytokines (ADCK), and particularly of anorectic leptin and of resistin in the mortality of PEW is strongly suspected. Convective techniques (ol-HDF) decrease leptin concentrations but induce a concomitant albumin loss which could be potentially harmful in malnourished patients. The aim of the prospective multicentric randomized study performed in France by the NUTRIPEPA GROUP is to compare one year evolution of 4 ADCK and seric albumin using HDF or HD and membranes with different cut-off.

Method: 47 patients responding to both criteria of albumin <35 g/l (mean of 3 dosages) and prognostic inflammatory and nutritional index (PINI) $\geq$ 1 were randomized to be treated using either polyester polyarylate (PEPA Nikkiso Japan) or polysufone, polyethersulfone dialyser (control) and followed for one year. Treatment consists in 3*4 hours HD session or in 3 HDF sessions with more than 20 liters reinjection/session. 24 patients were treated with HDF (HDF gr) : 11 with PEPA, 13 with control, and 23 with HD (HD gr) : 13 with PEPA, 10 with control. Oral nutritional supplementation was systematic, eventually completed by intradialytic parenteral nutrition. Albumin, leptin, adiponectin, ghrelin and resistin concentrations were determined at M0, M6, M9, M12. Delta concentration M0-M12 of albumin and of the 4 ADCK were compared with Wilcoxon test.

Results: At 12 months, decrease of leptin and of resistin was significantly higher in HDF group compare to HD group. There was no significant variation of adiponectin, ghrelin and albumin concentrations regardless of the technic or of dialyser cut-off.

Conclusion: In PEW, on a one year practice and regardless of the cut-off of the dialyser, HDF decreases both the anorexigenic adipokine leptin and resistin, adipokine implicated in insulin resistance, without harmfull incidence on seric albumin concentration. The decrease of concentrations of leptin and resistin obtained using ol-HDF could explain, at least in part, the reduction of one year mortality that we reported last year in preliminary results of NUTRIPEPA study.

Group	Δ M0-M12 Albumin (g/l)	Δ M0-M12 Leptin (ng/ml)	Δ M0-M12 Resistin (ng/ml)	Δ M0-M12 Ghrelin (pg/ml)	Δ M0-M12 Adiponectin (mg/ml)
HDF	3.02±5.09	50.6±103.7	4.6±11.3	-25.3±104.3	1.8±6.9
HD	2.02±3.94	-3.28±47	0.6±3.5	57±219.5	2.5±7.6
Wilcoxon test	NS	p=0.02	p=0.01	NS	NS

SO048

CREATININE INDEX AND IT'S ASSOCIATION WITH MORTALITY AND HOSPITALISATION AMONG INCIDENT HAEMODIALYSIS PATIENTS

Nandakumar Mooppil[1], Seema Aithal[1], Tripti Singh[1], Rajiva Ibakkanavar[1]

[1]*NKF Singapore, Medical, Singapore, Singapore*

Background and Aims: Studies have suggested that higher lean body mass (LBM) is associated with increased longevity among haemodialysis (HD) patients. It has been shown that creatinine index is a surrogate marker of lean body mass and can be estimated using a simplified equation based on age, gender, serum creatinine and KT/V(sp). The present study was conducted to investigate the association between estimated creatinine index and all-cause mortality in a large racially diverse cohort of incident HD patients. We also examined the relationship between creatinine index and hospitalisation incidence in this cohort.

Method: Incident patients (aged≥18 years) between January, 2010 and December, 2018 who survived six months of HD were included in this retrospective observational study. Baseline demographic data was collected at study commencement, followed by clinical and laboratory data during the 6 month exposure period. Patients were followed from the index date (last day of exposure period) until first of the following – death, withdrawal or end of study (June 30, 2019). The exposure of interest was Creatinine Index (CI) estimated using a simplified formula (Canaud et al 2014) based on patient demographics (age and gender), pre-dialysis serum creatinine and KT/V(sp). Patients were stratified into 4 groups based on CI quartiles - Q1(<=17.48), Q2(17.49-18.91), Q3(18.92-20.54) and Q4(20.55+). Primary outcome was all-cause mortality during the overall follow-up. Adjusted hazard ratios were estimated using a Cox regression model for association between CI quartiles and mortality. Negative binomial regression models were used to assess the relationship between CI quartiles and hospitalisation.

Results: A total of 3172 incident HD patients (mean age 60.4±11.5 years, 56.2% male, 57.4% Chinese and 70.4% with diabetes as cause of ESRD) were included in the study. During the median follow-up of 2.8 (1.4-4.7) years, 755 (23.8%) patients died. The mean creatinine index for entire cohort was 19.1±2.3 mg/kg/day. The patients in the lowest CI quartile (Q1) were older, females, had higher incidence of diabetes and comorbidity but lower levels of albumin, haemoglobin, BMI and SGA scores compared to higher quartiles (p<0.001). Following multivariate analysis the adjusted hazard of death were as follows - Q4 (aHR-1, reference), Q1 (aHR-2.14, 95%CI 1.56-2.94), Q2 (aHR-1.58, 95%CI 1.21-2.05), Q3 (aHR-1.33, 95%CI 1.05-1.68), p<0.001. Patients in the lowest quartile of CI (Q1) had 64% higher incidence of hospitalisation (IRR 1.64, 95%CI 1.36–1.98, p<0.001) compared with patients in Q4 (IRR-1, reference).

Conclusion: Creatinine index derived from a simplified equation is useful in predicting mortality and hospitalisation among Southeast Asian incident HD patients. Low CI was associated with increased risk of all-cause mortality and hospitalisation in our cohort. The present study is limited by the lack of data on residual renal function which might confound the results.

Table Association between creatinine index quartiles and all-cause mortality and hospitalisation among incident HD patients.

Creatinine Index quartiles (mg/kg/day)	No. deaths/No. at risk	Mortality rate / 100 PYAR	Adjusted HR* (95% CI)	No. hospitalisations / No. at risk	Hospitalisation rate / PYAR	Adjusted IRR* (95% CI)
Q1 (<= 17.48)	72/793	10.52 (8.23 - 13.3)	2.14 (1.56-2.94)	2274/793	3.42 (3.28 - 3.56)	1.64 (1.36-1.98)
Q2 (17.49 - 18.91)	36/793	5.16 (3.61 - 7.14)	1.58 (1.21-2.05)	1874/793	2.74 (2.62 - 2.87)	1.35 (1.16-1.57)
Q3 (18.92 - 20.54)	29/793	4.02 (2.70 - 5.78)	1.33 (1.05-1.68)	1875/793	2.64 (2.52 - 2.76)	1.26 (1.1-1.44)
Q4 (20.55+)- Ref	22/793	2.93 (1.83 - 4.43)	1 (Reference)	1453/793	1.95 (1.85 - 2.05)	1 (Reference)
P for trend	-	**<0.001**	**<0.001**		**<0.001**	**<0.001**

HR-Hazard ratio, IRR-Incidence rate ratio, PYAR-Person year at risk,

*Adjusted for age, sex, race, ESRD cause, SGA score, CCI score, medical dependency, intervening hospital events, albumin, haemoglobin, BMI.

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ANAEMIA MANAGEMENT IN CKD

SO049

HYPOXIA INDUCIBLE FACTOR-PROLYL HYDROXYLASE (HIF-PH) INHIBITION COUNTERACTS THE RENAL ENERGY METABOLISM ALTERATIONS IN THE EARLY STAGES OF DIABETIC KIDNEY DISEASE

Sho Hasegawa[1], Tetsuhiro Tanaka[1], Tomoyuki Saito[2], Kenji Fukui[1,2], Takeshi Wakashima[1,2], Masaomi Nangaku[1]

[1]*The University of Tokyo, Division of Nephrology and Endocrinology, Tokyo, Japan and* [2]*Central Pharmaceutical Research Institute, JT, Biological and Pharmacological Research Laboratories, Takatsuki, Japan*

Background and Aims: Hypoxia inducible factor (HIF)-prolyl hydroxylase (PH) inhibitors (also known as HIF stabilizers) increase endogenous erythropoietin production and serve as novel therapeutic agents against anemia in chronic kidney disease. Considering that HIF induces the expression of various genes, HIF stabilizers might have pleiotropic effects on the progression of kidney diseases as well as improvement in anemia. Interestingly, HIF induces the metabolic reprogramming from tricarboxylic acid (TCA) cycle to glycolysis as an adaptive response to hypoxia. However, it remains obscure how the metabolic reprogramming in renal tissue by HIF stabilization affects the pathophysiology of kidney diseases. Previous studies have shown accumulation of glucose and TCA cycle metabolites in diabetic renal tissue, which might be related to the progression of diabetic kidney disease (DKD). We hypothesized that HIF stabilization might reverse these metabolism alterations and conducted a proof-of-concept study using enarodustat (JTZ-951), an oral HIF-PH inhibitor.

Method: We utilized the streptozotocin-induced diabetic rat and alloxan-induced diabetic mouse models. Animals were divided into three groups: Control (normal animals eating normal food), DKD (diabetic animals eating normal food) and DKD+enarodustat (diabetic animals eating food mixed with enarodustat). Blood, urine and kidney samples were collected two weeks after grouping. Metabolism status in renal tissue were compared between groups from transcriptome and metabolome perspectives.

Results: Although plasma creatinine levels were not different between groups, enarodustat tended to reverse diabetic renal changes such as urinary albumin excretion, glomerulomegaly and glomerular basement membrane thickening (Figure 1). Transcriptome analysis has revealed that enarodustat counteracts the diabetic renal metabolism alterations; fatty acid and amino acid metabolisms were upregulated in diabetic renal tissue and downregulated by enarodustat, while glucose metabolism was upregulated by enarodustat. These symmetric metabolism alterations were confirmed by metabolome analysis (Figure 2); glycolysis and TCA cycle metabolites were accumulated, and amino acids were reduced in diabetic renal tissue, while these metabolism alterations were mitigated by enarodustat. Moreover, enarodustat alleviated the accumulation of glutathione disulfide (GSSG) in diabetic renal tissue and thus showed higher glutathione (GSH)/GSSG ratio, which suggested that enarodustat relieved oxidative stress in DKD.

Conclusion: HIF stabilization counteracts the renal energy metabolism alterations in the early stages of DKD, in association with the improvement in urinary albumin excretion and renal pathological abnormalities. Our study suggests that HIF stabilization may serve as a potential intervention targeting dysregulated energy metabolism of diabetic kidneys.

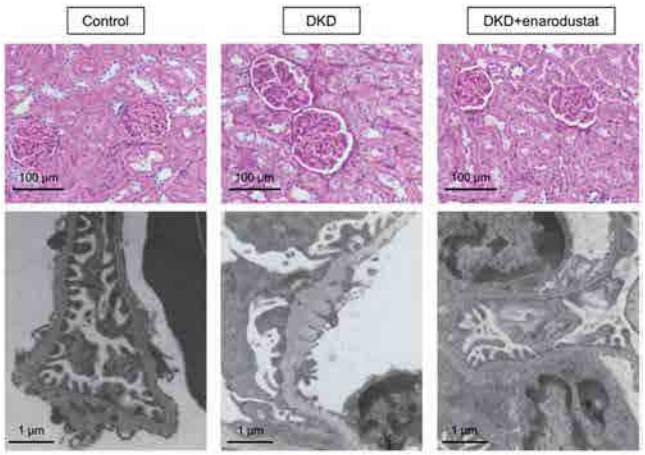


Figure 1

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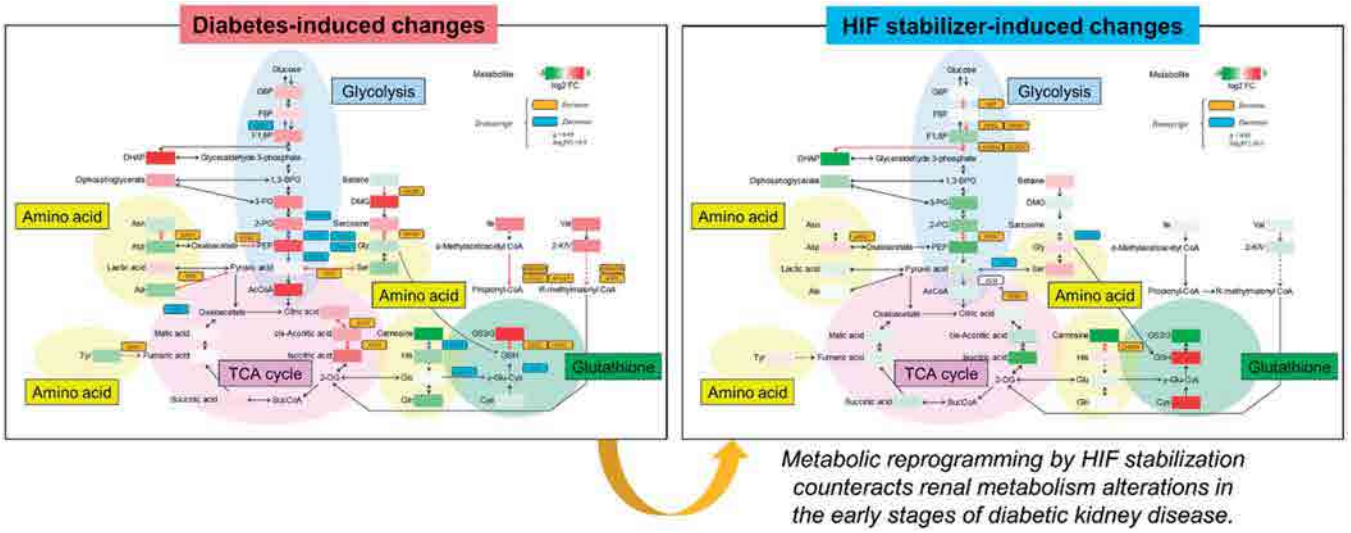

Diabetes-induced changes
HIF stabilizer-induced changes
Glycolysis
Amino acid
TCA cycle
Glutathione
Metabolite
log2 FC
Metabolic reprogramming by HIF stabilization counteracts renal metabolism alterations in the early stages of diabetic kidney disease.

Figure 2

SO050

DIFFERENT FERRIC CITRATE DOSE REGIMENS IN THE TREATMENT OF IRON DEFICIENCY ANAEMIA IN PATIENTS WITH NON-DIALYSIS-DEPENDENT CKD: THE COMPASS TRIAL

Pablo Pergola[1], Diogo Belo[2], Paul Crawford[3], Moustafa Moustafa[4], Dennis Vargo[5], Wenli Luo[5], Alexander Goldfarb-Rumyantezev[5]

[1]Renal Associates, P.A., San Antonio, United States of America, [2]Balboa Nephrology Medical Group, California Institute of Renal Research, Chula Vista, United States of America, [3]Research by Design, LLC, Chicago, United States of America, [4]South Carolina Nephrology and Hypertension Center, Orangeburg, United States of America and [5]Akebia Therapeutics, Inc., Cambridge, United States of America

Background and Aims: Ferric citrate (FC) is approved in the US as oral iron replacement for the treatment of iron deficiency anaemia (IDA) in adult patients with non-dialysis dependent (NDD) chronic kidney disease (CKD) and for the treatment of hyperphosphatemia in adult patients with dialysis dependent CKD. For IDA, a starting dose FC of 1 tablet three times daily (TID) is recommended with titration to maintain haemoglobin (Hb) at goal. This study was designed to investigate the possibility of dosing FC twice daily (BID) for flexibility in clinical practice. The efficacy and safety of different FC dosing regimens for the treatment of IDA were examined in adults with NDD-CKD.

Method: In this 48-wk, Phase 4, randomized, open-label, multicentre study, subjects with IDA of NDD-CKD (stage 3-5) were randomized 1:1 to receive 1 FC tablet (1gm containing 210mg ferric iron) TID or 2 tablets BID. At wk 12, subjects whose Hb increased $<$0.5 g/dL from baseline (BL) or was $<$10 g/dL had their dose increased to either 2 tablets TID or 3 tablets BID consistent with their original dosing regimen. This prespecified analysis reports data through wk 24. The primary endpoint was mean change in Hb from BL to wk 24. Secondary endpoints included mean change in transferrin saturation (TSAT), ferritin, and phosphate to wk 24.

Results: 206 subjects were randomized, 183 were included in this analysis after completing the 24-wk dose titration period. Groups were well matched with mean age of 69.5 +/- 10.32 years, 64% female and 54% had diabetes as a cause of CKD. Mean BL eGFR was 33.6 +/- 10.85 ml/min/1.73m^2 and Hb 10.45 +/-0.744 g/dL. In subjects who did not require an increase in the FC dose at wk 12, mean changes in Hb at wk 24 were 1.05 and 1.24 g/dL in the 1 tablet TID and 2 tablet BID dosage groups, respectively. In subjects who required an increase in the FC dose at wk 12, mean changes in Hb at wk 24 were 0.41 and 0.13 g/dL in the 2 tablet TID and 3 tablet BID groups, respectively. Mean changes in TSAT, ferritin and phosphate are presented in the Table. The incidence of TEAEs was 78.2% and 75.0% in the BID and TID groups, respectively. The most common AEs reported were diarrhoea, stool discoloration and constipation. The incidence of SAEs was 13.9% and 17.3% in the BID and TID groups, respectively. Five deaths were reported, none were deemed related to FC per the investigator.

Conclusion: FC was effective and generally well tolerated in the treatment of IDA in this NDD-CKD population. Subjects who had per protocol FC dose increases at wk 12 had less pronounced iron deficiency at BL and smaller increases in Hb suggesting an additional underlying cause of anaemia. Mean changes in Hb, TSAT, ferritin, and phosphate and AE profiles were similar in the BID and TID regimens as well as in 3 g/day and 4 g/day dosing groups supporting the potential for dosing flexibility with FC.

Clinicaltrials.gov identifier NCT03236246

Funding provided by Akebia Therapeutics, Inc.

SO051

PROSPECTIVE OPEN-LABEL EXPLORATIVE RANDOMISED SINGLE CENTRE COMPARATIVE STUDY TO DETERMINE THE EFFECTS OF VARIOUS INTRAVENOUS IRON PREPARATIONS ON HAEMOGLOBIN, HAEMETENICS, MARKERS OF KIDNEY FUNCTION, QUALITY OF LIFE AND SAFETY.

Xenophon Kassianides[1,2], Ahmed Zeidan[1], Sunil Bhandari[1,2]

[1]Hull University Teaching Hospitals NHS Trust, Academic Renal Department, Kingston Upon Hull, United Kingdom and [2]Hull York Medical School (HYMS), Kingston Upon Hull, United Kingdom

Background and Aims: Iron deficiency in Chronic Kidney Disease (CKD) is common. It frequently necessitates the use of intravenous (IV) iron for correction. A number of second and third generation preparations are now in clinical use with potentially increased efficacy and improved safety profiles. Concerns remain regarding the potential impact of intravenous iron on oxidative stress, kidney function, inflammation and endothelial function, which in turn may represent non-traditional cardiovascular risk factors.

The aim of this study is to verify whether three different IV iron preparations have similar safety, efficacy and effects on oxidative stress, inflammation, endothelial and renal function in a non-dialysis CKD population in the short term.

Method: This was a prospective open-label exploratory randomized, single-centre study comparing the efficacy and safety of three parenteral iron formulations (Iron Dextran (ID), Iron Sucrose (IS) and Iron Isomaltoside (IIM)). Patients with established CKD stages 3-5 and ferritin (SF) < 200microg/L and/or transferrin saturation (TS) <20% were recruited. They were randomized in a 1:1:1:1 ratio receiving a single infusion of ID 200mg IS 200mg, or IIM either at a low (200mg) or high dose (1000mg). Follow-up took place at 2 hours, 1 day, 1 week, 1 month and 3 months post-infusion. Response to iron was assessed using haemoglobin, TS and SF. Kidney function (Creatinine (Cr), eGFR) and proteinuria as a marker of injury (protein:creatinine, albumin:creatinine) were monitored. C-reactive protein (CRP) was used as an inflammatory indicator. Arterial response was monitored using Pulse wave velocity (PWVI). Quality of Life was assessed via the SF-36 questionnaire. Adverse events (AEs) were captured throughout the study, recorded for safety analysis and evaluation of relationship to treatment. Data is presented as means and standard error of the mean (SEM). Statistical analysis was carried out using ANOVA. A p value of <0.05 was statistically significant.

Results: : Forty patients were recruited and randomized ten to each group; 58% of the patients were male. The mean age was 58.8 years (±2.2). TS and SF rose in response to iron. Greater and more lasting ferritin repletion was seen in the group receiving 1000mg of IIM (pre-dose: 69.1 microg/L (±18.4); 3 months: 271.0 microg/L (±83.3)). All IV iron preparations led to a significant but transient rise in TS within the first 2 hours especially IIM 1000 group (17.8% to 98.7%; p-value <0.001) and IS (21.1% to 91.4%; p-value<0.01) to values >90%. These returned to baseline within 1 week. There was no statistical difference in haemoglobin concentration throughout both cumulatively and comparatively. CRP increased within one day but returned to normal values within one week – this was most pronounced with IS (pre-dose CRP: 8.1 (±3.3) 1-day CRP: 36.1 (±27.0); p=0.29). There was no short-term impact on renal function; mean Cr pre-dose: 234.6 umol/L (±16.6), to 216.6umol/L (±16.2) and mean eGFR pre-dose: 28.2 ml/min (±2.2) to 28.5 ml/min (±2.5). Proteinuria following infusion with IV iron was unchanged (pre-dose: 154.2 mg/mmol (±48.4); 2-hours post-dose: 127.5 mg/mmol (±45.2). Arterial stiffness (PWVI) did not increase following IV iron infusion irrespective of preparation or dosage. Quality of Life improved, which was more evident one month following infusion (pre-dose: 47.7 (±3.8); post-dose 54.4 (±4.3). There was one serious AE in the IIM high dose group with a death more than 2 weeks following infusion likely unrelated to infusion.

Conclusion: Both high and low dose intravenous irons are effective in replenishing the iron stores with significant increase in iron biomarkers. In the short-term there was no impact on kidney function, inflammation or vascular function. Intravenous iron, irrespective of impact on haemoglobin, translates to improvement in quality of life. Larger and more long-term studies are required to further assess safety.

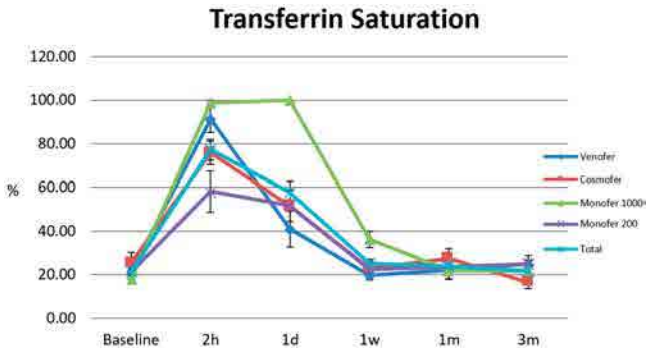


Figure:

SO052

EFFECT OF SEVERE RENAL IMPAIRMENT OR END-STAGE RENAL DISEASE ON THE PHARMACOKINETICS AND PHARMACODYNAMICS OF ROXADUSTAT, AN ORAL HYPOXIA-INDUCIBLE FACTOR PROLYL HYDROXYLASE INHIBITOR

Dorien Groenendaal-van de Meent[1], Virginie Kerbusch[2], Rudiger Kaspera[3], Begona Barroso-Fernandez[4], Piergiorgio Galletti[5], Gernot K. Klein[6], Martin Den Adel[7]

[1]Astellas Pharma Europe B.V., Clinical Pharmacology and Exploratory Development, Leiden, Netherlands, [2]PharmAspire BV, Wijchen, Netherlands, [3]Astellas Pharma Europe B.V., Clinical Pharmacology, Leiden, Netherlands, [4]Astellas Pharma Europe B.V., Drug Discovery Research, Leiden, Netherlands, [5]Astellas Pharma Europe B.V., Nephrology, Leiden, Netherlands, [6]APEX GmbH, Munich, Germany and [7]Astellas Pharma Europe B.V., Clinical Pharmacology and Exploratory Development, Leiden, Netherlands

Background and Aims: Roxadustat is an orally active hypoxia-inducible factor prolyl hydroxylase inhibitor used at titrated doses to treat anaemia in CKD patients. This study investigated the pharmacokinetics (PK), metabolic profile, pharmacodynamics, and safety of roxadustat in subjects with different degrees of renal function (RF).

Method: This was a phase 1, open-label study conducted in Germany and the United Kingdom (EudraCT Number: 2015-002565-28). Subjects were enrolled in four RF groups: normal RF (eGFR $\geq$90 mL/min/1.73 m^2); severely impaired RF (not on dialysis; eGFR $<$30 mL/min/1.73 m^2); end-stage renal disease (ESRD) on continuous ambulatory or automated peritoneal dialysis (CAPD/APD); or ESRD on 4-hour haemodialysis or haemodiafiltration (HD/HDF). Subjects in the normal RF, severely impaired RF, and ESRD on CAPD/APD groups received a single dose of 100-mg oral roxadustat on Day 1. A single-sequence design with two treatment periods (P1/P2) separated by a washout period was used for subjects with ESRD on HD/HDF; a single administration of 100-mg oral roxadustat occurred 2 hours after completion of a HD/HDF session (P1) and 2 hours before initiation of a HD/HDF session, 2 days after the previous session (P2). Plasma and urine PK of roxadustat and its circulating metabolites (*O*-glucuronide-, *O*-glucoside-, and sulphate of hydroxy-roxadustat) and plasma erythropoietin (EPO) were evaluated. Continuous heart rate monitoring was conducted.

Results: Of 73 screened subjects, 34 (46.6%) were enrolled and received roxadustat (normal RF, n=12; severely impaired RF, n=9; ESRD on CAPD, n=1; ESRD on HD/HDF, n=12). The geometric least-square mean ratio of area under the plasma concentration-time curve (AUC) from administration to infinity (AUC_{inf}) relative to subjects with normal RF was 223% (90% CI: 185, 268) and 195% (90% CI: 165, 229) in subjects with severely impaired RF and in those with ESRD on HD/HDF, respectively. Roxadustat's maximum concentration (C_{max}) and terminal elimination half-life ($t_{1/2}$) were comparable between groups. The PK of roxadustat and its metabolites were not affected by HD/HDF. In subjects with normal RF, the amount of roxadustat excreted unchanged in urine was $<$1%; urinary excretion and renal clearance of roxadustat and its metabolites decreased with lower baseline RF. Mean AUC_{inf} and $t_{1/2}$ for roxadustat's circulating metabolites were higher in subjects with severely impaired RF and with ESRD on HD/HDF than in those with normal RF. Metabolite to parent ratio of AUC_{inf} was $<$1% for *O*-glucuronide- and *O*-glucoside-roxadustat and $<$10% for sulphate of hydroxy-roxadustat. EPO baseline-corrected AUC from administration to last measurable concentration and EPO maximum effect were higher in subjects with severely impaired RF or with ESRD on HD/HDF than in those with normal RF.

Conclusion: The AUC for roxadustat and its metabolites was higher in patients with severely impaired RF or with ESRD on HD/HDF than in those with normal RF. Roxadustat's C_{max} and $t_{1/2}$ were comparable among all groups. Roxadustat and its metabolites were not significantly cleared by HD/HDF.

SO053

A REAL WORLD LONGITUDINAL ANALYSIS OF ANAEMIA TREATMENT PRESCRIPTIONS IN NON-DIALYSIS-DEPENDENT CHRONIC KIDNEY DISEASE PATIENTS, A CKDOPPS STUDY

Marcelo Lopes[1], Charlotte Tu[1], Jarcy Zee[1], Bryce Foote[2], Murilo Guedes[3], Katarina Hedman[4], Glen James[5], Antonio Alberto Lopes[6], Ziad Massy[7,8], Helmut Reichel[9], Ronald Pisoni[1], James Sloand[10], Sandra Waechter[11], Michelle Wong[12], Bruce Robinson[1], Roberto Pecoits-Filho[1]

[1]Arbor Research Collaborative for Health, DOPPS, Ann Arbor, United States of America, [2]Akebia Therapeutics, Medical Affairs, Boston, United States of America, [3]Pontificia Universidade Catolica do Parana, School of Medicine, Curitiba, Brazil, [4]AztraZeneca, Global Medical Affairs, MölNdal, Sweden, [5]AztraZeneca, Epidemiology, Cambridge, United Kingdom, [6]Universidade Federal da Bahia, Faculdade de Medicina da Bahia, Salvador, Brazil, [7] Univ Paris-Saclay, Univ Paris-Sud, UVSQ, CESP, Center for Research in Epidemiology and Population Health. Inserm UMRS 1018, Villejuif, France, [8] Ambroise Paré University Hospital, APHP, Division of Nephrology, Boulogne-Billancourt/Paris, France, [9]Nephrological Center, Villingen- Schwenningen, , [10]AztraZeneca, Global Medical Affairs, LocationGaithersburg, United States of America, [11]Vifor Fresenius Medical Care Renal Pharma, Renal Anaemia, Glattbrugg, Switzerland and [12] University of British Columbia, Department of Medicine, Vancouver, Canada

Background and Aims: Previously lacking in the literature, this analysis aims to comprehensively describe longitudinal patterns of anaemia management, including prescriptions of ESA and iron replacement, for non-dialysis dependent chronic kidney disease (NDD-CKD) stage 3 to 5 patients under nephrologist care.

Method: We analysed data from a prospective cohort of 2455 NDD-CKD patients from Brazil, Germany and the US, who were not using anaemia medications (oral iron, intravenous [IV] iron, or erythropoiesis stimulating agent [ESA]) at enrolment in the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDOPPS). We excluded 26% (N=862) of patients who were using any anaemia treatment from the source population at CKDOPPS study entry; we further excluded patients with (a) missing data for demographics and/or clinical history, or (b) no laboratory and medication data during follow-up. We reported the cumulative incidence (CI) of anaemia treatment initiation, stratified by biochemical parameters and patient characteristics. For patients that started therapy, we report the frequency of medication type at the moment of initiation, as well as switches and discontinuation over 12 months.

Results: The CI of any anaemia treatment initiation at 12 months was 18% for the whole sample, and 54% for patients with haemoglobin (Hb) <10 g/dL. For oral iron therapy, the CI at 12 months was 26% (19%, 32%) for TSAT<20%, and 22% (17%, 28%) for ferritin <100. For IV iron use, CI at 12 months was 6% (3%, 11%) for patients with TSAT<20% and 4% (2%, 7%) for patients with ferritin <100ng/mL. For ESA use, the CI at 12 months was 38% (29%, 47%) for patients with Hb <10 g/dL, and 11% (8%, 14%) for Hb 10 to <12 g/dL. Oral iron alone was the overwhelming first treatment option in the US (67%) and Brazil (56%); in Germany, a higher prevalence of ESAs (38%) and IV iron use (15%) was noted. Anaemia medication switches and discontinuation patterns, over 12 months, are outlined in the figure. The majority patients starting anaemia treatment were no longer on therapy one year later in Brazil (54%) and the US (51%); discontinuation of treatment was much lower in Germany (22%).

Conclusion: Anaemia treatment is initiated in a limited number of NDD-CKD patients with clinical signs that would indicate to do so, and many patients discontinue treatment, for reasons yet to be clarified. Although haemoglobin was the main factor associated with prescriptions, only about half of patients with Hb<10g/dL received any anaemia medication during a year. Oral iron was the treatment option most often prescribed, however given to only a quarter of iron deficient patients. We noticed country differences in the patterns of anaemia prescription and treatment discontinuation, over time, that could be due to regional policy and physician-led CKD anaemia management inequalities. These results provide longitudinal data supporting the concept that anaemia is sub-optimally managed among patients with NDD CKD in the real-world setting.

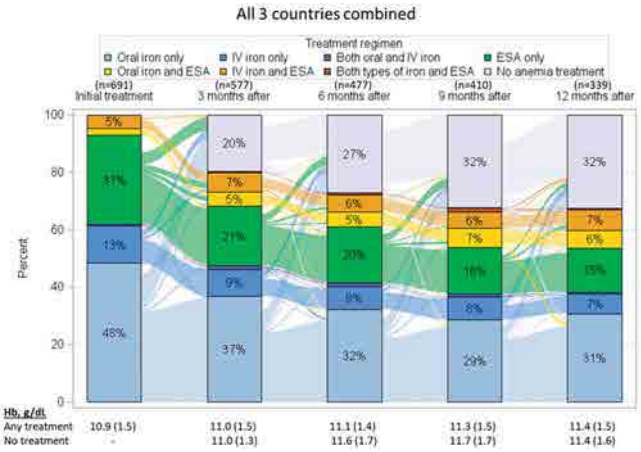


Figure: Longitudinal treatment patterns in the subset of patients who initiated anemia treatment, by country.

CLINICAL NEPHROLOGY 1

SO054

ONE-YEAR EFFICACY AND SAFETY OF THE LONG ACTING C5 INHIBITOR RAVULIZUMAB FOR THE TREATMENT OF ATYPICAL HAEMOLYTIC URAEMIC SYNDROME (AHUS) IN ADULTS

Thomas Barbour[1], Marie Scully[2], Gema Ariceta[3], Spero Cataland[4], Katherine Garlo[5], Nils Heyne[6], Yoshitaka Miyakawa[7], Marc Vallee[5], Yosu Luque[8], Sung-Soo Yoon[9], Jan Menne[10], David Kavanagh[11]

[1]Royal Melbourne Hospital, Kidney Care, Melbourne, Australia, [2]University College London Hospitals, Department of Haematology, London, United Kingdom, [3]University Hospital Vall d'Hebron, Paediatric Nephrology Department, Barcelona, Spain, [4]The Ohio State University Medical Center, Division of Hematology, Columbus, United States of America, [5]Alexion Pharmaceuticals Inc., Boston, United States of America, [6]Tübingen University Hospital, Tübingen, Germany, [7]Saitama Medical University, Department of General Internal Medicine, Saitama, Japan, [8]Sorbonne Université, Intensive Care Nephrology and Transplantation Department, APHP, Paris, France, [9]Seoul National University Hospital, Department of Internal Medicine, Seoul, Korea, Rep. of South, [10]Hannover Medical School, Department of Nephrology and Hypertension, Hannover, Germany and [11]Royal Victoria Hospital, National Renal Complement Therapeutics Centre, Newcastle upon Tyne, United Kingdom

Background and Aims: Ravulizumab is a long-acting C5 inhibitor, derived from eculizumab, that is dosed every 8 weeks. Ravulizumab was approved in the United States for patients with atypical haemolytic uraemic syndrome (aHUS) and it is currently under evaluation in the EU based on the phase 3 trial (NCT02949128) efficacy and safety results at 26 weeks in patients with aHUS. Here, we report longer term efficacy and safety of ravulizumab obtained from the trial during the ongoing extension period.

Method: This phase 3 trial was a single arm, global, open label study in adults ($\geq$18 years of age) with aHUS naïve to complement-inhibitor therapy. Ravulizumab was administered by intravenous infusion (IV) every 8 weeks during the maintenance phase. Patients fulfilling laboratory criteria for active TMA, ADAMTS13>5%, and negative STEC-HUS testing were eligible.

Patients that completed the 26-week initial evaluation period could enter the extension period. The primary endpoint was complete TMA response (normalisation of platelet count and lactate dehydrogenase [LDH], and $\geq$ 25% improvement in serum creatinine from baseline, measured at 2 separate assessments obtained at least 28 days apart). Secondary endpoints included changes from baseline in haematological parameters, kidney function, and FACIT-fatigue scores. Treatment emergent adverse events were also evaluated. Here, interim cumulative data on primary and secondary endpoints through at least 52 weeks are reported.

Results: Forty-seven of 56 enrolled patients completed the initial evaluation period and received at least one dose of ravulizumab in the extension period. All patients achieved complete inhibition of terminal complement as demonstrated by sustained suppression of free-C5 (<0.5 ug/mL). The proportion of patients achieving the individual components of complete TMA response improved during the extension period (Figure). At last follow-up, the number of patients achieving complete TMA response increased from 30/56 (53.6%) in the initial evaluation period to 34/56 (60.7%). Of the four additional patients that reached complete TMA response, three had a previous kidney transplant and one initiated treatment one month after TMA presentation. Improvement in FACIT-fatigue observed in the initial evaluation period was sustained in the extension period.

Although three new SAEs were reported during the extension period, there were no further fatal adverse events. As in the primary analysis period, no meningococcal infections occurred through the last patient follow-up.

Conclusion: In the extension period of the phase 3 trial, ravulizumab continued to have a good benefit: risk profile. At last follow-up, the cumulative efficacy of ravulizumab to treat complement mediated TMA in patients with aHUS improved to 61% from 54% in the initial evaluation period. Most AEs occurred in the first 26 weeks, and there were no meningococcal infections identified in the study. These results suggest that with ravulizumab further improvement in efficacy is possible with longer treatment with no compromise in safety and improved convenience of 8-week dosing intervals.

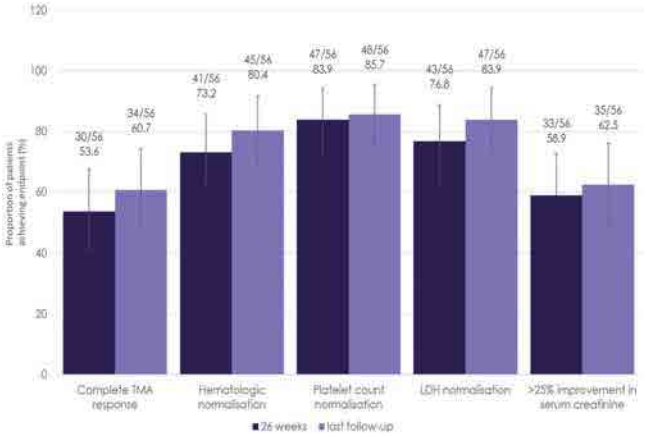


Figure: Complete TMA response and its components during initial 26 weeks and through all available follow-up data

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SO055

PROBIOTIC BIO-THREE DECREASES SERUM PHOSPHATE LEVELS WITH INVOLVEMENT OF BACTERIA IN GUT MICROBIOMA IN HEMODIALYSIS PATIENTS: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTOLLED STUDY.

Tetsuya Ogawa[1], Yumi Hosoda[1], Ai Horimoto[1], Yoko Nishizawa[1], KIYOTSUGU OMAE[1], Nobuo Nagano[1,2]

[1]Tokyo Women's Medical University Medical Center East, Department of Medicine, Tokyo, Japan and [2]Hidaka Hospital, Kidney Disease and Dialysis Center, Takasaki, Japan

Background and Aims: Recent studies revealed that the importance of the gut microbioma in the development and progression of CKD. Dysbiosis of the intestinal microbiota increases uremic toxin, which damage the epithelial tight junctions and increase the permeability of the intestinal wall via endotoxemia and systemic inflammation. Some articles reported that probiotics reduced the uremic toxin and decreased inflammation biomarkers in CKD patients, while others reported no remarkable changes. Meanwhile, we have already reported that oral administration of Bifidobacterium longum in a gastro-resistant seamless capsule decreases serum phosphate levels in patients receiving haemodialysis. The aim of this study is to evaluate the efficacy of probiotics by changes of serum data, including inflammation and intestinal flora in patients receiving hemodialysis.

Method: A 6-month prospective, randomized, double-blind, placebo-controlled study was conducted at three hemodialysis centers. As probiotic therapy, of three-combination probiotics (Bio-Three) tablets, each containing 2 mg of lactomin (Streptococcus faecalis T-110), 10 mg of Clostridium butyricum TO-A, and 10 mg of Bacillus mesentericus TO-A, were used. The patients receiving hemodialysis were randomly assigned to the Bio-Three group (n=37) and the placebo group (n=36). In both the Bio-Three group and the placebo group, patients orally received 6 tablets 3 times daily. We evaluated the effect of probiotic on the ratio of CRP to albumin as an inflammatory biomarker, other serum data and gut microbioma before and 6 month after the start of treatment. The gut microbioma composition was analyzed by a 16s rRNA gene-based sequencing protocol.

Results: The ratio of CRP to albumin did not change before and after treatment in both groups. The serum phosphate levels in the Bio-Three group significantly decreased after 6-month treatment, while did not change in the placebo group. In a 16s rRNA gene-based sequencing protocol analysis, the ratio of *Firmicutes, Actinomycetales* and *Neisseriaies* significantly changed after 6 month treatment in the only probiotic group. Meanwhile, serum phosphate levels were positively correlated with the number of *genus Haemephilus and gunus Neisseria* in the only probiotic group. Furthermore, serum phosphate levels were negatively correlated with the number of *genus Bifidobacterium* in the only probiotic group.

Conclusion: In this study, three-combination probiotics did not decrease systemic inflammation in hemodialysis patients. Meanwhile, three-combination probiotics might decrease serum phosphate levels, and the specific bacteria in the gut microbioma might contribute to the decrease of serum phosphate levels.

SO056 **THE CLINICAL AND IMMUNOLOGICAL IMPACT OF LOW DOSE RITUXIMAB IN CLINICAL NEPHROLOGY**

Sunu Alex[1]

[1]*Government medical college, Nephrology, Trivandrum, India*

Background and Aims: Currently, the dose of rituximab used in nephrology practice is mostly extrapolated from the dose used in lymphoproliferative disorders. It is possible that a lesser dose may suffice when treating a non-neoplastic disorder. We conducted this study to study the clinical response and CD19 B cell suppression with a single dose of 100mg rituximab in nephrology practice

Method: This was a single center prospective study of role of 100mg rituximab as initial dose in steroid dependent (SDNS), frequently relapsing nephrotic syndrome (FRNS), idiopathic membranous nephropathy (MN) and high immunologic risk kidney transplantation with subsequent doses based on CD19 B cell reconstitution.

Results: Following 100mg rituximab in 42 patients, CD19 B cell percentage decreased from 16.3±7.6 to 0.3±0.3, 1.9±1.7 and 4.0±4.5 by 30, 90 and 180 days respectively. At 30th day, 40(95.2%) had CD19 B cell count <1%. Of the 30 patients with SDNS and FRNS followed up for one year, 29(96.7%) went into remission at day 30. Remission was sustained in 23(76.6%) at day 180 and 21(70%) at 1 year. There was significant decrease [P <0.001] in the dose of steroids needed to maintain remission at 180 days following rituximab (0.27±0.02mg/Kg to 0.02±0.00mg/Kg). Of the five patients with MN, four patients achieved remission by 6 months. Remission was sustained in three patients by 1 year. Of the 7 kidney transplant recipients, 2 had antibody mediated rejections though CD19 B cells were suppressed even at one year.

Conclusion: Low dose of 100 mg rituximab is sufficient to deplete CD19 B cells for up to 90days and is effective in inducing remission in SDNS and FRNS and MN. Targeting subsequent doses depending on CD19 B cell reconstitution may prevent relapses, limit toxicity and be cost effective.

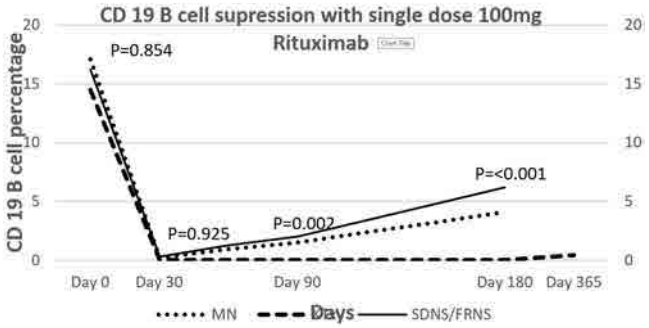


Figure:

SO057

BETA-BLOCKERS ARE ASSOCIATED WITH REDUCED MORTALITY IN PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION AND ADVANCED CHRONIC KIDNEY DISEASE: COHORT STUDY

Edouard L. Fu[1], Alicia Uijl[2,3], Friedo W. Dekker[1], Lars H. Lund[3], Gianluigi Savarese[3], Juan Jesus Carrero[4]

[1]Leiden University Medical Center (LUMC), Clinical Epidemiology, Leiden, Netherlands, [2]Julius Center for Health Sciences and Primary Care, Utrecht, Netherlands, [3]Karolinska Institute, Division of Cardiology, Department of Medicine, Sweden and [4]Karolinska Institute, Medical Epidemiology and Biostatistics, Sweden

Background and Aims: Beta-blockers reduce mortality and morbidity in patients with heart failure (HF) with reduced ejection fraction (HFrEF). However, patients with advanced chronic kidney disease (CKD) were underrepresented in landmark trials. We evaluated if beta-blockers are associated with improved survival in patients with HFrEF and advanced CKD.

Method: We identified 3906 persons with an ejection fraction <40% and advanced CKD (eGFR <30 mL/min/1.73m^2) enrolled in the Swedish Heart Failure Registry during 2001-2016. The associations between beta-blocker use, 5-year all-cause mortality, and the composite of time to cardiovascular (CV) mortality/first HF hospitalization were assessed by multivariable Cox regression. Analyses were adjusted for 36 variables, including demographics, laboratory measures, comorbidities, medication use, medical procedures, and socioeconomic status. To assess consistency, the same analyses were performed in a positive control cohort of 12,673 patients with moderate CKD (eGFR <60-30 mL/min/1.73m^2).

Results: The majority (89%) of individuals with HFrEF and advanced CKD received treatment with beta-blockers. Median (IQR) age was 81 (74-86) years, 36% were women and median eGFR was 26 (20-28) mL/min/173m^2. During 5 years of follow-up, 2086 (53.4%) individuals had a subsequent HF hospitalization, and 2954 (75.6%) individuals died, of which 2089 (70.1%) due to cardiovascular causes. Beta-blocker use was associated with a significant reduction in 5-year all-cause mortality [adjusted hazard ratio (HR) 0.86; 95% confidence interval (CI) 0.76-0.96)] and CV mortality/HF hospitalization (HR 0.87; 95% CI 0.77-0.98). The magnitude of the associations between beta-blocker use and outcomes was similar to that observed for HFrEF patients with mild/moderate CKD, with adjusted HRs for all-cause mortality and CV mortality/HF hospitalization of 0.85 (95% CI 0.78-0.91) and 0.88 (95% CI 0.82-0.96), respectively.

Conclusion: Despite lack of trial evidence, the use of beta-blockers in patients with HFrEF and advanced CKD was high in routine Swedish care, and was independently associated with reduced mortality to the same degree as HFrEF with moderate CKD.

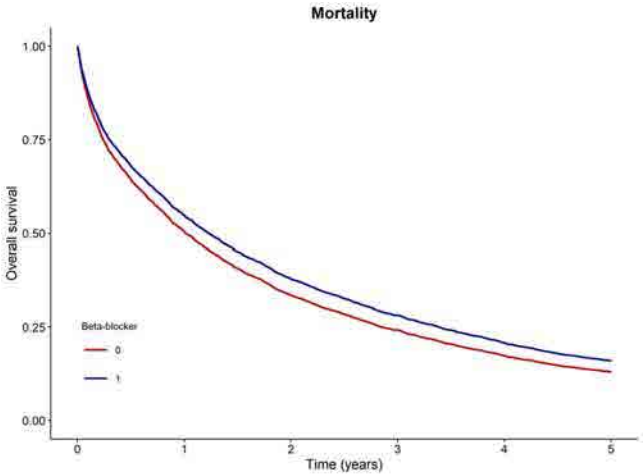


Figure: Adjusted survival curve for mortality in patients with HFrEF and advanced CKD according to beta-blocker use

Analyses were adjusted for age, sex, index year, duration of heart failure, outpatient location, follow-up location, NYHA class, ejection fraction, mean arterial pressure, heart rate, eGFR, smoking, atrial fibrillation, anemia, COPD, dilated cardiomyopathy, diabetes, hypertension, ischemic heart disease, peripheral artery disease, stroke and/or TIA, valvular disease, cancer in the previous 3 years, coronary revascularization, device implantation (CRT or ICD), RAS inhibitors, MRA, digoxin, diuretics, statins, anticoagulants, antiplatelets, nitrates, marital status, education level and income.

SO058

IGG4-RELATED KIDNEY DISEASE : A FRENCH NATIONWIDE RETROSPECTIVE COHORT STUDY

Anis Chaba[1], Mohamad Zaidan[2], BOFFA Jean Jacques[3,4], KARRAS Alexandre[5], Audard Vincent[6], SNANOUDJ RENAUD[7], Olivier Thaunat[8], Mathilde NOUVIER[9], DEVRESSE Arnaud[10], Dominique Joly[11], Jean Michel Halimi[12], CLAIRE CARTERY[13], Eric Daugas[14], Marie-Noelle Peraldi[15], LEGENDRE Mathieu[16], BELLIERE Julie[17], Stanislas Faguer[17], TITECA Dimitri[18], HANF William[19], Thierry Petitclerc[20], HANOUNA Guillaume[14], Jonathan Chemouny[21], GOUMRI Nabila[22], DUQUENNOY Simon[23], Eve Vilaine[24]

[1]Faculté de médecine de l'Université de Paris, Paris, France, [2]Bicetre Hospital AP-HP, Le Kremlin-Bicêtre, France, [3]Tenon Hospital (AP-HP) : Family Planning and Education Center, Paris, France, [4]Hospital Tenon Ap-Hp, Paris, France, [5]Hôpital Européen Georges-Pompidou, Paris, France, [6]Hôpital Henri-Mondor Ap-Hp, Créteil, France, [7]Hospital Foch, Suresnes, France, [8]Hospital Édouard Herriot, Lyon, France, [9]Lyon Sud Hospital Center, Pierre-Bénite, France, [10]Cliniques Universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, [11]Hôpital Necker, Paris, France, [12]Chru Hôpitaux De Tours, Tours, France, [13]Hospital Center De Valenciennes, Valenciennes, France, [14]Bichat-Claude Bernard Hospital, Paris, France, [15]Hospital _ Saint-Louis Ap-Hp, Paris, France, [16]Hospital Center University François Mitterand, Dijon, France, [17]Hospital Rangueil, Toulouse, France, [18]Hopital, Amiens, France, [19]Hospital Center Alpes-Leman Hospital Findrol, Contamine-sur-Arve, France, [20]Hôpital Aura Paris Plaisance, Paris, France, [21]CHU de Rennes, Rennes, France, [22]Hospital Louis Pasteur, Le Coudray, France, [23]Hospital Center Avranches-Granville, Granville, France and [24]Ambroise Paré Hospital (AP-HP), Boulogne-Billancourt, France

Background and Aims: IgG4 disease is a systemic fibroinflammatory disorder that may affect virtually any organ. IgG4-related kidney disease (IgG4-RKD) is a major manifestation, occurring in almost one third of patient. The present study addresses the diagnosis, management and outcome of French patients with IgG4-RKD.

Method: We conducted a retrospective observational study including patients with renal impairment due to IgG4-RKD from 32 centers. Clinical, biological, and imaging data, as well as management modalities and outcome, were retrieved from medical records.

Results: 74 patients, 64 males and 10 females, were diagnosed with IgG4-RKD between 1997 and 2019 and were included in the present study. The mean age at diagnosis was 65.2 ± 15-year-old. Renal involvement was present at diagnosis in 63% of cases. Nine (12%) patients had isolated renal involvement, whereas extra-renal involvement included retroperitoneal fibrosis (20%), auto-immune pancreatitis (49%), cholangitis (27%), and lung disease (22%). Renal imaging lesions were observed in 48 (64%) patients, and included renal hypertrophy, patchy lesions and pseudo-tumor solitary renal lesion. PET-CT scan was performed in 47 (65%) patients and showed hypermetabolic renal lesion(s) in 36% of cases. The presence of extra-renal hypermetabolic lesions was observed in 35 cases (74%). 43 %, 25% and 14% of patients presented with AKI, AKI-on-CKD, and isolated CKD, respectively. The mean serum creatinine level at diagnosis was 244 ± 140 µmol/L, corresponding to an eGFR of 69 ± 22ml/min/1.73m̀. Urinary sediment was most often bland. Mean urine protein-to-creatinine ratio was 1.27 g/g. of note, 26% of patients had more than 1 g/g. 82% of patients underwent a kidney biopsy showing tubulointerstitial involvement in all cases, 12 (16%) had additional glomerular involvement, mainly membranous nephropathy. The major additional laboratory abnormalities included polyclonal hypergammaglobulinemia, and increased serum IgG4 increase in 83% and 86%, respectively. Complement levels were decreased in 27 (37%) patients. Two patients were lost for follow-up and 69 patients were treated with corticosteroid therapy in 66 (89%) patients and 10 received Rituximab as first line therapy. The mean duration of follow-up was 28.8 ± 30 months. During follow-up, 22 (30%) patients relapsed, while 45 (62%) patients had persistent CKD at last follow-up, with a mean eGFR of 47±27 ml/min/1.73m̀. Seven (9%) patients progressed to ESRD and 7 died.

A significant response was achieved in 46 (62%) patients. Patients who received steroids higher than 0.5mg/kg/day had lower serum IgG4 levels (1.8 g/l versus 5.7 g/l, p=0.007) at last follow up but there was no significant difference observed in terms of renal function between the two groups (45.5 vs 48.8 ml/min/1.73m̀, p= 0.72). By univariate analysis, predictors of relapse were low C3 or C4 serum level (p=0.01), ANCA positivity (p= 0.02), renal radiological lesions (p=0.05). At last follow-up the eGFR was worse in patients with a serum creatinine diagnosis greater than 300 µmol/L (30.25 vs 57 ml/min/1.73m̀ p=0.0001) and more progressed to ESRD (p=0.03).

Conclusion: IgG4-RKD has been recently described and may affect middle-aged males. The disease presents as tubulointerstitial nephritis with glomerular involvement in 16% of cases. Disease response to corticosteroid therapy is favorable but is characterized by a high rate of relapses and a significant risk of persistent CKD in the majority of patient. Risk of ESRD and death in almost 20% of patients.

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PROGNOSIS IN HAEMODIALYSIS

SO059

ASSOCIATION OF ALL-CAUSE MORTALITY WITH PRE-HEMODIALYSIS PULSE PRESSURE IN CHRONIC HEMODIALYSIS PATIENTS

Hanjie Zhang[1], Alhaji Cherif[1], Peter Kotanko[1,2]

[1]Renal Research Institute, New York, United States of America and [2]Icahn School of Medicine at Mount Sinai, new york, United States of America

Background and Aims: Chronic and end-stage kidney disease patients experience significantly increased risk of cardiovascular morbidity and mortality due to multitude of interlinked pathophysiological processes inducing metabolic and inflammatory conditions. Pulse pressure (PP) reports cardiac and vascular conditions, where consistently high PP values are associated with atrial fibrillation, aortic insufficiency, arterial stiffness or arteriovenous malformation, and low PP values may be associated with aortic valve stenosis, cardiac insufficiency or cardiac tamponade. However, the association of pre-hemodialysis (pre-HD) PP with mortality among hemodialysis patients is not well understood. In this study, we aim to explore the extent to which PP is associated with mortality.

Method: We analyzed pre-HD PP (calculated as pre-HD SBP minus pre-HD DBP) between 1/2001 and 12/2012 in hemodialysis patients treated in U.S. Fresenius Medical Care facilities. A 3-months baseline period was defined as months 4 to 6 after hemodialysis initiation, all-cause mortality was noted during follow-up. Only patients who survived baseline were included. Censoring events were renal transplantation, modality change, or study end. We built Cox proportional hazards models with spline terms, allowing us to model nonlinear effects of pre-HD PP as a continuous variable and its relationship with all-cause mortality.

Results: We included 152,625 patients. Mean age was 60.8 years, 59% were white and 56% were male. During a median follow-up of 26.0 months 40.4% patients died. We found that for patients with pre-HD PP between 49.2 mmHg and 74.7 mmHg, were associated with better survival. In contrast, a PP below 49.2 mmHg and above 74.7 mmHg were associated with higher mortality. Similar nonlinear effects are seen in SBP for a given pre-HD PP value (see Fig. 1).

Conclusion: The association of pre-HD PP with mortality is nonlinear, and a better understanding of the nonlinearity will provide further insights into disentangling the associated mediators affecting its dynamics. Our findings may aid risk stratification in HD patients.

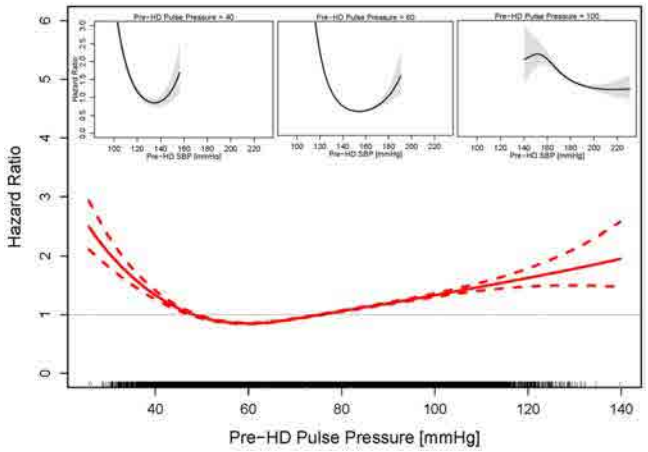


Figure 1: Association between pre-HD pulse pressure and all-cause mortality. HRs (solid line) and 95% CIs (dashed lines) of pre-HD pulse pressure. The tick marks on the x-axis represents individual patients.

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SO060

MONOCYTE-TO-LYMPHOCYTE RATIO, AN INDEPENDENT RISK FACTOR OF SURVIVAL IN HEMODIALYSIS PATIENTS: RESULTS FROM THE INTERNATIONAL MONDO CONSORTIUM

Rupert Bright[1], Xiaoling Ye[2], Kevin Woollard[1], Charles Dickson Pusey[1], Peter Kotanko[2,3], Neill Duncan[1]

[1]Imperial College Renal and Transplant Centre, London, United Kingdom, [2]Renal Research Institute, Research, New York, United States of America and [3]Icahn School of Medicine at Mount Sinai, Department of Nephrology, New York, United States of America

Background and Aims: Patients with end-stage kidney disease have a high prevalence of chronic inflammation and a higher risk of death. Previous work by our group has indicated a positive relationship between neutrophil counts and neutrophil-to-lymphocyte ratio (NLR) and mortality in a large and ethnically diverse dialysis population. Monocytes also have a crucial inflammatory role, but there has been limited study to date, an association between monocyte-to-lymphocyte ration (MLR) was reported in a small Chinese haemodialysis cohort. The aim of this analysis was to study the independent relationship between MLR and all-cause mortality in a large and ethnically diverse haemodialysis population.

Method: Four cohorts were described by phases of haemodialysis exposure: 1) acute phase cohort- first 90 days on HD as the baseline period with the subsequent 9 months as the follow-up period, 2) early-stable phase cohort- 91 days to the end of 1st year as the baseline followed with 1 year's follow-up period, 3) mid-stable phase cohort- 2nd year as the baseline and the following 1 year as the follow-up, and 4) late-stable phase cohort- 3rd year as the baseline followed by a 7 year follow-up period. All-cause mortality was recorded during the 4 phases. Kaplan-Meier (KM) curves were applied to explore the association between MLR quartiles with mortality in the 4 cohorts. Cox proportional hazards models with spline terms (adjusted for age, gender, race, body mass index, diabetic (DM) and congestive heart failure (CHF)) were applied to explore the association between MLR levels and all-cause mortality in the cohorts.

Results: A total of 20,848 patients were included in acute phase cohort; 19,575 in the early-stable phase cohort, 16,515 patients in the mid-stable cohort, and 13,708 patients in the late-stable phase cohort. Notably, patients with higher baseline MLR by quartile tended to be older, male and with a higher percentage of DM and CHF as comorbidities. Lower lymphocyte count and higher neutrophil count, NLR, CRP were associated with higher MLR quartile (Table 1), consistent with the observed association with other markers of inflammation and malnutrition: lower albumin, phosphate and higher ferritin. Adjusted all-cause mortality was observed to be higher in patients with higher MLR quartile both in the KM and spline analyses (Figure 1 a & b) in all phase cohorts (data not shown).

Conclusion: There is a positive relationship between higher levels of MLR and adjusted all-cause mortality across all phase cohorts, including long-term follow-up in this large and ethnically diverse haemodialysis population. Higher levels of MLR are seen in patients with DM and CHF and are consistently observed with other markers of inflammation and malnutrition. This work supports the findings made previously in a more a restricted cohort and warrants further mechanistic investigation.

Patients' baseline characteristics in the acute phase (first 90 days on dialysis)

MLR range	All		Q1 < 0.266		Q2 [0.266 - 0.356]		Q3 (0.366 - 0.484]		Q4 > 0.484		
Sample size	20,848		5,212		5,212		5,212		5,212		
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	P-value
Monocyte (%)	7.5	(3.0)	5.7	(2.0)	7.2	(2.2)	8.0	(2.6)	9.2	(3.7)	<.0001
Monocyte (x10^9/L)	0.5	(0.4)	0.4	(0.3)	0.5	(0.5)	0.6	(0.2)	0.7	(0.3)	<.0001
Lymphocyte (%)	22.2	(8.9)	28.9	(9.1)	23.8	(7.0)	20.4	(6.7)	15.5	(6.3)	<.0001
Lymphocyte (x10^9/L)	1.6	(1.3)	2.1	(1.8)	1.7	(1.5)	0.5	(0.1)	1.1	(0.5)	<.0001
MLR	0.4	(0.2)	0.2	(0.05)	0.3	(0.03)	0.4	(0.04)	0.7	(0.2)	<.0001
Neutrophil (%)	65.6	(12.4)	58.0	(11.8)	62.6	(10.8)	68.8	(12.2)	69.5	(12.8)	<.0001
Neutrophil (x10^9/L)	4.9	(2.9)	4.4	(3.4)	4.7	(3.4)	4.9	(1.9)	5.6	(5.2)	<.0001
NLR	4.0	(4.0)	2.5	(2.1)	3.2	(2.5)	3.9	(2.2)	8.5	(6.3)	<.0001
CRP	32.0	(39.2)	9.8	(15.5)	11.4	(18.1)	12.8	(19.2)	16.2	(22.6)	<.0001
Mortality per 1000 patient years	111.4		81.0		78.3		118.2		171.7		<.0001
Other biomarkers											
Serum albumin (mg/dL)	3.6	(0.5)	3.7	(0.5)	3.7	(0.5)	3.6	(0.5)	3.5	(0.5)	<.0001
Phosphate (mg/dL)	4.3	(1.5)	4.4	(1.6)	4.4	(1.5)	4.3	(1.5)	4.2	(1.5)	<.0001
BNP (pg/mL)	718.9	(1133.0)	605.1	(769.9)	628.2	(804.1)	636.8	(1357.9)	893.6	(1152.5)	0.159
Serum calcium (mg/dL)	8.6	(0.7)	8.7	(0.7)	8.7	(0.7)	8.6	(0.7)	8.6	(0.7)	<.0001
Cholesterol-C (mmol/L)	4.2	(1.1)	4.4	(1.2)	4.2	(1.1)	4.2	(1.1)	4.1	(1.1)	<.0001
HDL-C (mmol/L)	1.0	(0.5)	0.9	(0.5)	1.0	(0.4)	1.0	(0.4)	1.0	(0.5)	0.890
LDL-C (mmol/L)	2.5	(0.9)	2.5	(1.0)	2.5	(0.9)	2.5	(0.9)	2.4	(0.9)	0.009
Triglyceride (mmol/l)	4.1	(2.5)	4.4	(2.5)	4.2	(2.2)	4.0	(2.2)	3.7	(2.1)	<.0001
Ferritin (ng/mL)	330.1	(269.6)	305.6	(252.7)	317.3	(280.5)	327.1	(261.2)	372.3	(296.9)	<.0001
Iron (mcg/dL)	56.4	(23.0)	52.0	(19.7)	56.9	(23.1)	59.3	(25.5)	56.8	(23.9)	0.800
Transferrin (mg/dL)	187.5	(42.0)	191.3	(41.8)	190.4	(41.9)	184.9	(39.5)	182.3	(44.5)	<.0001
RBC count	3.5	(0.6)	3.6	(0.6)	3.5	(0.6)	3.5	(0.6)	3.5	(0.6)	<.0001
Hgbs t/c (%)	6.3	(1.3)	6.4	(1.4)	6.3	(1.3)	6.4	(1.1)	6.2	(1.3)	0.049
Platelet (count)	228.2	(78.1)	227.2	(75.6)	227.4	(76.1)	228.0	(76.8)	229.3	(83.4)	0.431
iPTH (pg/mL)	307.8	(260.8)	313.6	(267.9)	305.8	(258.1)	310.6	(257.2)	300.9	(259.6)	0.148
Uric acid (mg/dL)	6.2	(1.6)	6.2	(1.6)	6.2	(1.6)	6.2	(1.5)	6.1	(1.5)	0.560
25-OH vitamin D (ng/mL)	20.3	(12.6)	20.6	(13.7)	20.2	(11.8)	19.6	(12.0)	20.8	(13.0)	0.684
Demographic information											
Age at dialysis initiation (years)	63.8	(14.7)	60.5	(15.5)	63.1	(14.8)	64.9	(14.4)	66.7	(13.5)	<.0001
Gender male (%)	64.0		59.0		63.0		66.0		69.0		<.0001
Race: white (%)	85.2		80.2		84.4		86.5		89.6		<.0001
BMI	28.27	(10.43)	28.16	(8.55)	28.36	(13.25)	28.29	(9.83)	28.27	(9.57)	<.0001
Comorbidity											
Diabetic (%)	28.0		26.0		29.0		28.0		27.0		0.012
CHF (%)	22.0		19.0		21.0		24.0		25.0		0.003

Figure:

SO061

SEX DIFFERENCES IN MORTALITY AMONG PEOPLE WITH END-STAGE KIDNEY DISEASE: DO WOMEN ALWAYS LIVE LONGER?

Nicole De La Mata[1], Grace Macleod[2,3], Patrick Kelly[1], Brenda Rosales[1], Philip Masson[4], Rachael Morton[5], Angela Webster[1,6]

[1]The University of Sydney, Sydney School of Public Health, Camperdown, Australia, [2]The University of Sydney, School of Medicine, Camperdown, Australia, [3]The University of Notre Dame, School of Medicine, Fremantle, Australia, [4]Royal Free London NHS Foundation Trust, Department of Renal Medicine, United Kingdom, [5]The University of Sydney, NHMRC Clinical Trials Centre, Faculty of Medicine and Health, Sydney, Australia and [6]Westmead Hospital, Centre for Renal and Transplant Research, Westmead, Australia

Background and Aims: Female life expectancies consistently exceed males in the general population. Yet, this survival advantage may not persist in the presence of a chronic disease due to sex-based differences or healthcare inequities. We aimed to explore sex differences in survival among people with end-stage kidney disease (ESKD) compared to the general population.

Method: We included the entire ESKD population in Australia, 1980-2013 and New Zealand, 1988-2012 from the Australian and New Zealand Dialysis and Transplant Registry. These were linked to national death registers to ascertain deaths and their causes. We estimated relative measures of survival, including standardized mortality ratios (SMR), cumulative relative survival and expected life years lost, using general population data (adjusting for country, age, sex and calendar year) to account for background mortality.

Results: Of the 60,823 ESKD patients, there were 25,042 females (41%) and 35,781 males (59%). Overall 34,417 deaths occurred over the 368,719 person-years of follow-up where a similar proportion of females (57%) and males (56%) died. While mortality sex differences within the ESKD population were minor, once compared to the general population female ESKD patients had greater excess deaths, worse relative survival and greater life years lost compared to male ESKD patients. Female ESKD patients had 12 times (SMR:11.5; 95%CI:11.3-11.7) and males had 7 times (SMR:6.7; 95%CI:6.7-6.8) the expected deaths, with the greatest sex disparity among younger ages and from cardiovascular disease. Relative survival was consistently lower in females (0.57, 95%CI:0.57-0.58 in males vs 0.54, 95%CI:0.54-0.55 in females at 5 years), where the excess mortality was 9% higher (95%CI:7-12%) in female ESKD patients (Fig 1A), adjusting for year and age. The average life years lost for female ESKD patients was 4-5 years greater than male ESKD patients (Average life years lost 25.9 years, 95%CI:25.1-26.7 in males and 31.4 years, 95%CI:30.5-32.1 in females aged 15 years at ESKD) (Fig 1B). Kidney transplantation reduced the sex differences in excess mortality, with similar relative survival (p=0.42; Fig 1C) and average life years lost reduced to 3-4 years for females (Fig 1D).

Conclusion: The impact of ESKD is more profound for women than men with greater excess mortality, however kidney transplantation attenuates these differences. Our findings show that chronic diseases and sex can compound to produce worse outcomes where women lose their survival advantage in the presence of ESKD.

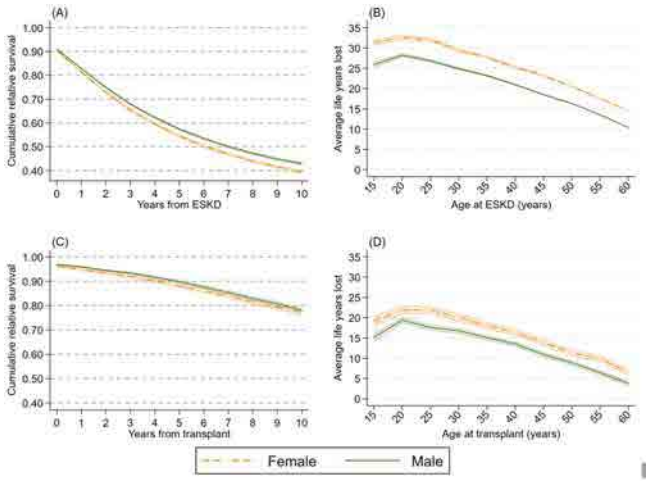


Figure 1. For people with end-stage kidney disease in (A)-(B), and kidney transplant recipients in (C)-(D), estimates of: (A) relative survival since ESKD diagnosis; (B) average life years lost* by age at ESKD; (C) relative survival since kidney transplant; (D) average life years* lost by age at kidney transplant.

*Adjusted for year, cause of kidney failure, pre-existing comorbidities, smoking status, ethnicity, dialysis modality (ESKD only), duration of dialysis (transplant only) and country.

SO062

TRENDS OF BASELINE-RISK OF MORTALITY AND OBSERVED 3-YEAR MORTALITY IN INCIDENT DIALYSIS PATIENTS IN GERMANY

Martin Wagner[1,2], Katherine Rascher[3], Heyke Cramer[1], Mathias Schaller[3], Rolf Dieter Bach[1], Gero Von Gersdorff[3]

[1]KfH - Board of Trustees for Dialysis and Kidney Transplantation, Neu-Isenburg, Germany, [2]University Hospital Wuerzburg, Dept. of Medicine I, Div. of Nephrology, Wuerzburg, Germany and [3]University Hospital Cologne, Dept. of Medicine II, Div. of Nephrology, Cologne, Germany

Background and Aims: The risk of mortality varies considerably among end stage kidney disease patients. As the population ages, patients on renal replacement therapy are presenting with an increasing number of non-renal complications such as heart failure and, subsequently, an increased mortality risk. Thus, in recent years, patient care in dialysis units has become more complex. In this study we describe trends in baseline risk of mortality and 3-year mortality risk in a sample of incident dialysis patients in Germany.

Method: The QiN (Quality in Nephrology) dataset is a registry-based observational study in which >90% of all patients treated in dialysis centers of the non-profit kidney care provider KfH are enrolled. In our analyses we included all adult patients beginning hemodialysis (HD) or peritoneal dialysis (PD) treatment between 2008 and 2014 who were enrolled in QiN within 6 months after inception of dialysis. Primary outcome was all-cause death within 3 years. Cox models were censored for transplantation and loss to follow-up. Baseline risk of mortality was assessed by the AROii score (Floege et al. 2015), a predictive model including patient characteristics, laboratory variables and dialysis parameters. In this score higher values indicate greater mortality risk.

Results: A total of n=20369 patients were analyzed, HD n=18255 (89.6%), PD n=2114 (10.4%). Baseline mortality risk increased over time: AROii score for the 2008/09 incidence cohort was median 8.1 (interquartile range 4.4; 11.9), for the 2010/11 cohort 8.8 (5.0; 12.0) and for the 2012-14 cohort 9.0 (5.0; 12.0), $p<0.001$. The AROii score was highly predictive for observed 3-year mortality (Hazard Ratio [HR] 1.196 [1.190; 1.203], $p<0.001$; C-statistic 0.736). In spite of higher baseline mortality risk in patients starting dialysis in more recent years, mortality was lower as compared to the earlier cohorts (HR 0.976 [0.964; 0.988), $p<0.001$). The results were mainly driven by HD patients. In PD patients baseline mortality risk increased, but no trend on mortality was observed.

Conclusion: Our results show that patients starting dialysis in Germany have become sicker over the last decade, as indicated by the AROii risk score. Simultaneously the observed risk of mortality decreased in recent years, indicating success of optimized medical treatment including dialysis therapy as well as non-nephrology medical care.

SO063

POOR REPORTING AND CONDUCT OF CLUSTER AND CROSSOVER RANDOMISED TRIALS IN THE HAEMODIALYSIS POPULATION

Prachi Kaushal[1], Daniel March[1,2], Helen Eborall[3], Laura Gray[3], James Burton[1,2,4]

[1]University of Leicester, Department of Cardiovascular Sciences, United Kingdom, [2]University Hospitals of Leicester NHS Trust, John Walls Renal Unit, [3]University of Leicester, Department of Health Sciences, United Kingdom and [4]Loughborough University, School of Sport Exercise and Health Sciences, United Kingdom

Background and Aims: There are fewer trials conducted in nephrology than any other speciality. Many trials fail to recruit to target and are therefore underpowered, resulting in unclear evidence and unlikely to be implemented into clinical practice. Carefully designed trials could improve the treatment options for haemodialysis patients. These could include designs other than individually randomised parallel group designs. We have reviewed cluster, stepped wedge and crossover randomised trials carried out in prevalent haemodialysis patients.

Method: A search for randomised controlled trials (RCTs) in haemodialysis patients was conducted across five databases (MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials and ClinicalTrials.gov) in October 2019. The first publication of a stepped wedge trial in haemodialysis was in 2013, so we searched from 2013-2019. Inclusion criteria were RCTs including adults receiving at least 3 months of haemodialysis. Once eligible studies were identified, we compared the sample size sections to the CONSORT requirements and extracted data on these parameters and assessed recruitment targets, attrition rates and primary outcome result.

Results: We identified 911 RCTs of which 13 (1.4%) cluster randomised trials, including one stepped wedge, and 145 (15.9%) crossover trials were identified. Data were extracted for 10 randomly selected crossover trials.

The total sample size required was not reported in 46% (n=6) cluster trials and 60% (n=6) crossover trials, with only 37.5% (n=3) of cluster trials and 50% (n=4) of crossover trials providing a justification for their sample size. In cluster trials, 13% (n=1) stated number of clusters required and 25% (n=2) gave the average cluster size, none of these stated the anticipated variance in cluster size and only 12.5% (n=1) stated the intracluster correlation (ICC) used to calculate the sample size, with none taking into account uncertainty in ICC. In 31% (n=4) of the cluster trials, the dialysis centre was the cluster and in the other 69% (n=9), the dialysis shift was the cluster. For crossover trials, within participant variability was only accounted for in 12.5% (n=1) of trials.

A CONSORT flow diagram was reported in 70% of the trials assessed, with 39% recruiting to target. There were also some differences seen between crossover and cluster designs. The average number of participants at the start of a cluster trial was 470, compared to 26 in crossover trials. Where able to assess, cluster trials had an average attrition rate of 25% this was lower in crossover trials, where the average attrition rate was 14%. Eighty five percent (n=11) of cluster trials had a primary outcome reaching statistical significance, however only 20% (n=2) of crossover trials reached statistical significance.

Conclusion: Cluster and crossover randomised trials are poorly reported. There was insufficient information provided for sample size calculations to be replicated in majority of trials. The average attrition rate was low in crossover trials, however a large proportion of these trials did not have a primary outcome reaching statistical significance, suggesting these trials could have been underpowered. Improvements in the design, conduct and reporting of cluster and crossover trials in the haemodialysis population is urgently required.

EXERCISE IN CKD

SO064

HEMODYNAMIC TOLERANCE OF EXERCISE WITH VIRTUAL REALITY PERFORMED DURING THE FIRST VERSUS THE SECOND PART OF THE HEMODIALYSIS SESSION.

Alicia Garcia-Testal[1], Rafael Garcia-Maset[1], José Antonio Gil-Gómez[2], Francisco José Martínez-Olmos[3], Noemi Valtueña-Gimeno[3], Lucia Ortega-Perez de Villar[4], Ana Ferrer-Salva[3], Jocelyne Piñón-Ruiz[3], KATARZYNA KARANDYSZ[3], Maari Elvi Amanda Lehtoviita[3], Pilar Royo-Maicas[5], Inmaculada Rico-Salvador[1], Víctor López Tercero[5], Delia Pans Alcaina[5], Hector Lavirgen Heras[5], Eva Segura-Ortí[3]

[1]Hospital de Manises, Nephrology, Manises, Valencia, Spain, [2]Universitat Politècnica de València, Instituto de Automática e Informática Industrial, Departamento de Sistemas Informáticos y Computación, Valencia, Spain, [3]Universidad Cardenal Herrera-CEU, CEU Universities, Physiotherapy, Alfara del Patriarca, Valencia, Spain, [4]Universidad Europea de Valencia, Physiotherapy, Valencia, Spain and [5]Hospital de Manises, Nephrology, Hemodialysis Unit, Manises, Valencia, Spain

Background and Aims: It is recommended intradialysis exercise implementation in the first part of the HD session to avoid hemodynamic instability or cramping, but the time restriction to exercise worsens clinical feasibility of exercise as a routine. Exercise using non-immersive virtual reality is a novel rehabilitation method for patients undergoing hemodialysis treatment. This method has shown in a pilot study improved physical function and health-related quality of life.

Objective: to determine effect of exercise with virtual reality during the first two hours and the last two hours of dialysis session on hemodynamic control.

Method: The design was a randomized clinical trial. Patients were randomized to exercise in the first (Start group) or last two hours (End group) of dialysis session. Intradialysis exercise consisted of a video game adapted to dialysis: Treasure hunting. It is a non-immersive virtual reality game in which the patient must catch some objectives avoiding obstacles by moving the lower limbs. The exercise session lasted from 20 to 40 minutes. Intensity was checked through the rate of perceived exertion. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), episodes of hypotension and episodes of clinical instability are monitored throughout the session. The intervention has already begun and will continue for twelve months. The control analysis is performed during the three months at rest prior to starting the intervention (Rest) and then the intervention begins, every three months. Now we present the results at thirth month with exercise (Exercise) . An mixed ANOVA of repeated measures is used to assess the effect of the intervention.

Results: 43 patients participated, 11 dropouts, 17 in Start group and 15 in End group. Mean age 73 years, males 28. The mean baseline (SD) was Body Mass Index 26.2 (5.5) kg/m^2, Overhydration 2.1 (1.3) liters, Kt/V was 1.65 (SD 0.21), Serum Albumin 3.84 (0.29) mg/dl and Hemoglobin 11.81(1.27) g/dl . Analysis by time Rest versus Exercise showed as mean (SD): HR 64 (8) vs 64 (7) bpm, SBP 143 (18) vs 141 (18) mmHg and DBP 61 (10) vs 60 (11) mmHg, no significant differences. The change in measurements at the end of dialysis showed in Rest vs Exercise were HR – 1.34 (5.7) vs -0.9 (5.9) bpm, SBP 1.2 (12) vs 2.65 (16) mmHg and DBP 2.65 (5.8) vs 1.09 (7.1) mmHg, no significant differences. Analysis by groups Start versus End showed as means (CI95%): HR 66 (62,69) vs 63 (59,67) bpm, SBP 145 (136,154) vs 136 (126,146) mmHg and DBP 63 (58,68) vs 56 (50,62) mmHg, no significant differences. The change in measurements at the end of dialysis showed in Start group vs End group neither showed significant differences. There were no differences between the groups regarding episodes of hypotension or clinical instability.

Conclusion: Performing intradialysis with virtual reality is well tolerated at any time during the session. This result improves the opportunities to implement exercise in hemodialysis.

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SO065 **TYPE OF EXERCISE INTERVENTION AND MUSCLE FUNCTIONS IN CHRONIC HEMODIALYSIS PATIENTS**

Łukasz Rogowski[1], Wioletta Dziubek[2], Kusztal Mariusz[3], Katarzyna Bulinska[2], Tomasz Gołębiowski[3], Marian Klinger[3], Krajewska Magdalena[3], Marek Wozniewski[2]

[1]Nonpublic Medical College, Wroclaw, , [2] University School of Physical Education, Physiotherapy, Wrocław, Poland and [3]Wroclaw Medical University, Nephrology and Transplantation Medicine, Wroclaw, Poland

Background and Aims: Decreased exercise capacity due to muscle weakness and exercise intolerance reduces the ability to perform activities of daily living in patients with end-stage kidney disease. Data on exercise type in dialysis population and its muscle effects are scarce. We aimed to determine the impact of training type (strength, resistance and mixed) on cardiovascular performance, muscle function (strength-speed parameters, electrophysiological function of muscles) in patients on hemodialysis maintenance.

Method: Eighty six dialysis patients underwent claster randomisation and were assigned to an exercise intervention groups: A - controlled endurance training during haemodialysis using rotors (MOTOmed letto2), B - controlled force training (resistance), C - Tai Chi training on non dialysis days. Intervention lasted 6 months, 3 times a week (A, B) and 2 times a week (C) for 60 minutes. The outcome measures were spiroergometry (VO2/VO2max), strength of the lower limbs and electromyographic examination. Values at the baseline and 6 months later were compared.

Results: 45 patients completed intervention period and were analysed. Mean age in group A was 64±12y (n-16), in B was 60,5±10y. (n-15) and in C – 68,5±9y. (n-14). Patients did not differ markedly between groups in term of sex, BMI, dialysis vintage and comorbidities.

After 6 months of training, VO2 and VO2max increased significantly only in group B (resistance training) Δ12.7 % for VO2 and 12.9% for VO2max but not in A and C group (Fig.1.). Regarding force torque of quadriceps (ΔPT) in isometric conditions the highest peak values were measured in group B (resistance training), namely increase by 13.6% ($p=0.0004$) in right (R) and 14% ($p<0.0001$) in left (L); in group A (endurance) 3.2% in R and 3.7% in L; in group C (Tai Chi group) by 7% ($p<0.05$) in R and 6.8% ($p<0.05$) in L. In terms of changes in electrophysiological function of right (QEMG_R) and left (QEMG_L) quadriceps, there were increases: for group A by 10.5% ($p<0.0001$) and 9.6% ($p<0.05$); B 9.7% ($p=0.0002$) and 20.1% ($p=0.0001$); for C by 4.5% and 6.2% for R and L, respectively (Fig.2).

In groups B and C significant increases in static force moments (Δ%PT) was associated with increases in electrophysiological action (Δ%QEMG), but in group A increase in EMG activity did not correspond with rise in muscle force (Fig.2).

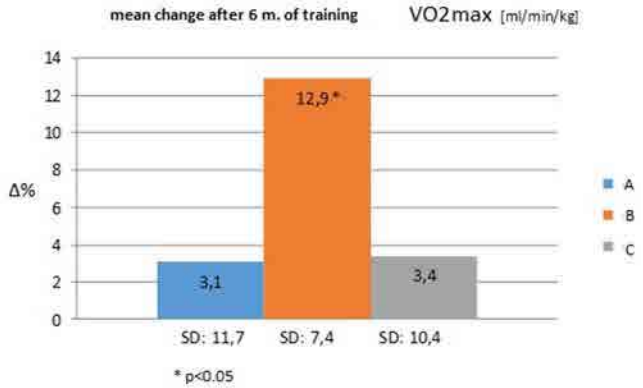


Fig.1

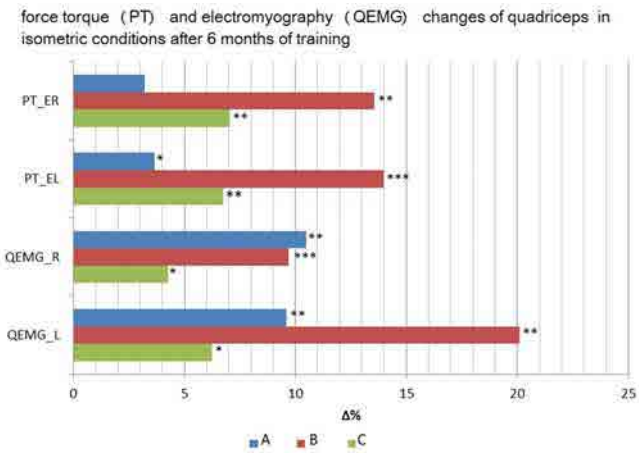


Fig.2

Conclusion: Differences in muscle strength and functions were observed after 6 months of various type of exercise intervention in dialysis patients. Resistance training during dialysis showed the largest improvement in cardiorespiratory function and isometric leg muscle strength.

SO066

IS OXYGEN-PULSE A GOOD SURROGATE MARKER OF STROKE VOLUME DURING PEAK EXERCISE IN CHRONIC KIDNEY DISEASE?

Shanmugakumar Chinnappa[1,2], Andrew Mooney[3,4]

[1]Doncaster and Bassetlaw Teaching Hospitals, Nephrology, United Kingdom, [2]University of Leeds, L.I.C.A.M.M, United Kingdom, [3]Leeds Teaching Hospitals, Nephrology, United Kingdom and [4]University of Leeds, United Kingdom

Background and Aims: As there is growing interest in the benefits of exercise training in chronic kidney disease (CKD), it is important to understand the utility of conventional exercise test parameters in quantifying the cardiopulmonary fitness of patients with CKD. Merely extrapolating information from studies of healthy volunteers and heart failure (HF) patients would not suffice. In the present study we evaluated one such parameter, the peak O_2-pulse [the rate of peak O_2 consumption (VO_{2max}) to peak heart rate (HR)] which is widely used as a surrogate for peak stroke volume (SV) in HF. We tested the hypothesis that peak O_2-pulse is a good surrogate marker for peak stroke volume in CKD.

Method: A cross sectional study of 70 asymptomatic male non-diabetic CKD patients [CKD stages 2-5 (pre dialysis)] without primary cardiac disease. Data from 35 healthy volunteers & 25 HF patients was used for comparison. Specialised cardiopulmonary exercise (CPX) test with CO_2 rebreathing technique was utilised to measure peak cardiac output (Q_t) and peak SV non-invasively. VO_{2max} was simultaneously measured. Peak O_2-pulse was calculated as *VO2max/Peak HR*. Peripheral O_2 extraction [$C(a\text{-}v)O_2$] was derived using Fick's equation, $VO_2 = Q_t \times C(a\text{-}v)O_2$. Pearson's correlation, univariate and multivariate analyses were applied. Results are presented as mean ± SD. $P<0.05$ is considered as significant.

Results: CKD patients had a mean age of 48.4 ± 12.6 years and a mean eGFR of 33.8 ± 25.5 ml/min. Whereas there was a very strong correlation between peak O_2-pulse and peak SV in HF ($R^2 = 0.81$), the correlation was less robust in CKD ($R^2 = 0.49$) (Fig 1). On multivariate analysis, in HF, peak SV was the major determinant of O_2 pulse ($\beta=1.03$). The β for peak $C(a\text{-}v)O_2$ was 0.44, both $P < 10^{-3}$. However, in CKD both peak SV ($\beta=0.76$, $P<10^{-3}$) and peak $C(a\text{-}v)O_2$ ($\beta=0.70$, $P<10^{-3}$) were significant determinants of O_2-pulse rendering O_2-pulse a poor surrogate of SV in CKD.

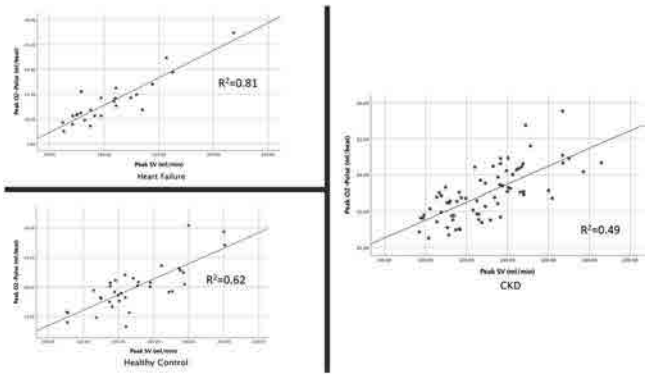


Figure 1: Association between peak O_2-pulse and peak stroke volume (SV) in CKD, heart failure and healthy control

Conclusion: Based on the above results we reject the hypothesis that peak O_2-pulse is a good surrogate marker of peak SV in CKD. The results highlight the pitfalls in the application of conventional CPX parameters in evaluating cardiopulmonary fitness in CKD. In view of the unique pathophysiology of the uraemic state further CKD-specific studies evaluating the central and peripheral determinants of aerobic exercise capacity are required.

SO067

VIRTUAL REALITY EXERCISE INTRADIALYSIS IMPACT ON PHYSICAL FUNCTION AND PHYSICAL ACTIVITY LEVEL: RANDOMIZED CONTROLLED TRIAL WITH FOLLOW-UP

Eva Segura-Ortí[1], Francisco José Martínez-Olmos[1], Alicia Garcia-Testal[2], Rafael Garcia-Maset[2], Noemi Valtueña-Gimeno[1], Lucia Ortega-Perez de Villar[3], Jocelyne Piñón-Ruiz[1], Ana Ferrer-Salva[1], KATARZYNA KARANDYSZ[1], Maari Elvi Amanda Lehtoviita[1], Francisco José Ferrer-Sargues[1], Pablo Salvador-Coloma[1], Inmaculada Rico-Salvador[2], Pilar Royo-Maicas[2], José Antonio Gil-Gómez[4]

[1]Universidad Cardenal Herrera-CEU, CEU Univerisities, Physiotherapy, Alfara del Patriarca, Spain, [2]Hospital de Manises, Nephrology, Manises, Spain, [3]Universidad Europea de Valencia, Physiotherapy, Valencia, Spain and [4]Universitat Politècnica de València, Instituto universitario de automática e informática industrial, Valencia, Spain

BACKGROUND AND AIMS. Despite the benefits reported by the implementation of exercise during dialysis, currently it is not a clinical routine. Non-immersive virtual reality (VR) is a feasible option to exercise and in a short pilot study of intadialysis VR exercise improved physical function (PF), Health-related quality of life (HRQoL) and physical activity (PA). The objective of this research was to investigate if a 12-weeks non-immersive VR exercise program intradialysis improves PF and PA.

METHODS: This was a crossover randomized controlled trial. Participants were randomized in a control-VR group (CVR) or VR-control group (VRC). There were two consecutive periods of 12 weeks, one control and one exercise period. The CVR started with a control period and followed by the exercise period, and the VRC did the opposite. PF and PA were assessed at four time points: baseline, 12, 24 and 36 weeks. The functional tests administered included the Short Physical Performance Battery (SPPB), gait speed in 4 meters, Timed Up-and-Go (TUG), balance with the one-legged stance test (OLST), Sit-to-Stand 10 (STS10) and Sit-to-Stand 60 (STS-60), 6 minute walking test (6MWT). Human Activity Profile (HAP) was used to assess PA level. Intradialysis exercise consisted of a video game adapted to dialysis: Treasure hunting. It is a non-immersive VR game in which the patient must catch some objectives avoiding obstacles by moving the lower limbs. The exercise session lasted from 20 to 40 minutes. Intensity was checked through the rate of perceived exertion (RPE). A mixed model of repeated measures were used to assess the effect of the intervention.

RESULTS: 47 subjects were included in the study, 22 subjects (median age 73.5 years; 13 males) in the CVR and 25 subjects (median age 72 years, 15 males) in the VRC. At 24 weeks we tested 33 subjects and at 36 weeks 31 patients were tested. The results of all functional tests improved after the exercise program (Gait speed in 4 meters -0.16 seconds, 95% CI -0.1- -0.2 VRC and -0.12 seconds, 95% IC -0.06–0.17 CVR; TUG -1.8 seconds, 95% CI -1.2–2.5 VRC and -1.3 seconds, 95% CI 0.1–2.7 CVR; OLST 6.2 seconds, 95% CI 2.6-9.8 VRC and 8.1 seconds, 95% CI 4.2-12.0 CVR; STS-10 -5.6 seconds, 95% CI -3.5–7.8 VRC and -6.0 seconds, 95% CI -4.0–7.9 CVR; and 6MWT 105.4 meters, 95% CI 76.2-134.6 VRC and CVR 59.5 meters, 95% CI 34.5-84.5). The VRC showed a significant increase in HAP (9.2, 95% CI 6.4-12.0) after the 12 weeks of exercise program. The CVR did not change during the first 12 weeks of no exercise, but showed a significant increase at 24 weeks after the end of the exercise program in HAP (7.4, 95% CI 3.8-11.0). The follow-up of 12 weeks after the end of the program in the VRC showed a significant decrease in function in the following tests (Gait speed in 4 meters -0.13seconds, 95% CI 0.08–0.18; STS-10 -1.4 seconds, CI 95% 0.11-2.65; and 6MWT -66.4 meters, 95% CI 43.5-89.2). During the follow-up period, at 24 weeks, the VRC showed a significant decrease in HAP (-7.7, 95% CI -11.0–4.4), there was no further decrease at 36 weeks. At 36 weeks, after 12 weeks of follow-up, participants in the CVR presented a significant decrease in HAP (-7.2, 95% CI -10.5–4.0).

CONCLUSIONS: A non-immersive VR exercise program during intradialysis improves PF and PA and HRQoL. Exercise benefits are not maintained after 12 weeks of follow-up.

SO068

EFFECTS OF BASELINE PHYSICAL FUNCTION AND 12 MONTHS EXERCISE TRAINING ON SURVIVAL IN PATIENTS WITH NON DIALYSIS DEPENDENT CHRONIC KIDNEY DISEASE

Sara Denguir[1], Matthias Hellberg[1], Helena Rydell[2], Martin Almquist[3], Naomi Clyne[1]

[1]Clinical Sciences, Lund, Lund University and Skåne University Hospital, Nephrology, Lund, Sweden, [2]Karolinska Institute and Karolinska University Hospital, Nephrology, Huddinge, Sweden and [3]Clinical Sciences, Lund, Lund University and Skåne University Hospital, Surgery, Sweden

Background and Aims: Low physical function is associated with increased mortality in patients on dialysis. Observational studies have shown an association between self-reported physical activity and survival in patients with chronic kidney disease (CKD). It is unclear whether exercise training can affect survival in patients with CKD. The purpose of this study was to investigate, whether level of physical function and exercise training, respectively, affect survival in patients with non-dialysis dependent CKD stages 3-5.

Method: The patients studied had participated in the RENEXC study comprising 12 months of endurance training in combination with either strength- or balance training. In this study the whole group was analyzed as both groups had improved their physical function with no between group differences. Physical function at baseline and after 12 months was assessed with a battery of tests. Patients were divided into 4 groups for each test: improved physical function by >10 %, no improvement, did not complete 12 months of exercise training and missing data. Effects of physical function at baseline and improvement in physical function after 12 months of exercise training on survival were analyzed using univariate and multivariate Cox regression analyses. Multivariate analyses were adjusted for age, sex, co-morbidity, time on dialysis and time as transplanted.

Results: This study comprised 151 patients, mean age 66±14 years, 65% men, measured GFR 22.5±8.2 ml/min/1.73 m^2. Median follow-up was 60 months.

Physical function at baseline was associated with a significantly better survival in univariate Cox regression analysis in the following tests: 6 Minute Walk Test (6MWT), handgrip strength right, functional reach and 30 seconds Sit-To-Stand (30s-STS). The decline in hazard ratio (HR) per unit in each test was 0.5 % in the 6MWT, 2.9 % in handgrip strength, 6.4 % in functional reach and 10.8 % in 30s-STS. Multivariate analyses showed that only 6MWT and 30s-STS were significantly related to survival. The decline in hazard ratio (HR) per unit in the multivariate analyses was 0.4 % in the 6MWT (HR 0.996, CI 0.994-0.998) and 5.7 % in 30s-STS (HR 0.943, CI 0.892-0.996).

Patients who completed 12 months of exercise training and improved their results by 10 % or more showed a significantly better survival compared with patients who completed 12 months of exercise training but failed to improve by at least 10 % in the following tests in the univariate analyses: handgrip strength right and left, isometric quadriceps strength left and 30s-STS. There was also a significantly better survival in the group that improved compared with the group that did not complete 12 months of exercise in the 6MWT, handgrip strength right and left, isometric quadriceps strength left and 30s-STS. In the multivariate analyses there were no significant differences between the group that improved and the group that did not improve in any of the physical function tests. The significant differences between the group that improved and the group that did not complete remained in the following tests: handgrip strength right (HR 7.83, CI 2.10-29.2) and left (HR 3.95, CI 1.31-11.9), isometric quadriceps strength left (HR 3.94, CI 1.78-8.74) and 30s-STS (HR 3.50, CI 1.58-7.77). The difference between the group that improved and the group that did not complete the training became significant in functional reach (HR 4.22, CI 1.99-8.94) and isometric quadriceps strength right (HR2.80, CI 1.35-5.80).

Conclusion: After adjustment for age, sex, co-morbidity, time on dialysis and time as transplanted overall endurance and muscular endurance at baseline were associated with a better survival. Patients who improved muscle strength, muscular endurance and balance showed a better survival compared with those who did not complete the study. There were no statistically significant differences between those who improved their physical function by at least 10% compared with those who did not.

BONE DISEASE IN DIALYSIS

SO069 **CIRCADIAN RHYTHMS OF THE BONE-MINERAL AXIS IN HEMODIALYSIS PATIENTS**

Yue Jiao[1], Chen Chen[2], John Larkin[1], Anke Winter[2], Len A Usvyat[1], Manuela Stauss-Grabo[2], Jeffrey Hymes[3], Franklin Maddux[4]

[1]Fresenius Medical Care, Global Medical Office, Waltham, United States of America, [2]Fresenius Medical Care Deutschland GmbH, EMEA Medical Office, Bad Homburg, Germany, [3]Fresenius Medical Care North America, NA Medical Office, Waltham, United States of America and [4]Fresenius Medical Care AG & Co. KGaA, Global Medical Office, Bad Homburg, Germany

Background and Aims: Chronic kidney diseases disrupt normal bone-mineral axis endocrine functions causing the onset of mineral bone disorders (MBDs). The general and hemodialysis (HD) populations have been found to exhibit diurnal rhythms in phosphate (PO4), calcium (Ca), and parathyroid hormone (PTH) regulation (Trivedi et al. J Nephrol. 2015), but reference values for fluctuations have not been established in HD patients and do not consider PO4 binder use. We profiled the diurnal rhythms of MBD labs overall and stratified by PO4 binder use in a large nationally representative HD population in the United States.

Method: We used prevalent in-center HD patient (vintage >90 days) data on adults (age ≥18 years) treated at a dialysis organization in 2018. Mean annual pre-HD blood PO4, corrected Ca, and intact PTH levels were computed in 2-hour periods through 24 hours for the population and stratified by binder use. HD initiation time was a varying exposure, allowing patients to switch time groups if blood draws occurred in multiple time periods. Mean MBD lab levels with 95% confidence limits were plotted using non-parametric smoothing spline models to fit data and calculate trajectories throughout the day.

Results: The population of adult HD patients (n=156,873) was: mean age 62.8±14.3 years, 57.1% male, 58.2% white race, 41.9% with diabetes, 19.6% with congestive heart failure, and HD vintage 1510±1289 days. Mean pre-dialysis albumin=3.8±0.4 g/dL, PO4=5.4±1.5 mg/dL, corrected Ca=9.1±0.6 mg/dL, PTH=468±333 pg/dL for the population. Mean PO4, corrected Ca and PTH levels varied remarkably by 0.9 mg/dL, 0.2 mg/dL, and 186 pg/dL throughout the day. For PO4 and PTH, nadir levels occurred from 0900 to 1100 hours (5.3±1.6 mg/dL and 473±340 pg/dL), followed by a rise to a mid-day peak from 1700 to 1900 hours (5.8±1.8 mg/dL and 562±401 pg/dL), and the highest levels had a peak time from 2300 to 0100 hours (6.2±2.1 mg/dL and 659±389 pg/dL) (Figure 1A & C). Corrected Ca showed relatively inverse fluctuations to PO4 and PTH, with peak levels from 1100 to 1300 hours (9.2±0.7 mg/dL) and nadir levels from 1900 to 2100 hours (9.0±0.7 mg/dL) (Figure 1B). Similar fluctuations and levels were observed for PO4 and PTH among patients using any phosphate binder type (90.7%), however, patients not using a phosphate binder exhibited absolute values that were persistently lower at every timepoint (Figure 1D & F). Corrected Ca levels were similar by any binder use (Figure 1E).

Conclusion: Our results suggest PO4, Ca, and PTH levels have a diurnal variation of 0.9 mg/dL, 0.2 mg/dL, and 186 pg/dL in hemodialysis patients. PO4 and PTH exhibit a nadir in the morning, a mid-day peak and a larger nocturnal peak. Ca exhibits relatively inverse diurnal fluctuations with PO4 and PTH. Patients using any binder exhibit similar fluctuations and levels of PO4 and PTH; while patients not requiring a binder have similar fluctuations, yet persistently lower levels of PO4 and PTH. Given PO4 binder and calcimimetic therapies are commonly used for treatment of MBDs based on pre-dialysis blood levels, these findings provide insights for further research and pose the question if algorithms are warranted to compute daily time-adjusted levels for MBD laboratories.

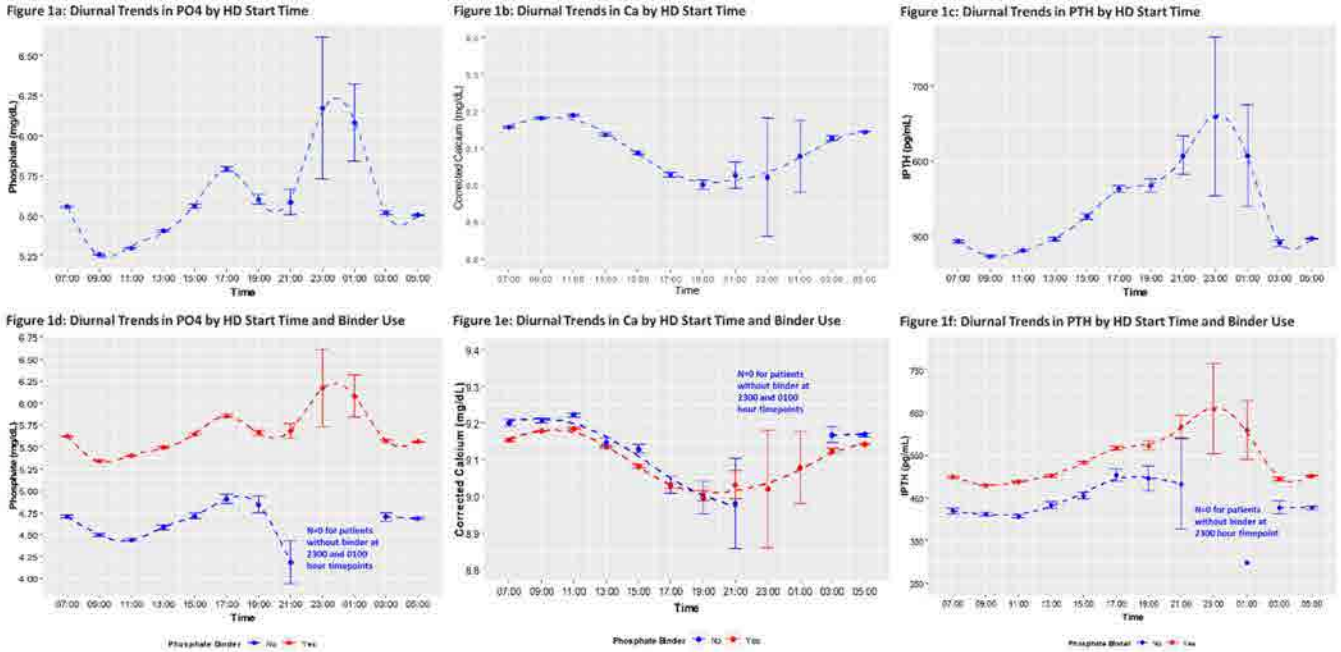


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SO070

THE SPECTRUM OF RENAL OSTEODYSTROPHY IN PREVALENT PERITONEAL DIALYSIS PATIENTS IN 21ST CENTURY - A HISTOMORPHOMETRIC ANALYSIS OF BONE BIOPSIES

Luciano Pereira[1,2,3,4], Juliana Magalhães[1,2], Luís Mendonça[1,2,3,4], Hugo Diniz[1,2,3,4], Maria João Sousa[4], Ricardo Neto[1,2,3,4], Catarina Carvalho[5], Ana Oliveira[1,2,3,4], Ana Beco[1,2,3,4], Joao M. Frazao[1,2,3,4]

[1]I3S - Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Porto, Portugal, [2]INEB - Instituto de Engenharia Biomédica, Nephrology and Infectious Diseases Group, Porto, Portugal, [3]Faculty of Medicine, University of Porto, Nephrology, Porto, Portugal, [4]São João Hospital Center, Nephrology, Porto, Portugal and [5]Hospital de Braga, Nephrology, Braga, Portugal

Background and Aims: The spectrum of renal osteodystrophy (ROD) in peritoneal dialysis (PD) patients remains to be clarified. Most studies are old and the results inconsistent. Also there were changes in clinical practice that may have influenced the bone histology in PD patients.

Method: In order to characterize ROD in prevalent PD population, we performed tetracycline-labelled bone biopsies in 49 PD patients with histomorphometric analysis according KDIGO guidelines. Exclusion criteria: history of kidney transplant, hemodialysis, treatment with agents interfering in bone metabolism (for example bisphosphonates). Hands and pelvis x-ray were performed to evaluate vascular calcification (VC) and to calculate the Adragão score. All patients were treated with biocompatible PD solutions, with calcium concentration of 1.25 mmol/L.

Results: Forty-nine patients participated in the study, with 32 biopsies analyzed so far. Mean age was 52.4±10.9 years, 16 male, 6 with diabetes mellitus, 23 on manual PD, median time on PD was 22.1 (3-61) months. Mean calcium, phosphate and PTH were 9.2±0.5 mg/dL, 4.9±1.0 mg/dL and 489.87±227.8 pg/mL, respectively. Vascular calcification was detected in 29% of patients and mean Adragão score was 1.13. Essential histomorphometric and selected data is represented in table 1:

Bone volume (BV) tended to be lower in diabetics - 17.1% (10.1-23.1) compared with non-diabetics – 22.6% (12.7-41.4) (p=0.07). Median bone formation rate (BFR) tended to be lower - 21.39 $\mu m^3/\mu m^2/y$ (8.2-53.2) in diabetic patients than in non-diabetics - 28.63 $\mu m^3/\mu m^2/y$ (3.5-89.77) (p=0.80). PTH levels also tended to be lower in diabetics – 384.8 pg/mL compared to non-diabetics – 514.1 pg/mL (p=0.14).

BV tended to be lower in patients with VC – 19.1% (10.1-27) compared with patients without VC - 22.6% (12.7-41.4) (p=0.23).

VC was detected on x-ray in all 6 patients with diabetes and only in 11.5% (3 in 26) of non-diabetic patients.

Conclusion: Similar to previous reports, the most frequent ROD pattern was ABD. However, PD patients with ABD had mean PTH of 405 pg/mL, a value well within the recommended KDIGO targets. This reinforces PTH as a far from ideal marker of bone turnover and suggests different targets for PTH levels in this seemingly highly susceptible population to ABD even when treated with low calcium dialysate.

The proportion of patients with normal bone was higher than previously published. This finding can be explained by differences in the classification of ROD and prescription of biocompatible PD solutions in all patients.

Diabetic patients tended to have lower BV and BFR. This finding is not surprising considering osteoblastic toxicity caused by advanced glycation end products. Also diabetic patients have a state of relative hypoparathyroidism.

In conclusion, the most frequent pattern was ABD. Diabetic patients on PD may be a different subgroup.

Table 1 – Comparison between identified histological subgroups

ROD type	**n**	**BFR/BS** ($\mu m^3/\mu m^2/y$) N: 18,25-40,15	**MLT** (days) N: 13,3-58,4	**BV/TV** (%) N: 16,8-22,9	**PTH** (pg/mL)	**ALP** (UI/L)	**Adragão Score** (0-8)	**Glucose load** (g/day)
Normal	4	21.9±3.6	12.3±5.4	22.8±3.41	518.3±155.9	125.8±37.4	1.5 (0-3)	47.6 (27.2-181.5)
Osteoporosis	1	36.49	5.8	15.7	214.2	195	8	54.4
ABD	12	9.83±4.0	23.0±15.3	18.3±4.3	404.84±173.6	116.9±57.0	1.17 (0-8)	81.6 (54.4-374.5)
sHPT	9	56.3±14.7	9.3±5.8	25.9±4.3	684.8±253.1	130±40	0.8 (0-4)	127 (27.2-295)
Osteo malacia	1	5.3	109	12.7	316	82	0	27.2

ABD – adynamic bone disease; sHPT – secondary hyperparathyroidism; BFR – bone formation rate; BS – bone surface; MLT – mineralization lag time; BV – bone volume; TV – tissue volume; ALP – alkaline phosphatase. Osteoporosis is not a classic ROD type and was defined as low bone volume, normal turnover and mineralization. In 5 patients dynamic data was not yet available.

SO071

18F-SODIUM FLUORIDE POSITRON EMISSION TOMOGRAPHY AND BONE HISTOMORPHOMETRY - COMPARISON BETWEEN ONLY BONE TURNOVER -BASED AND EXPERT EVALUATION -BASED CLASSIFICATION OF RENAL OSTEODYSTROPHY

Louise Caroline Aaltonen[1], Niina Koivuviita[1], Marko Seppänen[2], Inari Burton[3], Heikki Kröger[3,4], Kaj Peter Metsarinne[1]

[1]Turku University Hospital, Kidney Center, Department of Medicine, Turku, Finland, [2]Nuclear Medicine and Turku PET centre, University of Turku, Department of Clinical Physiology, Turku, Finland, [3]Institute of Clinical Medicine, University of Eastern Finland, Kuopio Musculoskeletal Research Unit (KMRU), Kuopio, Finland and [4]Kuopio University Hospital, Kuopio, Finland

Background and Aims: The diagnosis and the differentiation of renal osteodystrophy (ROD) are challenging. Bone biopsy is the golden standard, but it is invasive and not available in every center.

Bone turnover rate is defined by bone formation rate and/or activation frequency. Adynamic bone disease is defined as low turnover bone with reduced osteoblast- and osteoclast activities. Hyperparahyreoid bone disease or osteitis fibrosa is defined as high turnover bone with osteoclast- and osteoblast activities and fibrosis.

^{18}F- Sodium Fluoride positron emission tomography (^{18}F-NaF PET) is a noninvasive imaging technique that allows assessment of regional bone turnover.

The aim was to assess how well bone turnover –based classification of ROD correlates with the classification determined by an expert histomorphometrist (HK), and how these correlate with ^{18}F-NaF PET analysis

Method: A total of 24 dialysis patients underwent a ^{18}F-NaF PET scan. Fluoride activity was measured at the anterior iliac crest and in the lumbar region. An iliac crest bone biopsy was obtained within 4 weeks from the PET-scan. The diagnosis of bone histomorphometry was determined based on turnover-mineralization-volume (TMV) classification. Firstly, bone turnover was assessed using bone formation rate and activation frequency. Secondly, also other histomorphometric parameters (eg. osteoid volume, osteoid surface, resorption surface, mineralized surface, osteoblast and osteoclast surfaces and peritrabecular fibrosis) were also taking into account for classification of ROD by a histomorphometrist.

Results: Based on bone turnover parameters only, 12% of the patients had high turnover and 64% low turnover. When the diagnosis of renal osteodystrophy was made by a histomorphometrist, 40% had hyperparathyreoid bone/osteitis fibrosa and 24% adynamic bone disease or ostemalasia.

^{18}F-NaF PET's sensitivity to recognize hyperparathyreoid bone disease was 80% end specificity 100% (cut-of value 0.055).^{18}F-NaF PET's sensitivity to recognize adynamic bone disease was 100% and specificity 61% (cut-of value of fluoride-activity 0.038)

Conclusion: ^{18}F-NaF PET works well as a diagnostic tool, when the diagnosis of ROD is based on the histopathological evaluation. It remains unknown how variations in normal bone turnover rate can be detected in CKD patients by ^{18}F-NaF PET and if treatment decisions of ROD can be made only based on bone turnover.

SO072 **INCIDENCE OF FRACTURES BEFORE AND AFTER DIALYSIS INITIATION AMONG INCIDENT DIALYSIS PATIENTS**

Ken Iseri[1,2], Juan Jesus Carrero[3], Marie Evans[1], Li Felländer-Tsai[4], Hans Berg[4], Björn Runesson[1], Peter Stenvinkel[1], Bengt Lindholm[1], Abdul Rashid Tony Qureshi[1]

[1]Karolinska Institutet, Divisions of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, [2]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Japan, [3]Karolinska Institute, Department of Medical Epidemiology and Biostatistics and [4]Karolinska Institutet, Division of Orthopaedics and Biotechnology, Department of Clinical Science, Intervention and Technology

Background and Aims: The incidence of fractures is markedly higher in dialysis patients than in pre-dialysis patients, but it is not clear to what extent the initiation of dialysis as such is associated with accelerated fracture incidence or if fracture rates are already increasing prior to dialysis start among incident dialysis patients. Here we investigated the temporal pattern of occurrence of a first major osteoporotic fracture (MOF) among incident dialysis patients in the pre-dialysis period and in the period following dialysis initiation.

Method: We analyzed data from Swedish Renal Registry (SRR) and identified 9041 incident dialysis patients (2005 -2015; age 67 years, 67% men). We identified all first MOF (MOF_{first}) in hip, spine, humerus and forearm during 12 months before and after dialysis initiation. Using flexible parametric hazard models and Fine-Gray analysis accounting for competing risk of death and renal transplantation, we estimated adjusted fracture incidence rates and predictors of MOF_{first}.

Results: During the whole follow-up period, there were 361 fractures including 196 hip fractures. The crude incidence rate of MOF_{first} (n=157) before dialysis initiation was 17/1000 patient-years and after initiation of dialysis the incidence rate of MOF_{first} increased to 24/1000 patient-years. Overall the adjusted MOF_{first} incidence rates increased from 6 months before initiation of dialysis, fluctuated, and stabilized at a higher rate than that of the baseline rate after 12 months. The adjusted hip fracture rate rose steeply 3 months before dialysis initiation, declined 3 months after dialysis initiation, fluctuated, and then became stabilized. On the contrary, the adjusted incidence rates of other fractures, i.e., non-hip fractures, appeared to be stable all the time, before as well as after initiation of dialysis. Female gender, higher age and previous history of MOF had a negative impact on fracture incidence rates before and after dialysis initiation.

Conclusion: We conclude that the incidence of MOF_{first} is increasing already from 6 months prior to dialysis initiation among incident dialysis patients, and that there is a further increase following dialysis initiation. For hip fracture, which was the most common MOF, the temporal pattern of incidence rates was compressed to a high risk period lasting from 3 months before to 3 months after dialysis initiation, underlining the need of increased attention to prevent hip fractures in incident dialysis patients during this critical period.

SO073

IRON-RELATED PARAMETERS AND ANTI-ANAEMIC THERAPY IN HAEMODIALYSIS PATIENTS TREATED WITH SUCROFERRIC OXYHYDROXIDE: A 1-YEAR RETROSPECTIVE EUROPEAN CLINICAL DATABASE (EUCLID) ANALYSIS

Jayne Carey-George, Konstantin Gurevich[1], Rosa Ramos Sanchez[2], Charles Chazot[3], Anibal Ferreira[4], Attilio Di Benedetto[5], Astrid Feuersenger[6], Melanie Wolf[6], Hans-Juergen Arens[6], Sebastian Walpen[7], Stefano Stuard[8]

[1]Fresenius Medical Care Russia, Nephrology, Saint Petersburg, Russia, [2]NephroCare Spain, Nephrology, Madrid, Spain, [3]NephroCare France, Nephrology, Fresnes, France, [4]NephroCare Vila Franca de Xira, Nephrology, Vila Franca de Xira, Portugal, [5]NephroCare Italy, Medical Direction, Naples, Italy, [6]Fresenius Medical Care Deutschland GmbH, Bad Homburg, Germany, [7]Vifor Fresenius Medical Care Renal Pharma, Nephrology, Glattbrugg, Switzerland and [8]Fresenius Medical Care, Clinical & Therapeutical Governance, Bad Homburg, Germany

Background and Aims: This retrospective analysis of data from the European Clinical Database (EuCliD®) evaluated changes in iron-related parameters and use of concomitant anti-anaemic therapies in European haemodialysis (HD) patients treated with sucroferric oxyhydroxide (SFOH). Previous Phase 3 clinical studies and non-clinical studies have indicated that there is minimal iron absorption from SFOH. This study aimed to evaluate the changes in iron-related parameters among patients treated with SFOH in the real-world setting.

Method: De-identified patient data were extracted from a clinical database (EuCliD®) for adult HD patients newly prescribed SFOH routinely for up to 1 year (1 Jan 2015–1 Jan 2019). Levels of serum ferritin, transferrin saturation (TSAT) and haemoglobin were compared between baseline (BL; 3-month period before starting SFOH) and each quarterly period in the year after starting SFOH treatment (Q1–Q4). Proportions of patients receiving intravenous (IV) iron and erythropoiesis-stimulating agent (ESA) therapies, in addition to their mean weekly doses, during each quarter were recorded.

Results: The cohort included 1,096 patients with recorded SFOH prescriptions (mean age: 60.6 years; 65.8% male). There were small, but significant increases in ferritin from BL to Q1–Q4 ($P<0.05$ for all periods vs BL). There were also increases in TSAT ($P<0.05$ at Q1 and Q2 vs BL) and haemoglobin ($P<0.001$ at Q1 and Q3 vs BL) (**Table**). During the 1-year SFOH treatment period, the proportion of patients receiving IV iron therapy decreased ($P<0.05$ at Q2 and Q3 vs BL) and there was a significant reduction in the mean weekly dose of IV iron administered ($P<0.05$ at Q2 and Q3 vs BL). The use of ESA therapy also declined ($P<0.05$ at Q3 and Q4) and there was a significant decrease in the mean weekly dose of ESA during the 1-year SFOH follow-up period ($P<0.05$ for all periods vs BL).

Conclusion: This real-world study showed that SFOH treatment in routine clinical practice for up to 1 year was associated with small increases in iron-related parameters and decreases in the use and mean dose of concomitant anti-anaemic therapies in European HD patients. The results from this study indicate that SFOH treatment may be associated with the reduction in concomitant IV iron and ESA use in HD patients, in line with previous findings from the Phase 3 study.

Table: Iron-related parameters and concomitant IV iron and ESA use at baseline and during follow-up (Q1 to Q4) in the overall study cohort (N=1,096)

Iron-related parameter	Baseline (n=1,089)	Q1 (n=968)	Q2 (n=738)	Q3 (n=536)	Q4 (n=378)
Serum ferritin, μg/L	455.69 ± 331.43 (n=1,060)	480.82 ± 329.23** (n=901)	501.96 ± 329.54*** (n=704)	494.72 ± 320.2* (n=503)	488.25 ± 336.60* (n=348)
Serum TSAT, %	27.88 ± 12.07 (n=949)	29.38 ± 12.04* (n=768)	29.91 ± 12.09* (n=619)	29.33 ± 12.41 (n=435)	28.92 ± 11.65 (n=297)
Haemoglobin, g/dL	11.32 ± 1.24 (n=1,088)	11.47 ± 1.31** (n=968)	11.39 ± 1.39 (n=736)	11.55 ± 1.26** (n=534)	11.49 ± 1.31 (n=378)
Anti-anaemic therapy					
Patients receiving IV iron, n (%)	856 (78.6)	739 (76.3)	552 (74.8)*	388 (72.4)*	279 (73.8)
Mean IV iron dose, mg/week	54.40	51.42	48.54*	47.07*	49.98
Patients receiving ESA, n (%)	877 (80.5)	751 (77.6)	569 (77.2)	402 (77.1)*	282 (74.6)*
Mean ESA dose, units/week	6,618	5,945***	5,846*	6,126*	5,665*

All iron-related parameter values are mean ± standard deviation.

*$P<0.05$;

**$P<0.001$;

***$P<0.0001$ (vs baseline).

Abbreviations: ESA, erythropoiesis-stimulating agent; IV, intravenous; TSAT, transferrin saturation.

SO074

VASCULAR CALCIFICATION IN PREVALENT PERITONEAL DIALYSIS PATIENTS AND ITS RELATIONSHIP WITH CLINICAL AND BONE HISTOMORFOMETRIC PARAMETERS

Luciano Pereira[1,2,3,4], Juliana Magalhães[1,2], Ricardo Neto[1,2,3,4], Ana Oliveira[1,2,3,4], Ana Beco[1,2,3,4], Joao M. Frazao[1,2,3,4]

[1]I3S - Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Porto, Portugal, [2]INEB - Instituto de Engenharia Biomédica, Nephrology and Infectious diseases group, Porto, Portugal, [3]São João Hospital Center, Nephrology, Porto, Portugal and [4]Faculty of Medicine, University of Porto, Nephrology, Porto, Portugal

Background and Aims: Vascular calcification (VC) is associated to morbidity and mortality in chronic kidney patients. However, it remains to clarify the relationship between VC and renal osteodystrophy (ROD) evaluated by bone biopsy in peritoneal dialysis (PD) patients.

Method: In order to characterize the relationship between VC and ROD in prevalent PD population, we performed tetracycline-labelled bone biopsies with histomorphometric analysis according KDIGO guidelines. Hands and pelvis x-ray were performed to evaluate VC and to calculate Adragão Score. Exclusion criteria: previous kidney transplant, hemodialysis, treatment with agents interfering in bone metabolism (for example bisphosphonates). All patients were treated with biocompatible PD solutions, with calcium concentration of 1.25 mmol/L.

Results: Thirty-one patients participated in the study. Mean age was 52.32±11.09 years, 16 male, 6 with diabetes mellitus (DM), 22 on manual PD, median time on PD was 12 (3-61) months. Mean calcium, phosphate and PTH were 9.2±0.5 mg/dL, 4.9±1.0 mg/dL and 486.0±230.5 pg/mL, respectively. Most frequent diagnosed ROD pattern was adynamic bone disease (44.4%) followed by hiperparathyroid bone disease (33.3%) and normal bone (14.8%). VC was detected in 29% of patients and mean Adragão score was 1.13. However, 100% of diabetics had VC on x-ray compared to 12% of non-diabetics. Clinical, analytical and histomorphometric essential data is represented in table 1:

	Without VC	With VC	
Age (years)	50	59	**p=0.024**
Time on PD (months)	24	18	NS (p=0.495)
Total KT/V	2.5	2.0	**p=0.042**
Total creatinine clearance (ml/min)	117.5	121.1	NS (p=0.864)
Residual renal function (ml/min)	6.4	5.5	NS (p=0.564)
Diabetes (n)	0	6 (100%)	**p<0.001**
Total calcium (mg/dL)	9.2	9.2	NS (p=0.932)
Phosphate (mg/dL)	4.8	5.2	NS (p=0.309)
PTH (pg/mL)	492.2	470.7	NS (p=0.818)
25(OH)Vitamin D (ng/mL)	17.7	9.5	NS (p=0.276)
Sedimentation rate (mm/h)	57.9	91.1	**p=0.004**
BV/TV (%)	22.5	19.1	NS (p=0.186)
mBV/TV (%)	22	18.53	NS (p=0.166)
Tb.Sp (mcg)	248	274.9	NS (p=0.335)
Tb.N (mcg)	3.3	3.1	NS (p=0.564)
ObS/BS (%)	1.46	1.73	NS (p=0.78)
OcS/BS (%)	0.48	0.34	NS (p=0.602)
BFR/BS ($\mu m^3/\mu m^2/y$)	27.1	27.32	NS (p=0.982)
MLT (days)	21.2	17.0	NS (p=0.673)

BV – bone volume, TV – tissue volume, mBV – mineralized bone volume, Tb.SP – trabecular separation, Tb.N – trabecular number, ObS – osteoblast surface, BS – bone surface, OcS – osteoclast surface, BFR – bone formation rate, MLT – mineralization lag time.

Also no significant differences were observed between the patients with or without VC in ROD patterns on bone biopsy, glucose load in PD solutions, prescribed phosphate binders namely calcium-based binders, active vitamin D or calcimimetics.

In diabetic patients, bone volume tended to be lower (17.26% vs 22.54%; p=0.072) comparing to non-diabetics. Bone formation rate was similar in diabetics and non-diabetics (25.39 vs 27.71$\mu m^3/\mu m^2/y$) as mineralization lag time (18.7 vs 20.1 days).

Conclusion: ROD evaluated by bone biopsy and the proportion of PD patients with VC on x-ray were similar to previous reports. However, in the present study a striking difference in VC was detected in diabetics – all diabetic patients had VC demonstrated radiographically. This finding was not explained by differences in calcium, phosphate, PTH levels or other studied factors. So DM could be a strong risk factor to VC in this population. Also, patients with VC were older, with higher sedimentation rate and lower total KT/V.

It is possible that diabetic patients represent a different subgroup, particularly prone to lower bone volume and specially VC. They might benefit from higher dialysis dose and aggressive approaches to prevent or retard VC. This remains to be proved in properly designed prospective studies.

In conclusion, age, sedimentation rate, total KT/V and presence of diabetes were associated to VC in prevalent PD patients. Diabetics may be a subgroup of PD patients with very high risk of VC.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii81–iii83, 2020

GLOMERULONEPHRITIS 1

SO075

ADOPTIVE TRANSFER OF GINGIVA-DERIVED MESENCHYMAL STEM CELLS AMELIORATES LUPUS NEPHRITIS VIA INDUCTION OF CD4+HELIOS-FOXP3+ TREG THROUGH TARGETING OF CD39/CD73 SIGNALING PATHWAY

Zhenjian Xu[1], Junzhe Chen[1], Anping Xu[1]

[1]*Sun Yat-sen Memorial Hospital of Sun Yat-sen University, Nephrology, Guangzhou, P.R. China*

Background and Aims: Current approaches offer no cures for lupus nephritis. Accumulating evidence has revealed that manipulation of bone-marrow mesenchymal stem cells (BMSCs) may have the potential to treat lupus nephritis. While BMSC-based therapy faces many challenges such as limited cell availability, BMSCs from patients with autoimmune diseases are dysfunctional, use of BMSCs with long term has a potential risk on tumorigenesis and reduced clinical feasibility, we herein demonstrate that substitution of gingival-derived mesenchymal stem cells (GMSCs) results in significantly improved therapeutic effects on lupus-like disease model.

Method: Lupus-like disease has been induced with female New Zealand mixed (NZM) 2328 mice. In the study of prevention of lupus-like disease, GMSCs were injected i.v. into mice on age of 10 weeks. In some experiments, mice were injected with pre-treatment of GMSCs with CD39 or CD73 inhibitor. In the study of treatment of lupus-like disease, GMSCs were injected i.v. into mice on age of 20 weeks.

Results: In the study of prevention of lupus-like disease, infusion of GMSCs in NZM2328 mice significantly decreased the severity of lupus and kidney pathology scores, and down-regulated Th2, Tfh and Th17 cells. GMSCs significantly suppress activation and differentiation of B cells in vivo. Promotion of CD4+Helios-Foxp3+Treg cells following treatment with GMSCs, these increased Tregs were noted in spleen, LN and Kidney. Pre-treatment of GMSCs with CD39 or CD73 inhibitor significantly reversed the protective effect of GMSCs on lupus-like disease model. In the study of treatment of lupus-like disease, GMSCs can also treat the established disease.

Conclusion: The role of GMSCs in controlling lupus-like disease mostly depends upon CD39/CD73 signals and upon the induction of CD4+ Helios-Foxp3+Treg cells. GMSCs provide a promising approach for the treatment of lupus nephritis.

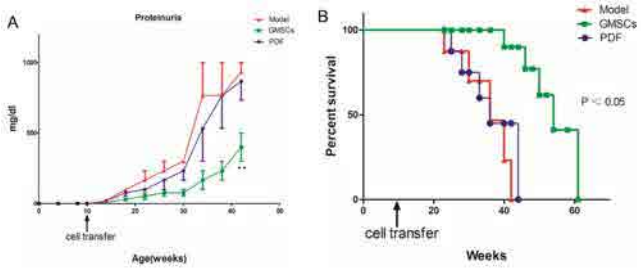


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SO076 EVOLOCUMAB HAS THERAPEUTIC EFFECTS ON EXPERIMENTAL MODEL OF FSGS

Taihei Suzuki[1], Masayuki Iyoda[1], Nobuhiro Kanazawa[1], Yukihiro Wada[1], Hirokazu Honda[1]

[1]*Showa University School of Medicine, Nephrology, Tokyo, Japan*

Background and Aims: Proprotein convertase subtilisin/kexin type 9 (PCSK9), which accelerates LDL-receptor degradation, plays a central role in dyslipidemia in nephrotic syndrome (NS). Intracellular LDL-C accumulation is supposed to damage podocytes through oxidative stress, foam cell formation, and apoptosis. In the present study, we investigate the effects of evolocumab (EVO), which is anti-PCSK9 monoclonal antibody, on a murine model of adriamycin-induced focal segmental glomerulosclerosis (FSGS) with NS in order to clarify the potential of EVO as a therapeutic agent in FSGS.

Method: Male BALB/c mice aged 9 to 11 weeks were divided into vehicle and intervention groups. The mice underwent subcutaneous injection of normal saline (FSGS-Vehicle group) or EVO (30 mg/kg) (FSGS-EVO group) and immediately after that, they were administered adriamycin (11.5 mg/kg) from tail vein. All mice were sacrificed on Day 14, and then morphological and functional analyses were performed.

Results: EVO treatment significantly reduced serum levels of LDL-C (mg/dl, 305.3 ± 77.1 vs. 159.1 ± 31.7, $p<0.01$) and PCSK9 (ng/ml, 652.9 ± 230.0 vs 311 ± 116.5, $p<0.001$). In addition, EVO treatment significantly improved renal function, including albuminuria (albumin/creatinine (Cr), 15.73 ± 1.26 vs. 7.32 ± 1.02, $p<0.001$), serum Cr (mg/dl, 0.48 ± 0.13 vs. 0.18 ± 0.044, $p<0.001$) and BUN (mg/dl, 80.08 ± 20.22 vs. 46.86 ± 9.60, $p<0.05$). Compatibly with the clinical data, the severity of glomerulosclerosis score (semi-quantification, 2.44 vs. 1.95, $p<0.001$) was ameliorated and podocyte density (number of podocyte/glomerulus, 2.61 vs. 7.54, $p<0.001$) was maintained in the FSGS-EVO mice compared with the FSGS-Vehicle mice.

Conclusion: Our findings provided novel insights into the protective effects of EVO on adriamycin nephropathy, indicating EVO as a potent therapeutic agent for FSGS.

SO077

A PROSPECTIVE RANDOMIZED STUDY ON PRE-EMPTIVE IMMUNOSUPPRESSIVE TREATMENT IN LUPUS NEPHRITIS PATIENTS WITH ASYMPTOMATIC SEROLOGICAL REACTIVATION

Desmond Yap[1], Colin Siu On Tang[1], Ho Yin Chung[2], Julia Chan[3], Joseph M. W. Lo[4], Benjamin Y. F. So[1], Daniel Tak Mao Chan[1]

[1]University of Hong Kong, Division of Nephrology, Department of Medicine, Hong Kong, Hong Kong, P.R. China, [2]University of Hong Kong, Division of Rheumatology and Clinical Immunology, Department of Medicine, [3]Queen Elizabeth Hospital, Division of Rheumatology, Department of Medicine and [4]Kwong Wah Hospital, Renal Unit, Department of Medicine & Geriatrics, Hong Kong, Hong Kong, P.R. China

Background and Aims: The optimal management for asymptomatic serological reactivation (ASR) in lupus nephritis (LN) patients remains undefined. Our previous retrospective study suggested that pre-emptive treatment with moderate increase of immunosuppression may reduce subsequent clinical flares.

Method: This prospective study randomized LN patients with ASR (defined as >2-fold increase of anti-dsDNA to >100 IU/mL, with or without change in complement level, and absence of clinical lupus exacerbation) to receive pre-emptive treatment ('Pre-emptive' group) or unchanged management ('Control' group). Pre-emptive treatment included increasing prednisolone dose to 0.5 mg/kg/D, and the dose of mycophenolate to 1g/D or azathioprine to 75 mg/D, then tapered over 12-16 weeks back to the original dosages.

Results: Thirty-four patients were randomized (17 in each group). Pre-emptive group showed lower anti-dsDNA and higher C3 levels after 12 weeks compared with Controls (90.3±58.3 IU/mL vs. 153.8±92.9 IU/mL, and 98.7±33.4 mg/dL vs. 81.8±26.2 mg/dL, respectively; $p<0.001$ for both) (Figure 1). Pre-emptive group showed significantly lower incidence rates of all clinical flares and renal flares during subsequent 9 months of follow-up compared with Controls (11.7% vs 47.1%, p=0.01; and 0% vs 17.7%, p=0.03; respectively). Mean time-to-flare was 6.4±4.2 months and 5.2±3.4 months in Pre-emptive and Control groups respectively (p=0.77). There was no clinically significant adverse event.

Conclusion: Our results suggest that pre-emptive moderate increase of immunosuppressive treatment reduces the risk of disease flare in LN patients with ASR and is well tolerated.

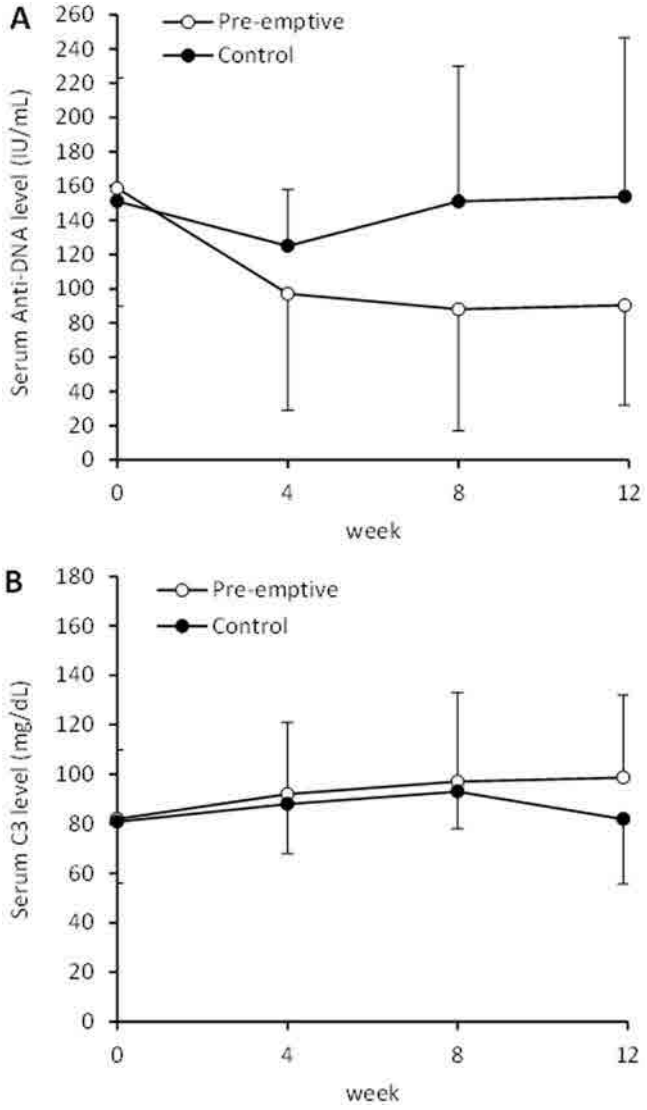


Figure 1. Serial changes in (A) anti-dsDNA level and (B) C3 level in lupus nephritis patients with asymptomatic serological reactivation who have or have not received pre-emptive immunosuppressive treatment.

ASPECTS OF CKD PATHOPHYSIOLOGY 1

SO078

APABETALONE, A BROMODOMAIN AND EXTRA-TERMINAL (BET) PROTEIN INHIBITOR, REDUCES ALKALINE PHOSPHATASE IN CVD PATIENTS, IN MICE, AND IN CELL CULTURE SYSTEMS

Dean Gilham[1], Laura Tsujikawa[1], Sylwia Wasiak[1], Ravi Jahagirdar[1], Li Fu[1], Phoebe Ho[1], Christopher Halliday[1], Christopher Sarsons[1], Stephanie Stotz[1], Brooke Rakai[1], Kenith Lebioda[1], Jan Johansson[2], Michael Sweeney[2], Norman Wong[1], Kamyar Kalantar-Zadeh[3], Mathias Haarhaus[4], Ewelina Kulikowski[1]

[1]Resverlogix, Calgary, Canada, [2]Resverlogix, San Francisco, United States of America, [3]University of California Irvine, Irvine, United States of America and [4]Karolinska University Hospital, Stockholm, Sweden

Background and Aims: Elevated serum alkaline phosphatase (ALP) independently predicts major adverse cardiac events (MACE) by contributing to vascular calcification and endothelial dysfunction arising in chronic kidney disease (CKD) and cardiovascular disease (CVD). Apabetalone is an orally active inhibitor of bromodomain and extra-terminal (BET) proteins – epigenetic readers that modulate gene expression involved in vascular inflammation and calcification. Here we examined apabetalone's effects on ALP post-hoc in recent clinical trials, then performed mechanistic studies into apabetalone's impact on tissue non-specific ALP (TNALP) expression in mice and cell culture.

Method: Serum ALP was determined in CVD patients in phase 2 trials (3 month ASSERT and 6 month SUSTAIN & ASSURE) and in the phase 3 BETonMACE CVD outcomes trial, including subpopulations with CKD (eGFR$<$60 mL/min/1.73m^2). Apabetalone's effect on expression of TNALP (gene symbol *ALPL*) was examined in mice, cultured primary human hepatocytes (PHH), HepaRG, HepG2, vascular smooth muscle cells (VSMCs), and vascular endothelial cells by real-time PCR. TNALP protein levels were assessed by immunoblots and flow cytometry. ALP enzyme activity was measured in enzymatic assays.

Results: In phase 2 trials, baseline serum ALP independently predicted MACE (hazard ratio [HR] 1.6, 95% CI 1.2-2.2, p=0.001). In the 3 month ASSERT trial, apabetalone dose dependently reduced serum ALP (p$<$0.001 vs placebo). Prominent reductions in ALP were apparent in patients on apabetalone (n=331) vs placebo (n=166) in combined analysis of the ASSURE & SUSTAIN trials (median % change -11 vs -3.2; p$<$0.001). In the subset with CKD, patients on apabetalone (n=69) had greater reduction in serum ALP than placebo (n=22; p=0.008). Strikingly, ALP reductions in phase 2 correlated with reduction in MACE (HR 0.58, 95% CI 0.44-0.77, p$<$0.001). Consistent with phase 2, BETonMACE saw serum ALP reduced by 6.8 U/L with apabetalone (n=1082) vs placebo (n=1070; p$<$0.001) at 24 weeks. At the conclusion of BETonMACE, fewer MACE occurred in the CKD subgroup with apabetalone (n=124) vs placebo (n=164; HR 0.50 95% CI 0.26-0.96 p=0.032). Neither apabetalone nor statins that control low-density lipoprotein cholesterol inhibited recombinant TNALP enzyme activity, implying that decreased serum ALP activity in patients reflected reduction in TNALP production rather than inhibition of the enzyme.

Liver-derived TNALP accounts for ≈50% of circulating ALP. In the liver of mice on high fat diet, apabetalone or JQ1 (BET inhibitors with different chemical scaffolds) reduced *Alpl* mRNA (p$<$0.001) with corresponding trends in TNALP activity. In PHH, HepaRG, & HepG2 cells, apabetalone dose dependently suppressed *ALPL* expression by 60-80%. In HepG2 cells, apabetalone reduced TNALP protein ($>$55%, p$<$0.001), enzyme activity ($>$ 40%; p$<$0.001), and % of TNALP positive cells (15-30%; p$<$0.001). MZ1, which promotes degradation of BET proteins, downregulated *ALPL* / TNALP similar to apabetalone. In VSMCs, apabetalone or JQ1 suppressed *ALPL* gene expression, TNALP protein levels, and enzyme activity, leading to decreases in extracellular calcium deposition. In addition, apabetalone downregulated *ALPL* expression in human aortic, umbilical vein, and brain microvascular endothelial cells by 50-70%.

Conclusion: Apabetalone lowers serum ALP in clinical trials, which is consistent with reduced hepatic production of TNALP - the most abundant ALP isoform. Further, apabetalone downregulates *ALPL* gene expression in vascular cell types while reducing calcification. Together, BET-dependent epigenetic modulation of ALP by apabetalone can affect several pathogenetic processes, and thereby improve cardiovascular outcomes. This study provides insights to the CVD event reductions observed in the CKD subpopulation in the BETonMACE Phase 3 trial.

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SO079 **ASYMPTOMATIC HYPERURICEMIA, A REGULATOR OF INNATE IMMUNITY IN CHRONIC KIDNEY DISEASE.**

Qiuyue Ma[1], Roland Immler[2], Monika Prünster[2], Paola Romagnani[3], Markus Sperandio[2], Hans-Joachim Anders[1], Stefanie Steiger[1]

[1]Hospital of the LMU Munich, Department of Medicine IV, Division of Nephrology, Munich, Germany, [2]Walter-Brendel-Center of Experimental Medicine, Institute of Cardiovascular Physiology and Pathophysiology, Biomedical Center, LMU Munich, Planegg-Martinsried, Germany and [3]University of Florence, Department of Biomedical Experimental and Clinical Sciences "Maria Serio", Florence, Italy

Background and Aims: Asymptomatic hyperuricemia (HU) is common among patients with chronic kidney disease (CKD) but the causative role of HU on CKD progression remains controversial. Two large multi-center randomized controlled trials (RCTs), the CKD-FIX and the PERL study, have now disproven a causal relation. On the other hand, a causative role of persistent HU exists with gouty arthritis but a rapid correction of HU with urate lowering therapy can also elicit acute gout attacks. This suggests a more complex role of HU in this context. Hence, we hypothesized that soluble uric acid (sUA) has immunomodulatory effects on leukocyte function during the immune response to monosodium urate (MSU) crystals.

Method: Alb-creERT2;*Glut9*$^{lox/lox}$ and *Glut9*$^{lox/lox}$ control mice were injected with tamoxifen and placed either on a chow or high-fat diet with inosine to induce HU with or without CKD. After two weeks, MSU crystals or vehicle were injected into air pouches or postcapillary venules in the cremaster muscle of transgenic mice. Leukocyte infiltration and the extent of inflammation were assessed by flow cytometry, intravital microscopy, ELISA, and colorimetric assays. Human blood neutrophils and CD14+ monocytes were isolated from CKD stage G2-4 (n=10) and CKD stage G5 (n=18) patients or healthy individuals (n=15). Neutrophil transwell migration assays were performed and the number of migrated human neutrophils towards chemoattractants determined by flow cytometry. Human blood CD14+ monocytes were treated with MSU crystals or lipopolysaccharide *ex vivo*, and the expression of inflammatory mediators determined by RT-PCR and flow cytometry.

Results: We found that the presence of HU impaired leukocyte recruitment into MSU crystal-injected air pouches of mice with or without CKD. Intravital microscopy revealed that HU specifically reduced leukocyte adhesion, extravasation, and leukocyte-related tissue inflammation. The CKD-mediated attenuation of MSU crystal-induced inflammation was fully reversible by treating HU with urate lowering therapy such as rasburicase. In blood neutrophils isolated from healthy individuals, sUA diminished β2 integrin activation and expression, and hence impaired neutrophil migration e*x vivo*. An impaired migratory capability was also observed in neutrophils from CKD stage G2-4 or G5D patients. Moreover, sUA attenuated Toll-like and TNFα receptor-induced human monocyte activation, a process depending on the intracellular uptake of sUA via the urate transporter SLC2A9 (GLUT9), the only urate transporter expressed by these immune cells.

Conclusion: We identify sUA as an endogenous modulator of innate immunity. HU modulates neutrophil migration by altering efficient β2 integrin activation and suppresses pattern recognition receptor-driven monocyte activation via SLC2A9 in gouty arthritis related or unrelated to CKD (see Figure). This process provides a molecular explanation for several previously unexplained clinical phenomena in the context of gouty arthritis and renal failure.

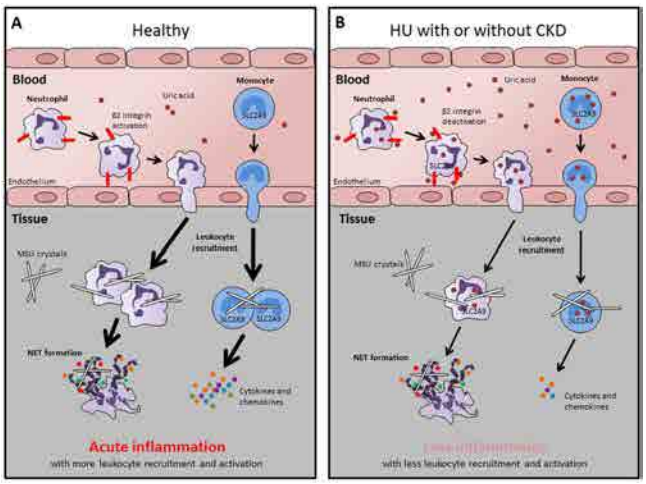


Figure: Schematic of the regulatory effects of HU on innate immunity during CKD. (**A**) During sterile inflammation like acute gouty arthritis, leukocytes migrate from the blood into the inflamed joint. For their migration, neutrophils require β2 integrin expression and activation. Once leukocytes enter the inflamed joint, they get activated by MSU crystals leading to neutrophil extracellular trap (NET) formation and the release of pro-inflammatory mediators by monocytes. (**B**) In the setting of CKD, HU suppresses β2 integrin activation in neutrophils, and induces an unresponsiveness of monocytes following sUA uptake via SLC2A9, which results in impaired leukocyte recruitment. Therefore, the inflammatory response to MSU crystals is diminished due to a lower number of neutrophils that can form NETs and a suppressed SLC2A9-mediated inflammatory monocyte phenotype.

SO080

NOVEL EVIDENCE OF THE "PULMO-RENAL INTERACTION" AS A DISEASE DRIVER IN PATIENTS WITH CKD AND COPD

Stefan Schunk[1], Christoph Beisswenger[1], Christian Herr[1], Felix Ritzmann[1], Triem Sarah[1], David Schmit[1], Albert Omlor[1], Rudolf Jörres[2], Henrik Watz[3], Tobias Welte[4], Claus Vogelmeier[5], Stephen Zewinger[1], Danilo Fliser[1], Robert Bals[1], Thimoteus Speer[1]

[1]Saarland University Hospital, Homburg, Germany, [2]LMU, Munich, Germany, [3]Pneumologisches Forschungsinstitut an der LungenClinic Grosshansd. GmbH, Großhansdorf, Germany, [4]Medizinische Hochschule Hannover, Hannover, Germany and [5]Philipps-University Marburg, Marburg, Germany

Background and Aims: Chronic kidney disease (CKD) and chronic obstructive pulmonary disease (COPD) represent a global public health problem worldwide. As such, both conditions are associated with high disease-related morbidity and mortality. However, it is unclear whether the presence of CKD aggravates the clinical course of COPD and vice versa.

Method: In a novel murine model of cigarette smoke (CS)-induced lung injury combined with an adenine nephropathy model, kidney and lung inflammation, and fibrosis were studied. Moreover, in 2,314 patients with stable COPD enrolled in the prospective, multi-centre COSYCONET study, urinary Dickkopf-3 (DKK3), a biomarker of kidney injury and CKD progression was quantified. The association between urinary DKK3 and trajectories of forced expiratory pressure in 1 second (FEV1) and estimated glomerular filtration rate (eGFR) during a median follow-up of 37.1 months, exercise capacity, risk of exacerbation, and mortality was determined.

Results: In the CKD-COPD animal model, the presence of kidney injury was associated with increased systemic and pulmonary inflammation, impaired pulmonary function, as well as more severe damage of the lung architecture. Moreover, CS enhanced kidney fibrosis. Accordingly, in the COPD patients from the COSYCONET study, higher urinary DKK3 was associated with declining FEV1 during follow-up (OR 3.36, 95% CI 2.22-5.08). Moreover, high urinary DKK3 was associated with higher risk for exacerbation (OR 1.24, 95% CI 1.03-1.50), lower 6-minute walking distance, and higher all-cause mortality (HR 1.49, 95% CI 1.08-2.05). Importantly, high urinary DKK3 was associated with declining eGFR during follow-up (OR 2.23, 95% CI 1.22-4.07) independently from baseline kidney function and proteinuria, which was confirmed by a machine learning approach.

Conclusion: These data uncover a novel pathophysiological link between CKD and COPD. Patient with COPD and concomitant CKD are at high risk for worsening pulmonary function and adverse outcomes. Elevated urinary DKK3 allows identification of COPD patients with progressive CKD. Measurement of urinary DKK3 in patients with COPD may therefore represent a novel tool for risk stratification and the identification of patients, who might in particular benefit from preventive therapeutic strategies to prevent progression of COPD and CKD as well.

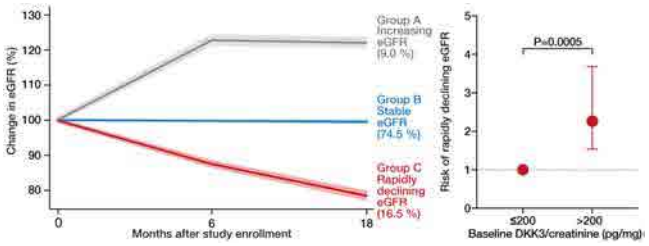


Figure:

SO081

LITHIUM EXPOSURE AND OCCURENCE OF CHRONIC KIDNEY DISEASE IN THE IRISH HEALTH SYSTEM: A COHORT STUDY

Mark Behan[1], Leonard Browne[1,2], Stack Austin[1,2,3]

[1]University of Limerick, Graduate Entry Medical School, Limeirck, Ireland, [2]University of Limerick, Health Research Institute, Limerick, Ireland and [3]University Hospital Limerick, Department of Nephrology, Limerick, Ireland

Background and Aims: Lithium is implicated as a causative factor in the development and progression of chronic kidney disease (CKD). Few studies have assessed the independent impact of plasma levels and duration of lithium therapy on CKD progression. We examined the influence of lithium on CKD progression in the Irish health system.

Method: We utilised data from the Irish Kidney Disease Surveillance System (IKDSS) to explore associations of lithium levels and duration of exposure with kidney function in a regional cohort. A retrospective cohort study was conducted between 1999 to 2014 from the Midwest Region. All adult patients with lithium levels were identified and followed longitudinally. Kidney function was assessed at baseline and longitudinally using serum creatinine and estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI. Patients with < 2 lithium values, missing data on creatinine were excluded. The index date was the date of the first lithium blood test. Toxicity from lithium was defined as levels >1.2mmol/L as per NICE guidelines while duration of treatment was calculated based on patient –years of exposure as determined by positive blood lithium levels. Relationships between baseline kidney function, lithium levels, duration of exposure and each patients most recent eGFR value on follow up were assessed using multiple linear regression

Results: We identified 1,978 patients exposed to lithium from 1999-2014, mean age was 47.4 (15.6), 45.1% were men, eGFR [median (IQR)] at baseline was 84.4 (32.1) ml/min1.73㎡ and the median duration of exposure was 3.0 years (IQR=4 years). Frequency of lithium testing increased from 1.77 in 1999 to 2.66 in 2014. In multiple linear regression, the final eGFR on follow-up was significantly lower in older patients (-0.48 ml/min/1.73㎡ per year increase in age), P<0.001; in patients with elevated baseline lithium levels (-2.18 ml/min1.73㎡ lower per unit increase), P<0.05, with long duration of exposure (-1.42 ml/min/1.73㎡ lower for each year on lithium), P<0.001, and for patients with low GFR at baseline (P<0.001). Together these variables explained 58% of the variation in the final model.

Conclusion: Both the magnitude of and the duration of lithium exposure are both independently associated with CKD progression among lithium users in the Irish health system. Higher baseline lithium values had a more deleterious impact on kidney function. Continued efforts should be expended in minimising the risks of lithium induced nephrotoxicity through switching to alternatives and dose reduction when over possible.

Funding: This study is funded by the Health Research Board and the Midwest Research and Education Foundation (MKid).

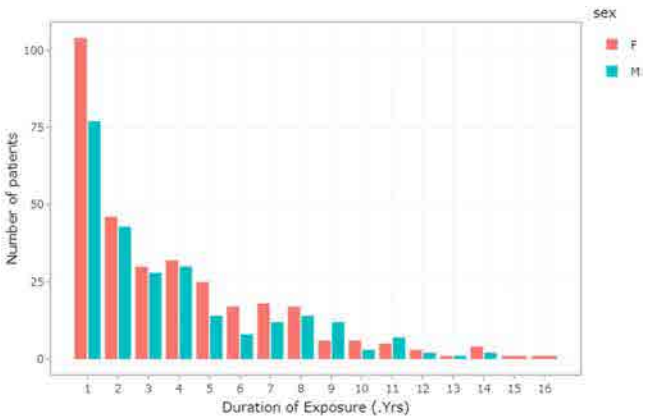


Figure 1. Distribution of the duration of lithium treatment.

SO082 **LATENT TRANSFORMING GROWTH FACTOR BETA BINDING PROTEIN (LTBP4) CAN REGULATE RENAL FIBROSIS AND ALTER INFLAMMATION AND MITOCHONDRIAL DYSFUNCTION IN CHRONIC KIDNEY DISEASE (CKD)** ÷ ÷

Chi-Ting Su[1,2], Tzu-Ming Jao[3], Jenq-Wen Huang[4]

[1]National Taiwan University Hospital, Yun-Lin & Taipei Branch, Nephrology, Taiwan, R.O.C., [2]University of Pittsburgh, Human Genetics, Graduate School of Public Health, Pittsburgh, United States of America, [3]National Taiwan University, Graduate Institue of Toxicology, Taipei, Taiwan, R.O.C. and [4]National Taiwan University, Internal Medicine, Taipei, Taiwan, R.O.C.

Background and Aims: Transforming growth factor beta (TGF-beta) has been well known as a key factor for fibrosis and inflammation. LTBPs regulate TGF-beta signalling in complicated ways. Disruption and loss of LTBP4 expression is associated with abnormal accumulation of extracellular matrix (ECM) and altered TGF-beta activation. However, the role of LTBP4 in chronic kidney disease remains largely unknown. We aim to explore the mechanisms of LTBP4-related regulation in kidney disease.

Method: To investigate the impact of LTBP4 on tubulointeresitial fibrosis (TIF), we generated LTBP4-overexpression human renal proximal tubule cells (HK-2), treated with exogenous TGF-beta and established a fibroblasts-HK-2 co-culture system using rat fibroblasts (NRK-49F) and HK-2 cells. Moreover, to create TIF model, we performed unilateral ureteral ligation (UUO) in *Ltbp4S*-/- mice and wild-type (WT) mice to check ECM deposition and phenotypic alterations. In addition, we performed RNA-Sequencing analysis to understand transcriptomic changes associate with LTBP4 overexpression.

Results: Up-regulation of Ltbp4 in fibrotic kidney was noted in TIF model with UUO and in renal tissue with diabetic nephropathy. LTBP4-overexpression reduced epithelial-mesenchymal transition (EMT) with showing increased epithelial-cadherin, reduced vimentin and collagen I in the co-culture system. Moreover, higher expression of fibronectin, collagen I and alpha-smooth muscle actin (alpha-SMA) were noted in fibrotic kidneys in *Ltbp4S*-/- mice compared with changes in WT mice, suggesting inflammation condition could be altered by the absence of Ltbp4S. The inflammatory change in renal tissue in UUO model was studied with F4/80 stain. Increased macrophage infiltration and increased monocyte chemoattractant protein-1 (MCP-1) expression were detected in *Ltbp4S*-/- mice compared with that in WT mice. In addition, LTBP4-overexpression reduced mitochondrial biogenesis.

Conclusion: Ltbp4 acted as a regulator of fibrosis and inflammation in fibrotic kidneys. TGF-beta- induced EMT were clearly enhanced in ltbp4 deficient environments, accompanied with reduced macrophage infiltration, which could be the major mechanism related to LTBP4/TGF-beta pathways. Furthermore, altered ATP production and usage as well as mitochondria respiration could be regulated by LTBP4 in renal failure.

CARDIOVASCULAR DISEASES IN DIALYSIS

SO083

VASCULAR STIFFNESS ESTIMATED NON-INVASIVELY USING PULSE WAVE PROPAGATION CORRESPONDS TO VASCULAR BIOPSY FINDINGS

Malgorzata Debowska[1], Bengt Lindholm[2], Lu Dai[2], Jacek Waniewski[1], Abdul Rashid Tony Qureshi[2], Peter Stenvinkel[2], Jan Poleszczuk[1]

[1]Nalecz Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Department for Mathematical Modeling of Physiological Processes, Warsaw, Poland and [2]Karolinska Institutet, Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden

Background and Aims: Patients with chronic kidney disease (CKD) are at high risk of cardiovascular disease (CVD) due to complex processes in the uremic milieu linked to CKD - mineral and bone disorders (CKD-MBD). These processes alter structure and function of heart and vasculature e.g. by causing ectopic calcification that makes vessels stiffer thus affecting pulse (pressure) wave profiles. Our study aimed to derive patient-specific parameters using pulse wave propagation model including arterial stiffness and compare those parameters with cardiovascular status including biopsy proven severity of vascular calcification.

Method: In a group of 81 CKD (stage 5) patients undergoing living donor kidney transplantation, the degree of medial calcification in epigastric artery was histologically graded as 0 (n=22), 1 (n=31), 2 (n=21) and 3 (n=7) representing *no*, *minimal*, *moderate* and *extensive* signs of vascular calcification, respectively. Concomitantly 82 features were determined including demographic and anthropometric features, blood biomarkers related to CKD - MBD and other measurements. Pressure profiles (circles in Fig. 1) in radial artery were recorded using applanation tonometer (SphygmoCor, AtCor Medical, Australia) and used to derive patient-specific parameters from a mathematical model describing blood flow and pressure in 55 major arteries.

Results: The model was able to reproduce all recorded pressure profiles with high accuracy with average relative error less than 8% (compare solid line and circles in Fig. 1). Vascular stiffness, derived from the model, in arterial branches located in the area of artery for which calcification was histologically quantified, was significantly higher for higher calcification score (p-value < 0.001). The estimated stiffness correlated with the level of troponin T (rho=0.65**), advanced glycation end-products (by skin autofluorescence, rho=0.55*), osteoprotegerin (rho=0.44**), hepcidin 25 (rho=0.32*, interleukin 6 (rho=0.29*) and choline (rho=0.28**), (‘**’ and ‘*’ denote p-value < 0.01 and 0.05, respectively). Stiffer arteries were found in patients with diagnosed CVD (p-value < 0.01).

Conclusion: We demonstrate that a mathematical model based on a single peripheral recording of pulse pressure profile has the potential to provide information about cardiovascular status in the individual patient. Also, the estimated stiffness correlates well with several well-established CVD risk factors. Our mathematical model of the arterial tree, if validated in larger cohorts of patients, may be used as computational tool to predict vascular stiffness without need of arterial biopsy.

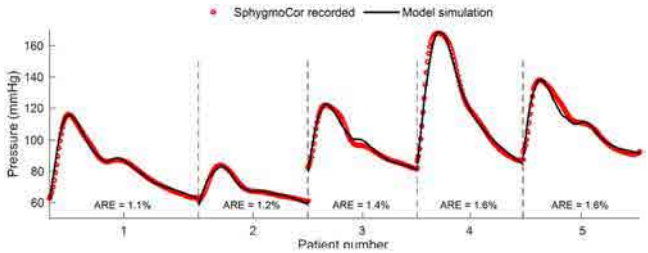


Fig. 1. Examples of recorded pressure waves in radial artery (circles) and their reproduction by mathematical model (solid line) in 5 patients. ARE: average relative error.

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SO084 **SILDENAFIL DRUG IN HEMODIALYSIS PATIENTS WITH PULMONARY HYPERTENSION**

Maha Abdelmoneim Behairy Said[1], Tamer El Said[1], Abdelrahman Elbraky[1,2], Hazem Khorshid[2], Waleed Anwar[1], Gamal Mady[1]

[1]Ain Shams University, Internal medicine and Nephrology, Cairo, Egypt and [2]Ain Shams University, cardiology, Cairo, Egypt

Background and Aims: Pulmonary hypertension (PH) is not an uncommon progressive condition in prevalent hemodialysis (HD) patients, associated with high morbidity and mortality. Sildenafil drug has limited studies about the efficacy of the drug and optimal dose among prevalent HD patients with PH. Aim of the study to assess the effects of sildenafil drug on estimated Pulmonary Artery pressure value (ePAP) mmHg via transthoracic Doppler Echocardiography and 6-minute walk test (6MWT) among hemodialysis patients with pulmonary hypertension.

Method: Randomized, double-blind, placebo-controlled clinical trial, from December 2018 to May 2019, involving 60 eligible patients on regular adequate HD with PH, estimated Pulmonary Artery Pressure (ePAP) $\geq$35 mmHg via Doppler echocardiography. HD patients with mean age 52.6$\pm$10.8 year divided randomly into 3 groups: Group 1 (20 patients) received 25 mg sildenafil, group 2 (20 patients) received 50 mg sildenafil and group 3 (20 patients) who received placebo as daily dose treatment for 3 months duration. Every patient in the study was subjected to full history taking and clinical examination. Exclusion Criteria: Current treatment of pulmonary hypertension, patient with evident history of cardiac diseases or chronic pulmonary diseases or systemic autoimmune diseases, portal hypertension, HIV, patients with uncontrolled hypertension or severe anaemia or hypersensitivity to sildenafil, treatment with any drugs that may interact with sildenafil all were excluded from the study. Transthoracic echocardiography was done at the begging of the study and after three months in mid-week non-dialysis day for assessment of the change in ePAP, pulmonary artery pressure calculated using the modified Bernoulli equation, and assessment of right ventricular functions . Exercise capacity assessment by 6MWT to assess the clinical response to the drug, was done for every patient at the start of the study and after 3 months of treatment. Clinically meaningful change estimate for the 6MWT considered as increase more than 30 meters.

Results: Significant increase in mean of 6 MWT in both group 1,2 received 25 mg,50 mg sildenafil respectively after 3 m duration of treatment versus non-significant change in placebo group as basal 6 MWT was (171 $\pm$45, 214 $\pm$58, 175 $\pm$39) meters in group 1,2 and placebo group respectively (p>0.05). Means 6 MWT post-treatment were (205 $\pm$57, 258 $\pm$59, 182 $\pm$49) meters (P<0.001) in group 1, 2&3 respectively, as post Hoc test results, showed significant increase in 6MWT2 in group 2 in comparison to group 1 and placebo group *(P<0.01)*, as shown in figure (1).There was a significant decrease in e PAP in each group of studied groups after treatment (P<0.01). As mean basal ePAP1 measures were (48 $\pm$9, 43.5 $\pm$16, 48.5 $\pm$12) mmHg in group 1,2,3 respectively (P>0.05).There were no significant differences between the studied groups regarding means of ePAP2 post-treatment were (42 $\pm$9, 39 $\pm$15, 44.5$\pm$8) mmHg in group 1,2,3 respectively (P>0.05). However, the degree of severity of PH was more improved after treatment duration with sildenafil as in group 1 there were 5 patients downgraded from moderate to mild and 2 patients downgraded from severe to moderate after treatment. In group 2 there were 4 patients downgraded from moderate to mild PH and 2 patients downgraded from severe to moderate PH. In 3rd group (placebo group) only one patient downgraded from moderate to mild PH. There were 4 patients dropouts from the study two of them from group 2 (receiving 50mg) due to sildenafil related side effects appeared through the study.

Conclusion: This a clinical trial confirmed the efficiency of both 50mg and 25mg sildenafil daily dose in reducing e PAP and improving functional exercise capacity in chronic haemodialysis patients with pulmonary hypertension disease.

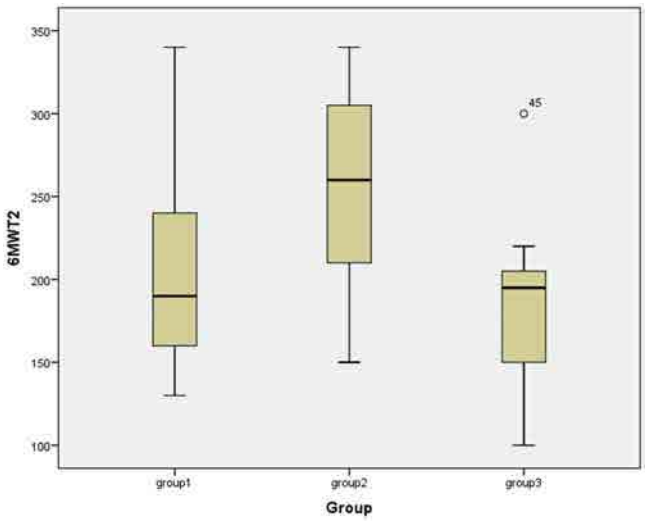


Figure:

SO085

CIRCULATING PCSK9 LEVEL PREDICTS RISK OF CARDIOVASCULAR EVENTS AND DEATH IN HEMODIALYSIS PATIENTS

Hyeon Seok Hwang[1], Jin Sug Kim[1], Yang-Gyun Kim[1], So-Young Lee[2], Shin Young Ahn[3], Hong Joo Lee[4], Dong-Young Lee[5], Sang ho Lee[1], Ju-Young Moon[1], Kyung Hwan Jeong[1]

[1]Kyung Hee University, Internal Medicine, Division of Nephrology, Seoul, Korea, Rep. of South, [2]CHA Bundang Medical Center, Internal Medicine, Division of Nephrology, Seoul, Korea, Rep. of South, [3]Korea University College of Medicine, Internal Medicine, Division of Nephrology, Seoul, Korea, Rep. of South, [4]Seoul Red Cross Hospital, Internal Medicine, Division of Nephrology, Seoul, Korea, Rep. of South and [5]Veterans Health Service Medical Center, Internal Medicine, Division of Nephrology, Seoul, Korea, Rep. of South

Background and Aims: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a promising new target for prevention of cardiovascular (CV) events. However, the clinical significance of circulating PCSK9 is unclear in hemodialysis (HD) patients.

Method: A total of 353 HD patients were prospectively enrolled from June 2016 to May 2018 in a K-cohort. Plasma PCSK9 level was measured at the time of study enrollment. Patients were classified into three groups based on PCSK9 tertile. The primary endpoint was defined as composite of CV event and death from any cause.

Results: Plasma PCSK9 level was positively correlated with total cholesterol level in patients with statin treatment. However, PCSK9 was not related to plasma inflammatory (high-sensitivity C-reactive peptide, monocyte chemoattractant protein-1, interleukin-6) or calcification-related markers (osteoprotegerin and receptor activator of nuclear factor kappa-B ligand). Multivariate linear regression analysis revealed that baseline statin treatment and serum glucose, albumin, and total cholesterol were independent determinants of circulating PCSK9 levels. In Cox-regression analysis, PCSK9 tertile 3 was associated with a 1.99-fold risk for composite events (95% CI, 1.08–3.66), and it was associated with a 2.26-fold risk for CV events (95% CI, 1.11–4.62) after adjustment for multiple variables. PCSK9 tertile 3 provides additional prognostic power to predict composite events in subgroups with higher levels of high-sensitivity C-reactive peptide and LDL.

Conclusion: In conclusion, higher circulating PCSK9 level independently predicted CV events and death in HD patients. These results suggest the importance of future studies regarding the effect of PCSK9 inhibition on reduction of CV events.

SO086

SNF472 CONSISTENTLY SLOWS PROGRESSION OF CORONARY CALCIFICATION IN PATIENTS ON HEMODIALYSIS: SUBGROUP ANALYSIS OF THE CALIPSO STUDY

Paolo Raggi[1,2], Antonio Bellasi[3], David Bushinsky[4], Jordi Bover[5], Mariano Rodriguez[6], Markus Ketteler[7], Smeeta Sinha[8], Rekha Garg[9], Claire Padgett[9], Joan Perelló[10,11], Alex Gold[9,12], Glenn Chertow[12]

[1]Mazankowski Alberta Heart Institute, Edmonton, Canada, [2]University of Alberta, Medicine, Edmonton, Canada, [3]ASST Papa Giovanni XXIII, Research, Innovation and Brand Reputation Unit, Bergamo, Italy, [4]University of Rochester Medical Center, Medicine, Rochester, United States of America, [5]Fundació Puigvert and Universitat Autònoma, IIB Sant Pau, REDinREN, Nephrology, Barcelona, Spain, [6]Hospital Universitario Reina Sofia, IMIBIC, REDinREN, Nephrology, Córdoba, Spain, [7]Robert-Bosch-Krankenhaus, General Internal Medicine and Nephrology, Stuttgart, Germany, [8]Salford Royal NHS Foundation Trust, Renal Medicine, Salford, United Kingdom, [9]Sanifit Therapeutics, Research and Development, San Diego, United States of America, [10]Sanifit Therapeutics, Research and Development, Palma, Spain, [11]University of the Balearic Islands, Palma, Spain and [12]Stanford University, Medicine, Palo Alto, United States of America

Background and Aims: In the CaLIPSO study, SNF472 significantly attenuated progression of coronary artery calcium (CAC) volume score compared with placebo. This pre-specified analysis examined the effect of SNF472 on CAC progression in key subgroups of patients in CaLIPSO.

Method: Patients with a CAC Agatston score of 100 to 3500 at baseline were randomized to SNF472 300 mg (n=92), SNF472 600 mg (n=91), or placebo (n=91), infused during hemodialysis (HD) thrice weekly for 52 weeks. Patients received standard of care therapy, including phosphate binders and calcimimetics as determined by investigator. The primary endpoint (change in log CAC volume score from baseline to week 52 in the combined dose groups vs placebo) was analyzed for patients who received SNF472 or placebo and had an evaluable CT scan post-randomization (modified ITT population). Sensitivity analysis was also performed for the per protocol population of patients that met entry criteria, received 80% of scheduled treatment, completed the study procedures, and had both a baseline and week 52 evaluable CT scan. The analysis plan pre-specified key subgroups: age, sex, diabetes, dialysis vintage, and arteriosclerotic cardiovascular disease (ASCVD), as well as baseline use of non-calcium phosphate binders, calcium-based phosphate binders, calcimimetics, activated vitamin D, warfarin, or statins.

Results: Demographics and disease characteristics were similar across the treatment groups. Age (mean±SD) at baseline was 63.6±8.9 years and 39% of the patients were female; 62% had diabetes and 41% had prior ASCVD. Median dialysis vintage was 42.4 months; 33% had received hemodialysis for ≥5 years. Concomitant medications at baseline were: non-calcium phosphate binders, 62%; calcium-based phosphate binders, 28%; calcimimetics, 31%; activated vitamin D, 51%; warfarin, 8%; and statins, 64%. CAC volume progression was 11% for the combined dose groups and 20% for placebo (p=0.016). Treatment differences for CAC volume score progression from baseline to week 52 were similar across the subgroups (FIGURE). All interaction p-values were non-significant, and comparisons favored SNF472 vs placebo in each subgroup for both the modified ITT and per protocol population.

Conclusion: SNF472 treatment for 52 weeks attenuated CAC progression compared with placebo in all subgroups of the CaLIPSO study. These results support the potential benefit of SNF472 across a broad population of patients with cardiovascular calcification. Future studies are needed to determine the effects of SNF472 on cardiovascular events in patients receiving HD.

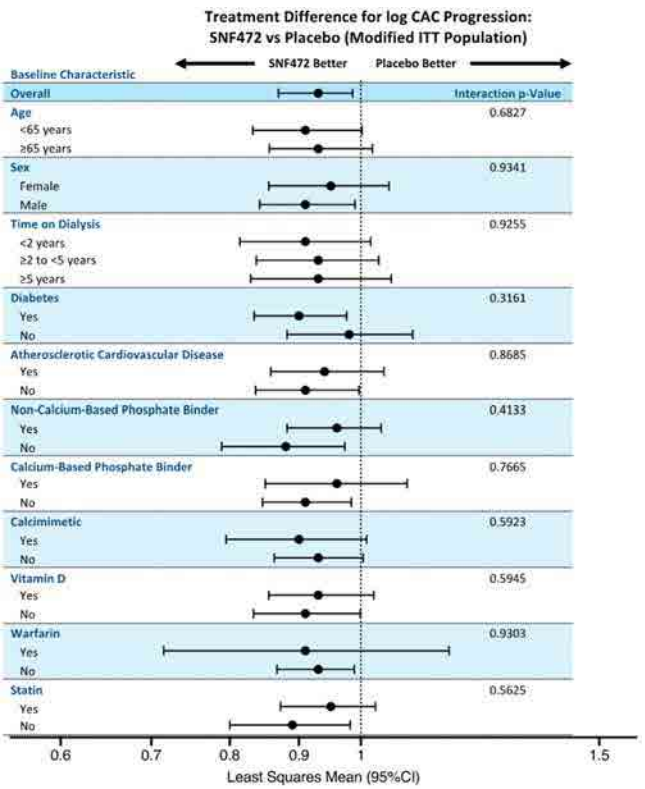


Figure:

SO087

RISK OF INTRADIALYTIC HYPOTENSION BY DAY OF THE WEEK IN MAINTENANCE HEMODIALYSIS

Simon Correa[1,2], Xavier E. Guerra-Torres[3], Sushrut S Waikar[1,2,4], Finnian R. Mc Causland[1,2]

[1]Brigham and Women's Hospital, Division of Renal Medicine, Boston, United States of America, [2]Harvard Medical School, [3]Hospital Universitario Príncipe de Asturias, Nephrology Section, Alcala de Henares, Spain and [4]Boston University Medical Center, Renal Section, Boston, United States of America

Background and Aims: Intradialytic hypotension (IDH) affects up to 50% of maintenance hemodialysis (HD) patients and is associated with a higher risk of cardiovascular (CV) events and mortality. CV events are more common on the days of dialysis and are most pronounced following the longer interdialytic interval. We wished to investigate if the rates of IDH differed according to dialysis day.

Method: We examined data from adult patients undergoing in-center thrice-weekly maintenance HD (N= 975 patients/n=59,004 sessions from a large dialysis organization [LDO] and N=1,838 patients/n=64,407 sessions from the Hemodialysis [HEMO] Study). We fit random effects logistic regression models to determine the association of day of HD (Mon/Tue [HD_1]; Wed/Thu [HD_2]; Fri/Sat [HD_3]) with various definitions of IDH. Models were adjusted for age, sex, race, Kt/V, membrane flux, heart failure, peripheral vascular disease, diabetes, access type (catheter vs. fistula vs. graft), pre-dialysis blood urea nitrogen, ultrafiltration rate, pre-HD systolic blood pressure (SBP). IDH definitions included Nadir90 (nadir intra-HD SBP <90mmHg), Nadir90/100 (nadir intra-HD SBP <90mmHg if pre-HD SBP <160mmHg or <100mmHg if pre-HD SBP ≥160mmHg), Fall20 (pre-SBP minus nadir SBP ≥20mmHg) and Fall30 (pre-SBP minus nadir SBP ≥30mmHg).

Results: Mean age was 60 years, 44% were female and 38% were black in the LDO cohort, while mean age was 58 years, 56% were female and 63% were black in HEMO. Nadir90 occurred in 15% of LDO and 11% of HEMO sessions; Nadir90/100 occurred in 18% of LDO and 14% of HEMO sessions; Fall20 occurred in 76% of LDO and 68% of HEMO sessions; Fall30 occurred in 60% of LDO and 50% of HEMO sessions. Overall, a monotonic increase in the risk of IDH was observed for HD_2 and HD_3 compared with HD_1 for all IDH definitions in both cohorts (see Table and Figure).

IDH definition	Study Cohort	HD1	HD2		HD3	
		OR (95% CI)	OR (95% CI)	P-value	OR (95% CI)	P-value
Nadir90	LDO	Ref	0.98 (0.91-1.05)	0.55	1.08 (0.94-1.24)	0.26
	HEMO	Ref	1.10 (1.02-1.18)	0.01	1.26 (1.13-1.40)	<0.001
Nadir90/100	LDO	Ref	1.04 (0.97-1.11)	0.26	1.09 (0.97-1.24)	0.16
	HEMO	Ref	1.09 (1.02-1.17)	0.008	1.31 (1.19-1.45)	<0.001
Fall20	LDO	Ref	1.19 (1.11-1.26)	<0.001	1.21 (1.08-1.36)	0.001
	HEMO	Ref	1.20 (1.14-1.26)	<0.001	1.35 (1.25-1.47)	<0.001
Fall30	LDO	Ref	1.17 (1.10-1.24)	<0.001	1.28 (1.15-1.43)	<0.001
	HEMO	Ref	1.18 (1.12-1.24)	<0.001	1.35 (1.25-1.46)	<0.001

Conclusion: We observed a consistent monotonic increase in the risk of IDH for HD_2 and HD_3, compared with HD_1 in two separate cohorts of maintenance HD patients. Potential explanations may relate to progressive reduction in post-HD weight during the dialytic week, or perhaps more aggressive ultrafiltration in advance of the longer interval. Further research to determine the underling mechanisms is necessary to guide practicing nephrologists when individualizing the HD prescription.

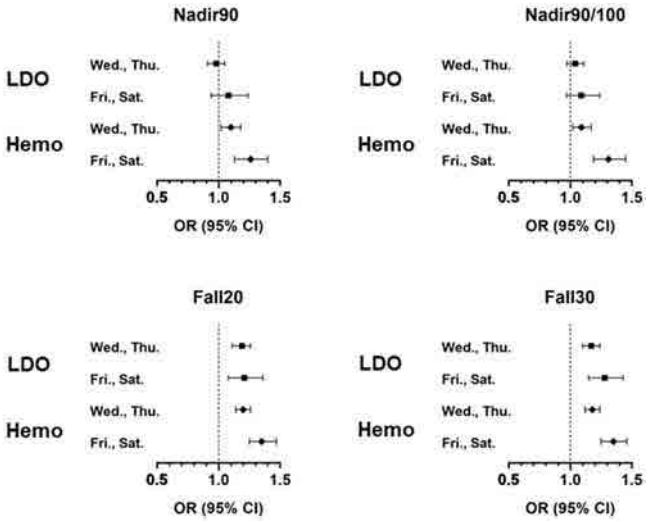


Figure:

SO088 **BURDEN OF VALVULAR HEART DISEASE IN HAEMODIALYSIS RECIPIENTS**

Mohamed Elewa[1,1], Anu Jayanti[1]

[1]*Manchester Royal Infirmary, Renal Medicine, Manchester, United Kingdom*

Background and Aims: Valvular heart disease (VHD) is highly prevalent in maintenance haemodialysis patients. This high prevalence is associated with poor outcomes and higher mortality [Samad et al., Journal of the American Heart Association, 6 (10), (2017)]. Previous large studies found VHD prevalence between 14% and 16% among prevalent haemodialysis patients [2018 USRDS Annual Data Report | Vol 2] [Hickson et al., Journal of the American College of Cardiology, 67(10), (2016)]. KDIGO consensus group identified several evidence gaps where research is necessary in order to improve our understanding of diagnosis and management of VHD in this population [Marwick et al., Kidney international, 96 (4), (2019)]. The aim of our study is to assess the burden of VHD in a large cohort of haemodialysis recipients in one center in the United Kingdom (UK).

Method: This is a retrospective cross-sectional evaluation of valvular heart disease in prevalent haemodialysis patients. Prevalent haemodialysis recipients were defined as patients established on haemodialysis for $\geq$ 3 months. Echocardiographic data was collected for all patients. Patients were considered to have VHD if they had significant aortic (AVD) or mitral valve disease (MVD) based on standard echocardiographic criteria. These valvular diseases are classified as mild, moderate or severe. Here, we report some descriptive statistics from our data.

Results: The study group includes 544 prevalent haemodialysis patients. Mean age was 62 years (SD 15.28), 40% females and 60% were males. Median dialysis vintage was 1.9 years (IQR 1, 3.2) [Range: 0.2, 10.2]. 14 % of patients received home-based hemodialysis and 86% received in-center dialysis. 30% of patients were actively awaiting a transplant. A total of 1155 echocardiography studies were reviewed. Of the 425 patients who had an echocardiogram; 34% (n=143) had evidence of VHD as defined above. Significant AVD was identified in 18% of patients (n=78). The dominant lesion was aortic regurgitation in 11%, and aortic stenosis in 7% of patients. 20% of patients (n=85) had significant MVD with mitral valve stenosis in 0.7% of patients (n=3) and mitral regurgitation in 18% of patients. 5% of patients had cardiothoracic intervention (n=21) for valvular heart disease, which included aortic valve replacement (n=9), transcatheter aortic valve implantation (TAVI) (n=9), and mitral valve replacement (n=3).

Conclusion: We found that at least one third (34%) of patients in this cohort had significant VHD- higher than the previously published figures. The numbers are likely to be higher, if echocardiogram information was available for all patients in the study. Timely echocardiographic studies and follow-up imaging for those with established disease are essential to identify patients with significant VHD, in order to establish impact of disease on both dialysis delivery and patient symptoms.

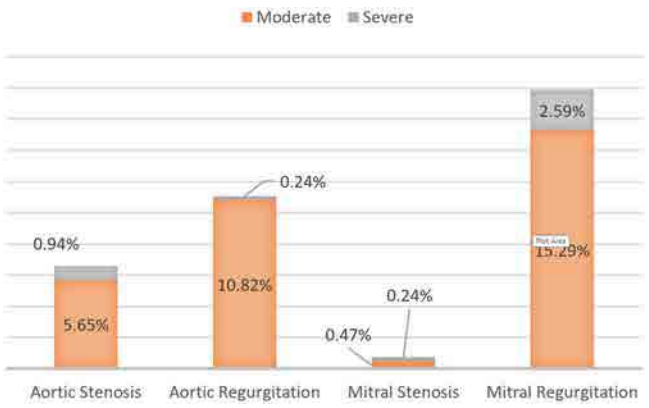


Figure: Burden of valvular heart disease in haemodialysis patients (n=425)

NOVELTIES IN CYSTIC DISEASE

SO089 THE EVOLUTION OF THE RENAL FUNCTION IN A COHORT OF ITALIAN PATIENTS WITH ADPKD: AN ANALYSIS BY THE JOINT MODEL

Marco Galliani[1], Elio Vitaliano[1], Silvana Chicca[1], Antonio Paone[1], Luca Di Lullo[2], Maria Elena Tosti[3], Alfonso Mele[4], Luca Calvaruso[5], Graziella D'Arrigo[6], Giovanni Luigi Tripepi[6], Carmine Zoccali[6]

[1]Hospital Sandro Pertini, UOC Nefrologia, Dialisi e Litotrissia, Roma, Italy, [2]OSPEDALE - L. Parodi Delfino, UOC Nefrologia e Dialisi, Colleferro, Italy, [3]Istituto Superiore di Sanita, National Center for Global Health, Roma, Italy, [4]Istituto Superiore di Sanita, Roma, Italy, [5]Agostino Gemelli University Polyclinic, UOC Nefrologia, Roma, Italy and [6]Consiglio Nazionale Delle Ricerche-IFC, Clinical Epidemiology of Renal Diseases and Hypertension, Reggio Calabria, Italy

Background and Aims: The natural history of ADPKD has been defined in numerous studies in various countries and in various genetic and environmental contexts but the problem has not yet been studied in sufficiently large studies in the Italian population. We have studied the evolution of ADPKD in a cohort of 445 incident patients enrolled in a time span between 2012 and 2016 in 28 nephrological centers in 3 regions of central Italy. The main demographic and clinical characteristics of this cohort are reported below.

[GRAPHICS]

Method: The analysis was carried out on a sample of 296 patients with at least 2 creatinine measurements prior to ESKD and with eGFR at onset $\geq$45 ml/min/1.73m^2. The median follow-up was 15 years (range 1-42 years). The analysis of the data was carried out with the Joint model, an approach that allows the simultaneous modeling of longitudinal (repeated over time) and time to event ESKD or GFR$<$45 ml/min/1.73m^2 data. This approach produces two sub-models: a longitudinal model (mixed linear model, sub-model A in the table) and a time to event model (Cox model, survival sub-model B in the Table). The two models are mutually associated through an analytical structure that quantifies the relationship between the variables of interest.

[GRAPHICS]

[GRAPHICS]

Results: The average eGFR decline in the entire population was -2.13 ml/min/1.73m^2/year. In males the decline in GFR was significantly higher than in females (M: -2.63 ml/min/1.73m^2; in F -1.74 ml/min/1.73m^2/year, p $<$0.005) while it was not significant differences are observed for the different age groups considered separately in the two sexes (p = 0.158 in the M; p = 0.625 in the F).

In the longitudinal model the age at diagnosis $>$30 years and the presence of hypertension were significantly associated with an accelerated decline in GFR and patients older than 50 years exhibited a reduction by 35 ml/min/1.73m^2 greater than those younger than 30 years. In the survival model the GFR trend and sex were associated with the risk of renal survival. For each incremental baseline unit of GFR the risk for ESKD decreased by 16% (HR: 0.84) and in females the risk was about one third compared to males (HR: 0.31).

Conclusion: This study, the first to apply the joint model in the analysis of the evolution of renal function in ADPKD and the first in a sizeable cohort in Italy, provides important information on the progression of polycystic kidney disease in an incident series of Italian patients with ADPKD.

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SO090 EVALUATING PAIN IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Ragada El-Damanawi[1], Tess Harris[2], Laura Cowley[3], Fiona Karet[4], Michael Lee[5], Thomas Hiemstra[1]

[1]Cambridge Clinical Trials Unit, University of Cambridge, United Kingdom, [2]PKD Charity, London, United Kingdom, [3]Patient Led Research Hub, United Kingdom, [4]University of Cambridge, Division of Renal Medicine and Departments of Medical Genetics, United Kingdom and [5]University of Cambridge, Department of Anaesthesia, United Kingdom

Background and Aims: Chronic pain is prevalent in Autosomal Dominant Polycystic Kidney Disease (ADPKD) and is associated with a substantial quality of life burden. Literature describing ADPKD-related chronic pain (ACP) is limited, and generic pain management strategies are suboptimal with patients often reporting inadequate relief. Furthermore, the absence of a validated and widely accepted pain assessment tool (PAT) in ADPKD has posed a significant barrier to better pain management and research. We established an ADPKD PAT (APAT) and confirmed its feasibility and validity through administration to ADPKD patients participating in a randomised high water intake trial (NCT02933268).

Method: A collaboration of key stakeholders (patients, ADPKD experts, trialists and pain specialists) constructed an ADPKD pain conceptual framework consisting of eight prioritized pain assessment domains. We constructed an APAT from components of previously validated pain assessment tools covering each of the prioritized pain domains. The finalized APAT was administered to participants in a feasibility trial which randomised adult ADPKD patients with an eGFR$\geq$20mls/min/1.73m^2 to prescribed high water intake (HW) or ad libitum water intake (AW group) over eight weeks. Participants were asked to complete the APAT at least twice (baseline and week 8), although more frequent submissions were permitted.

Results: 93% (39/42) of trial participants with CKD stages 1-4 completed a total of 129 questionnaires. Each participant completed a median of 3 (range 1-10) questionnaires. In terms of baseline characteristics; mean age of respondents was 47$\pm$13 years, 90% (35) were White British ethnicity, and 59% (23) were female. Median disease duration was 14.2 (IQR 7.0-25.9) years, 69% had enlarged kidneys, 64% had hypertension and hepatic cysts were present in 59%.

Pain (52%) and associated analgesic use (29%) were prevalent. Participants with pain were more likey to report interference with mobility (25% vs 0%), self-care (20% vs 0%) and usual activities (31% vs 1%) compared to those with no pain ($p<0.001$. Pain was also associated with a higher risk of anxiety and depression (RR 2.97, CI 1.70-5.20, p=0.000). Pain severity was predicted by traditional risk factors of disease progression including increasing age (OR 1.07, p=0.009), eGFR<60mls/min/1.73m2 (OR 5.45, p=0.021), and hypertension (OR 12.11, p=0.007), but not kidney size, consistent with findings of previous studies. Neuropathic descriptors were not commonly used, while continuous and intermittent descriptors were more frequently selected by patients to describe their pain quality (figure).

The APAT achieved good internal consistency (Cronbach's alpha coefficient =0.91) and test-retest reliability was demonstrated with domain intra-class correlation coefficients ranging from 0.62-0.90.

Conclusion: A bespoke APAT including components of previously validated pain assessment tools was reliable in evaluating pain in patients with ADPKD, and was acceptable to participants. Pain was prevalent among participants and associated with a substantial emotional and physical burden. The APAT represents a viable instrument for standardised evaluation of ADPKD pain in observational and interventional research.

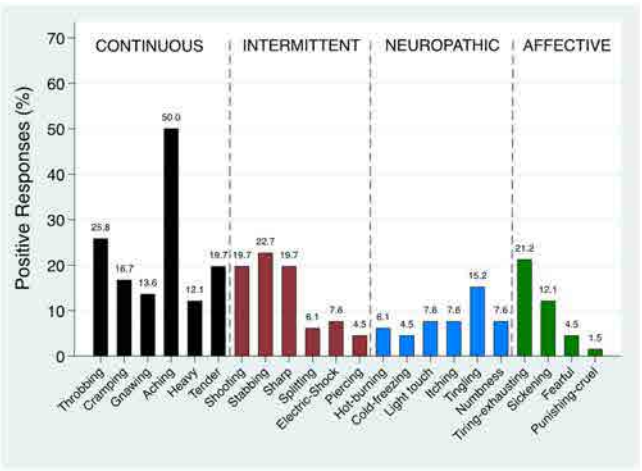


Figure:

SO091

URINE-TO-PLASMA UREA RATIO, AS SURROGATE MARKER FOR URINE CONCENTRATING CAPACITY, IS ASSOCIATED WITH DISEASE PROGRESSION IN ADPKD

Judith E. Heida[1], Ronald Gansevoort[1,2], Lianne Messchendorp[1], Esther Meijer[1], Niek F. Casteleijn[1], Wendy E. Boertien[1], Debbie Zittema[1]

[1]University Medical Center Groningen, Nephrology, Groningen, Netherlands and [2]On behalf of the DIPAK consortium

Introduction Predicting disease progression in autosomal dominant polycystic kidney disease (ADPKD) patients poses a challenge, especially in early stage disease when renal function is not yet affected. The ongoing formation and growth of cysts causes the urine concentrating capacity to decrease from early on in the disease. We therefore hypothesized that the easy and inexpensive to measure urine-to-plasma urea ratio (UPU ratio), which is assumed to be surrogate for maximal urine concentrating capacity, can be used as marker to predict disease progression in ADPKD.

Methods The UPU ratio was calculated by dividing urea concentration in a fasting morning spot urine sample by plasma urea concentration adjusted for plasma creatinine concentration. First, we validated the UPU ratio in 30 ADPKD patients who underwent a prolonged water deprivation test to measure the maximal urine concentrating capacity. Thereafter, the association of the UPU ratio with renal outcome was evaluated in 583 ADPKD patients participating in the DIPAK observational cohort (inclusion criteria: age>18 years, eGFR >15 mL/min/1.73m^2, no concomitant diseases affecting eGFR, without V2 receptor antagonist prescription). Kidney function was assessed as eGFR by the creatinine based CKD-EPI formula, height adjusted total kidney volume (htTKV) by MRI and copeptin (surrogate for vasopressin) by ELISA.

Results In the water deprivation test participants (n=30), the UPU ratio was strongly correlated with maximal urine concentrating capacity ($R = 0.67$, $p<0.001$). This association remained significant after correcting for sex, age, htTKV and eGFR (st. $\beta = 0.53$, $p = 0.007$). In these subjects maximal urine concentrating capacity as well as UPU ratio were associated with the rate of eGFR decline during a median follow-up of 6.3 yr (12 eGFR assessments per patient) assessed using linear mixed modeling, also when corrected for sex, baseline age and eGFR ($\beta = 0.009$, $p = 0.04$, and $\beta = 5.56$, $p<0.001$, resp.). We subsequently corroborated in the larger DIPAK observational cohort (n=583, 58% female, mean age 47 yr median eGFR 60 mL/min/1.73m^2 and htTKV 898 ml/m), that the UPU ratio was significantly associated with rate of eGFR decline during a median follow-up of 4.0 yr (6 eGFR assessments per patient): $\beta = 0.23$, $p = 0.005$. This association remained significant when corrected for sex, baseline age and eGFR ($\beta = 0.32$, $p<0.001$) and even when additionally corrected for Mayo class, PDK mutation and copeptin ($\beta = 0.40$, $p <0.001$). Stepwise backward multivariate regression analysis resulted in a final model including the UPU ratio, PKD mutation, Mayo Class and copeptin. Cox survival analysis showed that a lower baseline UPU ratio (indicating less urine concentrating capacity) was significantly associated with a higher risk to develop the combined renal endpoint of incidence of start of kidney replacement therapy, eGFR <15 mL/min/1.73m^2 or eGFR decrease >40% during follow-up (adjusted Hazard Ratio per SD = 1.39, $p = 0.007$). Limiting the aforementioned analyses to the subgroup of patients with relative early stage disease (n=122, age <40 yr and eGFR >60 mL/min/1.73m^2) rendered essentially similar results, with an adjusted β for UPU ratio in the final model of 0.33 ($p = 0.04$). In this subgroup with a limited number of events (n=10), Cox survival analysis did not reach formal significance (adjusted HR per SD: 2.67, $p = 0.055$).

Conclusion The UPU ratio, which is calculated from routine laboratory measurements, predicts renal prognosis in ADPKD in addition to other, more laborious to measure and expensive risk markers. Notably, this marker of urine concentrating capacity also shows promise in early-stage disease.

SO092 REDUCED QUALITY OF LIFE IN ADPKD PATIENTS WITH CKD STAGE 1-3: THE CYSTIC I QUALITY OF LIFE STUDY

Jean Winterbottom[1], Roslyn Simms[1], Albert Ong[1]

[1]*The University of Sheffield, Academic Nephrology, Infection Immunity and Cardiovascular Disease, Sheffield, United Kingdom*

Background and Aims: ADPKD is the most common inherited kidney disease in man, a major cause of end-stage renal disease and is a significant medical and economic burden across Europe. However the impact of this major disease on the quality of life of patients with preserved kidney function has not been systematically explored.

Method: The CYSTic 1 study was an academic prospective study designed to study the natural history of ADPKD, the impact of the disease on individual patients and the health economic costs on care systems across Europe in adult patients with preserved kidney function (eGFR $\geq$30 mls/min). Around 400 patients were recruited from 6 expert centres across Europe (Belgium, France, Italy, Netherlands, Spain, UK) with baseline clinical data recorded including HR-QOL (Health-Related Quality of Life) incorporating a Kidney Disease QOL short form (KDQOL-SF v1.3 questionnaire), renal MRI for TKV (Total Kidney Volume) and DNA for genotyping. Here we report initial results based on baseline HR-QOL data in the UK patients.

Results: Detailed analysis was conducted on 76 patients recruited from a single centre (UK) whose mean age was 43 years, 53.9% were female with a mean eGFR-EPI of 69ml/min/1.73m^2 and mean height-adjusted TKV (Ht-TKV) of 664ml/m. The cohort was subdivided by groups based on eGFR stage (I, II, III), Ht-TKV (<>750ml/m) and genotype (PKD1 v PKD2/NMD) and correlated with HR-QOL scores. As expected, age, hypertension and Ht-TKV were significantly associated with eGFR stage. Of interest, flank pain was more frequently reported in patients with smaller kidneys (Ht-TKV<750) and patients with PKD1 more likely to be hypertensive. All QOL scores (SF36) were significantly lower in patients with progressively lower eGFR except for emotional well-being whereas Symptom/problem (p=0.043) and Sleep (p=0.021) (KDQOL-SF1.3) were significantly worse in patients with lower kidney function. SF36 scores for Physical functioning (p=0.001), General health (p=0.026) and physical component summary (PCS) (P=0.019) decreased in patients with more advanced disease defined by larger kidneys (ht-TKV>750).

Conclusion: In ADPKD patients with stage 1-3 chronic kidney disease (CKD), stepwise lower QOL scores were consistently found and significantly associated with decreasing eGFR. A notable reported item was disturbed sleep. Unexpectedly, patients with smaller kidneys reported significantly more flank pain. PKD1 patients and those with large kidneys were more likely to be hypertensive. Our results suggest that the impact of ADPKD on patients with stage 1-3 CKD is underestimated. Future work will investigate possible national differences and the relationship of HR-QOL with markers of disease within the entire cohort.

SO093

LONGITUDINAL DATA ON TREATMENT DURATION AND COMPLIANCE FROM AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE CLINICAL TRIALS WITH TOLVAPTAN

Xiaolei Zhou[1], Diana Garbinsky[1], John Ouyang[2], Eric Davenport[1], Indra Agarwal[2], Dorothee Oberdhan[2]

[1]RTI Health Solutions, Research Triangle Park, NC, United States of America and [2]Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD, United States of America

Background and Aims : Observation of impactful clinical outcomes in a clinical trial setting for ADPKD is challenging due to the life-long progressive nature of ADPKD and longer-term associated outcomes of interest in this population (e.g., renal function decline, cardiovascular events, and mortality). Since 2004, the tolvaptan (TOL) clinical trial program enrolled subjects in multiple clinical studies with the opportunity to enroll in subsequent clinical trials for treatment and outcomes evaluation.

Method : Data from 6 ADPKD studies (protocols 156-04-250, 156-04-251, 156-06-260, 156-09-284, 156-09-290, 156-08-271) were pooled and evaluated over time for overall treatment duration, treatment time, and treatment gaps. Treatment duration for the individual clinical trials ranged from 1 week to up to 3 years.

Results : Overall, 1,437 subjects received TOL in these ADPKD clinical trials. For these subjects, the mean overall treatment duration was 4.1 years (3.8 years on treatment) with a maximum of 9.7 years (9.0 years on treatment). In this cohort, 513 subjects (35.7%) received TOL treatment for more than 5 years. Mean treatment compliance was 94.1%. Overall, 723 subjects (50.3%) received TOL treatment in $\geq$2 trials, with a median treatment gap duration between trials of 0.1 years (maximum, 5.6 years). At least 7 years of follow-up data are available for estimated glomerular filtration rate in 241 subjects (mean at baseline, 78.6 mL/min/1.73m^2) and for total kidney volume in 130 subjects (mean at baseline, 1,816.9 mL).

Conclusion : This analysis provides longitudinal follow-up over an extended timeframe in a large number of subjects treated with TOL, with the greatest number of subjects being enrolled in clinical trials enriched for rapidly progressing ADPKD. Treatment compliance over years was reasonably good despite treatment gaps.

SO094

HUMAN URINE-DERIVED RENAL EPITHELIAL CELLS PROVIDE INSIGHTS INTO THE PATHOGENICITY OF PKHD1 VARIANTS

Elisa Molinari[1], Shalabh Srivastava[1], Becky Dewhurst[1], John Sayer[1,2]

[1]Newcastle University, Translational and Clinical Research Institute, Newcastle, United Kingdom and [2]The Newcastle upon Tyne Hospitals NHS Foundation Trust, Renal Services, Newcastle, United Kingdom

Background and Aims: A 26 year old woman was referred for the investigation of polycystic kidney disease. There was no family history of renal disease and no obvious extra-renal manifestations. A GEMINI ciliopathy gene panel was performed which identified two heterozygous sequence changes (segregating from each parent) in *PKHD1*: a missense variant c.7964A>C, p.(His2655Pro), listed as a pathogenic variant in association with ARPKD on the Human Gene Mutation Database and a synonymous variant c.6900C>T, p.(Asn2300Asn). The pathogenicity of the synonymous *PKHD1* variant is not clear. It is reported as a variant of unknown significance on ClinVar and has a low population frequency in the gnomAD cohort. The altered nucleotide is weakly conserved, but the same heterozygous change has been previously reported in an individual prenatally presenting with multicystic kidneys together with a missense variant on the other allele. We aim to confirm the pathogenicity of this variant in our patient, analysing its effects on the splicing of *PKHD1* mRNA.

Method: *PKHD1* is expressed at low levels in the leukocytes, therefore it can be difficult to analyse the splicing of *PKHD1*, using routine methods that involve RNA extraction from the blood. Urine-derived renal epithelial cells were isolated and cultured from two wild type individuals and from the patient and total RNA was extracted from these cells. RT-PCR and RT-qPCR were carried out to analyse the effects of the synonymous variant on the splicing of the *PKHD1* gene in renal epithelial cells.

Results: RT-PCR revealed that *PKHD1* is alternatively spliced both in the controls and in the patient and Sanger sequencing following T-cloning of PCR products revealed that both controls and the patient express an in-frame transcript and a shorter transcript with a 47 nucleotide loss in the exon 43 of *PKHD1*, that leads to a frame-shift and to the formation of a premature stop codon. We hypothesized that, although both mRNA isoforms are expressed in controls as well as in the patient URECs, the variant p.(Asn2300Asn) may shift the expression ratio between the two transcript isoforms in favour of the shorter, out-of-frame transcript. We designed and tested two sets of transcript-specific primers and performed a SYBR-green based RT-qPCR on controls and patient URECs cDNA. RT-qPCR, revealed that *PKHD1* is expressed at lower levels in patient URECs, compared to controls. Specifically, the in-frame *PKHD1* isoform is expressed at lower levels in patient URECs, compared to controls, whereas the levels of the shorter transcript leading to a frame-shift are higher in patient cells.

Conclusion: Using urine-derived renal epithelial cells as a source of kidney-specific RNA, we confirmed the pathogenicity of the *PKHD1* synonymous variant p.(Asn2300Asn), which leads to an increased expression of an out-of-frame *PKHD1* transcript, predicted to result in a truncated protein and expressed at lower levels also in control cells. The significance of this isoform in control renal epithelial cells is unclear.

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ANAEMIA TREATMENT IN CKD: A CHANGING SCENARIO

MO001

ROXADUSTAT FOR THE TREATMENT OF ANAEMIA IN CHRONIC KIDNEY DISEASE PATIENTS NOT ON DIALYSIS: A PHASE 3, RANDOMISED, OPEN-LABEL, ACTIVE-CONTROLLED STUDY

Jonathan Barratt[1], Branislav Andrić[2], Avtandil Tataradze[3], Michael Schömig[4], Michael Reusch[5], Udaya Valluri[5], Christophe Mariat[6]

[1]University of Leicester, Leicester, United Kingdom, [2]Health Center Krusevac, Krusevac, Serbia, [3]National Center of Urology, Tbilisi, Georgia, [4]Center for Dialysis and Nephrology, Heilbronn and Neckarsulm, Germany, [5]Astellas Pharma Europe B.V., Leiden, Netherlands and [6]CHU St Etienne, Service Nephrologie Dialyse Transplantation, St Etienne, France

Background and Aims: Roxadustat is an orally administered hypoxia-inducible factor prolyl hydroxylase inhibitor for the treatment of anaemia in patients (pts) with chronic kidney disease (CKD). Efficacy and safety of roxadustat compared with darbepoetin alfa (DA) for the treatment of anaemia in CKD pts not on dialysis (NDD) was assessed in a randomised, open-label, active-controlled phase 3 study. Results from a protocol-specified interim analysis, performed after pts had either completed ≥36 weeks of treatment or had withdrawn from the study, are presented here.

Method: This study (CL-0610) enrolled pts with NDD CKD stages 3-5 and anaemia (haemoglobin [Hb] ≤10.5 g/dL) and randomised them to receive roxadustat or DA. Following prescribed initial doses (weight-based), dose adjustments were permitted, with the goal of correcting and maintaining Hb. The primary endpoint was Hb response, defined as Hb ≥11.0 g/dL and an Hb increase from baseline (BL) of ≥1.0 g/dL in pts with BL Hb >8.0 g/dL, or an increase of ≥2.0 g/dL in pts with BL Hb ≤8.0 g/dL, during the first 24 weeks of treatment without rescue therapy. Key secondary endpoints included change in serum lipids, time to first IV iron use, change in mean arterial pressure (MAP), and occurrence of hypertension. Noninferiority of roxadustat to DA was declared if the lower bound of the two-sided 95% confidence interval (CI; roxadustat – DA) for change in Hb was >-0.15. Adverse events (AEs) were assessed across the study and are presented as events/100 patient exposure years (PEY) unless otherwise specified. The full analysis set (FAS) included pts who received ≥1 dose of study drug and had ≥1 post-dose Hb assessment. The per protocol set (PPS) included FAS pts who did not meet exclusion criteria. The safety analysis set (SAF) included pts who received ≥1 dose of study drug.

Results: As of 15 June 2018, 616 pts were randomised to receive roxadustat (n=323) or DA (n=293); of these 616 pts, 395 pts (roxadustat, n=194; DA, n=201) were still receiving treatment and 89 pts had completed ≥2 years of treatment (roxadustat, n=55; DA, n=34). In the PPS, 89.5% (n=256) of roxadustat pts responded in the first 24 weeks compared with 78.0% (n=213) of DA pts, for a difference of 11.51% (95% CI: 5.66%, 17.36%), thereby establishing roxadustat's noninferiority to DA. Noninferiority of roxadustat to DA was also demonstrated for MAP and time to occurrence of hypertension. In the FAS, superiority of roxadustat to DA was demonstrated for low-density lipoprotein (LDL) and time to first IV iron use. (**Table**) In the SAF, overall incidence of AEs was comparable between roxadustat and DA (85.8% and 84.6%, respectively).

Conclusion: This analysis demonstrates that roxadustat was noninferior to DA in correction of Hb levels during the first 24 weeks of treatment in pts with NDD CKD stages 3-5 and anaemia. Safety profiles were comparable between groups. Final analysis of this study's data will be presented at the congress.

Table. Summary of Results for Key Secondary Efficacy Endpoints

Endpoint (Population)	Test	Statistics (units)	Result (95% CI)	Conclusion	Non-inferiority Criteria
LDL change from baseline to average of Weeks 12-28 (FAS)	Superiority	LSM difference (mmol/L)	-0.404 (-0.510, -0.297)	Superiority met (*P*-value <0.001)	-
Time to first IV iron use during first 36 weeks (FAS)	Superiority	Hazard ratio	0.46 (0.27, 0.80)	Superiority met (*P*-value=0.006)	-
MAP change from baseline to average of Weeks 20-28 (PPS)	Non-inferiority	LSM difference (mmHg)	-0.362 (-1.577, 0.852)	Non-inferiority met	Upper bound <1 mmHg
Occurrence of hypertension during first 36 weeks (PPS)	Non-inferiority	Hazard ratio	0.827 (0.56, 1.22)	Non-inferiority met	Upper bound <1.3

Common (>10 events/100 PEY in both groups) AEs included hypertension (roxadustat, 28.4; DA, 37.3), end-stage renal disease (roxadustat, 24.3; DA, 24.3), decreased estimated glomerular filtration rate (roxadustat, 12.1; DA, 13.0), and peripheral oedema (roxadustat, 12.1; DA, 12.6).

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MO002

OPHTHALMOLOGICAL EFFECTS OF ROXADUSTAT IN THE TREATMENT OF ANAEMIA IN CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS IN A PHASE 3, RANDOMISED, DOUBLE-BLIND, ACTIVE-COMPARATOR CONVERSION STUDY

Yasir Sepah[1,2], Quan Dong Nguyen[2], Yusuke Yamaguchi[3], Yoshikatsu Majikawa[3], Michael Reusch[4], Tadao Akizawa[5]

[1]Ocular Imaging Research and Reading Center, Sunnyvale, United States of America, [2]Byers Eye Institute, Stanford School of Medicine, Stanford, United States of America, [3]Astellas Pharma, Inc., Tokyo, Japan, [4]Astellas Pharma Europe B.V., Leiden, Netherlands and [5]Showa University School of Medicine, Tokyo, Japan

Background and Aims: Roxadustat is an orally administered hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) approved in China for the treatment of dialysis-dependent (DD) and non–dialysis-dependent chronic kidney disease (CKD) anaemia, and in Japan for the treatment of DD CKD anaemia. An acceptable safety profile as well as noninferiority of roxadustat to darbepoetin alfa (DA), measured by haemoglobin (Hb) change from baseline (BL), was shown in patients (pts) with DD CKD in a Japanese phase 3, randomised double-blind, double-dummy study (CL-0307). Some nonclinical data suggest that HIF stimulation may promote angiogenesis, thereby increasing the risk of certain retinal pathologies. As such, this report focuses on a prospective analysis of ophthalmological/retinal-related events observed during the 24-week study period of the aforementioned phase 3 study.

Method: Japanese pts with DD CKD were randomised 1:1 to receive roxadustat three times weekly or DA once weekly; doses were titrated to maintain Hb between 10–12 g/dL. Ophthalmological/retinal-related outcomes were evaluated in pts who received ≥1 dose of study drug (SAF) and included emergence of adverse events assessed by the investigator and ophthalmological findings based on assessments performed by centralised grading. Ophthalmic imaging (colour fundus photography, optical coherence tomography) and assessment of visual acuity were performed at BL, Week 12, and Week 24 or at study discontinuation according to Ophthalmic Image Acquisition Guidelines. Each investigator evaluated the ophthalmic images and assessed the clinical relevance of any changes. Central evaluation of ophthalmological examination results was then performed by two independent specialists who were blinded to study treatment. During central evaluation, the reviewers assessed ophthalmic images in accordance with the Safety Independent Ophthalmology Review Charter. If graders' results disagreed, adjudication was performed by a blinded, independent grader who did not participate in the primary review of the patient data. Grading results and visual acuity were analysed descriptively.

Results: In the SAF, a total of 302 pts were randomised to receive either roxadustat (n=150) or DA (n=152). At BL, previous or concurrent retinal vascular disorders were present in 41.3% (62/150) and 37.5% (57/152) of pts in the roxadustat and DA groups, respectively; 32.7% (49/150) and 27.6% (42/152) of pts presented with a history of both diabetes mellitus and retinal vascular disorders, respectively. The mean (SD) duration of exposure to study drug was 146.7 (45.8) days in the roxadustat group and 154.7 (37.4) days in the DA group. The proportion of pts with new or worsening retinal haemorrhages during the treatment period was 32.4% (n=46/142) with roxadustat and 36.6% (n=53/145) with DA. In a subgroup analysis of pts with no retinal haemorrhage at BL, the proportion of pts with new retinal haemorrhages was 19.1% (n=18/94) with roxadustat and 25.0% (n=24/96) with DA during the treatment period; in pts with ≥1 retinal haemorrhage at BL, the proportion of pts with new or worsening retinal haemorrhages was 58.3% (n=28/48) with roxadustat and 59.2% (n=29/49) with DA during the treatment period. From BL, no clinically meaningful changes in visual acuity or retinal thickness were found in either treatment group. Similarly, from BL, no clinically meaningful changes were found in the proportion of pts exhibiting intra-/sub-retinal fluid, hard exudates, or cotton wool spots in either treatment group.

Conclusion: These findings suggest that, during the 24-week treatment period, DD CKD pts treated with roxadustat were not at an increased risk of ophthalmic abnormalities—including retinal haemorrhages or increased retinal thickness—compared with pts treated with DA.

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DIETARY APPROACHES IN CKD: PROMOTING QUALITY OVER QUANTIFY

MO003 ADHERENCE TO DIETARY GUIDELINES IN ADULTS UNDERGOING MAINTAINANCE HAEMODIALYSIS: THE DIET-HD STUDY

Valeria Saglimbene[1,2], Guobin Su[3], Marinella Ruospo[1], Juan Jesus Carrero[4], Giovanni Strippoli[5]

[1]Diaverum, Medical office, Sweden, [2]University of Sydney, School of public health, Australia, [3]Karolinska Institutet, Department of Global Public Health, Sweden, [4]Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Sweden and [5]University of Bari, Department of Emergency and Organ Transplantation, Italy

Background and Aims: While clinical guidelines emphasize dietary modifications as a cornerstone component in the management of patients undergoing dialysis, the adherence to these recommendations has been poorly quantified. The aim of this study is to evaluate the extent of adherence to diet guidelines for adults treated with long-term haemodialysis within the European patients included in the multinational cohort of the "DIETary intake, death and hospitalization in adult with ESKD treated with Haemodialysis" (DIET-HD) study.

Method: Cross-sectional analysis of the DIET-HD study in 6906 adults undergoing haemodialysis in 10 European countries. Patients responded to the Global Allergy and Asthma European Network (GA^{2}LEN) Food Frequency Questionnaire, and dietary intakes were estimated to evaluate the adherence to the European Best Practice Guidelines nutritional recommendations.

Results: Patients showed low adherence to the daily recommended intake of phosphorous (<1000mg, met by 25% of participants) and potassium (<2730mg, met by 28% of participants). Almost half the participants achieved targets for energy (>30 kcal/kg, 45% of participants) and calcium (<800mg/day, 53% of participants) intake, while the recommended sodium (<2300mg/day) and proteins intake (≥1.1g/kg) was achieved in 85% and 67% of participants, respectively. Adherence to renal guidelines varied across participating countries, but followed the same pattern. Only 1% of patients adhered to all six recommendations at the same time.

Conclusion: Adherence to dietary guideline recommendations is poor, particularly regarding phosphorus, potassium, calcium and energy intake.

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GLOMERULONEPHRITIS 2

MO004

THE SAFETY PROFILE OF REPEAT RITUXIMAB TREATMENT IN ANCA-ASSOCIATED VASCULITIS - A 10 YEAR SINGLE CENTRE STUDY

PEK GHE TAN[1], Jennifer O'Brien[1], Megan Griffith[1,2], Marie Condon[1], Tom Cairns[1], Jeremy Levy[1], Charles Pusey[1,2], Stephen McAdoo[1,2]

[1]Imperial College Healthcare NHS Trust, Specialist Nephrology Clinic, London, United Kingdom and [2]Imperial College London, Centre for Inflammatory Disease, London, United Kingdom

Background and Aims: Rituximab is a proven effective induction and remission-maintenance treatment in patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Studies have identified hypogammaglobulinemia, infection, and late-onset neutropenia as potential adverse events. There is limited data on long-term outcomes following extended periods of B-cell depletion therapy with rituximab in AAV cohorts. We conducted a retrospective study to examine the safety profile of repeated rituximab treatment in AAV.

Method: All patients with AAV treated with rituximab between 1st January 2008 and 31st December 2018 were identified through local dispensary database. Patients were stratified into low (≤4g), medium (>4g to ≤8g) and high (>8g) dose groups according to the cumulative rituximab dose received until 1st October 2019. Baseline characteristics and events including death, opportunistic and severe infections (defined as infections required hospitalization and/or intravenous antibiotic administration), neutropenia (neutrophil count ≤1.5x10^9/L), hypogammaglobulinemia (IgG level≤5.0), infusion reactions and malignancy diagnosed post-rituximab treatment were examined and compared between the groups.

Results: 364 patients (49% male, 52 year old mean age) received rituximab for treatment of active disease or remission maintenance. 49%(n=175) had repeat rituximab treatments (267/513 treatment courses for relapsing disease and 247/513 for remission maintenance). There were 262 (72%), 70(19%) and 32(9%) patients in low-, medium- and high-dose groups respectively. The median cumulative rituximab dose for each group was 2g, 6g and 12g ($p<0.001$). Low-dose group patients were older (59 and 40 years, $p<0.001$) and more likely to have renal-limited disease compared to high-dose groups (19%vs4%; $p<0.05$). Conversely, there were more ear-nose-throat (ENT) /ocular limited (41% and 13%; $p<0.05$) and antiproteinase 3 (PR3)-ANCA positive disease (56% vs 38%, $p<0.05$) in high-dose compared to low-dose group. The overall median duration of follow up was 72 months (QR: 28-135months)(Table1).

Outcomes (Table2):

Infections: no difference in serious or opportunistic infection rate between groups (1.2 vs 0.1 vs 0.1infections/patient/year; p=0.18). 77% of opportunistic infections across all groups were related to herpesvirus (e.g. Cytomegalovirus/Herpes Zoster/Herpes Simplex) reactivation.

Hypogammaglobulinemia: incidence was comparable between groups (9.7% vs 10% vs 9%, p=0.91). Overall median time to event was 5 months from first rituximab.

Neutropenia: 101 patients had recorded neutropenia after rituximab (Low-dose: 32%; medium-dose 16% and High-dose: 22%, $p<0.05$). All were related to concurrent immunosuppressants (e.g. Azathioprine, cyclophosphamide or mycophenolate) or infection. Events resolved after withdrawal or reduction of concurrent immunosuppressant or treatment of underlying infection.

Cancer: No difference in malignancy rate between groups (6% vs 14% vs 3%, p=0.22). 39 malignancies reported in 32 patients post rituximab treatment. The two commonest reported cancers were skin (36%) and breast cancer (21%)

Deaths: 58 patients died during the study period. Mortality rate in the low and medium-dose groups were comparable (82% survival at 30 month after last rituximab). Conversely, there were no deaths in the high-dose group.

Conclusion: In this large, single-centre cohort of patients with AAV, we did not observe an increased incidence of adverse events with increasing cumulative rituximab exposure. This likely reflects physician bias in patient selection for repeat treatment and suggests that in selected patients, extended periods of rituximab treatment might be safe. The superior survival seen in high-dose group was likely related to higher proportion of ENT/ocular limited vasculitis.

Baseline Characteristics	≤ 4000mg (N=262, 72%)	>4000-≤8000mg (N=70, 19%)	>8000mg (N=32, 9%)	P-value
Age, years (median, QR)	59 (44-69)	46 (28-61)	40 (28-48)	<0.01
Female (N,%)	128 (49%)	35 (50%)	22 (69%)	0.10
ANCA serology				
PR3	99 (38%)	42 (60%)	18 (56%)	
MPO	106 (40%)	15 (21%)	3 (9%)	
Negative	28 (11%)	11 (16%)	6 (19%)	
EGPA	12 (4.5%)	0	1 (3%)	
PR3/MPO+ antiGBM	7 (2.7%)	0	1 (3%)	
PR3/MPO + lupus	7 (2.7%)	0	3 (9%)	
MPO+PR3	3 (1.1%)	3 (4%)	0	<0.05
Hypertension	146 (56%)	33 (49%)	18 (56%)	0.31
Diabetes	53 (22%)	15 (22%)	8 (25%)	0.99
Dyslipidemia	131 (53%)	35 (52%)	20 (63%)	0.59
Estimated Glomerular Filtration Rate <ml/min/1.73m²	174 (71%)	27 (39%)	7 (22%)	<0.05
Organ involvement				
Renal Limited	50 (19%)	3 (4%)	0 (0%)	
Respiratory Limited	3 (1%)	5 (7%)	1 (3%)	
ENT/Ocular Limited	33 (13%)	11 (16%)	13 (41%)	
Systemic	175 (67%)	51 (73%)	18 (56%)	<0.05
Cumulative Rituximab Dose (median, QR, gram)	2 (2.0-3.0)	6 (5.38-7.00)	12 (10.25-14.93)	<0.01
Follow up duration (median, QR, months)	93 (15-83)	299 (59-328)	181 (107-264)	<0.01

Table 1: Baseline Characteristics of all groups

Figures:

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MO005

HIGH LEVELS OF FIVE SPECIFIC FECAL METABOLITES IN IGA NEPHROPATHY PATIENTS SUPPORT THE HYPOTHESIS OF THE INTESTINAL-RENAL AXIS CONNECTION

Claudia Curci[1], Fabio Sallustio[2], Nada Chaoul[3], Angela Picerno[3], Gabriella Lauriero[3], Chiara Divella[3], Vincenzo Di Leo[3], Maria De Angelis[4], Luigi Macchia[3], Anna Gallone[1], Renato Monteiro[5], Francesco Pesce[3], Loreto Gesualdo[3]

[1]University of Bari, Department of basic medical sciences, neurosciences and sense organs, Bari, Italy, [2]University of Bari, Department of Interdisciplinary medicine, Bari, , [3]University of Bari, DETO, Bari, Italy, [4]University of Bari, Department of soil, plant and food sciences,, Bari, Italy and [5]INSERM, Center for research on inflammation, Paris,

Background and Aims: The IgA nephropathy (IgAN) is the most frequent primitive glomerulonephritis. In the last years, the role of mucosal immunity in IgAN, together with that of the gut microbiota in the activation of innate and adaptive immune cells, has gained

importance. Particularly interesting is the role of the microbiota and intestinal immunity in IgAN. BAFF and APRIL can be produced by the intestinal epithelium, in response to signals triggered by TLRs once activated by the commensal bacteria present in the intestinal lumen, representing the link between microbiota and intestinal immunity. To date, even if hypothesized, this relationship in IgAN patients has not been investigated.

Here, we studied the intestinal-renal axis connections analyzing levels of BAFF, April and intestinal-activated B cells in IgAN patients.

Method: Serum and fecal samples were collected from 44 IgAN patients, 22 non-IgA glomerulonephritides (controls) and 22 healthy subjects (HS) with similar clinical features. BAFF and APRIL serum levels were measured by ELISA assay. Metabolomic analysis of fecal microbiome was performed using Biochrom 30 series amino acid analyzer and gas-chromatography mass spectrometry/solid-phase microextraction (GC-MS/SPME) analysis. B cell subsets were investigated by FACS.

Results: IgAN patients had increased serum levels of BAFF cytokine compared to the control group of patients with non-IgA glomerulonephritis and compared with HS ($p<0.0001$and $p=0.012$, respectively). We found that serum BAFF levels positively correlated with the levels of 24h-proteinuria in IgAN patients ($r2 = 0.2269$, $p <0.001$).

We correlated serum BAFF levels with fecal concentration of 5 different metabolites of 30 IgAN patients, which were previously investigated for the fecal microbiota. These organic compounds had been found at significantly higher levels in the feces of IgAN patients compared to HS. Serum BAFF levels positively correlated with the levels of fecal metabolites: 4-(1,1,3,3-tetramethylbutyl) phenol ($r2 = 0.2882$, $p = 0.0027$), p-tert-butyl-phenol ($r2 = 0.386$, $p = 0.0003$), methyl neopentyl phthalic acid ($r2 = 0.3491$, $p =0.0007$), hexadecyl ester benzoic acid ($r2 = 0.2832$, $p =0.003$) and furanone A ($r2 = 0.1743$, $p = 0.024$).

Serum levels of APRIL were significantly increased in IgAN patients respect to control groups (4.49 ± 0.54 vs 2.27 ± 1 ng/ml, $p=0.0014$). We found a correlation between APRIL and serum creatinine ($r2 = 0.159$, $p =0.04$) and eGFR ($r2 = 0.2395$, $p =0.0082$), while no correlation was found between APRIL and fecal metabolite levels in IgAN patients. In addition, we found that subjects with IgAN have a significantly higher proportion of circulating Bregs, Memory B cells and IgA secreting-plasmablasts activated at the intestinal level (CCR9+INTB7+) compared to HS.

Conclusion: The results of our study showed for the first time an important correlation of serum levels of BAFF with intestinal microbiota in patients with IgAN, confirming the hypothesis of the pathogenic role of intestinal mucosal hyperresponsiveness in the IgAN patients. The intestinal-renal axis plays a crucial role in Berger's glomerulonephritis, whose complex pathogenesis may contribute several factors as genetics, pathogens and food.

MO006

INFLAMMASOME ACTIVATOR NLRP3 HYPOMETHYLATION IS ASSOCIATED WITH GLUCOCORTICOID RESISTANCE IN PATIENTS WITH IDIOPATHIC NEPHROTIC SYNDROME.

Simona Granata[1], Gabriele Stocco[2], Marianna Lucafò[2], Erik Bonten[3], Robert McCorkle[3], Giuliana Decorti[2], Giovanni Gambaro[1], William E Evans[3], Gianluigi Zaza[1]

[1]University of Verona, Renal Unit, Department of medicine, Verona, Italy, [2]University of Trieste, Department of Life Sciences, Trieste, Italy and [3]St. Jude Children's Research Hospital, Hematological Malignancies Program, and Department of Pharmaceutical Sciences, Memphis, United States of America

Background and Aims: We have previously shown that the Nod-like receptor protein-3 (NLRP3) gene is over-expressed in leukocytes of many patients with chronic kidney disease, and studies have also shown that hypomethylation and overexpression of NLRP3 are associated with glucocorticoid resistance in acute lymphoblastic leukemia. Therefore, we hypothesized that hypomethylation of the NLRP3 promoter my cause glucocorticoid resistance in patients with Idiopathic Nephrotic Syndrome (INS) associated with minimal change disease (MCD) or focal glomerulosclerosis (FSGS).

Method: We assessed NLRP3 and Caspase 1 (CASP1) promoter methylation by SNuPE reaction in germline DNA from leukocytes of 14 glucocorticoid-resistant and 18 glucocorticoid-sensitive adult INS patients (discovery cohort) and 7 glucocorticoid-resistant and 14 glucocorticoid-sensitive pediatric INS patients with MCD/FSGS (validation cohort). The effects of NLRP3 inflammasome on glucocorticoid resistance were validated *in vitro* in human monocytic cell lines (THP-1 and U937).

Results: Methylation of CpG islands in the CASP1 promoter was undetectable in both groups whereas NLRP3 promoter methylation was significantly lower in glucocorticoid-resistant compared to glucocorticoid-sensitive in both adults and children.

The AUROC curve was 81.2% (p=0.0003) in adults and 73.5% (p=0.0002) in children demonstrating the capability of NLRP3 methylation to discriminate glucocorticoid-resistant versus glucocorticoid-sensitive.

Activation of the NLRP3 inflammasome by LPS/ATP reduced glucocorticoid receptor expression and increased glucocorticoid resistance in U937. Consistently, knockdown of NLRP3 in THP-1 increased sensitivity to glucocorticoids.

Conclusion: Our findings demonstrate a novel mechanism whereby INS patients develop resistance to glucocorticoids via leukocyte epigenetic changes of NLRP3 and reveal a new potential clinical biomarker to early detect this condition.

MO007

A PHASE 1B MULTIPLE ASCENDING-DOSE STUDY OF A CD6 TARGETED THERAPY, ITOLIZUMAB, IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH OR WITHOUT ACTIVE PROLIFERATIVE LUPUS NEPHRITIS

Kenneth Kalunian[1], Richard Furie[2], Jai Radhakrishnan[3], Vandana Mathur[4], Joel Rothman[5], Catherine Kim[5], Cherie Ng[5], Stephen Connelly[5], Krishna Polu[5], Chaim Putterman[6]

[1]University of California San Diego, Rheumatology, La Jolla, United States of America, [2]Northwell Health, Rheumatology, Great Neck, United States of America, [3]Columbia University, Nephrology, New York, United States of America, [4]MathurConsulting, Nephrology/Clinical Research, Woodside, United States of America, [5]Equillium, Inc. and [6]Albert Einstein College of Medicine, Rheumatology, New York, United States of America

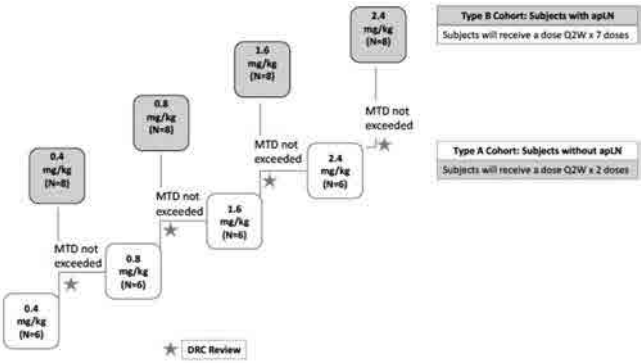
Background and Aims: Lupus nephritis (LN) is a leading cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients. T cells are believed to play a central role in the pathogenesis of both SLE and LN. CD6 is a co-stimulatory receptor, predominantly expressed on T cells, that binds to activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen presenting cells and various epithelial and endothelial tissues. The CD6-ALCAM pathway plays an integral role in modulating T cell activation, proliferation, differentiation and trafficking, and is central to immune mediated inflammation. Itolizumab (EQ001) is a humanized IgG1 monoclonal antibody that binds CD6, blocks the interaction between CD6 and ALCAM, and inhibits both the activation and trafficking of T cells. Inhibiting the CD6-ALCAM pathway with itolizumab potentially represents a promising therapeutic approach for the treatment of LN. The aim of this study is to assess the safety and tolerability, pharmacokinetics, pharmacodynamics, and clinical activity of subcutaneously administered itolizumab in patients with SLE with and without active proliferative lupus nephritis (apLN).

Method: This cohort-based dose escalation study includes two types of patients: The Type A cohort will enroll ~24 patients with SLE without apLN (all treated with itolizumab) and the Type B cohort will randomize in a blinded manner ~36 patients (3:1, itolizumab:placebo) with biopsy-proven ISN/RPS class III or IV (± V) apLN who have had inadequate response to induction and/or post-induction maintenance treatment, exhibiting urine protein to creatinine ratio [UPCR] ≥1 g/g and active serology. Within both the Type A and Type B cohorts, up to 4 dose groups will be tested (**Figure**). Background treatments for SLE or LN are allowed. Following 4 weeks of treatment in a new higher dose Type A cohort and recommendation by an independent safety data review committee (DRC), the dose studied in the Type A cohort may then be studied in a Type B Cohort for a 12-week treatment duration (**Figure**).

The primary endpoint is the safety and tolerability of itolizumab. Efficacy endpoints (in the Type B cohorts) include UPCR, estimated glomerular filtration rate, prednisone dose requirements, renal response, Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), FACIT Fatigue Scale, serologic markers, and other patient reported outcomes. In Type A cohort patients, clinical responses and pharmacologic activity will be assessed based on changes in serologic markers, SLEDAI-2K, FACIT Fatigue Scale. Pharmacodynamic markers, including markers that may allow future risk stratification, urinary ALCAM and CD6, will be examined in both cohort types.

Results: The study is ongoing. Six patients have been enrolled in Type A Cohort 1 (0.4 mg/kg dose) and completed both treatment and 4 weeks of post-treatment follow-up. The mean age was 59.5 (12.9) years, 100% were female; 67% were Hispanic/Latino; and 50% were White, and 50% were Black. Duration of SLE ranged from 3 years to 31 years. Concomitant medications for lupus included prednisone (83%, dose range 2.5 mg – 10 mg), methotrexate (33%), and anti-malarials (33%). Baseline SLEDAI-2K (mean 7.5 [2.2]) was based on findings of alopecia (83%); arthritis (67%); mucosal ulcers and rash (50% each); fever, increased dsDNA, and low complement (17% each). There were no adverse events. Additional data from this ongoing study will be presented.

Conclusion: Itolizumab, a monoclonal antibody blocking the CD6-ALCAM pathway, is a novel experimental treatment for LN. This is the first trial of itolizumab in patients with SLE and apLN. Data from the first cohort of patients suggest that the drug is safe and well-tolerated at a dose of 0.4 mg/kg over a 4-week treatment period. Additional cohorts of patients with SLE and apLN are currently being enrolled.



Figure

MTD = maximum tolerated dose

MO008

B LYMPHOCYTE SUBSET CHANGES IN PRIMARY MEMBRANEOUS NEPHROPATHY

Nooshin Dalili[1], Fatemeh Pour-Reza Gholi[1], Katayoun Hasanzadeh[1], Sara Assadiasl[2]

[1]Department of Nephrology, Labbafinejad Medical Center, CKDRC, Shahid Beheshti University of Medical Sciences, Tehran, Iran and [2]Molecular Immunology Research Center, Tehran University of Medical Sciences, Tehran, Iran

Background and Aims: Primary membranous nephropathy (PMN) is the most common cause of nephrotic syndrome (NS) in adults. Rituximab a chimeric monoclonal anti-CD20 antibody has been supposed to eliminate autoantibody-producing B cells via direct signaling, complement-mediated cytotoxicity (CMC), and antibody-dependent cellular cytotoxicity (ADCC). According to the fact that a wide range of B lymphocytes may carry this marker, we aimed to identify which subset is more (or less) frequent in PMN patients and which one is more affected by rituximab administration.

Method: Three groups were enrolled in the present study. They included a healthy control group and two patient groups having the clinical, laboratory, and pathological diagnostic criteria of PMN, comprising either patients on standard treatment or patients on standard treatment plus rituximab. The latter group was studied just before receiving rituximab (pre-rituximab) and two months later (post rituximab). Peripheral blood mononuclear cells (PBMCs) were isolated using Ficoll-hypaque (inno-train, Germany) gradient. Afterward, cells were adjusted to a concentration of 1 _ 106 cells/mL and stained with mouse antihuman CD19-Cy5-conjugated antibody (Cytognos, Spain), mouse antihuman CD24-PE-conjugated antibody (Cytognos, Spain), and mouse antihuman CD38-FITC-conjugated antibody (Cytognos, Spain). Flow cytometry performed by FACS Calibur (BDFacs Calibur Becton Dickinson, USA).

Results: The total lymphocyte percentage was higher in PMN patients receiving either standard treatment or rituximab than in healthy controls (standard-treatment vs. control: P value = 0.001, pre-rituximab vs. control: P value =0.001). In post-rituximab analysis, CD19+ cell count showed notable reduction (P value = 0.003)

B CD19+CD24+CD38- cells, representing the memory B cell population, did not show any significant difference between healthy controls and patients. Furthermore, the count of these cells did not decrease significantly two months after rituximab administration. The subset of CD19+CD24-CD38+ B lymphocytes, a class of naïve/mature lymphocytes with normal function, was significantly higher in the control group than in standard treatment patients (P value = 0.01). However, no statistically significant difference was found in CD19+CD24-CD38+B lymphocytes neither between the rituximab and control groups nor between pre-rituximab and post-rituximab patients.

Conclusion: The number of regulatory B cells decreased in both standard treatment and rituximab-receiving PMN patients and the proportion of naïve/mature B-lymphocytes was lower in the former group. Moreover, the memory B cells count did not reduce significantly two months after rituximab administration. Hence, it might be the best choice to target the memory B cell subset in immunosuppressive therapy while avoiding the Breg or naïve/mature B lymphocyte depletion to obtain more favorable sustained outcomes.

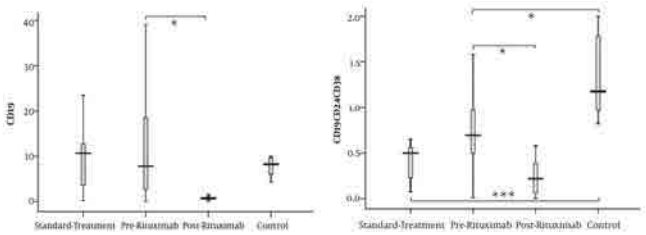


Fig 1. Right Panel: CD19+ cells frequency (percentage in lymphocytes) in four groups of standard treatment (steroid + immunosuppressive), pre-rituximab (steroid + immunosuppressive + rituximab), post-rituximab (2 months after RTX administration), and healthy controls; *P < 0.05 **P < 0.001 ***P < 0.0001

Left Panel: CD19+CD24highCD38high cells frequency (percentage in CD19+ cells) in four groups of standard treatment (steroid + immunosuppressive), pre-rituximab (steroid + immunosuppressive + rituximab), post-rituximab (two months after RTX administration), and healthy controls; *P < 0.05 **P < 0.001 ***P < 0.0001

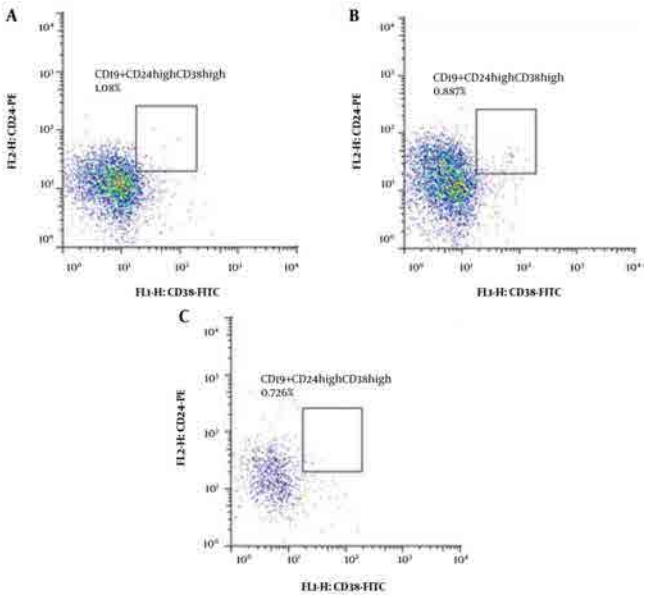


Fig 2. CD19+CD24highCD38high cells frequency (percentage in CD19+ lymphocytes) in A: healthy controls, B: standard treatment patients (steroid + immunosuppressive), and C: pre-rituximab treatment patients (steroid + immunosuppressive + rituximab)

CLINICAL OUTCOMES IN TRANSPLANTATION 2

MO009

NEUTRALIZATION OF UPAR WITH AN ANTI-UPAR ANTIBODY AMELIORATES RECURRENT FSGS SERA INDUCED PODOCYTE INJURY

Flavio Vincenti[1], Priyanka Rashmi[2], Andrea Alice Da Silva[2], Jun Shoji[1], Charles Craik[3], Minnie Sarwal[2]

[1]University of California San Francisco Parnassus Campus, Kidney Transplantation, San Francisco, United States of America, [2]University of California San Francisco Parnassus Campus, Surgery, San Francisco, United States of America and [3]University of California, San Francisco, Pharmaceutical Chemistry, San Francisco, United States of America

Background and Aims: The role of suPAR as a biomarker and/or causative factor in the pathogenesis of recurrent FSGS remains unclear (Harel E., et al. Transplantation 2020; 104:54-60). While anti-suPAR antibodies have been shown to block suPAR induced podocyte injury in mouse models of FSGS, this beneficial effect has not yet been demonstrated in FSGS patients.

We report here the inhibitor effects of 2G10, a fully human anti-suPAR antibody that blocks the interaction of suPAR with the B3 integrin on podocytes.

Method: The immortalized podocyte cell line was developed by transfection with the temperature sensitive SV40 T gene. These cells proliferate at the "permissive" temperature (33°C) and are considered undifferentiated. After transferring to the "nonpermissive" temperature (37°C), they enter growth arrest and by day 10-14 express markers of differentiated podocytes *in vivo*, such as nephrin, podocin, CD2 associated protein (CD2AP), synaptopodin, and known molecules of the slit diaphragm ZO-1, α, β, and γ-catenin, and P-cadherin. The podocytes were cultured in RPMI medium supplemented with insulin, transferrin, selenium, sodium pyruvate (ITS-A, Gibco #513000), 10% FBS and penicillin/streptomycin. After differentiation for 14 days, cells were serum starved for 1h. Serum from rFSGS patients or from a control patient was added (4% final) and cells were cultured for an additional 24h. After fixation in PFA/sucrose. actin cytoskeleton was visualized by labeling with rhodamine-conjugated phalloidin. DAPI was used for nuclei staining. Cells were imaged by confocal microscopy at 40X magnification and the number of cells with intact stress fibers were counted. For rescue of stress fibers, podocytes were cultured in the presence of a fully humanized anti uPAR antibody (2G10, 1 ug/ml; Duriseti S, J Biol Chem, 2010, 285:26878-88) or an isotype IgG control antibody (1 ug/ml).

Results: Sera from three patients with recurrence of FSGS after transplant were used in the study. Podocyte culture in the presence of sera from all three patients caused significant depolarization of stress fibers as determined by number of stress fiber positive cells (30%, 59% and 49% reduction with respect to untreated podocytes respectively). Treatment of podocytes with control sera did not cause any significant changes (data not shown). Culture of podocytes with patient sera in the presence of 2G10 antibody against uPAR rescued stress fibers (Fig 1A and 1B). On the other hand, a control human IgG was unable to rescue the loss of stress fibers induced by sera from recurrent FSGS patients.

Conclusion: The therapeutic potential of a human anti-suPAR antibody in samples from patients with recurrent FSGS has not been previously demonstrated. The in vitro findings of 2G10 antibody on preserving the stress fibers in human podocytes from the disrupting effect of the sera of patients with recurrent FSGS suggest that antibodies that block suPAR could be effective in preventing recurrence of FSGS.

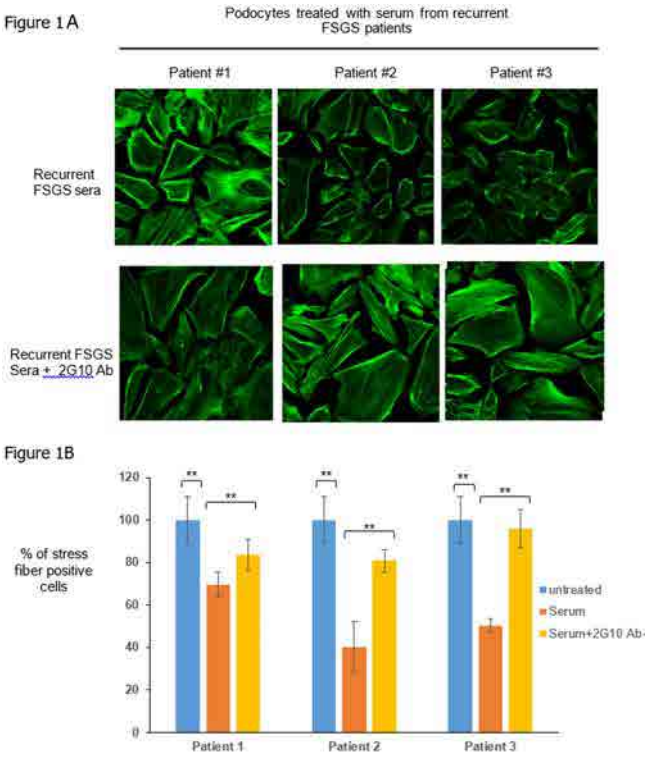


Figure 1A and 1B

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MO010

TREATMENT STRATEGIES OF ANTIBODY MEDIATED REJECTION IN KIDNEY TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Jesmar Buttigieg[1,2], Jon Jim Kim[2,3], Stephen Mason[4,5], Brian Camilleri[2,6], Ahmed Halawa[2,7]

[1]Mater Dei Hospital, Renal Division, Department of Medicine, Imsida, Malta, [2]Faculty of Health and Life Science, Institute of Learning and Teaching, University of Liverpool, Liverpool, United Kingdom, [3]Paediatric Nephrology Department, Nottingham Children Hospital, Nottingham, United Kingdom, [4]Palliative Care Institute Liverpool, Academic Palliative & End of Life Care Centre, University of Liverpool, Liverpool, United Kingdom, [5] School of Medicine Postgraduate / CPD Unit, School of Medicine, University of Liverpool, Liverpool, United Kingdom, [6]Renal Unit, Ipswich Hospital, East Suffolk and North Essex Foundation Trust, Ipswich, United Kingdom and [7]Renal Transplant Unit, Sheffield Teaching Hospitals, NHS Trust, Sheffield, United Kingdom

Background and Aims : Antibody mediated rejection (AMR) remains accountable for the majority of death-censored graft failure following the first year of kidney transplantation. Despite significant advances in transplant immunology and immunosuppressive agents, long-term graft survival has not improved significantly. The objective of this systematic review and meta-analysis is to determine the optimal treatment strategy for AMR by investigating the effect on kidney function, proteinuria, donor specific antibody (DSA), histopathology, graft survival, adverse events and patient survival.

Method : MEDLINE (PubMed), Scopus, Cochrane Central Register of Controlled Trials and ClinicalTrials.gov databases were systematically searched following the PRISMA guidelines. Any kidney transplant study conducted between 1997-2018, which investigated treatment strategies for biopsy-proven AMR, and reported at least one of the following outcomes; serum creatinine, glomerular filtration rate (GFR), proteinuria, DSA, histopathology scores, graft survival, adverse events and/or patient survival were eligible for inclusion. Risk of bias was evaluated using the Cochrane Risk of Bias Tool for randomised controlled trials (RCTs) and the ROBINS-I tool for non-randomised controlled studies.

Results : Our analysis identified a total of 27 studies consisting of 6 RCTs and 21 non-randomised controlled studies. Together these studies included 1,237 transplant recipients; 748 patients with acute AMR (AAMR) and 489 with chronic AMR (CAMR). Meta-analysis identified significantly better 1-year graft survival in patients with AAMR when treated with Rituximab in addition to plasmapheresis and intravenous immunoglobulin (IVIG) compared to plasmapheresis and IVIG alone [risk ratio (RR): 0.48, 95% confidence interval (CI): 0.27-0.86, Z=2.46, P=0.01, I^2=0%] (Fig-1A). Pooled analysis of GFR in the AAMR group was not possible due to insufficient data. There was no significant difference in the GFR at 6-12 months after treatment of CAMR with IVIG plus Rituximab compared to no treatment [mean difference: 0.36, 95% CI: -11.80-12.52, Z=0.06, P=0.95, I^2=89%] (Fig-1B). Similarly, there was no significant difference in the 1-year graft survival after treatment of CAMR with IVIG plus Rituximab compared to no treatment [RR: 0.77, 95% CI: 0.42-1.40, Z=0.86, P=0.39, I^2=9%] (Fig-1C). Late diagnosis of AMR and established transplant glomerulopathy seem associated with graft dysfunction and poor prognosis. Additionally, declining GFR and proteinuria seem to impact considerably on the overall outcome of the graft. Pooled analysis of proteinuria, DSA titres, and histopathology scores was not possible due to insufficient data. Similarly, pooled analysis of adverse events was not possible; however, these therapeutic strategies were generally well tolerated and associated with excellent patient survival throughout the included studies. Novel therapeutic approaches seem promising, but currently there is insufficient evidence for their routine use in AMR. The risk of bias ranged between low-risk to high-risk throughout the included RCTs and between moderate-risk to critical-risk amongst the non-randomised controlled studies.

Conclusion : This systematic review and meta-analysis outlines the treatment of AMR in kidney transplantation using the current best available evidence. We identified low-quality evidence in favour of treatment with combined plasmapheresis, IVIG and Rituximab in AAMR. Treatment of established CAMR does not seem advantageous in terms of graft function and survival. Additionally, the treatment of AMR is particularly heterogeneous between transplant centres, reflecting the lack of good quality evidence to guide practice. RCTs conducted via multicentre collaboration are urgently required to establish the optimal therapeutic strategies and validate models for predicting therapeutic response in AMR.

Figure 1A: Forest plot illustrating graft survival at 1-year after treatment of acute AMR with the addition of Rituximab to plasmapheresis and IVIG compared to no Rituximab.

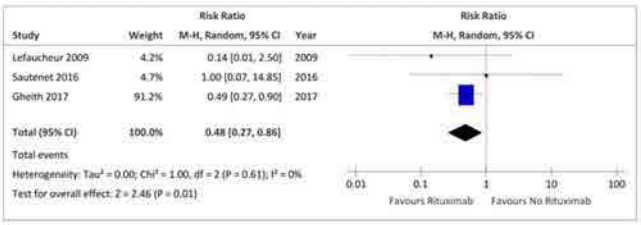


Figure 1B: Forest plot illustrating GFR at 6-12 months after treatment of chronic AMR with combined IVIG and Rituximab compared to no treatment.

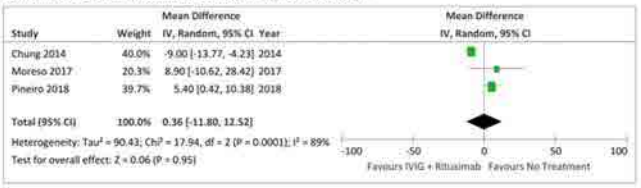


Figure 1C: Forest plot illustrating graft survival at 1-year after treatment of chronic AMR with combined IVIG and Rituximab compared to no treatment.

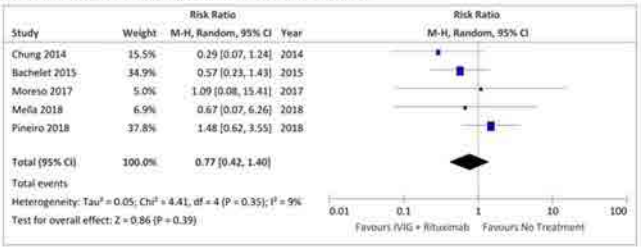


Figure:

MO011

A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF VITAMIN K SUPPLEMENTATION TO IMPROVE VASCULAR HEALTH IN KIDNEY TRANSPLANT RECIPIENTS

Jennifer Lees[1,2], Alastair Rankin[1,2], Keith Gillis[2], Luke Zhu[1], Elaine Rutherford[1], Giles Roditi[1,2], Miles Witham[3], Alan G. Jardine[1], Patrick Mark[1,2]

[1]University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom, [2]NHS Greater Glasgow and Clyde, Glasgow, United Kingdom and [3]University of Newcastle, Newcastle, United Kingdom

Background and Aims: Vascular stiffness (VS) and calcification (VC) are markers of cardiovascular disease which are prevalent in kidney transplant recipients (KTR) and associated with subclinical vitamin K deficiency. We tested the hypothesis that vitamin K supplementation would reduce VS and VC in prevalent KTR in the Vitamin K for kidney Transplant Organ Recipients: Investigating vEssel Stiffness (ViKTORIES) trial.

Method: In a single-centre, phase II, parallel-group, randomised, double-blind, placebo-controlled trial (ISRCTN22012044), KTR were randomised 1:1 to vitamin K (menadiol diphosphate 5mg) or placebo thrice weekly for one year. The primary outcome was between-group difference in VS (ascending aortic distensibility by cardiac magnetic resonance imaging) at 1 year by ANCOVA adjusted for the baseline value, age and duration of end-stage kidney disease. Secondary outcomes included VC (coronary artery calcium score on non-contrast computed tomography), cardiac structure and function (on cardiac magnetic resonance imaging), blood pressure, eGFR, proteinuria and quality of life. All outcomes were assessed by intention-to-treat with secondary per-protocol analyses. Missing data were multiply imputed as a sensitivity analysis for the main outcomes. The trial was conducted in accordance with the Declaration of Helsinki and was approved by the West of Scotland Research Ethics Committee 4 (Ref: 17/WS/0101). The results were combined in a meta-analysis with other published data.

Results: Ninety participants were randomised to vitamin K (n=45) or placebo (n=45) and included in the analysis. Baseline demographics, clinical history and immunosuppression regimens were similar between groups: mean age 57.6 ± 9.6 years, 70% male, with median time after transplantation 7.8 (IQR 3.5 - 13.9) years. There was no impact of vitamin K versus placebo on VS after 12 months (-0.2 (-0.5 - 0.2) vs. -0.3 (-0.6 - 0.1) $x10^{-3}$ $mmHg^{-1}$; p=0.60), nor on VC (184 (52 - 315) vs 44 (-89 - 177) units; p=0.11), nor on any other outcome measure. Medication adherence was very good in both groups (90 vs. 95%; p=0.58). Achieved power was 85%. Serious adverse events were common (vitamin K: 26.7 vs. placebo: 60.0%): all serious adverse events were classified as expected. Multiple imputation of missing data had no impact on results of VS or VC outcomes. Combining these with other published results, vitamin K supplementation has no significant observed effect on VS or VC, though with few available studies for analysis.

Conclusion: In this heterogeneous cohort of prevalent KTR, vitamin K supplementation did not reduce VS or VC over 1 year. Improving vascular health in patients with established kidney disease is likely to require a multifaceted approach.

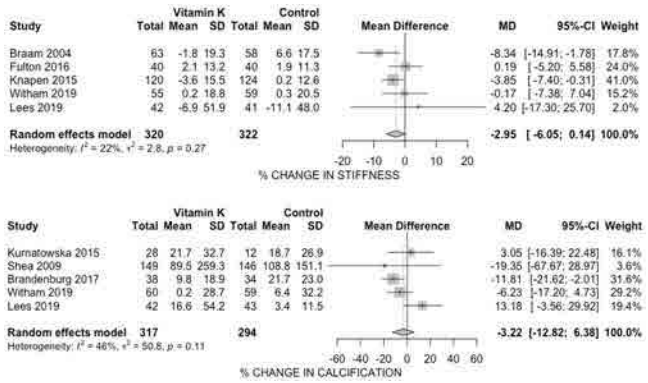


Figure:

MO012

IS IT SAFE TO USE INTERLEUKIN-2 RECEPTOR ANTAGONIST INDUCTION THERAPY IN 2DR MISMATCH RENAL TRANSPLANTS IN TACROLIMUS ERA?

Hatem Kaies Ibrahim Elsayed Ali[1], Ahmed Daoud[2], Mahmoud Mohamed[3], Karim Soliman[4]

[1]University Hospitals of Birmingham, Renal, Birmingham, United Kingdom, [2]Medical institute, Houston, United States of America, [3]University of Tennessee, Tennessee, United States of America and [4]university of south carolina, United States of America

Background and Aims: 2DR HLA mismatch indicates high immunological risk renal transplant. Induction therapy with rabbit Anti-thymocyte Globulin (r-ATG) and IL-2 Receptor Antagonist (IL-2RA) resulted in marked reduction of acute allograft rejection rate and improved graft survival. However, the outcomes in 2DR (HLA-DR) mismatched renal transplant recipients (RTRs) in the era tacrolimus-mycophenolate mofetil maintenance immunosuppression remains understudied.

Method: Using data from the United States organ procurement and transplantation network, all 2 DR mismatched RTRs with panel reactive antibodies <20% maintained on tacrolimus and mycophenolate mofetil immunotherapy between 2000 and 2017 were retrospectively reviewed. Data including age, sex, gender, ethnicity, functional status, diabetes, body mass index, cold ischemia time, number of previous transplants, panel reactive antibodies, donor type, donor age, HLA-mismatches, number of acute rejection episodes, induction therapies, maintenance immunotherapy, recipients and graft survival were collected. Based on induction therapies administered, RTRs were divided into 2 groups: (r-ATG) and IL-2RA groups. Poisson regression analysis was used to assess effect of induction therapies on acute rejection episodes. Cox hazard regression analysis was used to assess effect of different induction therapies on patient and graft survival

Results: 3379 patients received IL2-RA while 3677 patients received ATG for induction. There were no significant differences between both groups in terms of acute rejection episodes (95% CI ranges from 0.95 to 1.068, P=0.805), graft survival (95% CI: 0.91 - 1.06, P=0.712), or patient survival (95% CI: -0.949 - 1.12, P=0.43) .

Conclusion: This study revealed no significant difference in acute rejection episodes, patient or graft survival when utilizing ATG vs IL-2RA in 2DR HLA mismatched renal transplant recipients with PRA<20%, in the tacrolimus-based maintenance immunosuppression era. Therefore, IL2-RA is a safe induction therapy in this group of patients and non-inferior to –ATG induction therapy.

MO013

PATERNAL SAFETY OF THE USE OF MYCOPHENOLIC ACID BY KIDNEY TRANSPLANT RECIPIENTS. RESULTS OF THE EMVARON STUDY

Paloma Leticia Martin-Moreno[1], Ana I. Sánchez-Fructuoso[2], Auxiliadora Mazuecos[3], Marisa Mir[4], Isabel López López[5], Ana González-Rinne[6], Armando Coca[7], Natalia Ridao[8], Valero Rosalía[9], Ana Ventura Galiano[10], Néstor Toapanta[11], Ernesto José Fernández-Tagarro[12], Mónica Pérez-Mir[13], Leónidas Cruzado-Vega[14], Carlos Jimenez[15]

[1]Clinica Universidad de Navarra and Instituto de Investigación Sanitaria de Navarra (IdiSNA), Nephrology Department, Pamplona, Spain, [2]Hospital Clinico San Carlos, Nephrology Department, Madrid, Spain, [3]Hospital Puerta del Mar, Nephrology Department, Cádiz, Spain, [4]Hospital del Mar, Nephrology Department, Barcelona, Spain, [5] Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Hospital Universitario Reina Sofía, Nephrology Department, Córdoba, Spain, [6]Hospital Universitario de Canarias, Nephrology Department, Tenerife, Spain, [7]Hospital Clínico Universitario, Nephrology Department, Valladolid, Spain, [8]Hospital Universitario Central de Asturias, Nephrology Department, Oviedo, Spain, [9] H.U. Marqués de Valdecilla, IDIVAL, Universidad de Cantabria, Nephrology Department, Santander, Spain, [10]Hospital Universitari i Politécnic La Fe, Transplant Unit, Valencia, Spain, [11]Hospital Vall d'Hebron, Nephrology Department, Barcelona, Spain, [12]Complejo Hospitalario Universitario Insular Materno-Infantil, Nephrology Department, Las Palmas, Spain, [13]Hospital Universitari Germans Trias i Pujol, Nephrology Department, Badalona, Barcelona, Spain, [14]Hospital General de Elche, Nephrology Department, Elche, Spain and [15]Hospital Universitario La Paz, Nephrology Department, Madrid, Spain

Background and Aims: Mycophenolic acid (MPA) is one of the most used immunosuppressive drugs. It is teratogenic in women with a typical embryopathy profile. Regarding its effect on the children of male kidney transplant recipients, although clinical evidence does not indicate a greater risk of malformations, the European Medicines Agency and the Spanish Agency for Medicines and Health Products introduced in 2015 the recommendation to use contraceptive methods because of their genotoxic potential.

For this reason, we propose to study the results of the Spanish Kidney Transplant Centers.

Method: Multicenter retrospective observational study in which 15 Kidney Transplant Centers have participated. Of 3934 men $\leq$ 60 years old that received a kidney transplant between 2000 and 2015, 3023 were contacted, and 159 men who fathered at least one post-transplant pregnancy (total 252 fetuses) were included. We compared the incidence of abortions and live births with malformations among those who received MPA at the time of conception vs. those who did not.

Results: In the 252 fetuses (characteristics in table 1) there was an exitus and no differences were detected in the incidence of abortions between the group exposed to MPA (n = 230) and the unexposed group (n = 22), 11.3% vs 18.2%, p = 0.31. Among the 221 live-born fetuses, no differences were found in congenital malformations between the group exposed to MPA (n = 203) and the unexposed (n = 18) 4.9% vs. 16.7%, p = 0.07. Among the malformations described, the typical embryopathy profile of the MPA was not found.

Conclusion: According to the data of this retrospective national multicenter study, the use of MPA in male kidney transplant recipients does not cause a greater number of abortions or congenital malformations.

For these reasons, and given the evidence also published by other groups, it seems necessary to reevaluate the recommendation given on contraception in men treated with MPA.

Table 1. Demographic and clinical characteristics of the group exposed to Mycophenolate Acid (MPA) vs non-exposed.

	MPA N= 230	NO –MPA N= 22	p
Male age (years)	31.2 $\pm$ 5.7	32.9 $\pm$ 5.2	ns
Hypertension (n,%)	83.2%	86.4%	ns
Diabetes mellitus (n,%)	5.3%	9.1%	ns
Body Mass Index (Kg/m2)	26.6 $\pm$ 4.1	26.9 $\pm$ 4	ns
Time from transplant to conception (months)	63.3 $\pm$ 45.6	44.6 $\pm$ 38.6	ns
Serum creatinine (mg/dL)	1.5 $\pm$ 0.5	1.7 $\pm$ 0.5	ns
Female age (years)	33.1 $\pm$ 4.5	34.1 $\pm$ 5.5	ns
Body Mass Index (Kg/m2)	24 $\pm$ 3.5	21.5 $\pm$ 2.7	ns
Preeclampsia (n,%)	2.3 %	0	
Children's weight (kg)	3.1 $\pm$ 0.6	3.2 $\pm$ 0.5	ns

Male and female ages and body mass index, time from transplant to conception, serum creatinine and children's weight are expressed as media and standard deviation.

MO014

BORDERLINE T-CELL REJECTION IN RENAL TRANSPLANTATION: ARE WE AWARE OF THE REAL IMPACT IN GRAFT SURVIVAL?

Carolina Figueiredo[1], Rita Leal[1,2], Clara Pardinhas[1], Filipe Mira[1,2], Luís Rodrigues[1,2], Lidia Santos[1], Catarina Romãozinho[1], Helena Sá[1,2], Arnaldo Figueiredo[3,4], Rui Alves[1,4]

[1]Centro Hospitalar e Universitário de Coimbra, Nephrology, Portugal, [2]Faculdade de Medicina da Universidade de Coimbra, Clínica Universitária de Nefrologia, Portugal, [3]Centro Hospitalar e Universitário de Coimbra, Urology and Kidney Transplantation, Portugal and [4]Faculdade de Medicina da Universidade de Coimbra, Portugal

Background and Aims: Histological findings that meet criteria for borderline changes "suspicious" for acute T cell mediated rejection (BR) as defined by the Banff Classification (2017) are frequently seen. However, its clinical significance, as well as the appropriate clinical management, are still controversial. Our goal was to compare clinical outcomes of kidney transplant recipients with biopsy proven BR versus acute T cell mediated rejection (aTCMR) and the influence of treating BR rejection in graft outcomes.

Method: A retrospective cohort study was performed in all kidney transplant recipients with biopsy proven BR and aTCMR between January 2012 and December 2018. Data related to donor and recipient demographics, treatment and subsequent evolution of serum creatinine, proteinuria and graft survival were collected. Mean time at follow up was 31.2 ± 29.1 months.

Results: We included 91 patients with biopsy proven T cell rejection of which 34 (37.4%) had a BR and 57 (62.6%) aTCMR: 39 (68.4%) IA, 9 (15.8%) IB, 7 (28.1%) IIA and 2 (3.5%) IIB. There was no difference between groups (BR vs aTCMR) regarding age (45,5 vs 48,1, p=0,38), sex (male 73% vs 60%, p=0,27) or race (Caucasian 100% vs 93%, p=0.114). For both groups, deceased donor was more frequent (82% vs 95%, p=0.074), and there was no difference in cytotoxic PRA (mean 4.5 ± 9.2 vs 3.7 ± 12.8, p=0.762) or number of compatibilities (mean 2.2 ± 1.2 vs 2.4 ± 1.3, p=0.539).

At the time of rejection diagnosis, the mean time of transplant was similar between groups (32.9 ± 43.6 vs 42.3 ± 67.4 months, p=0.467), but estimated glomerular filtration rate (GFR) was significantly higher in patients with BR when compared to aTCMR (32.0 ± 22.5 vs 19.9 ± 13.1 ml/min/1.73m^2, p=0.009). We found no significant difference in proteinuria at the time of biopsy between the 2 groups.

Treatment with steroids was started in 20 (58.8%) patients with BR and all the patients with aTCMR were treated with steroids with or without thymoglobulin, depending on the Banff class. Fourteen (41.2%) patients with BR were followed closely with no acute interventions.

At 1-year post biopsy, graft survival was 70%, and we found no significantly statistical difference between the two groups (79.4% vs 64.3%, p=0.129). In patients with preserved graft, there was no difference in GFR (41.9 ± 17.7 vs 37.7 ± 19.8, p=0.401) at 12 months post biopsy for both groups. When performing Kaplan-Meyer survival curves at follow-up, we also found no difference between BR and aTCMR (57.6 ± 7.1 vs 43.6 ± 5.5 months, p=0.157) (Figure 1).

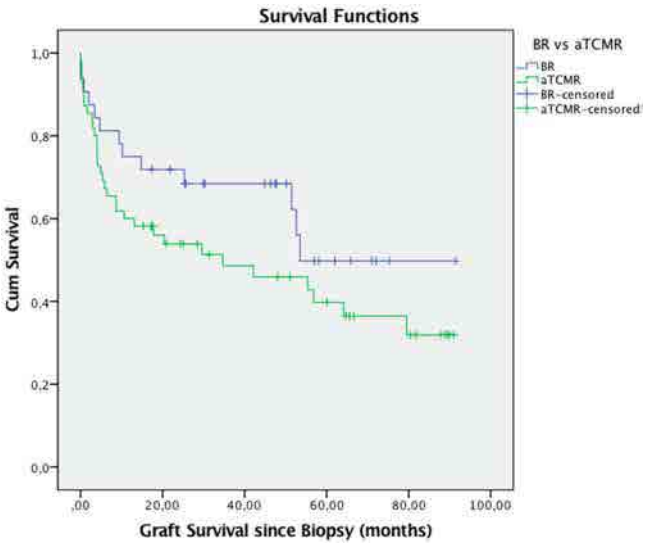


Figure 1: Kaplan Meyer survival curves: BR and aTCMR

When analyzing the BR group (N=34) and comparing the patients that were treated (N=20) versus the patients with conservative approach (N=14), we found no difference in demographic features, sCr at biopsy (3.0 ± 1.1 vs 2.8 ± 2.1 mg/dl, p=0.696) and time post-transplant (28.1 ± 43.2 vs 39.7 ± 44.8 months, p=0.454). Graft survival at 1-year was 80% for treated patients and 79% for non-treated patients, p=0.919 and GFR for patients with preserved graft was not different between groups (43.9 ± 21.0 vs 39.7 ± 13.5 ml/min/1.73m2, p=0.572). When performing survival curves, we found that treated patients had almost the double time with functioning graft compared to non-treated patients (71.9 ± 8.5 vs 41.3 ± 6.2 months, p=0.104), although not statistically different probably due to the small sample size (figure 2).

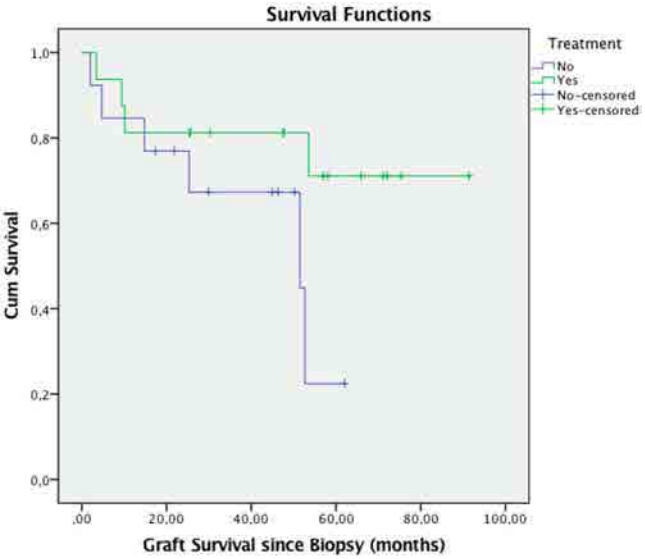


Figure 2: Kaplan Meyer survival curves: treated and untreated BR

Conclusion: Our study showed that despite having better GFR at time of biopsy, patients with BR (overall and treated) did not present better graft survival nor graft function at 1 year post biopsy or at follow up, compared with aTCMR. We also found a tendency to better graft survival in patients with BR treated with steroids compared with conservative approach. These results reinforce the importance of borderline rejection in graft outcomes and that the decision of whether to treat or not can influence long-term outcomes.

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EVERYDAY ISSUES DURING HAEMODIALYSIS

MO015

HAEMODIALYSIS VASCULAR ACCESS THROMBOSIS: AN ANALYSIS OF EVENTS FROM THE PROACTIVE IV IRON THERAPY IN HAEMODIALYSIS PATIENTS (PIVOTAL) TRIAL

Peter Thomson[1], Patrick Mark[1], Michele Robertson[2], Donal Reddan[3], Alan G. Jardine[1], Claire White[4], Chante Reid[4], Stefan D. Anker[5], Sunil Bhandari[6], Kenneth Farrington[7], Philip A. Kalra[8], John McMurray[9], Charles R.V. Tomson[10], David Wheeler[11], Christopher G. Winearls[12], Ian Ford[2], Iain Macdougall[4]

[1]Queen Elizabeth University Hospital, Renal & Transplant Unit, Glasgow, United Kingdom, [2]University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom, [3]National University of Ireland,, School of Medicine, Galway, Ireland, [4]King's College Hospital, Renal Unit, London, United Kingdom, [5]Charite University, Department of Cardiology, Berline, Germany, [6]Hull and East Yorkshire Hospitals NHS Trust, Renal Medicine, Hull, United Kingdom, [7]Lister Hospital, Renal Unit, Stevenage, United Kingdom, [8]Salford Royal Foundation Trust, Renal Medicine, Manchester, United Kingdom, [9]University of Glasgow, Department of Cardiovascular Medicine, Glasow, United Kingdom, [10]Freeman Hospital, Renal Medicine, Newcastle upon Tyne, United Kingdom, [11]University College London, Centre for Nephrology, London, United Kingdom and [12]University of Oxford, Oxford Renal Unit, Oxford, United Kingdom

Background and Aims: Haemodialysis vascular access thrombosis (VAT) is a common occurrence that undermines the safe and effective delivery of haemodialysis (HD) and has been associated with anaemia therapy. In the Proactive IV Iron Therapy in Haemodialysis Patients trial (PIVOTAL), proactive high-dose intravenous iron dosing was compared with reactive low-dose intravenous iron dosing. VAT was a pre-specified secondary endpoint. Here we present data detailing the VAT events in PIVOTAL, alongside univariate and multivariate analyses of risk association, testing the hypothesis that VAT may be independently associated with a proactive iron dosing regimen.

Method: In PIVOTAL 2141 adults with end-stage kidney disease within 12 months of initiating regular HD were randomised 1:1 to either high-dose intravenous iron administered proactively, or low-dose intravenous iron administered reactively, on the basis of monthly Ferritin and Transferrin saturation levels. Erythropoiesis Stimulating Agents were dosed sufficiently to maintain a haemoglobin of 100 to 120g/L. Vascular access use was recorded at baseline and on a monthly basis. VAT was regarded as a safety event with investigators mandated to record such events. VAT was defined clinically, with investigators expected to report thrombotic occlusion of the access (either arteriovenous or catheter thrombosis) significant enough to prevent further effective use without intervention.

Baseline demographic, blood pressure and laboratory data underwent univariate analysis with regard to first event of VAT. Primary patient demographics (age, gender, primary renal disease, randomised treatment arm) were put forward for inclusion in a multivariable cox proportional hazards model alongside variables that associated on univariate testing with $\alpha<0.05$. Analyses were performed using SAS software, version 9.4 (SAS Institute).

Results: 2141 eligible patients were randomised, of whom 877/2141 (41.0%) were using a central venous catheter (CVC), 1209/2141 (56.5%) an arteriovenous fistula (AVF), and 55/2141 (2.6%) an arteriovenous graft (AVG) at baseline. Over a median follow up of 2.1 years, 480/2141 (22.4%) experienced a VAT event; 194/887 (21.9%) of CVC patients; 263/1209 (21.8%) of AVF patients; and 23/55 (41.8%) of AVG patients.

On univariate testing VAT events associated with diabetes as a cause of kidney failure (HR 1.44, 95%CI 1.19 to 1.74, p<0.001), AVG use at baseline (HR 2.37, p<0.001), digoxin use (HR 2.35, p=0.002), and diuretic use (HR 1.24, p=0.02). Angiotensin receptor blocker (ARB) use associated with less VAT (HR 0.66, p=0.013), as did male gender (HR 0.74, p=0.002), and never having smoked (HR 0.68, p=0.008). No association was seen with age, AVF use, CVC use, blood pressure, history of cardiovascular (CV) disease, atrial fibrillation, other CV medications, C-reactive protein, haemoglobin, transferrin saturation, ferritin or randomised treatment group (Proactive 262/1093 (24.0%) v Reactive 218/1048 (20.8%), HR 1.15, p=0.12) .

Multivariate analysis found diabetes as a cause of kidney failure (HR 1.45, p<0.001), AVG use (HR 2.29, p<0.001), digoxin exposure (HR 2.48, p<0.001) and diuretic exposure (HR 1.25, p=0.018) to independently associate with VAT. Male gender (HR 0.75, p=0.002), never smoked (HR 0.68, p=0.004) and ARB use (HR 0.66, p=0.011) were found to independently associate with lower risk of VAT. Investigation of interaction between significant predictors found diuretic use in AVF patients to reach nominal significance (p=0.033). No other significant interactions being demonstrated.

Conclusion: In PIVOTAL, VAT affected nearly one quarter of the cohort over a median of 2.1 years. Diabetes as a cause of kidney failure, active smoking, AVG use, female gender, exposure to digoxin, and exposure to diuretic were independently associated with VAT, but this was not the case with higher iron dosing. ARB use was independently associated with lower risk.

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MO016

MYOCARDIAL INFARCTION IN THE PIVOTAL STUDY OF IV IRON IN HAEMODIALYSIS: A PRE-SPECIFIED SECONDARY ANALYSIS

Mark Petrie[1], Pardeep Jhund[2], Michele Robertson[3], Patrick Mark[2], Eugene Connolly[2], Michael Macdonald[2], Claire White[4], Chante Reid[4], Stefan D. Anker[5], Sunil Bhandari[6], Kenneth Farrington[7], Philip A. Kalra[8], Charles R.V. Tomson[9], David Wheeler[10], Ian Ford[3], John McMurray[2], Iain Macdougall[4]

[1]University of Glasgow, BHF Cardiovascular Research Centre, gLASGOW, United Kingdom, [2]University of Glasgow, BHF Cardiovascular Research Centre, Glasgow, United Kingdom, [3]University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom, [4]King's College Hospital, Department of Renal Medicine, London, United Kingdom, [5]German Center for Cardiovascular Research, Department of Cardiology, Berlin, Germany, [6]Hull Royal Infirmary, Department of Renal Medicine, Hull, United Kingdom, [7]Lister Hospital, Department of Renal Medicine, Stevenage, United Kingdom, [8]Salford Royal NHS Foundation Trust, Department of Renal Medicine, Salford, United Kingdom, [9]Newcastle Freeman Hospital, Department of Renal Medicine, High Heaton, United Kingdom and [10]University College London, Department of Renal Medicine, London, United Kingdom

Background and Aims: Coronary artery disease is prevalent in patients with CKD but how often a myocardial infarction (MI) occurs in patients on maintenance haemodialysis, and the prognostic importance of these MIs, is uncertain. The PIVOTAL trial investigated the effects of proactive high-dose versus reactive low-dose intravenous (IV) iron in incident haemodialysis patients. We now report the rates of MI, sub-types of MI, and the prognostic importance of these MIs, as well as the effect of high versus low dose iron on this event.

Method: This was a pre-specified secondary analysis of 2141 patients enrolled in the PIVOTAL trial. All potential endpoints in the trial, including MIs were adjudicated by a blinded Endpoint Adjudication Committee. The outcomes of time-to-first MI (type 1 or type 2 MI, STEMI or NSTEMI) and the composite outcome of MI and death due to MI were reported. In addition to time-to-first MI, we also analysed recurrent events, to account for the cumulative burden of events over time, as well as case-fatality related to MI. The time-to-event analyses of the primary, secondary and post hoc outcomes were performed in the intention-to-treat population using Cox proportional hazards regression, with treatment group as the only explanatory variable. The Kaplan–Meier method was used to estimate event rates. Recurrent events were analysed using the proportional-means model of Lin et al. and described in the form of mean frequency functions.

Results: 8.4% of patients experienced a MI over a median of 2.1 years follow-up. Rates of type 1 MIs (3.2/100 patient years) were 2.5 times higher than type 2 MIs (1.3/100 patient years). NSTEMIs (3.3/100 patient years) were 6.6 times more common than STEMIs (0.5/100 patient years). Mortality was high after non-fatal MI (30-day and 1-year mortality were 11.3% and 39.8%, respectively). In time-to-first event analyses, proactive high-dose IV iron reduced the rate of non-fatal MI (HR 0.69, 95% CI 0.51-0.93; p=0.01) and the composite endpoint of non-fatal and fatal MI (HR 0.69, 95% CI 0.52-0.93, p=0.015) (Figure) when compared to low dose reactive IV iron. The benefits of a proactive high-dose IV iron strategy were seen in type 1 MIs but not type 2 MIs.

Conclusion: Most MIs in patients on HD were type 1 and NTEMIs. Patients randomised to the high-dose group of PIVOTAL had a substantial reduction in fatal and non-fatal MI compared to those in the low-dose group.

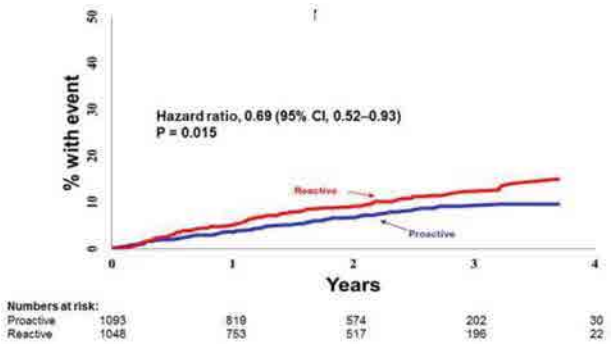


Figure:

CLINICAL NEPHROLOGY 2

MO017

ANTITHROMBOTIC THERAPIES AND CLINICAL OUTCOME OF ATRIAL FIBRILLATION IN ADULT HD-PATIENTS: LARGE LONG-TERM COHORT STUDY ON GERMAN NETWORK DATA.

Karl August Brensing[1], Anna Ochsmann[1], Heyder Omran[2], Gerhard Lonnemann[3], Helmut Reichel[4], Johannes Duttlinger[3]

[1]Nierenzentrum Bonn, Dialysis Unit, Bonn, Germany, [2]St. Marien Hospital Bonn, Cardiology, Bonn, Germany, [3]Deutsche Nierenzentren eV, WiNe Institute, Düsseldorf, Germany and [4]Nephrological Center, Villingen-Schwenningen, Germany

Background and Aims : ESRD (end stage renal disease) patients on hemodialysis (HD) with persistent atrial fibrillation (AF) are at high risk for cardio-vascular events, severe bleeding and rapid vascular/valvular calcification. In such patients standard vitamin-K based oral anticoagulation (VK-OAC) is debated, since prospective OAC studies are missing and smaller short-term register data showed conflicting results. Our study evaluated risk-factors, use of anticoagulants and clinical long-term outcome in a large representative German HD-cohort.

Method : After informed consent, we analysed pseudonymized benchmarking data (2013-2018) of 16226 adult chronic HD patients treated in a German outpatient dialysis network (Verband Deutsche Nierenzentren, DN) based on quarterly electronically transmitted data. Diagnoses were coded by "International Classification of Diseases (ICD)" and drugs via "Anatomical Therapeutical Chemical (ATC)" codes.

Results : At baseline in 2013, 2812 (17%) HD-patients had AF as coded diagnosis. AF-prevalence increased significantly ($p<0.001$) with age (< 65 yrs: 7%; 65-<75 yrs: 22% >75 yrs: 34%) without gender differences. Baseline CHA2DS2-Vasc (4.0/1.5) and HAS-Bled (3.2/0.9) risk scores indicated high risk for embolism and bleeding. Median observation time was 2.1 yrs (Range: 0–6 yrs.). Apart from dialysis-related heparin-supply four main approaches were applied: No active therapy, standard VK-OAC+/- aspirin/clopidogrel (VK-OAC+/-Asp/Clop), heparin-based therapy (Heparin+/-Asp/Clop) or only anti-thrombocyte drugs (Asp/Clop).

Baseline risk scores were not related to any adverse events. Outcome data are shown in the Table: event rates were low (8.8%) and comparable for all anticoagulant therapies, especially for cerebral adverse events (3.8%, range 3.3-4.5%). Patients on any anti-thrombotic therapy had similar outcome rates as patients without anticoagulant therapy. The latter had fewer overall bleeding events (3.8% vs. 5.0%; NS).

Finally, overall actual 6-yr mortality rates were high (55.8%; median survival 4.4 yrs) and significantly ($p<0.001$) lower for patients without anti-coagulant therapy (48.9%; median survival 6.0 yrs) than for patients on anti-coagulant therapy (59.5%; median survival 4.0 yrs) with highest mortality on VK-OAC based therapy (60.3%; $p<0.001$).

Conclusion : De-novo cerebral event-rates were rather low (<0.8%/yr) and similar for all anti-thrombotic therapies and even for patients with no active therapy, suggesting major beneficial impact of regular dialysis-related heparin-supply. Since actual 6-yr mortality was high and survival was significantly better in patients without anticoagulants than for VK-OAC or other active therapy, we need prospective studies comparing anticoagulants even with no drugs and/or new interventional approaches (i.e. left atrial appendage closure) to provide valid future guidelines.

Table:

Mean (SD) Baseline N = Median use (2013-2018)	Total cohort 2812	No active Therapy 951 (34%) 17%	VK-OAC/+/- Asp/Clop 712(25%) 30%	Heparin +/-Asp/Clop 268(10%) 10%	Asp/Clop 675(24%) 24%	Three active Therapies 1655 (59%) 64%
Male/Female	61/39%	59/41%	62/38%	60/40%	64/36%	62/38%
Age	75 (9)	76 (10)	75 (9)	75 (10)	76 (9)	75 (9)
CHA2DS2-Vasc	4.0 (1.5)	3.9 (1.5)	4.0 (1.5)	4.1 (1.5)	4.1 (1.5)	4.1 (1.5)
HAS Bled	3.2 (0.9)	2.9 (0.7)	3.0 (0.8)	3.4 (0.9)	3.9 (0.7)	3.4 (0.9)
Cerebral Infarction	2.9%	2.6%	3.4%	1.9%	3.3%	3.1%
Cerebral	0.9%	0.7%	0.7%	1.5%	1.2%	1.0%
Bleeding	1.0%	1.2%	0.8%	0.4%	1.0%	0.8%
Systemic	4.9%	3.8%	4.9%	5.6%	4.7%	5.0%
Embolism	55.8%	48.9% (a)	60.3% (b)*	57.1%(c)**	59.6%(d)*	59.5% (e)*
All bleeding	4.4	6.0	4.1	4.0	4.0	4.0
Actual 6-yrs Mortality Median (yrs)						

(*) a vs. b/d/e; $p<0.001$ and (**) a vs. c; $p<0.05$

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MO018

CARDIOVASCULAR EFFECTS OF UNILATERAL NEPHRECTOMY IN LIVING KIDNEY DONORS AT FIVE YEARS

Anna Price[1,2], William Moody[1,2], Victoria Stoll[1,2], Ravi Vijapurapu[1,2], Manvir Hayer[1,2], Luca Biasiolli[3], Chris J Weston[1], Rachel Webster[2], Roman Wesolowski[2], Kirsty McGee[1], Amreen Kaur[1], Nicola Edwards[1,4], Boyang Liu[1,2], Luke Pickup[1,2], Ashwin Radhakrishnan[1,2], Jonathan Law[1,2], Colin Chue[2], Richard Steeds[1,2], Charles Ferro[1,2], Jonathan Townend[1,2]

[1]University of Birmingham, Birmingham, United Kingdom, [2]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom, [3]Oxford Centre for Magnetic Resonance, Oxford, United Kingdom and [4]Green Lane Cardiovascular Service, Auckland, New Zealand

Background and Aims: Chronic kidney disease (CKD) is a highly prevalent risk factor for cardiovascular disease with an inverse relationship between estimated glomerular filtration rate (eGFR) and increases in all-cause and cardiovascular mortality. Living kidney donation provides a model to study the cardiovascular effects of a reduced kidney function in previously healthy subjects without comorbidities. We report follow up results in a group of kidney donors and healthy controls who underwent cardiovascular assessment at baseline, 12 months and 5 years after nephrectomy in the CRIB-DONOR studies (NCT01028703, NCT02973607).

Method: A longitudinal blinded end point study of kidney donors (n=50) and healthy controls (n=45) followed up between May 2017 to May 2019. Participants underwent a cardiac MRI (3.0 Tesla) for assessment of left ventricular (LV) size, mass, systolic function (ejection fraction and 3-dimensional feature tracking) and aortic distensibility. Clinical assessment included; office and 24-hr ambulatory blood pressure measures, measurement of arterial stiffness (SphygmoCor) and blood and urine analysis.

Results: Mean follow up time was 5.7 ± 0.7 yrs. Mean eGFR in donors was 95 ± 15 ml/min/1.73m^2 prior to donation, 65 ±13ml/min/1.73m^2 at 12 months and 67 ± 14 ml/min/1.73m^2 at 5 years. This compared with an annual decline in eGFR of -1ml/min/1.73m^2 in healthy controls. Despite a rise in LV mass at 12 months in the original study, by 5 years, LV mass in donors was no different to controls (113 ± 31g vs. 115 ± 30g, p=0.707). There was also no significant difference in LV volumes or LV geometry. At 5 years, 3D global longitudinal strain (donors -16.2 ± 2.5% vs. controls -14.9 ± 2.1%, p=0.007) and 3D global circumferential strain (donors -19.0 ± 2.5% vs. controls -17.7 ± 2.2%, p=0.004) were marginally greater in donors than controls.

Markers of vascular stiffness (pulse wave velocity and augmentation index) were increased in donors compared to controls at 12 months but at 5 years they were not significantly different. No changes in office or ambulatory blood pressure were observed at any time point in donors or controls. At 5 years, uric acid was significantly greater in donors than controls (335 ± 83 µmol/L vs. 276 ± 7, p=<0.001) and had increased after the 12 month time point despite an improvement in eGFR. At 12 months the prevalence of a detectable troponin and levels of fibroblast growth factor-23 were greater in donors compared to controls, but this effect was lost at 5 years

Conclusion: The reduction in eGFR associated with nephrectomy in living kidney donors in the absence of intrinsic renal disease or comorbidity does not lead to adverse changes in cardiovascular structure and function at 5 years. This study offers reassurance to living kidney donors and the transplant community but should prompt further work into the causes of cardiovascular disease in CKD as we have found no medium term deleterious cardiovascular effects of an isolated reduction in eGFR.

MO019

AURORA PHASE 3 TRIAL DEMONSTRATES VOCLOSPORIN STATISTICAL SUPERIORITY OVER STANDARD OF CARE IN LUPUS NEPHRITIS (LN)

Dawn J. Caster[1], Neil Solomons[2], Simrat Randhawa[2], Robert B. Huizinga[2]

[1]University of Louisville School of Medicine, School of Medicine, Louisville, United States of America and [2]Aurinia Pharmaceuticals, Inc., Victoria, Canada

Background and Aims: Voclosporin (VCS) is a novel high potency calcineurin inhibitor (CNI) with a favorable metabolic profile and a consistent predictable dose response potentially eliminating the need for therapeutic drug monitoring. The Aurinia Renal Response in Active Lupus with Voclosporin (AURORA) study, involving 357 patients with active LN, was a Phase 3 global, double-blind, placebo-controlled RCT designed to evaluate the efficacy and safety of VCS (23.7mg BID) vs placebo in combination with mycophenolate (MMF, 2 g/day) and rapidly tapered low dose oral steroids.

Method: The primary endpoint was renal response (RR) at 52 weeks. RR was defined as UPCR of $\leq$ 0.5 mg/mg, eGFR $\geq$ 60 mL/min, or no confirmed decrease from baseline in eGFR of $>$ 20%, presence of sustained, low dose steroids and no administration of rescue medication.

Results: AURORA met its primary endpoint, achieving statistically superior RR rates of 40.8% for voclosporin vs. 22.5% for the control (OR 2.65, 95% CI; $p < 0.001$). The benefits of VCS were also seen for all predetermined secondary endpoints, achieving statistical significance in favor of VCS for RR at 24 weeks, partial renal response (PRR) at 24 and 52 weeks, time to achieve UPCR $\leq$ 0.5, and time to 50% reduction in UPCR. Prespecified confirmed eGFR decreases $>$30% were similar in both groups, with 10.1% reported in the VCS group and 10.2% in the control arm ($p = 0.971$). No significant differences were seen at any timepoints in the study. Furthermore, all pre-specified subgroup analyses (age, sex, race, biopsy class, region, and prior MMF use) also favored VCS. VCS was well tolerated with no unexpected safety signals. Similar SAEs were reported in the VCS group (20.8%) and in the control arm (21.3%). Infection was the most commonly reported SAE with 10.1% of VCS patients versus 11.2% of patients in the control arm. Overall mortality in the trial was low, with 6 deaths observed; 1 in the VCS arm and 5 in the control group. Additionally, the VCS arm showed no significant decrease at week 52 in eGFR or increase in BP, lipids or glucose.

Conclusion: While maintaining a comparable safety profile, VCS plus standard therapy achieved a statistically superior RR over one year compared to placebo plus standard therapy in adults with active LN.

MO020

EFFICACY AND SAFETY OF THE LONG-ACTING C5 INHIBITOR RAVULIZUMAB IN PATIENTS WITH POSTPARTUM ATYPICAL HAEMOLYTIC URAEMIC SYNDROME

Anja Gäckler[1], Vladimir Dobronravov[2], Gaetano La Manna[3], Andrew Denker[4], Peng Liu[4], Ulf Schoenermarck[5], Maria Vinogradova[6], Sung-Soo Yoon[7], Manuel Praga[8]

[1]Essen University Hospital, Essen, Germany, [2]FSBEI HE I.P. Pavlov SPbSMU MOH, St. Petersburg, Russia, [3]Azienda Ospedaliera Universitaria Policlinico Sant'Orsola Malpighi, Bologna, Italy, [4]Alexion Pharmaceuticals Inc., Boston, United States of America, [5]Medizinische Klinik IV, Klinikum der Universität, Munich, Germany, [6]National Medical Research Center of Obstetrics and Gynecology, Moscow, Russia, [7]Seoul National University Hospital, Korea, Rep. of South and [8]University Hospital 12 de Octubre, Madrid, Spain

Background and Aims: Atypical haemolytic uraemic syndrome (aHUS) triggered by pregnancy is a rare and under-recognised disease caused by dysregulation of the alternative complement pathway that occurs in approximately 1 in 25,000 pregnancies. The 311 phase 3 trial (NCT02949128) showed that ravulizumab, a long-acting C5 inhibitor built on eculizumab, with a maintenance dosing interval of 8 weeks, is efficacious in treating aHUS. In this analysis, we report outcomes in a subgroup of patients with postpartum-aHUS enrolled in the 311 study.

Method: This was a global, phase 3, single-arm, multicentre trial evaluating the efficacy and safety of ravulizumab in adults ($\geq$18 years of age) with aHUS naïve to complement inhibitor treatment. The primary endpoint was complete thrombotic microangiopathy (TMA) response (simultaneous platelet count normalisation [$\geq$150 x 10^9/L], lactate dehydrogenase [LDH] normalisation [$\leq$246 U/L] and $\geq$25% improvement in serum creatinine at 2 separate assessments $\geq$28 days apart) through the 183-day initial evaluation period. Additional efficacy endpoints were: time to complete TMA response, haematological normalisation (platelet count and LDH), dialysis requirement status, and change in eGFR.

Results: Eight patients with postpartum-aHUS (mean age 36 [$\pm$8] years) were diagnosed within 12 days of delivery. Seven patients were white and one was Asian. Six patients (75%) had received plasma exchange/infusion before ravulizumab therapy; five (63%) were on dialysis. Complete TMA response was achieved in 7/8 patients (87.5%) in a median time of 32 days. Haematological normalisation was observed in all patients. By Day 29, all five patients on dialysis at baseline had discontinued dialysis, and by Day 183 all eight patients had improved CKD stage (defined based on eGFR value) by $\geq$1 category. Three possible treatment-related adverse events (non-serious) were noted in two patients (arthralgia and nasopharyngitis; urinary tract infection). All patients survived and no meningococcal infections occurred.

Conclusion: This is the first prospective analysis of a C5 inhibitor in postpartum-aHUS. Treatment with ravulizumab resulted in rapidly improved haematological and renal outcomes with no unexpected adverse events identified when administered at 8-weekly dosing intervals through intravenous infusion.

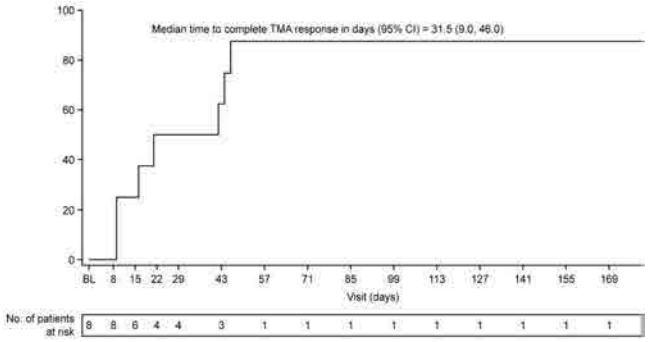


Figure: Median time to complete TMA response

Kaplan–Meier graph depicting time to complete TMA response.

BL, baseline; CI, confidence interval; TMA, thrombotic microangiopathy.

MO021

GALECTIN 3 LEVEL IS REDUCED BY TREATMENT WITH SODIUM BICARBONATE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Mirela Dobre[1,2], Neil Patel[2], Hima Sapa[2], Edward Horwitz[2], Michal Melamed[3], Thomas Hostetter[4]

[1]University Hospitals Cleveland Medical Center, Medicine, Division of Nephrology and Hypertension, Cleveland, United States of America, [2]Case Western Reserve University, Cleveland, United States of America, [3]Albert Einstein College of Medicine of Yeshiva University - Jack and Pearl Resnick Campus, United States of America and [4]University of North Carolina at Chapel Hill, United States of America

Background and Aims: Circulating cardiac biomarkers implicated in the pathogenesis of heart disease are a non-invasive platform to assess the cardiovascular disease (CVD) burden in individuals with chronic kidney disease (CKD). Galectin 3 is a 26 kDa β-galactoside-binding lectin that has a graded and positive association with CKD stages. In animal models, inhibition of galectin-3 prevents myocardial fibrosis. These pre-clinical findings have not been replicated in randomized controlled studies in humans. Metabolic acidosis of CKD has been shown to be associated with adverse CVD outcomes. We sought to examine whether correction of metabolic acidosis of CKD leads to lower circulating levels of Galectin 3, as an expression of myocardial fibrosis.

Method: A total of 95 participants with stages 3 and 4 CKD and a serum bicarbonate level between 21-25 mEq/L, were randomized to receive sodium bicarbonate at a dose of 0.4 mEq/kg/day once a day or placebo for two years at two clinical sites in US. Galectin 3, was measured at study baseline and after one year.

Results: Fifty participants were randomized to sodium bicarbonate and 45 to placebo. Mean age (SD) was 61.4 (10.2) years, 48% were women, 57% were non-Hispanic black, and 40% were non-Hispanic white, 61% had diabetes mellitus and 90% had hypertension at baseline. Mean baseline serum bicarbonate level was 23.5 (SD 1.7), mean (SD) baseline eGFR was 38.8 (11.2) ml/min/1.7m^2 and mean (SD) baseline systolic BP was 130 (17) mmHg. There were no differences in baseline characteristics between treatment groups.

Compared to the placebo group, participants randomized to sodium bicarbonate had statistically significant change in the levels of Galectin 3 after one year of treatment (-7.12% vs 7.76% and -1.25 vs 1.54 ng/ml, p=0.03 in the sodium bicarbonate vs. placebo group, respectively, Figure). In subgroup analyses by CKD stages, participants with stage 3A randomized to sodium bicarbonate observed the highest decrement in Galectin 3 levels (-19.2% vs 14.7%, p=0.01; -3.3% vs -4.8%, p=0.49; and -7.4% vs 29.1%, p=0.09; for CKD 3B, 3B and 4, respectively).

Conclusion: The level of Galectin 3 was reduced in patients with CKD 3 and 4 treated with sodium bicarbonate. This provides a framework for future therapeutic interventions aimed at reduction of myocardial fibrosis in patients with CKD and metabolic acidosis.

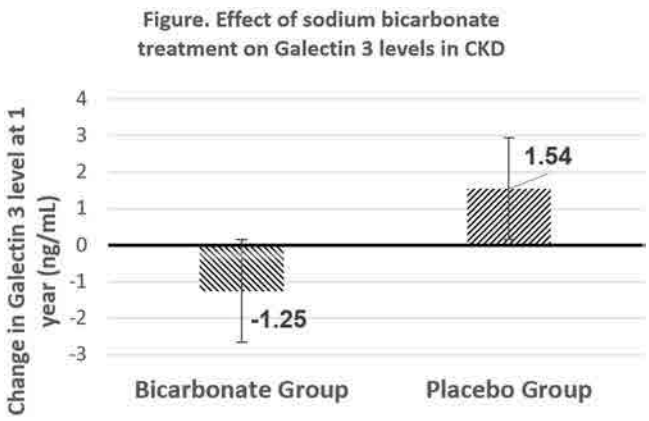


Figure:

ASPECTS OF CKD PATHOPHYSIOLOGY 2

MO022

URINARY PHOSPHATE/UREA RATIO, A NEW TOOL TO EVALUATE ADHERENCE TO PHOSPHATE DIETARY INTERVENTIONS IN CKD PATIENTS

M. Victoria Pendon-Ruiz de Mier[1,2], Rafael Santamaria[1,2], Cristian Rodelo-Haad[1,2], Juan. R Muñoz-Castañeda[1,2], Cristina Membrives[1], Rodrigo Lopez-Baltanas[1], M. Dolores Lopez-Zamorano[2], Alejandro Martin-Malo[1,2], Francisco Caravaca[3], Sagrario Soriano Cabrera[1,2], Mariano Rodriguez[1,2]

[1]Instituto Maimónides de Investigación Biomédica de Córdoba, Córdoba, Spain, [2]Hospital Universitario Reina Sofia, Nephrology, Córdoba, Spain and [3]Infanta Cristina Hospital, Nephrology, Badajoz, Spain

Background and Aims: In chronic kidney disease (CKD) patients, phosphate (P) restriction is crucial for the control of mineral metabolism. Many reports indicate that P intake doesnot correlate with 24-hour phosphaturia. Different sources of P (organic or inorganic) have different intestinal absorption rates. Different proportions of organic and inorganic P in diet might be the reason for the lack of correlation between phosphorus intake and phosphaturia. Therefore, we aimed to evaluate if the source of dietary P rather than the total amount of P ingested determines total phosphaturia and it was accessed to what extent inorganic P intake modifies phosphaturia

Method: A 3-day dietary survey was performed in 71 stages G2-3 CKD patients with metabolic syndrome to estimate the amount and source of P in the diet. Blood and 24-hour urine-samples were collected. Total phosphaturia, fractional excretion of P (FeP%), urinary P/eGFR ratio (mg/day/GFR that reflects the urine P excretion relative to renal function), P/creatinine ratio, urinary urea /Cr ratio, and urinary P/urea ratio (that reflects daily intestinal absorption of P relative to the amount of proteins absorbed and metabolized) were evaluated. P/urea ratio was categorized into tertiles and contrasted in terms of the other variables analyzed (T1=<0.027 mg/mg, T2=0.027-0.033 mg/mg, T3= >0.033 mg/mg). Statistics were performed using R 3.6.2, RStudio, Tidyverse, and tableone v0.10.0 packages.

Results: Patients' age was 61±9 years, and eGFR was 68±21 ml/min/1.73m^2. Estimated P intake was 869±289 mg/day. According to sources, P intake was 64% from animal sources, 22% from vegetable sources, and 14% from inorganic P. Total P intake did not correlate with urinary P (r=0.18, p=0.12), urinary P/eGFR (r=-0.32, p=0.79), or FeP (r=-0.08, p=0.48). Figure 1 shows that patients ingesting more P have a greater intake of inorganic P. There was a correlation between P intake and P/Urea ratio (p=0.008). Patients in the upper urinary P/urea tertile showed the highest daily P intake (p=0.04), and inorganic P (p=0.03). These patients from tertile 3 also showed the highest amount of urinary P excretion (p=0.04).

Conclusion: Urinary P/urea reflects the total P intake and, more importantly, provides information about the amount of inorganic P. Therefore, the P/urea ratio may be used to guide the appropriate nutritional advice for CKD patients.

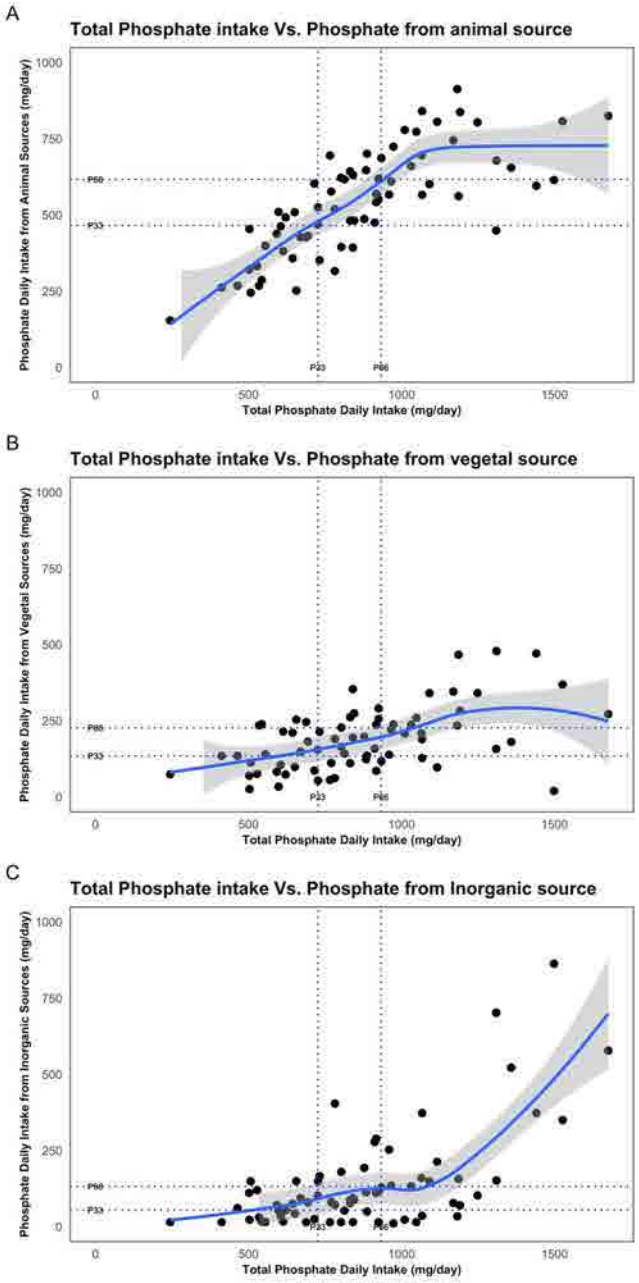


Figure: Correlation between daily phosphate intake and the different sources of phosphate on the diet, a. Animal, b. Vegetal, c. Inorganic. Dotted lines represent tertiles.

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MO023

SARCOPENIA, CHRONIC KIDNEY DISEASE AND RISK OF MORTALITY: FINDINGS FROM 426,839 INDIVIDUALS IN THE UK BIOBANK

Thomas Wilkinson[1], Joanne Miksza[2], Luke Baker[1], Courtney Lightfoot[1], Emma Watson[3], Thomas Yates[4], Alice Smith[1]

[1]University of Leicester, Department of Health Sciences, Leicester, United Kingdom, [2]Leicester Real World Evidence Unit, Leicester, United Kingdom, [3]University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom and [4]Leicester Biomedical Research Centre, Leicester Diabetes Centre, Leicester, United Kingdom

Background and Aims: Sarcopenia describes a degenerative and generalised skeletal muscle disorder involving the loss of muscle mass and function. In studies of the general population, sarcopenia is associated with adverse outcomes including falls, functional decline, frailty, and mortality. However it remains an under-recognised yet important clinical problem in an ever-increasing ageing and multimorbid renal population. Whilst sarcopenia has been widely studied in end-stage renal disease, there is limited evidence of its prevalence and effects in those not requiring dialysis, particularly in large cohort studies and using the latest sarcopenia definitions. Using the UK Biobank, we aimed to identify the prevalence of sarcopenia in individuals with non-dialysis CKD and its association with mortality.

Method: 426,839 participants were categorised into a CKD (defined as eGFR <60ml/min/1.73m^2 not requiring dialysis) and a non-CKD comparative group (no evidence of CKD). Sarcopenia was diagnosed using criteria from the EWGSOP2: 'probable sarcopenia' (low handgrip strength (HGS) <27 and 16kg, males and females respectively); 'confirmed sarcopenia' (low HGS plus low muscle mass, appendicular lean mass <7.0 and 5.5 kg/m^2 as measured by bioelectrical impedance); and 'severe sarcopenia' (low HGS and muscle mass plus slow gait speed). Patients requiring existing renal replacement therapy were excluded. All-cause mortality was extracted from data linkage to national death records with a median follow up of 9.0 years. Data were analysed using Cox survival models.

Results: CKD (non-dialysis dependent) was identified in n=7,623 individuals (mean age 62.7 (±5.9) years, 44% male, eGFR 52.5 (±7.7) ml/min/1.73m^2) compared to n=419,216 in the non-CKD comparative group (mean age 56.1 (±8.1) years, 47% male). 'Probable sarcopenia' was identified in 9% of individuals with CKD compared to 5% in those without CKD (P<0.001). 'Confirmed sarcopenia' was observed in 0.3% of those with CKD (vs. 0.2% in the non-CKD group, P<0.001). 0.2% of CKD patients satisfied all three criteria ('severe sarcopenia') compared to 0.03% in those without CKD (P<0.001). In CKD, sarcopenia was significantly associated with all-cause mortality: 'probable sarcopenia', unadjusted hazard ratio (HR) 1.95 (95%CI 1.57 to 2.42), P<0.001 (Figure 1); 'confirmed sarcopenia', HR 5.1 (2.5 to 10.3) P<0.001; 'severe sarcopenia', HR 5.1 (1.9 to 13.5) P=0.001.

Conclusion: In the largest cohort of its kind, probable sarcopenia was present in 9% of individuals with non-dialysis CKD. The risk of sarcopenia was significantly higher in those with CKD than those without. Regardless of criteria used, CKD patients with sarcopenia were approximately 2-5 times more likely to die than those without sarcopenia. Worryingly, the risk of sarcopenia was elevated even in patients with early stage mild to moderate CKD. Our results show that sarcopenia, including just the presence of low muscle strength, is an important predictor of mortality in early non-dialysis CKD. Measuring sarcopenia as standard practice may identify those most at risk of future adverse events and in need of appropriate interventions to mitigate its negative effects.

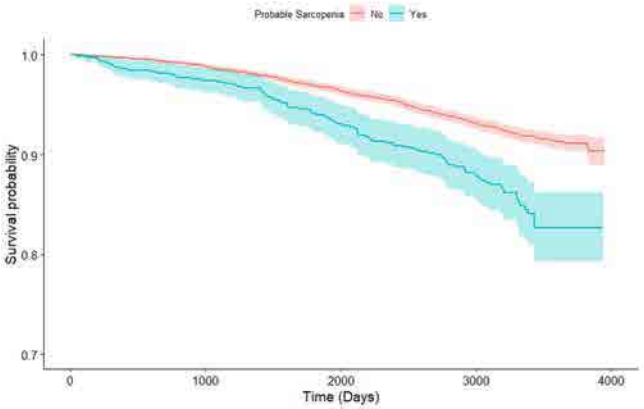


Figure 1. Survival curve for CKD patients with and without probable sarcopenia

MO024

WHAT IS THE BEST PREDICTABLE LIPID SUBFRACTION FOR CARDIOVASCULAR OUTCOMES AND ALL-CAUSE MORTALITY IN PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE?

Yaerim Kim[1], Jeongsoo Yoon[2], Jin Hyuk Paek[1], Woo Yeong Park[1], Kyubok Jin[1], Seungyeup Han[1], Kwon Wook Joo[3], Dong Ki Kim[3]

[1]Keimyung University School of Medicine, Department of Internal Medicine, Daegu, Korea, Rep. of South, [2]Yoon's Internal Medicine Clinic, Daegu, Korea, Rep. of South and [3]Seoul National University Hospital, Department of Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Dyslipidemia is an essential parameter for the prediction of cardiovascular disease (CVD). We aimed to investigate the most valuable subfraction of lipid for predicting CVD in patients with chronic kidney disease (CKD).

Method: We retrospectively reviewed the National Health Insurance Service database for people who received nationwide health screening in 2009. All subjects exposed with lipid-lowering agent before screening were excluded. The population was divided as control, early CKD (eGFR 45-60 ml/min/m^2), and advanced CKD (eGFR <45 ml/min/m^2) by estimated glomerular filtration rate. Each subfraction of lipid profile, including LDL, TG, HDL, and TG/HDL, was categorized by decile, and the reference was the fifth decile. The end-point of the study was major adverse cardiovascular events (MACCE). The hazard ration (HR) of MACCE was calculated using Cox regression models after adjustment of multiple covariates.

Results: A total of 3,634,915 examiners were included in this study, with 66,810 (1.8%) and 404,315 (11.1%) in advanced and early CKD, respectively. For all populations, LDL, TG, HDL, and TG/HDL showed a linear relationship to MACCE. Except HDL, all subfraction showed positive correlation with the risk for MACCE: adjusted HR (aHR) in tenth decile, 1.45 (1.42-1.49) in LDL; 1.25 (1.22-1.28) in TG; 1.30 (1.27-1.33) in TG/HDL; 0.88 (0.85-0.90) in HDL. Although these patterns were similar in TG, HDL, and TG/HDL for all-cause mortality, only LDL showed different pattern for the two outcomes. In the subgroup analysis using LDL, according to the renal function, the significance for the outcomes and a linear pattern was decreased in the advanced CKD group. For the TG/HDL, although the significance was deceased, the linear pattern has maintained in the advanced CKD group (Fig 1).

Conclusion: The pattern and significance of lipid subfraction were different according to the grade of renal function. Thus, TG/HDL should be additionally considered with LDL as a target variable in patients with advanced CKD.

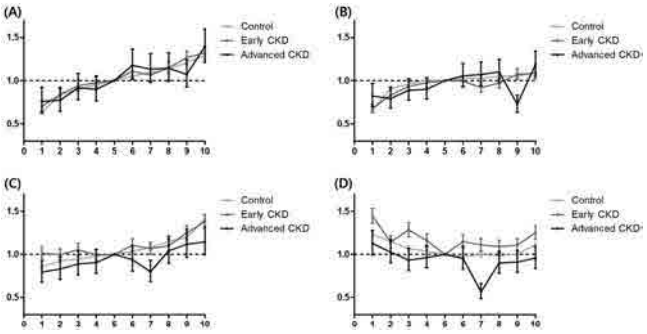


Figure: The pattern of risk for MACCE and all-cause mortality using TG/HDL and LDL in according to stage of chronic kidney disease.

MO025

ADVANCED GLYCATION END PRODUCTS (AGES) AND SOLUBLE RECEPTOR FOR AGES (SRAGE): ASSOCIATION WITH RISK OF MORTALITY IN CHRONIC KIDNEY DISEASE PATIENTS

Elena Dozio[1], Lara Caldiroli[2], Silvia Nerini[3], Elena Vianello[1], Federico Ambrogi[4], Piergiorgio Messa[2,5], Massimiliano Marco Corsi Romanelli[1,6], Simone Vettoretti[2]

[1]Università degli Studi di Milano, Department of Biomedical Science for Health, Milan, Italy, [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Unit of Nephrology Dialysis and Kidney Transplantation, Milan, Italy, [3]ASST Grande Ospedale Metropolitano Niguarda, Department of Clinical Microbiology, Milan, Italy, [4]Università degli Studi di Milano, Department of Clinical Sciences and Community Health, Milan, Italy, [5]Università degli Studi di Milano, Department of Clinical Sciences and Community Health, Milan, Italy and [6]IRCCS Policlinico San Donato, Operative Unit SMeL-1 Laboratory Medicine, San Donato Milanese, Italy

Background and Aims : In chronic kidney disease patients (CKD), excessive oxidative stress, uremia and chronic inflammation may increase the production of advanced glycation end-products (AGEs) which in turn promote CKD-related morbidities and mortality. Much attention has recently been paid to the soluble receptor for AGEs (sRAGE), as a marker of inflammation, oxidative stress, atherosclerosis and heart failure. sRAGE is a decoy receptor that prevents AGEs binding to RAGE, the cell membrane form of the receptor, and RAGE-related detrimental effects.

Both AGEs and sRAGE accumulate in CKD due to the increased production and reduced kidney filtration. Recently, we reported an association between higher levels of sRAGE and mortality in hemodialysis and peritoneal dialysis patients. Whether AGEs, sRAGE and its different isoforms, namely the membrane-cleaved receptor cRAGE and the endogenous secretory form esRAGE, may also work as prognostic factors for mortality in non-dialysis CKD patients is not known.

Method : We quantified plasma sRAGE and esRAGE levels in 111 CKD patients (mean $\pm$ SD age: 77.71 $\pm$ 10.24 years, eGFR: 24.86 $\pm$ 11.06 ml/min, male gender: 74.86%) by ELISA. Florescent AGEs and glycated albumin (GA) were quantified by AGEs-specific fluorescence (excitation: 365 nm, emission: 414-445 nm) and the quantILab assay (Werfen, Italy), respectively. The cRAGE form was estimated by subtracting esRAGE from sRAGE and the ratio cRAGE/esRAGE was calculated. AGEs were normalized against total proteins. Patients were screened for malnutrition and malnutrition-inflammation score (MIS) was calculated (4-8: risk of malnutrition, >8: malnutrition). The Cox proportional-hazards model was used for investigating the association between variables and survival time. Median follow-up time was 40 months.

Results : Mean levels of sRAGE, esRAGE and cRAGE were 2317 $\pm$ 1224 pg/ml, 648 $\pm$ 453 pg/ml and 1669 $\pm$ 901 pg/ml, respectively. The mean value of cRAGE/esRAGE ratio was 2.82 $\pm$ 0.96. AGEs/total protein content was 433.2 A.U., GA was 21.3 $\pm$ 7.5 % and MIS 5.98 $\pm$ 4.67. During the follow up, 28 patients died. Univariate Cox regression indicated a prognostic role for mortality for age (HR: 1.100, 95%CI: 1.041-1.163, $p < 0.001$), AGEs/total protein (HR: 1.004, 95%CI: 1.000-1.007, $p < 0.05$), esRAGE (HR: 1.001, 95%CI: 1.041-1.001, $p < 0.01$), cRAGE/esRAGE (HR: 0.5390, 95%CI: 0.331-0.888, $p < 0.05$) and MIS (HR: 1.079, 95%CI: 1.025-1.137, $p < 0.01$). After adjusting for age and MIS, the associations were still significant for esRAGE (HR: 1.001, 95%CI: 1.0002-1.001, $p < 0.01$) and cRAGE/esRAGE ratio (HR: 0.572, 95%CI: 0.347-0.943, $p < 0.05$), with AGEs/total protein at the margin of statistical significance (HR: 1.004, 95%CI: 0.9997-1.007, $p = 0.0726$).

Conclusion : In CKD higher levels of esRAGE and lower cRAGE/esRAGE ratio may have a prognostic role for mortality. Since esRAGE acts as a decoy receptor for AGEs and thus has a cytoprotective effect, from a pathological point of view the observed association with esRAGE but not cRAGE was quite surprisingly. One potential explanation is that AGEs increases all sRAGE isoforms, but esRAGE accumulation was greater than that of cRAGE due to a different synthesis/catabolism that needs further investigations.

In conclusion, in CKD patients esRAGE and cRAGE/esRAGE seem to be useful supportive tools to identify high risk patients.

MO026

TREATMENT WITH ACTIVE VITAMIN D DOES NOT IMPROVE LEFT VENTRICULAR HYPERTROPHY BUT FURTHER INCREASES FGF23 AND ACCELERATES CKD PROGRESSION IN CHILDREN

Maren Leifheit-Nestler[1], Anne Schoen[1], Jennifer Deppe[1], Aysun Karabay Bayazit[2], Łukasz Obrycki[3], Nur Canpolat[4], Ipek Kaplan Bulut[5], Karolis Azukaitis[6], Gabriele Stangl[7], Rouven Behnisch[8], Rukshana Shroff[9], Justine Bacchetta[10], Uwe Querfeld[11], Franz Schaefer[12], Dieter Haffner[1]

[1]Hannover Medical School, Department of Pediatric Kidney, Liver and Metabolic Diseases, Hannover, Germany, [2]Cukurova University School of Medicine, Department of Pediatric Nephrology, Turkey, [3]The Children's Memorial Health Institute, Department of Nephrology, Kidney Transplantation and Arterial Hypertension, [4]Istanbul University Cerrahpasa Faculty of Medicine, Department of Pediatric Nephrology, [5]Ege University Faculty of Medicine, Division of Pediatric Nephrology, Department of Pediatrics, [6]Vilnius University, Clinic of Pediatrics, Faculty of Medicine, [7]Martin Luther University Halle-Wittenberg, Institute of Agricultural and Nutritional Sciences, [8]University Heidelberg, Institute of Medical Biometry and Informatics, [9]Great Ormond Street Hospital for Children and Institute of Child Health, Department of Pediatric Nephrology, [10]Hospices Civils de Lyon, Centre de Référence des Maladies Rénales Rares, Hôpital Femme Mère Enfant, [11]Charité Universitätsmedizin Berlin, Department of Pediatrics, Division of Gastroenterology, Nephrology, and Metabolic Medicine and [12]University Heidelberg, Division of Pediatric Nephrology, Center for Pediatrics and Adolescent Medicine

Background and Aims: Elevated FGF23, activation of the renin-angiotensin-aldosterone system (RAAS), and vitamin D and Klotho deficiency promote left ventricular hypertrophy (LVH) and LV fibrosis in chronic kidney disease (CKD). Whether treatment with active vitamin D affects uremic cardiomyopathy and/or FGF23/Klotho system in CKD is unclear.

Method: 5/6 nephrectomized (5/6Nx) rats, as a well-established model of CKD, were dose-dependently treated with calcitriol for 10 weeks and the cardiac phenotype, including local RAAS activation, was investigated compared to untreated 5/6Nx and sham-operated rats. Additionally, 38 children with eGFR $\leq$ 30 ml/min/1.73 m^2 selected from the Cardiovascular Comorbidity in Children with CKD (4C) study were enrolled in a case-control study. Nineteen children were started on active vitamin D treatment with either calcitriol or calcidiol (average dosage 0.4 µg/day), and 19 CKD children with non-active vitamin D treatment matched for age, eGFR, serum calcium, parathyroid hormone, and phosphate served as controls. LV mass index (LVMI), LVH prevalence (LVMI >95th percentile), intact (iFGF23) and C-terminal FGF23 (cFGF23), and soluble Klotho (sKlotho) were assessed at baseline and after nine months.

Results: In 5/6Nx rats, FGF23 synthesis in bone and heart was enhanced compared to sham-operated rats, and calcitriol further stimulated its expression in bone only. Renal Klotho expression was reduced in 5/6 rats and almost normalized after calcitriol treatment. 5/6Nx induced cardiomyocyte growth and LV fibrosis, and calcitriol treatment significantly ameliorated both. Cardiac RAAS genes, such as angiotensinogen, renin, angiotensin-converting-enzyme, and angiotensin II receptor type I, were significantly upregulated in 5/6Nx rats compared to sham-operated animals, and normalized by calcitriol treatment.

In the 4C study cohort, median plasma cFGF23 and iFGF23 were significantly elevated in both groups, whereas sKlotho was not altered compared to healthy children. Forty-seven percent and 42% of active vitamin D-treated patients and controls, respectively, received blood pressure (BP) medications, however diastolic BP was slightly but significantly enhanced in both groups compared to healthy children. Mean LVMI and LVH prevalence of 47% in active vitamin D-treated patients and controls did not differ at baseline. After nine months, median cFGF23 and iFGF23 were significantly increased in active vitamin D-treated patients compared to controls. sKlotho levels were decreased in the active vitamin D-treated group compared to baseline but not in controls. A significant decline in median eGFR was observed in active vitamin D group but not in controls. Likewise, the median eGFR change during the observation period was higher in the active vitamin D group compared to controls. Median LVMI as well as frequency of LVH did not change significantly during vitamin D treatment, nor in controls. Consequently, final median LVMI as well as percentage of patients with LVH did not significantly differ between groups.

Conclusion: Calcitriol treatment in 5/6Nx rats improves cardiac hypertrophy and fibrosis, reduces uremia-induced cardiac RAAS gene expression, and improves renal Klotho expression. By contrast, treatment with active vitamin D does not decrease the prevalence of LVH in children with advanced CKD compared to matched controls. This may be due to further enhancement of FGF23 levels, faster progression of CKD associated with reduced Klotho in active vitamin D-treated patients and/or concomitant treatment with RAAS inhibitors. The latter may blunt the favorable effects of calcitriol on the activated RAAS.

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HEALTH SERVICES FOR RENAL PATIENTS

MO027

EVALUATING THE FEASIBILITY AND IMPACT OF A MOBILE PHONE TEXT MESSAGING INTERVENTION ON ADHERENCE TO DIETARY RECOMMENDATIONS IN PATIENTS ON HAEMODIALYSIS (KIDNEYTEXT)

Jessica Dawson[1,2,3], Katrina L Campbell[4,5], Jonathan Craig[6], Allison Tong[2,7], Armando Teixeira-Pinto[2,7], Mark A Brown[8,9], Kirsten Howard[7], Martin Howell[7], Rabia Khalid[2], Kamal Sud[10,11,12], Aravinda Thiagalingam[1,13], Clara K Chow[13,14], Vincent W Lee[1,2,11]

[1]The University of Sydney, Westmead Clinical School, Westmead, Australia, [2]The Children's Hospital at Westmead, Centre for Kidney Research, Westmead, Australia, [3]St George Hospital, Nutrition and Dietetics, Sydney, Australia, [4]Griffith University, Menzies Health Institute, Brisbane, Australia, [5]Metro North Hospital and Health Services, Allied Health Services, Brisbane, Australia, [6]Flinders University, College of Medicine and Public Health, Adelaide, Australia, [7]The University of Sydney, Sydney School of Public Health, Sydney, Australia, [8]St George Hospital, Department of Renal Medicine, Kogarah, Australia, [9]University of New South Wales, St George and Sutherland Clinical School, Sydney, Australia, [10]Nepean Hospital, Department of Renal Medicine, Kingswood, Australia, [11]Westmead Hospital, Department of Renal Medicine, Westmead, Australia, [12]The University of Sydney, Nepean Clinical School, Sydney, Australia, [13]Westmead Hospital, Department of Cardiology, Westmead, Australia and [14]The University of Sydney, Westmead Applied Research Centre, Westmead Clinical School, Sydney, Australia

Background and Aims: Nutritional management is an important, but complex, component of treatment for people on haemodialysis. Dietary recommendations are poorly adhered to, and novel strategies to improve self-management are needed. The aim of this study was to determine the feasibility and effectiveness of a mobile phone text message intervention to improve dietary behaviours in people on haemodialysis.

Method: We conducted a six-month, multi-centre randomised controlled trial (2:1) in patients on maintenance haemodialysis. Participants who were randomised to receive the KIDNEYTEXT intervention received three semi-tailored text messages per week for six months plus usual care. The control group received usual care. The primary outcome was a composite outcome to determine feasibility, using: recruitment rate, retention rate, adherence to dietary recommendations and acceptability. Adherence to dietary recommendations was defined as meeting 3 of 4 nutrition guidelines (potassium, phosphorus, sodium and protein). Acceptability was evaluated by semi-structured interviews to elicit perspectives regarding satisfaction, acceptability and change in behaviours. Secondary outcomes included serum electrolytes, interdialytic weight gain (IDWG) and dietary intake. Trial registration - ACTRN12617001084370.

Results: In total, 130 participants were recruited (87 intervention, 43 control) from six haemodialysis units in Sydney, Australia. 48% of eligible patients consented to participate and 114 participants (88%) completed the trial. Whilst there was no significant difference in adherence to dietary recommendations at 6 months (p=0.14), there were significant reductions in dietary intake of potassium (p=0.01), phosphorus (p=0.003), sodium (p=0.031) and protein (p=0.024) in intervention participants compared to control. Compared to control participants, intervention arm had a significant increase in the number of participants meeting IDWG guidelines (p=0.005) and significant reduction in average IDWG (p=0.024). There was a significant reduction in the number of phosphate binders prescribed in the intervention arm compared to control at 6 months (p=0.03). There was no significant difference in serum electrolytes between the 2 arms at 6 months. Semi-structured interviews explored acceptability, with 5 themes emerging: clear and comprehensive, engaging with consistent and relevant content, maintaining attention with timely reminders, sustaining interest through ongoing care and generic messages inadequate to prompt dietary change.

Conclusion: A mobile phone text message intervention targeting dietary behaviours in people on haemodialysis is feasible and has the potential to change dietary behaviours and improve clinical parameters, such as fluid management and pill burden. Future trials evaluating the effect of a mobile phone text message intervention on patient-centred and clinical outcomes in the haemodialysis population is warranted.

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MO028 BARRIERS TO HOME HEMODIALYSIS IN SASKATCHWAN CANADA: RESULTS FROM A PROVINCIAL SURVEY

Bhanu Prasad[1], Maryam Jafari[2], Lucas Diebel[3], Sachin Shah[4]

[1]Regina General Hospital, Saskatchewan Health Authority, Medicine, Regina, Canada, [2]Dr. T Bhanu Prasad Medical Prof Corp, Medicine, Regina, Canada, [3]College of Medicine, University of Saskatchewan, Medicine, Saskatoon, Canada and [4]St. Paul's Hospital, Saskatchewan Health Authority, Medicine, Saskatoon, Canada

Background and Aims: Home hemodialysis (HHD) offers similar, and perhaps even superior clinical outcomes to in-center hemodialysis (HD) at a fraction of the cost. HHD remains underutilized as remote HD patients in the province of Saskatchewan often relocate or travel hundreds of kilometers weekly in order to receive dialysis related care. Many barriers to accessing and utilizing HHD have been described, but the degree to which these factors impact our province's residents has not been quantified. In quantifying these barriers we can better design better protocols to address the unique barriers leading to low utilization of HHD in our province. The purpose of this study was to determine the barriers to receiving HHD in the province of Saskatchewan.

Method: We conducted a cross sectional survey of in-center HD patients across the province of Saskatchewan, Canada. A total of 740 in-center HD patients (two academic sites, 7 satellite units) were approached by study coordinators. 421 patients (n=268 in the main units and n=153 in the satellite units) agreed to participate in the study. A five-point Likert scale survey was created to identify barriers to HHD with questions addressing HHD awareness and knowledge, accessibility, home constraints, impact on family members, and risks, fears, beliefs surrounding HHD. Responses were anonymous and tabulated using a data collection tool. Survey data were summarized using descriptive statistics.

Results: 41.7 % of participants had more than 12 years of formal education. 12% lived on reserve, 18% on farm, and 70% in town/city. The median (interquartile range=IQR) distance of home to in-center dialysis units was 12 (5-80) kilometers. Only 76% of patients were aware of HHD. 46% of patients felt they had no understanding of the benefits or risks of HHD. Despite only 8% of patients being told they were unsuitable for HHD by their nephrologist, only 28% had ever considered it as a treatment option. Other prominent barriers to HHD were: satisfaction with in-center HD (76%), medical supervision during HD (76%), opportunity to socialize with in-center HD patients (73%), increase in utility payments (54%), and fear of having a major health event at home (51%). Other home constraints (space, inability to make modifications to the home) also figured prominently (35%).

Conclusion: In this study, we identified patient specific barriers to HHD in a prevalent cohort of HD patients. Several barriers were identified with a few consistent themes being identified, including deficiencies in knowledge and awareness, home constraints, and perceived benefits of in-center care (satisfaction with current care, socializing with patients and staff, and fear of a catastrophic event at home). The most frequently reported knowledge barrier was a lack of understanding of the benefits and risks of HHD. These findings suggest that not enough patients are receiving formal education, or active involvement in deciding which modality they would be most suitable for them when initiating dialysis. In center dialysis is considered the 'default' option for many patients, resulting in limited education on HHD. Changing the culture surrounding in-center dialysis as the 'default' method of dialysis requires broader physician, allied health professional, and system level recognition of the potential benefits HHD could offer patients. Differences in remuneration for HHD and in-center HD also pose an obstacle to ensuring patients are making truly informed choices when it comes to in-center HD versus HHD. While the study does not reflect views of all the patients, this information will be valuable in designing an educational program to improve adoption of HHD within our province.

MO029 CLINICAL AND SOCIAL ADVANTAGES OF REMOTE PATIENT MONITORING IN HOME DIALYSIS

Massimo Morosetti[1], Maria Iolanda Famà[2]

[1]ASL Roma 3 - Presidio Ospedaliero G. B. Grassi, Nephrology, Ostia Lido, Roma, Italy and [2]Vree Health Italia S.r.l, Roma, Italy

Background and Aims: Home dialysis (both extracorporeal and peritoneal) can improve the management and the quality of life of patients affected by end stage renal disease. Remote patient monitoring (RPM) can improve the care of Patients in home dialysis: RPM may detect early problems, ensure compliance and give both clinicians and patients a sense of reassurance regarding the clinical management. These advantages may translate into improved outcomes and increased uptake on home dialysis therapies.

For these reasons, the Doctor Plus® NEPHRO program has been created. Clinical and social advantages derived from remote patient monitoring by the Doctor Plus® NEPHRO program versus the standard of care were evaluated.

Method: Patients included in the remote monitoring program, by the Nephrology Unit of ASL 3 in Rome (Italy), from July 2017 and April 2019, were analyzed. Each patient was observed for at least 4 months, up to 22 months.

Patients received a Doctor Plus® NEPHRO KIT composed by clinical devices to measure systolic and diastolic pressure, heart rate, body weight and oximetry. Clinical data were automatically sent from electronic devices to the HUB included into the provided KIT and from the HUB to the Vree Platform operating at the Nephrology Unit. All devices, included HUB and Vree Platform, were classified as medical device class IIa.

The SF-12 questionnaire was also administered by remote nurses and the level of satisfaction with the program Doctor Plus® NEPHRO was evaluated.

Results: We observed 16 patients (56,3% males, mean age 62 years), 14 in Peritoneal Dialysis and 2 in Home Hemodialysis. A total number of 35.720 clinical measures were collected during the observational period.

During this length time, systolic pressure was reduced in 69% of patients and diastolic pressure was reduced in 62,5% of patients. Systolic pressure decreased from 137,8 to 130,2 mmHg ($p<0,0002$) and diastolic pressure decreased from 80,5 to 76 mmHg ($p>0,0002$). Mean heart rate decreased in 50% of patients from 69,4 bpm to 68,8 bpm ($p<0,0046$).

During the same period, clinical monitoring generated 58 early clinical interventions: 11 non planned visits at Nephrological Centre and 47 calls from nephrologist to patients (0,5 visits per month and 2,2 calls per month). In 35 cases pharmacological therapy has been modified (in 80% of cases treatment modified was the hypertension therapy).

Due to the increase of clinical monitoring, Patients accesses to ER are decreased of 29%.

SF-12 questionnaire showed an improvement in the perceived health status in all patients. Reduction of 15% in workdays lost were registered in both patients and caregivers.

Conclusion: Doctor Plus® NEPHRO resulted as a useful tool for the Nephrology Center in order to monitor patients who performed home dialysis. Data collected by the remote monitoring program have shown an improvement in clinical outcomes and the possibility to prevent some clinical complications thus reducing clinical emergencies and the hospitalization rate. Moreover, the possibility for patients and caregivers to complain with morbidity remaining in a home setting, results in the improvement in quality of life.

Finally, the possibility to avoid hospitalizations, emergency accesses and transfers to hemodialysis is important for cost saving with a more appropriate use of healthcare resources.

MO030

PATIENT SAFETY IN A LARGE MULTINATIONAL RENAL SERVICES PROVIDER NETWORK

Belén Marrón[1], Israel Silva[2], Charlotta Wollheim[3], Carlos Lucas[4], Marietta Torok[5], Filiz Akdeniz[2], Suzanne Pearce[2], Ulf Westesson[6], Fernando Macário[7]

[1]Diaverum Renal Services, Corporate Home Therapies & Patient Safety Director. Medical Office, Mälmo, Sweden, [2]Diaverum Renal Services, Corporate Nursing Director. Medical Office, Mälmo, Sweden, [3]Diaverum Renal Services, Corporate Data Management Director. Medical Office, Mälmo, Sweden, [4]Diaverum Renal Services, Corporate Medical Protocols & Standarization Director. Medical Office, Mälmo, Sweden, [5]Diaverum Renal Services, Corporate Medical Integrations Director. Medical Office, Mälmo, Sweden, [6]Diaverum Renal Services, Corporate Data Protection Director. Medical Office, Mälmo, Sweden and [7]Diaverum Renal Services, VP Medical Office, Mälmo, Sweden

Background and Aims: Patient safety is considered of paramount importance under any qualified provision of care, but results from routine tracking of incidents have scarcely been reported, even when that may negatively impact survival.

To analyze all types of incidents in a multinational renal service provider network from Jan.1st to Sept. 30th, 2019.

Method: For the last 10 years, our institution has tracked all incidents under a structured process program, as well as, educated our staff in the importance of proactively reporting and analyzing incidents in a quarterly basis at the clinic, by country and globally. Incidents are categorized in 4 different types: A-Patient related; B-Staff and visitors; C-Products and D-Equipment. Different incident codes are assigned to each type.

Results: A total of 68.399 incidents (2.7 incidents/patient/year) have been reported during Q1-Q3 2019 (higher than in 2018: 2.2). This means an increase of 20% in the total number of reported incidents. Total incidents/1000 treatments was 17.1 (12.1 patient-related incidents). Reporting follows a heterogeneous pattern among countries, being lowest in Argentina and highest in the UK. Top 5 reported incidents were as follows: Codes A15 (voluntarily shortened treatment) and A14 (Patient did not show up), both related to patient adherence to treatment, accounted for 36% of total incidents, vascular access (VA) complications (A4) for 10.5%, change of dialyzer and/or blood lines due to clotting (A2) for 8.6% and recurrent minor monitor malfunction (D1) for 6.7% of incidents. Codes related with unexpected death or cardiorespiratory arrest are not present among the total global top 10 incidents.

Conclusion: Detailed tracking of incidents and comparison between countries have potential to increase quality of care. Room for improvement recently made the Corporate Medical Office to launch new strategies on VA management, anticoagulation and patient compliance, among others. This large series may help other institutions to better monitor and standardize patient safety.

MO031

EFFECTS OF PREDICTIVE MODELLING RISK DIRECTED INTERVENTIONS ON HOSPITALIZATION RATES IN HAEMODIALYSIS PATIENTS

Sheetal Chaudhuri[1], Sophia Rosen[1], John Larkin[1], Len A Usvyat[1], David Sweet[2], Allison Vinson[2], Stephanie Johnstone Steinberg[2], Franklin Maddux[3]

[1]Fresenius Medical Care, Global Medical Office, Waltham, United States of America, [2]Fresenius Medical Care North America, Waltham, United States of America and [3]Fresenius Medical Care AG & Co. KGaA, Global Medical Offoce, Bad Homburg, Germany

Background and Aims: End Stage Kidney Disease (ESKD) patients have high hospitalization rates. We have developed and deployed a predictive model to identify in-centre haemodialysis (HD) patients at an increased risk for all-cause hospitalization within the next 12 months. The model was used in a pilot called Dialysis Hospitalization Reduction Program (DHRP) to identify patients predicted to be at risk of >=6 hospital admissions and provide additional interdisciplinary team intervention. We investigated the impact of the DHRP on hospitalization rates in HD patients.

Method: We used data from 45 clinics in South Alabama/Florida Panhandle regions of the United States who participated in DHRP pilot starting January 2016. The predictive model used more than 200 variables to stratify patients as high risk (>=6 admissions), medium high risk (>=3 admissions) and medium low risk (>=1 admission) and low risk (<1 admission). For patients identified at high risk of hospitalization, social workers assessed psychosocial barriers and offered additional psychosocial intervention to target those barriers. Dietitians utilized a high risk assessment looking at weight, nutrition, and access to food and supplements. Resident nurses assessed high risk patients focusing on anaemia, adequacy, access, blood pressure, fluid management, prior hospitalizations, glycaemic control and risk of skin ulcers and blood stream infection Data from patients at the participating clinics was collected and yearly hospital admission and day rates per patient year were calculated 2 years prior to (2014, 2015) and 3 years after (2016-2018) pilot start. Comparison clinics were chosen from neighbouring regions in South and North Florida (43 and 45 clinics respectively).

Results: Over the study period the number of patients ranged from 4661 to 5672 in the DHRP pilot clinics, 5416 to 5947 in South Florida control clinics, and 6087 to 7596 in North Florida control clinics. Hospitalization rates in pilot clinics during the first year of the DHRP remined similar to the rates during the two years preceding the pilot start. In the second and third years of the DHRP, pilot clinics showed reductions in hospital admission and day rates. At control clinics in both regions the hospital admissions and day rates showed increasing trends while DHRP clinics showed decreasing trends over the study period (Figures 1a and 1b).

Conclusion: These findings suggest predictive model risk directed interdisciplinary team interventions associate with lower hospitalization rates in HD patients, compared to controls. Further studies are needed to confirm these results.

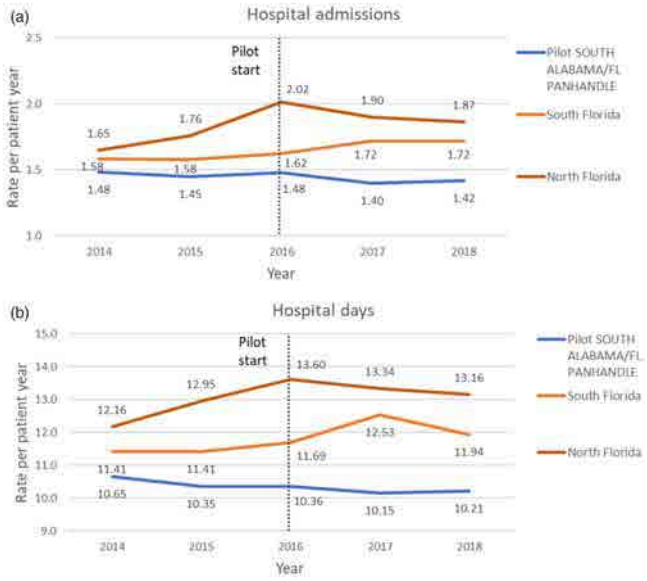


Figure 1a

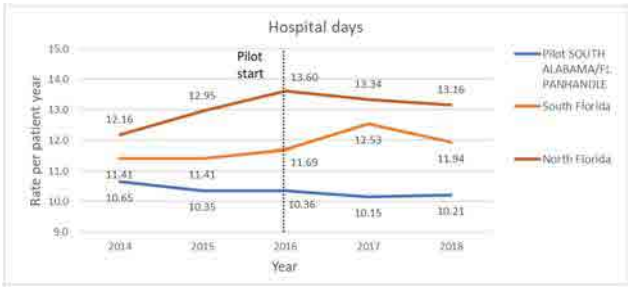


Figure 1b

Nephrology Dialysis Transplantation 35 (Supplement 3): iii000–iii000, 2020

GENETICS IN NEPHROLOGY

MO032 PODOCIN REGULATES THE SIZE OF THE GLOMERULAR PORE

Máté Kétszeri[1], Violetta Antal[1], Gusztáv Schay[2], Anita Ungvári-Veres[1], Katalin Pászty[2], Miklós Kellermayer[2], Dóra Karancsiné Menyhárd[3], Kálmán Tory[1]

[1]MTA-SE Lendület Nephrogenetic Laboratory, 1st Department of Pediatrics, Semmelweis University, Budapest, Hungary, [2]Department of Biophysics and Radiation Biology, Semmelweis University, Budapest, Hungary and [3]MTA-ELTE Protein Modeling Research Group and Laboratory of Structural Chemistry and Biology, Eötvös Loránd University, Budapest, Hungary

Background and Aims: Podocin is a major component of the glomerular slit diaphragm. It is encoded by *NPHS2*, the most frequently mutated gene in steroid-resistant nephrotic syndrome. We previously showed that podocin oligomerization occurs exclusively through the C-terminal helical region and is responsible for mediating interallelic interactions of *NPHS2*. Podocin anchors the main slit diaphragm component nephrin to the podocyte cell membrane. The shortest dimension of the glomerular pore (3,5-4nm) is determined by the distance between two neighboring nephrin molecules in cis position and – according to our structural model – corresponds perfectly to the distance between the nephrin binding domains of two podocin molecules in an oligomer. We therefore hypothesized that podocin regulates the distance between nephrin molecules, thus affecting the size of the glomerular pore. Here we aimed to explore the effects of podocin variants on the distance between neighboring nephrin molecules.

Method: Wild type nephrin was tagged with C-terminal YPet or mRuby3 fluorescent proteins and the two constructs were transiently coexpressed in HEK293 cells, together with podocin variants of different oligomer-forming capacity. We verified the plasma-membrane localization of the fluorescently labelled nephrin molecules by confocal microscopy. Förster resonance energy transfer (FRET) was measured between the fluorescently labelled nephrin molecules in living cells. In a second set of experiments the fluorescent tags (Ypet and mCherry) were inserted in the extracellular part of nephrin at a distance of ten amino acids from the N-terminal end of the transmembrane domain. The fluorescence decay curves measured by time-correlated single photon counting (TCSPC) (Chronos BH, ISS Inc.) were decomposed into lifetime components, and the longest lifetime population – most suitable for long-range FRET – was used for further calculations. Nonparametric tests were used to analyze the data.

Results: Similar results were obtained with the extracellular and the intracellular tags. FRET efficiency was increased in the presence of the wild type podocin ($p<0.0005$ with both extracellular and intracellular tags), but remained unaltered in the presence of the monomer-forming R286Tfs*17 podocin. Similar to R286Tfs*17, the other pathogenic podocin variants (R138Q, A284V and F344Lfs*4) did not alter the FRET efficiency, irrespective of the different effect of these mutations on podocin oligomerization and localization. On the other hand, the coexpression of the R229Q podocin variant, which is benign in the homozygous state, resulted in a similarly high FRET efficiency as the wild type podocin. The FRET efficiency measured between extracellularly labelled nephrin molecules in the presence of the V290M podocin variant correlated with its clinically hypomorphic effect: it fell between that of the wild type and the R286Tfs*17 podocin, being statistically different from both.

Conclusion: Wild type podocin significantly reduces the distance between the nephrin molecules in cis: the shortest dimension of the glomerular pore. Several pathogenic podocin variants do not. The FRET efficiency between the nephrin molecules correlates with the clinical effect of the podocin variants. We thus suggest that a major function of podocin is the regulation of the critical dimension of the glomerular pore.

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MO033

THE DUAL ETAR/AT1R BLOCKER SPARSENTAN SLOWS RENAL DISEASE, IMPROVES LIFESPAN, AND ATTENUATES HEARING LOSS IN ALPORT MICE: COMPARISON WITH LOSARTAN

Dominic Cosgrove[1], Brianna Dufek[1], Duane Delimont[1], Daniel Meehan[1], Gina Samuelson[1], Jared Hartsock[2], Grady Phillips[2], Ruth Gill[2], James Hasson[3], Celia Jenkinson[3], Radko Komers[3], Michael Anne Gratton[2]

[1]Boys Town National Research Hospital, Omaha, United States of America, [2]Washington University, St. Louis, United States of America and [3]Retrophin, Inc., San Diego, United States of America

Background and Aims: In Alport syndrome (AS), endothelin type A receptor (ET_AR) activation plays a role in both renal and inner ear pathologies. Currently, angiotensin converting enzyme inhibitors or angiotensin II type 1 receptor (AT_1R) blockers are the standard of care for patients with AS; however, these drugs have not been shown to improve hearing. Previously, we showed that sparsentan (SP), a dual ET_AR/AT_1R inhibitor, prevented increases in proteinuria, fibrosis, glomerulosclerosis, and glomerular basement membrane dysmorphology. The AS mouse model lifespan was extended when SP treatment was started at 3 weeks (W) of age (pre-proteinuric). Here we compare the effect of SP and the AT_1R blocker losartan (LS) on lifespan and proteinuria in AS mice treated from 4 W, and on hearing loss and associated inner ear pathology in AS mice treated from 3 W to 8.75 W.

Method: Wild type (WT) and AS mice were treated daily with vehicle (V), 60, 120, or 200 mg/kg SP (SP60, SP120, or SP200) by oral gavage, or 20 mg/kg LS by daily oral gavage from 3-4 W of age and in drinking water at 10 mg/kg from 4-8.75 W. Three studies were conducted: early intervention for hearing from 3-8.75 W (V, SP120, and LS, n=5) or for assessment of laminin α2, laminin α5, and collagen IVα1 expression in stria vascularis from 3-7 W (V, SP200, and LS, n=7), and for lifespan with treatment from 3 W (V, n=10) or from 4 W (LS, SP60, or SP120, n=5). Urinary protein/creatinine (UP/C) was assessed weekly during the lifespan study. In the hearing study, the auditory brainstem response (ABR) assessed hearing ability and sensitivity to noise at 8-9 W (n=5). The cochleae were preserved and transmission electron microscopy was used to assess severity of strial pathology and to measure strial capillary basement membrane (SCBM) thickness (n=5-7). Accumulation of extracellular matrix in SCBM was determined in mice treated with V, SP200, or LS by immunofluorescence microscopy using antibodies to laminin α2, laminin α5, or collagen IVα1.

Results: In AS mice treated with SP from 4 W, SP120 significantly ($P<0.05$) increased median lifespan by 34 days compared to LS-treated mice, and by 50.5 days compared to V-treated mice (Figure 1). AS mice treated with SP60 or LS initiated at 4 W did not have a significant difference in lifespan compared to V. At 8 W, SP120 but not SP60 or LS significantly ($P<0.05$) attenuated the increase in UP/C compared to V (UP/C mg/mg mean±SD 8 W: 47±16 V; 31±6 LS; 61±44 SP60; 20±3 SP120). Notably, development of UP/C at 11 W in AS-SP120 mice was significantly attenuated ($P<0.05$) compared to that in AS-LS mice (UP/C mg/mg mean±SD 11 W: 58±8 LS; 77±51 SP60; 18±10 SP120). In hearing studies, although both SP120 and LS significantly ($P<0.05$) prevented SCBM thickening compared to AS-V mice (mean SCBM width±SD nm: 57.8±2.1 WT-V; 67.6±5.5 AS-V; 54.7±2.4 AS-SP120; 55.0±5.9 AS-LS), post-noise ABR thresholds at 16 kHz were significantly improved only in AS-SP120 mice compared to AS-V mice (*$P<0.05$; Figure 2). AS-LS post-noise hearing did not differ from that of AS-V mice. Moreover, SP200 tended to ameliorate increases in expression levels of laminin α2, laminin α5, and collagen IVα1 to a greater extent than LS in the SCBM of AS mice. Finally, dysmorphology of the stria vascularis was noted in LS but not SP120-treated AS mice.

Conclusion: SP120 provided significant nephroprotection in AS mice when treatment was started at 4 W, significantly extending lifespan beyond that of mice treated with LS while delaying the development of proteinuria. SP120 treatment in AS mice reduced the SCBM width. Moreover, SP120 treatment significantly attenuated noise-induced hearing loss in AS mice whereas LS was without effect. These pre-clinical studies, if successfully translated to the clinic, may suggest that sparsentan offers a novel, dual-therapeutic approach in AS by reducing both renal injury and hearing loss.

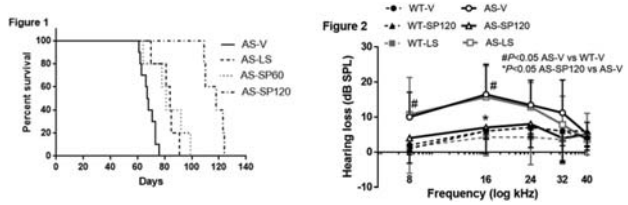


Figure:

MO034 ANALYSIS OF A MOUSE MODEL FOR MCTO DUE TO THE MUTATION OF MAFB TRANSACTIVATION DOMAIN

Toshiaki Usui[1], Naoki Morito[1], Yuki Tsunakawa[2], Hyojung JEON[2], Michito Hamada[2], Seiya Mizuno[3], Satoru Takahashi[2], Kunihiro Yamagata[1]

[1], Department of Nephrology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan, [2], Department of Anatomy and Embryology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan and [3], Transborder Medical Research Center, University of Tsukuba, Tsukuba, Japan

Background and Aims: Transcription factor MafB in podocytes is essential for podocyte differentiation and maintenance. Previous works identified a missense mutation in the transactivation domain of MAFB as the cause of multicentric carpotarsal osteolysis (MCTO). MCTO is a condition involving progressive osteolysis of the carpal and tarsal bones. MCTO patients also develop with focal segmental glomerulosclerosis (FSGS) and renal failure (MCTO nephropathy). However, the pathogenesis of MCTO *in vivo* is unclear.

Method: In order to address this question, we generated an MCTO mouse model using the CRISPR/Cas9-mediated genome editing. This mouse has a human MCTO mutation c.176C>T, (p.Pro59Leu). *Mafb* $^{MCTO/MCTO}$ mice were obtained by crossing *Mafb* $^{MCTO/WT}$ mice. Control animals were *Mafb* $^{WT/WT}$ mice. Sequencing analysis was performed to confirm the integration of the MCTO mutation on F2 generations. We checked urine of these mice every 4 weeks, and biochemical and histological analysis were performed at 26 weeks-ages. RNA-seq analysis of the isolated glomeruli of these mice was performed at 10 weeks-ages.

Results: Interestingly, *Mafb* $^{MCTO/MCTO}$ newborn mice exhibited a 10% lower body weight than control mice. The differences were still observed at 2 weeks, with *Mafb* $^{MCTO/MCTO}$ mice presenting a 23% lower body weight than control animals. The length of femoral bones in *Mafb* $^{MCTO/MCTO}$ mice was shorter than that of control. MCTO model mice exhibit growth deficiency. In addition, *Mafb* $^{MCTO/MCTO}$ mice resulted in albuminuria at 4 weeks-ages from postnatal periods and became persistent. Renal histological analysis in adult stage revealed FSGS-like glomerular lesions in *Mafb* $^{MCTO/MCTO}$ mice. In electron microscope analysis, microvillous transformation of the foot processes of podocytes in Bowman's space and foot processes effacements were seen in *Mafb* $^{MCTO/MCTO}$ mice. These phenotypes are similar to that seen in MCTO nephropathy patients. Subsequently, we performed RNA-seq analysis of isolated glomeruli to gain insight into the molecular mechanism of the MCTO mutation. We found *Cldn1*, gene expression in mature podocytes caused profound proteinuria, was significantly increased in *Mafb* $^{MCTO/MCTO}$ glomeruli.

Conclusion: This study is significant for revealing the mechanism of MCTO and contributes to the development of an alternative treatment against MCTO nephropathy by providing model mice for use.

MO035

HISTORICAL CONTROL ANALYSIS DEMONSTRATES SUPERIOR REDUCTION OF PLASMA GLOBOTRIAOSYLCERAMIDE BY VENGLUSTAT COMPARED WITH PLACEBO OR AGALSIDASE BETA IN CLASSIC FABRY DISEASE PATIENTS

Dominique P. Germain[1,2], William Wilcox[3], Patrick Deegan[4], Kejian Liu[5], Eric Hailman[6], Alberto Ortiz[7], Vijay Modur[6]

[1]University of Versailles, Paris-Saclay University, Division of Medical Genetics and INSERM U1179, Montigny, France, [2]French Referral Center for Fabry Disease, Garches, France, [3]Emory University School of Medicine, Atlanta, United States of America, [4]Addenbrooke's Hospital, Lysosomal Disorders Unit, Cambridge, United States of America, [5]Sanofi Genzyme, Bridgewater, United States of America, [6]Sanofi Genzyme, Cambridge, United States of America and [7]IIS-Fundacion Jiminez Diaz UAM, Madrid, Spain

Background and Aims: Fabry disease (FD) is a rare, X-linked, genetic disorder caused by pathogenic variants in the gene for the lysosomal enzyme alpha-galactosidase A (αGal-A). The progressive accumulation of glycosphingolipids, most notably globotriaosylceramide (GL-3), leads to renal, cardiovascular, and other clinical manifestations over decades. In a single-arm phase 2 study, glucosylceramide synthase inhibition with venglustat led to a reduction in lysosomal GL-3 inclusions in skin capillary endothelial cells, as well as a progressive reduction in plasma GL-3 to normal levels by 26 weeks, with a continued decrease to low-normal levels after 3 years of therapy. We used patient data from a previously completed placebo-controlled phase 3 study of agalsidase beta (Fabrazyme) as historical control to compare the effect of venglustat treatment with placebo over 6 months and with agalsidase beta over 3 years.

Methods: In the venglustat phase 2 study, previously untreated classic FD patients were treated with daily venglustat for up to 3 years (NCT02228460, NCT02489344). For comparison to placebo, change in plasma GL-3 levels after 26 weeks of venglustat treatment was compared with matched historical control data from previously untreated classic FD patients who were treated for 20 weeks with placebo in the phase 3 agalsidase beta study (Eng et al, N Engl J Med 345:9, 2001). For comparison to agalsidase beta, the historical control arm was matched patients treated with agalsidase beta in the phase 3 study; change in plasma GL-3 was compared at multiple time points up to 3 years. Entry criteria and baseline characteristics were similar between the two studies. Due to the much larger numbers of patients in the phase 3 agalsidase beta study, venglustat patients were matched 1:X (variable match) with control (placebo or agalsidase beta) patients based on propensity scores using baseline variables of age, plasma GL-3, gender, UPCR (< 500 vs 500-1000 vs >1000 mg/g), and eGFR (<80 vs >= 80 mL/min/1.73m^2) as matching variables. Plasma GL-3 was measured at Sanofi Genzyme by LC/MS/MS, using the same method for the two studies, with controls in place to assure assay consistency.

Results: Venglustat patients (N=11) were matched to 19 patients for the placebo comparison and to 28 patients for comparison to Fabrazyme. All patients in all 3 groups were male and had elevated plasma GL-3, UPCR <500 mg/g, and eGFR ≥80 mL/min/1.73m^2 at baseline. Mean ages in the 3 groups were 26.6, 25.7, and 26.5 years after matching, respectively. Venglustat treatment for ∼6 months led to a highly significant reduction in plasma GL-3 compared to placebo of 3.62 vs 1.06 μg/mL ($p < 0.0001$). Long-term treatment with venglustat yielded similar reductions in plasma GL-3 compared to agalsidase beta for the first year of treatment, but while GL-3 levels reached a plateau with agalsidase beta, the reduction with venglustat continued with longer treatment and was significantly greater than that of agalsidase beta after 2 years ($p=0.0351$) or 3 years ($p=0.0081$) (Figure). Plasma GL-3 levels after 3 years of treatment were 1.90 and 4.44 μg/mL for venglustat and agalsidase beta, respectively (normal range ≤7.02 μg/mL).

Conclusions: Glucosylceramide synthase inhibition with venglustat led to a significantly greater reduction in plasma GL-3 compared to placebo after 6 months, and treatment for 2-3 years led to a significantly greater reduction in plasma GL-3 compared with agalsidase beta. These results highlight the potential of long-term treatment venglustat to reverse the accumulation of GL-3 in classic FD.

MO036

SINGLE NUCLEOTIDE POLYMORPHISMS OF THE CYP24A1 AND KL GENES ARE ASSOCIATED WITH THE EXTENT OF ARTERIAL CALCIFICATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Guillermo Solache-Berrocal[1,2], Valeria Rolle-Sóñora[3], Noelia Martín-Fernández[4], Serafí Cambray[5], José Manuel Valdivielso[2,5], Isabel Rodríguez[1,2]

[1]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Cardiac Pathology Research Group, Oviedo, Spain, [2]Instituto de Salud Carlos III, REDinREN, [3]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Bioestatistics and Epidemiology Platform, Oviedo, Spain, [4]Hospital Universitario Central de Asturias (HUCA), Nuclear Medicine Unit, Oviedo, Spain and [5]Biomedical Research Institute IRBLleida, Vascular and Renal Translational Research Group, Lleida, Spain

Background and Aims: Individuals with chronic kidney disease (CKD) constitute a population with an exceptionally high cardiovascular risk. Vascular calcification, a common finding in these patients, is a known contributor to cardiovascular disease and several studies suggest it has a certain genetic component. Single nucleotide polymorphisms (SNPs) associated with the extent of calcification in CKD patients could therefore be used to predict individual susceptibility to calcification and subsequent increased cardiovascular risk. We consequently searched for associations of SNPs from candidate genes of known implication in the pathogenesis of vascular calcification (encoding cytokines, extracellular matrix proteins, members of the RANK/RANKL/OPG axis and vitamin D metabolism proteins) with the extent of arterial calcium deposits in order to improve the risk prediction of cardiovascular events in CKD patients.

Method: The study was performed in 1439 individuals from the NEFRONA population, which include CKD patients (stages 2-3, 4-5, and dialysis) as well as healthy controls recruited from 81 Spanish hospitals. Individuals were genotyped with the iPLEXGOLD MassARRAY technology and Assay Design v4 software for 61 SNPs from 22 genes. A continuous vascular calcification score was calculated from the echogenicity of atherosclerotic plaques detected by ultrasonography in the carotid and femoral arteries. Among several other clinical variables, the presence of cardiovascular events during a 4-year follow up was collected. Association of SNPs with calcification extent was identified by univariate linear regression models. Multiple linear regression with backward elimination was used for the selection of an appropriate SNP-based model adjusted by age, sex and CKD stages. Finally, a Cox proportional hazard regression model was applied for the prediction of cardiovascular risk.

Results: Arterial calcification scores were higher with increasing age, male sex, and advanced CKD stages (all $p<0.001$), as expected. Univariate linear regression analyses of all SNPs with the arterial calcification score as dependent variable retrieved p-values <0.05 for 6 six of them (rs11568820, rs2248359, rs2296241, rs3102735, rs385564 and rs495392), which were selected for subsequent analyses. These polymorphisms were next included in a multivariate linear regression model with CKD stage, age and sex as additional independent variables. Only rs2296241 of *CYP24A1* (estimate 0.36, 95% CI 0.14 to 0.58, p=0.001 for homocygous GG) and rs495392 of *KL* (estimate -0.39, 95% CI -0.69 to -0.09, p=0.011 for homocygous TT) remained independently associated with the extent of calcium deposits. Finally, using Cox regression models, it was determined that both the CKD stage (HR [for dialysis stage]=8.34, 95% CI 4.59 to 15.15, $p<0.001$) and the calcification score (HR=2.05, 95% CI 1.67 to 2.54, $p<0.001$) predicted the development of cardiovascular events. Considering all possible risk factors, no differences were found in the rate of development of cardiovascular events according to the genotype for the two associated polymorphisms: rs2296241 HR=1.13, 95% CI 0.87 to 1.48, p=0.36; rs495392 HR=0.80 95% CI 0.63 to 1.03, p=0.08.

Conclusions: Polymorphisms of *KL* and *CYP24A1* genes are associated with the extent of calcification in CKD individuals although they lack the capacity to predict cardiovascular events. However, the echogenic determination of the extent of arterial calcium deposits in CKD patients seems a promising non-invasive, non-irradiating method for the scoring of calcification and even the prediction of cardiovascular events. Further genetic association studies using this technique could therefore yield valuable results.

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EXPANDING THE PATIENT'S VOICE IN NEPHROLOGY WITH PATIENT OUTCOME MEASURES

MO037 SYMPTOM MONITORING WITH FEEDBACK TRIAL (SWIFT) PILOT TO EXPLORE THE FEASIBILITY AND ACCEPTABILITY OF ELECTRONIC PATIENT REPORTED OUTCOME MEASURES (E-PROMS) DATA CAPTURE AND FEEDBACK

Andrea Viecelli[1], Kathryn Dansie[2], Stephen McDonald[2], Shilpanjali Jesudason[3], Emily Duncanson[2], Paul Bennett[4], Rachael Morton[5]

[1]Princess Alexandra Hospital, Woolloongabba, Australia, [2]SAHMRI (South Australian Health and Medical Research Institute), Adelaide, Australia, [3]Kidney Health Australia, Adelaide, Australia, [4]Satellite Healthcare San Jose, San Jose, United States of America and [5]NHMRC Clinical Trials Centre, Camperdown, Australia

Background and Aims: People on haemodialysis (HD) often experience overwhelming and debilitating symptoms of fatigue, pain, nausea, itching, sleeping problems and depression that contribute to poor quality of life. Trials in oncology have shown that active symptom monitoring can improve quality of life and survival, but it remains unknown if this intervention is effective in people on HD. The use of PROMs is increasing in nephrology care; but they are not routinely collected in kidney registries. The SWIFT pilot aims to assess the feasibility and acceptability of tablet-based symptom monitoring with feedback to clinicians in preparation of a large-scale, registry-based cluster-randomised trial to assess the clinical- and cost-effectiveness of this intervention in HD (SWIFT; ACTRN12618001976279).

Method: This pragmatic, multicenter cluster-randomised controlled pilot study tests the hypothesis that 3-monthly tablet-based PROMs monitoring using the Integrated Palliative Outcome Scale-Renal Symptom Tool with electronic feedback to clinicians using the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) compared with usual care will improve health-related quality of life measured by EQ-5D-5L and is technically feasible and clinically acceptable to patients, nurses and nephrologists in different HD settings. Acceptability and feasibility outcomes are assessed through a process evaluation using the Medical Research Council framework: (1) patient acceptability of ePROMS (5-point Likert scale; focus groups with 20 purposively sampled participants), (2) feasibility of embedding ePROMS in routine care (response rates, time from data capture to feedback, ease of generating PROMs reports by the ANZDATA registry), (3) acceptability and usefulness of ePROMs data for nephrologists and nurses (qualitative semi-structured interviews with thematic analysis).

Results: 163 adult patients from 4 HD units across Australia were enrolled (83 in the intervention units and 80 to the control units) and completed baseline PROMs, representing 77% of eligible patients (range 44-90%). At 3-months, 61% of enrolled patients in the intervention units completed the PROMs (range 48-73%). Reasons for non-completion included transfer to another unit and lack of ability to read English. Severe or overwhelming symptoms were reported by 30 of 83 enrolled patients (36%) at baseline and by 32 of 62 (52%) at 3 months. Technical feasibility was demonstrated by successful development of a Qualtrics survey platform presented on tablet computers, use of QR reader codes for linkage with the ANZDATA registry which captures clinical outcomes, and linkage to the relevant survey for the patient's allocation and trial timepoint. Emails containing a short report of any symptoms identified as severe or overwhelming along with a summary of evidence-based guidelines for management of those symptoms were sent to and opened by treating clinicians. Assessment of patient and clinician acceptability of the feedback mechanism is ongoing.

Conclusion: Electronic symptom monitoring in adults on HD with feedback to clinicians is feasible and provides a template for ongoing registry-based monitoring of PROMs to facilitate patient-centred care and the infrastructure for future evaluations of interventions to improve patients' quality of life and survival.

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GLOMERULONEPHRITIS 3

MO038

ANTIMYELOPEROXIDASE AND PROTEINASE 3 ANTIBODIES ARE A USEFUL MARKER AS NEPHRITIS FLARE PREDICTOR IN ANCA-ASSOCIATED VASCULITIS

Eva Rodriguez[1], Ana Belén Latze[1], Milagros Sierra[2], Ana María Romera[3], Diego Siedel[3], Irene Agraz[4], Maria Jose Soler Romeo[4], Juliana Draibe[5], Francisco José De la Prada[6], Javier Villacorta[7], Anna Buxeda[1], Adriana S. Ochoa[1], Inés Lozano[1,8], Xavier Duran[9], Julio Pascual[1]

[1]Parc de Salut Mar, Nephrology, Barcelona, Spain, [2]Hospital San Pedro, La Rioja, Nephrology, Logroño, , [3]Hospital Universitario de Ciudad Real, Nephrology, Ciudad Real, Spain, [4]Hospital Universitario Valle Hebrón, Nephrology, Barcelona, Spain, [5]Hospital Universitario Bellvitge, Nephrology, Hospitalet, Spain, [6]Hospital Uinversitario Virgen de la Macarena, Nephrology, Sevilla, Spain, [7]Hospital Universitario Ramón y Cajal, Nephrology, Madrid, Spain, [8]Laboratorio de Referència de Catalunya, Barcelona, Spain and [9]AMIB . Institut Hospital del Mar Investigación Médica, Barcelona, Spain

Background and Aims: The diagnostic utility of ANCA antibodies in ANCA associated-vasculitis (AAV), antiproteinase 3 (PR3) and myeloperoxidase (MPO) testing is now undisputed, but the clinical utility of serial MPO/PR3 testing to predict relapses, remain controversial. The aim of this study was to analyze the relevance of serum MPO and PR3 antibody level assessment in the management of AAV. We sought to determine whether MPO and PR3 antibody levels correlated with renal disease activity, and whether an increase could predict a nephritis flare.

Method: Retrospective multicenter study including AAV-patients with renal involvement from 7 nephrology departments belonging to the Spanish Glomerular Study Group (GLOSEN). The main inclusion criteria were that MPO antibodies were detected by ELISA (Multiplex assay) and PR3 using chemioluminescence immunoassay. For statistical purpose a continuous variable were calculated, called delta MPO/PR3(ΔMPO y ΔPR3) that reflects change in antibodies levels 6 months before renal flare. Clinical data were recorded since complete remission of first nephritis diagnosis flare until second renal relapse.

Results: 113 AAV-patients with pauci-inmune necrotizing glomerulonephritis were included, 59 (52.2%) women, mean age (64.3±14.8 years), 85 patients (75.2%) MPO-AAV and 28 (24.8%) PR3-AAV, after a mean follow-up of 5±4.8 years, 54 renal relapses occurred in 40 (52,6%) MPO-AAV patients and in 14 (57.1%) PR3-AAVpatients. Serum **MPO levels** were significant higher in relapser-patients compared with non-relapser patients, 3±1.2 months before nephritis relapse [(n=32) 19.2±12.2 IA vs (n=38) 3.2±5.1 IA, p<0.001)]. **Δ MPO levels** were significant higher in relapse-patients compared with non-relapser patients [(n=32) 8.3±12 IA vs (n=38) 0.9±3.1.1 IA, p=0.001). The discrimination value of the MPO antibody levels 3 months before renal relapse were established by means of a ROC curve: AUC of 0.82 (95% CI 0.73 to 0.92; p<0.001) and the MPO cut-off value predicting renal relapse were established in 8.3 IA. The discrimination value of the ΔMPO were established by means of ROC curve: AUC of 0.76 (95% CI 0.63 to 0.88; p<0.001), ΔMPO cut-off value were established in an increase of MPO levels of 3.7 IA. **Serum PR3** levels were significant higher in relapser-patients 2.8±1.4 months before relapse [(n=14) 58.6±6.6 IA vs (n=7) 2.0±0.6 IA, p<0.001)] and **Δ PR3 levels** were significant higher in relapse-patients compared with non-relapser patients [(n=14) 57.5±28.5 IA vs (n=7) 0.8±0.2. IA, p<0.001)]. The discrimination value of the PR3 3 months before flare and Δ PR3 antibody levels were established by means of ROC curve: AUC 1.

Conclusion: Our results show that MPO antibodies, measured by Multiplex assay, could be a useful predictor of glomerulonephritis flare in AAV-patients. MPO levels 3 months before renal flare seems a good marker confirmed by ROC curve results, MPO cut-off value with the best sensitivity and specificity in predicting renal relapse was established in 8.3 IA. Δ MPO levels show that increase in titers ≥ 3.7 IA 6 months before renal flare, predict nephritis relapse However, PR3 antibodies are not a useful predictor marker, rise in antibodies level indicate renal vasculitis activity.

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MO039

THE 24-WEEK INTERIM ANALYSIS RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE II STUDY OF ATACICEPT IN PATIENTS WITH IGA NEPHROPATHY AND PERSISTENT PROTEINURIA

Jonathan Barratt[1], James A. Tumlin[2], Yusuke Suzuki[3], Amy Kao[4], Aida Aydemir[5], Yulia Zima[5], Gerald Appel[6]

[1]Leicester General Hospital, John Walls Renal Unit, Leicester, United Kingdom, [2]Emory University School of Medicine, GA Nephrology, Atlanta, United States of America, [3]Juntendo University Faculty of Medicine, Department of Nephrology, Tokyo, Japan, [4]EMD Serono Research and Development Institute, Inc., Immunology, Billerica, United States of America, [5]EMD Serono Research and Development Institute, Inc., Billerica, United States of America and [6]Columbia University Medical Center, Division of Nephrology and Hypertension, New York, United States of America

Background and Aims: IgA nephropathy (IgAN) is the most common primary glomerulonephritis in the world. Despite being described over 50 years ago, there remains no approved therapy for this common global cause of kidney failure. The central pathogenic feature in IgAN is the formation of circulating IgA containing immune complexes which have the propensity to deposit in the kidneys and trigger glomerular inflammation and tubulointerstitial scarring. The primary substrate for immune complex formation is an excess of poorly O-galactosylated polymeric IgA1 (Gd-IgA1) in the circulation. These IgA1 O-glycoforms are thought to trigger the formation of IgA and IgG autoantibodies. Atacicept is a human TACI-Ig fusion protein that inhibits B cell-stimulating factors, BLyS and APRIL, and has been associated with reductions in levels of serum IgA and IgG, as well as reductions in mature B cells and plasma cells. A number of studies have shown elevated levels of BLyS, APRIL and Gd-IgA1 in IgAN patients which have been linked to worse clinical outcomes. IgAN patients with persistent proteinuria >1 g/day are at increased risk of progression to end-stage renal disease. This Phase II study examines the safety and efficacy of atacicept in reducing pathogenic Gd-IgA1 levels and measures of renal activity in IgAN.

Method: This Phase II study (NCT02808429) enrolled patients with IgAN and proteinuria ≥1 g/day or 0.75 mg/mg on 24-hour urine protein-creatinine ratio (UPCR) despite maximal standard of care therapy (angiotensin converting enzyme inhibitor and/or angiotensin receptor blocker). Enrolled patients were randomized 1:1:1 to receive placebo or atacicept 25mg or 75mg once weekly by subcutaneous injection. The primary endpoint was a change in proteinuria by 24-hour UPCR at Week 48; key secondary endpoints included change in eGFR, serum immunoglobulin and Gd-IgA1 levels.

Results: Data from the 24-week interim analysis are reported here for enrolled patients (placebo=5; atacicept 25mg=6; atacicept 75mg=5). A consistent, dose-dependent reduction in serum immunoglobulins (IgA, IgG and IgM) and, in particular, Gd-IgA1 (Figure) were observed through Week 24. In parallel, proteinuria (24-hour UPCR) showed a higher median % reduction from baseline with atacicept at Week 24: -18.67% and -25.34% with atacicept 25 mg and 75 mg, respectively, vs +0.098% with placebo (Figure). eGFR remained stable over time. TEAEs were reported by 81% of the subjects. TEAEs were mild or moderate in severity, with no severe TEAEs reported. No serious related events, events with severe hypogammaglobulinemia or fatal outcome were reported.

Conclusion: These 24-week interim analysis results provide early proof of concept for the potential treatment of atacicept in patients with IgAN and persistent proteinuria.



Figure: Median changes from baseline in serum Gd-IgA1 and 24-hour UPCR at Week 24

MO040

LONG-TERM FOLLOW-UP OF IGA NEPHROPATHY PATIENTS AT HIGH RISK OF PROGRESSION ACCORDING TO THE THERAPEUTIC APPROACH EMPLOYED: A MULTICENTER RETROSPECTIVE STUDY OF 947 PATIENTS

Federico Alberici[1], Ivano Baragetti[2], Francesca Ferrario[2], Serena Ponti[3], Chiara Salviani[4], Lucia Del Vecchio[5], Francesca Viazzi[6], Antonello Pani[7], Carlo Manno[8], Giuliano Boscutti[9], Grazia Di Cesare[10], Claudio Pozzi[11]

[1]University of Brescia, Brescia, Italy, [2]Bassini Hospital, Cinisello Balsamo, Italy, [3]ASST Valtellina e Alto Lario, Sondrio, Italy, [4]ASST Spedali Civili, Brescia, Italy, [5]ASST Lecco, Lecco, Italy, [6]University of Genova, Genova, Italy, [7]AO Brotzu, Cagliari, Italy, [8]University of Bari, Bari, Italy, [9]Azienda sanitaria universitaria Giuliano Isontina, Trieste, Italy, [10]University of Milano Bicocca, Monza, Italy and [11]Independent Researcher, Lecco, Italy

Background and Aims: IgA-nephropathy (IgA-N) is a frequent cause of CKD and ESRD. The optimal therapeutic approach and the role of glucocorticoids and immunosuppression is still debated. Aim of this study was to perform a survey across several Italian centers focusing on the long-term outcome of patients with IgA-N at high risk of progression stratified according to the therapeutic approach employed.

Method: All the consecutive patients affected by biopsy proven IgA-N, proteinuria >1g/day and a follow-up longer than 24 months have been collected across 48 centers. The population has been divided in three groups according to the therapeutic approach: group-1 received ACEi or ARBs alone, group-2 a six months course of glucocorticoids while group-3 glucocorticoids and immunosuppressive drugs. Primary endpoints have been ESRD free-survival, halving of the eGFR free-survival and rate of non-responders (NR, proteinuria >1 g/day). Secondary endpoints have been assessment of the prognostic role of the time average proteinuria (TAP) as well as of the time average slope of proteinuria (TASP) and rate of severe adverse events (SAEs).

Results: 947 patients have been included and followed for a median time of 60 months (IQR 24-96). Baseline eGFR and proteinuria in the three groups have been respectively 68.1 (95%CI 63.9-72.4)-67.8 (95%CI 65.3-70.3)-63.3 (95%CI 58.5-68.1) ml/min/1.73m2 (p=0.191) and 2.38 (95%CI 2-2.77)-2.65 (95%CI 2.49-2.82)-3.26 (95%CI 2.89-3.64) g/day (p<0.001). Respectively 76/586 (13%) and 28/167 (17%) of the patients in group-2 and 3 required re-treatment with glucocorticoids alone or in combination with immunosuppressive drugs after a median of 24 months from the first cycle.

ESRD free-survival has been longer in the group-2 (p=0.004) (*figure, panel A*); at subgroup analysis this was restricted to the patients with a eGFR<50 ml/min (p=0.004) (*figure, panel B*) while only a trend was observed in the ones with eGFR ≥50 ml/min (p=0.0631). The halving of the eGFR free-survival has been longer in group-2 only when limiting the analyses to the subgroup with eGFR<50 ml/min (p=0.026) (*figure, panel C*).

The proportion of NR has been significantly lower in group-2 compared to group-1 throughout the first 36 months of follow-up (*figure, panel D*); of note being NR during the first 36 months increased the risk of developing ESRD during the follow-up (OR 4 95%CI 2.2-7.3, p<0.0001). The TAP and TASP of the first 24 months have been higher in the patients developing ESRD (respectively, mean 2.48 95%CI 2.14-2.82 and 0.81 95%CI 0.70-0.92) compared to the other patients (mean 1.12 95%CI 1.2-1.32 and 0.59 95%CI 0.56-0.61) (p<0.0001 for both comparisons). Of note the 24 months TASP of group-2 was lower compared to group-1 (respectively mean 0.56 95%CI 0.54-0.59 and 0.79 95%CI 0.71-0.87) (p<0.0001).

The rate of patients experiencing SAEs during the first 6 months of therapy in the three groups has been respectively 2%, 7% and 16%; of these withdrawn of the therapeutic approach employed has been necessary in 67%, 21% and 48%. During the whole follow-up the number of SAEs per 100 patients/years has been respectively 1.9-2.7 and 2.5 in the 3 groups.

Conclusion: In this large multicenter retrospective survey, the use of glucocorticoids in patients with IgA-N at high risk of progression has been associated to longer ESRD free-survival, longer time to the halving of the eGFR in the subgroup with eGFR <50 ml/min, lower rate of non-response during the first 36 months of follow-up as well as lower TASP during the first 24 months. The overall rate of SAEs has been low but higher in the group receiving glucocorticoids alone or in combination with immunosuppressors.

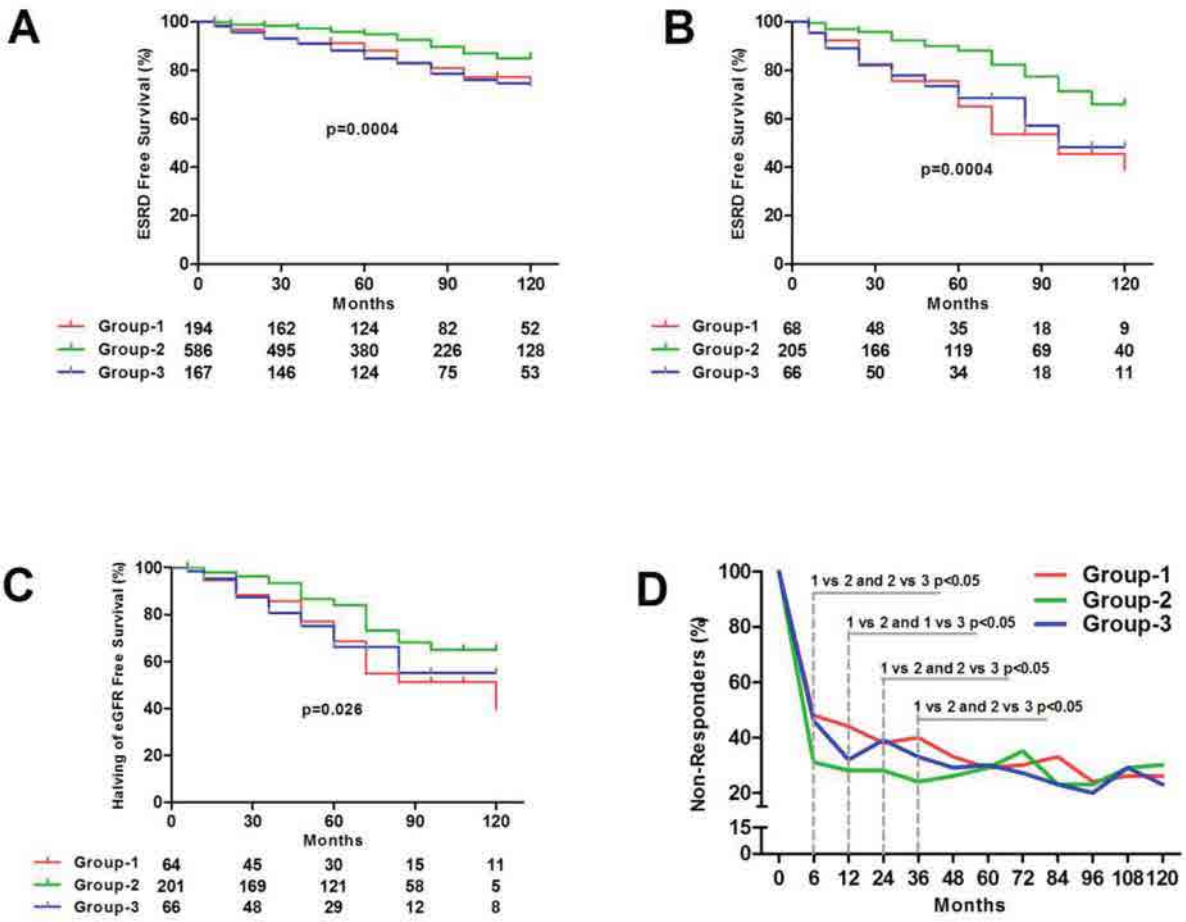


Figure:

MO041

URINE PROTEOMICS FOR PREDICTION OF DISEASE PROGRESSION IN PATIENTS WITH IGA NEPHROPATHY

Michael Rudnicki[1], Justyna Siwy[2], Heather Reich[3,4], Ralph Wendt[5], Mark Lipphardt[6], Dita Maixnerova[7], Björn Peters[8,9], Miroslaw Banasik[10], Ana Sanz[11], Alberto Ortiz[11], Bernd Stegmayr[9], Vladimir Tesar[7], Harald Mischak[2], Joachim Beige[5]

[1]Medical University Innsbruck, Dept. of Internal Medicine IV - Nephrology and Hypertension, Innsbruck, Austria, [2]mosaiques diagnostics GmbH, Hannover, Germany, [3]University of Toronto, Dept. of Medicine, Toronto, Canada, [4]University Health Network, Div. of Nephrology, Toronto, Canada, [5]Hospital St. Georg, Division of Nephrology and KfH Renal Unit, Leipzig, Germany, [6]University Medical Centre Göttingen, Dept. of Nephrology and Rheumatology, Göttingen, Germany, [7]1st School of Medicine, Charles University, Dept. of Nephrology, Prague, Czech Republic, [8]Skaraborg Hospital, Dept. of Nephrology, Skövde, Sweden, [9]Umeå University, Dept. of Public Health and Clinical Medicine, Umeå, Sweden, [10]Wroclaw Medical University, Dept. of Nephrology and Transplantation Medicine, Wroclaw, Poland and [11]Research Health Institute-Fundación Jiménez Díaz, Madrid, Spain

Background and Aims: Although IgA nephropathy (IgAN) is the most common primary glomerulonephritis in many parts of the world, risk of progressive kidney function decline is significant. Furthermore, the effect of immunosuppressive treatment in IgAN currently remains uncertain. There is no validated tool to predict disease progression or response to treatment. To serve this unmet need, we aimed at developing a urinary biomarker-based algorithm that predicts fast disease progression in patients with IgAN, thus enabling a personalized risk stratification and potentially improving patient management.

Method: In this multicenter study in 7 centers in Europe and in Canada urine samples were collected as part of clinical routine at time of biopsy in n= 300 patients (63% male, age 42±14 years) with biopsy proven IgAN. The follow-up data were collected for at least one year. Progressive disease was defined as an annual loss of kidney function (estimated glomerular filtration rate, eGFR) of more than -5ml/min/1.73m^2 per year or when end-stage kidney disease (ESKD) was reached. The institutional review boards of each of the participating centers approved this study.

Urine samples were analyzed using capillary electrophoresis coupled mass spectrometry (CE-MS). Whole proteome/peptidome profile was obtained for each sample.

This study received funding from the European Union's ERA PerMed program.

Results: Urine proteome/peptidome profiles were obtained from n=294 patients. On average, 2383 peptides were detected per sample. The data were subsequently divided into a discovery (n=154) and validation cohort (n=140). The comparison of the progressors (n=35) and non-progressors (n=119) in the discovery cohort resulted in the definition of more than 100 significant peptides. These included mainly fragments from collagen, mostly type 1 (decreased in progressors) and from different blood derived proteins like alpha-1-antitrypsin, alpha-2-HS-glycoprotein and apolipoproteins (increased in progressors). The distribution of the 100 most significant peptides in the progressor and non-progressor group is shown in the figure. The peptides were combined into a classifier using support vector machine. After optimizing the classifier employing a take-one-out procedure combined with n-1 cross-validation, the urine-peptide based algorithm enabled separation of progressors versus no progressors with an accuracy of 90% in take-one-out cross-validation. This classifier was subsequently applied to the validation cohort and resulted in highly significant separation of progressive from non-progressive IgAN patients. Furthermore, this classifier will be further applied blinded in an independent well characterized multicenter cohort of 267 IgAN patients.

Conclusion: We identified a urinary proteome profile which was associated with progressive loss of GFR in patients with IgAN. Further validation of this profile in an independent cohort is ongoing. The data indicate that CE-MS-based urinary proteomics enables identifying IgAN patients at high risk of disease progression. These patients may benefit from aggressive immunosuppressive treatment. Upon validation of the classifier in an independent cohort, its value in predicting response to immunosuppression will be assessed, aiming at establishing an innovative strategy that could improve patient management and personalize treatment of IgAN patients.

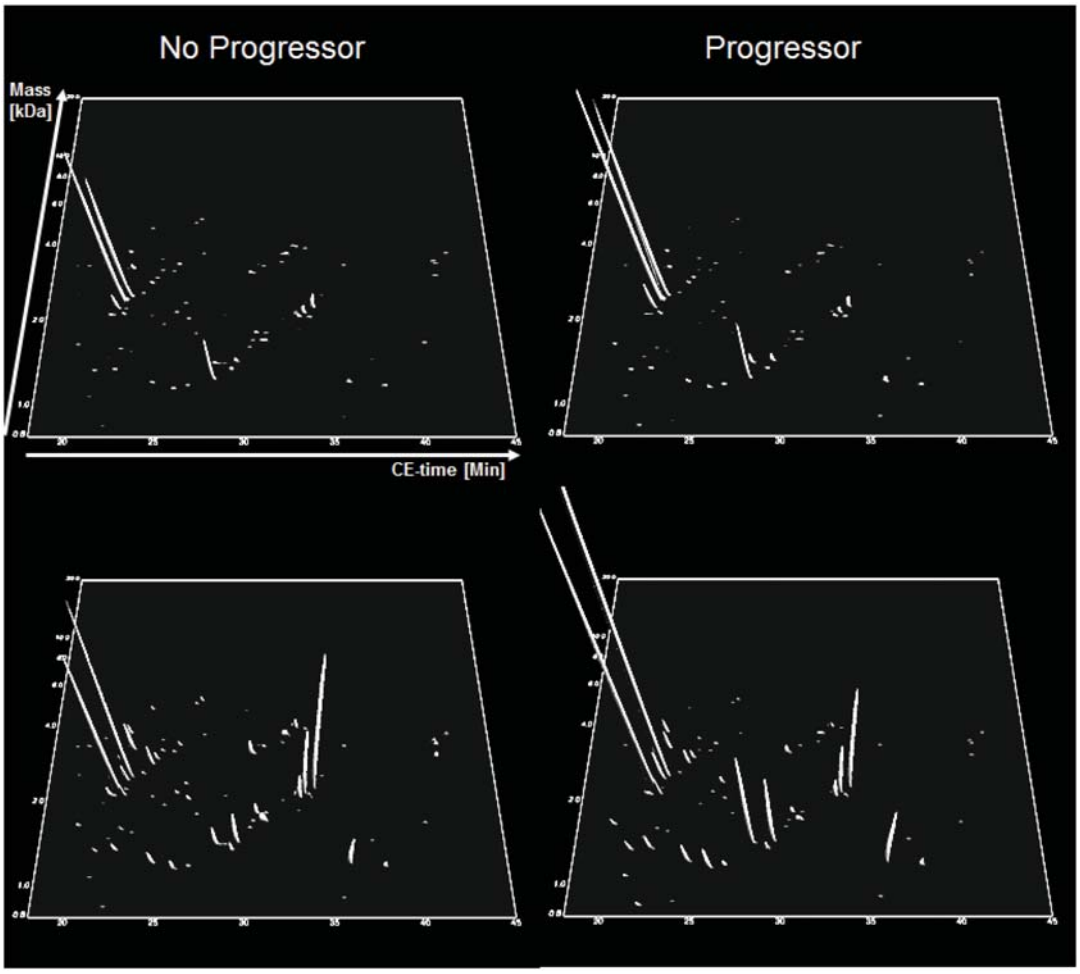


Figure: Distribution of the 100 most significant peptides in the progressor and no progressor group of IgAN patients. The molecular mass (on a logarithmic scale) is plotted against normalized migration time. Signal intensity is encoded by peak height. In the lower panel the most intensive peptides were omitted and the other peptides showed in fivefold magnification

MO042

LNP023: A NOVEL ORAL COMPLEMENT ALTERNATIVE PATHWAY FACTOR B INHIBITOR FOR THE TREATMENT OF GLOMERULAR DISEASE

Nicholas Webb[1], Boerje Haraldsson[1], Anna Schubart[1], Julie Milojevic[1], Peter End[1], Thomas Holbro[1], Guido Junge[1]

[1]*Novartis Pharma AG, Basel, Switzerland*

Background and Aims: The alternative complement pathway (AP) provides the central amplification loop of complement activation and is critically involved in a number of diseases including C3 glomerulopathy (C3G), paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic uremic syndrome. There is also evidence for AP dysregulation in IgA and membranous nephropathies (IgAN, MN). Novartis has developed a highly selective oral low molecular weight inhibitor of complement Factor B, a key AP protease. LNP023 potently blocks AP activation *in vitro* and *in vivo* and is efficacious in passive Heymann nephritis in rats, suggesting an important role of the AP in classical-pathway mediated nephropathies.

Method: LNP023 was tested at increasing single or multiple ascending doses in a Phase I safety, tolerability, pharmacokinetic (PK) and pharmacodynamic study in healthy volunteers. Complement inhibition was measured by the *ex vivo* Wieslab assay and by quantifying fragment Bb level.

Results: LNP023 was well tolerated at all doses from 5 mg to 400 mg (single dose) and from 25 mg to 200 mg bid for 14 days (multiple dose). There were no deaths, SAEs or AEs leading to study drug discontinuation in LNP023-treated subjects. LNP023 dose-dependently inhibited the AP complement system. Based on the Wieslab assay, maximal inhibition of AP activity (80% or more) was observed 2 hours after a single dose of 10 mg or higher. The level of Bb decreased until 12 hours post-dose. Approximately 30% to 50% decrease in Bb, relative to baseline, was achieved for subjects receiving a single dose of LNP023 of 5mg or higher. For both assays, the duration of this inhibition was dependent upon the dose administered. Persistent inhibition was obtained in the multiple dose cohorts, the magnitude of inhibition being dose-dependent for the Wieslab assay but not for Bb. PK studies showed rapid drug absorption and no evidence of food effect. The plasma clearance was moderate and the terminal half-life was around 20h. There was an under-proportional dose-exposure relationship. Among other mechanisms, binding to highly expressed target (Factor B) is believed to affect clearance and thus exposure.

Following a successful proof of concept Phase 2 study in PNH (data not shown), LNP023 is currently being investigated in three ongoing Phase 2 studies in IgAN (NCT03373461), C3G (NCT03832114) and MN (NCT04154787). The IgAN study has an adaptive seamless design; the first part has recently completed, 46 patients having received 3 months of one of three LNP023 doses or placebo. The study remains blinded; however, similar to the FIH study safety appears excellent, with only one treatment-emergent SAE (inhalation of chlorine gas) and two SAEs in the post-treatment follow-up period. No patient discontinued randomised treatment for any reason. There were no episodes of proven infection with encapsulated bacteria. The independent data safety monitoring committee have endorsed the study proceeding to the second part with the addition of a fourth LNP023 dose and recruitment is ongoing, completion being anticipated in mid-2020.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii143–iii148, 2020

CKD AND NUTRITION

MO043

IDENTIFICATION OF INDOXYL SULFATE PRODUCER PHENOTYPES BY ORAL TRYPTOPHAN CHALLENGE TEST: A MICROBIOTA-BASED PERSONALIZED NUTRITIONAL APPROACH

Ting-Yun Lin[1], Szu-Chun Hung[1]

[1]*Taipei Tzu Chi Hospital, Division of Nephrology*

Background and Aims: Indoxyl sulfate (IS), one of the most representative gut-derived uremic toxins, has been implicated in the pathogenesis of cardiovascular disease in patients with chronic kidney disease (CKD). However, current approaches to IS reduction are not optimized. IS is converted from indole, a gut bacterial metabolite of dietary tryptophan, by two hepatic enzymes CYP2E1 and SULT1A1 (**Figure 1A**). Given that the interplay between microbes and host is associated with various phenotypes of medical importance, we hypothesized that the effects of a particular diet on individuals differ from person to person. In the present study, we measured individualized IS production using a fixed-dose loading of tryptophan. We aimed to characterize variable IS producer phenotypes and identify person-specific host and microbiome features associated with the variability.

Method: We developed an oral tryptophan challenge test (OTCT) to determine the individual IS producing capacity. Plasma and urine samples were collected at baseline after overnight fasting, and were then collected at 4, 8, 12, 24, 36 and 48 hours after oral administration of L-tryptophan at a dose of 2 gm. All participants were on a low tryptophan diet during the pharmacokinetic study of IS production following OTCT. Positive (above baseline) components of the area under the curve (AUC) were calculated to indicate IS production because of the variable nature of the baseline IS. Information on dietary patterns was obtained using a semiquantitative food frequency questionnaire (FFQ) validated for assessment of major nutrients in the diets of Taiwanese vegetarians and omnivores. Tryptophan and IS concentrations were quantified by high performance liquid chromatography. CYP2E1 and SULT1A1 single nucleotide polymorphism genotyping was analyzed by TaqMan PCR assay. The gut microbiome was assessed by metagenomic next-generation sequencing.

Results: We enrolled 40 healthy volunteers to undergo the OTCT. The mean age of the participants was 33 $\pm$ 7 years; 27.5% were men (n=11), and 40% were vegetarians (n=16). Participants were stratified into quartiles of baseline-adjusted AUC of IS. High interpersonal variability in IS production following OTCT was observed (**Figure 1B**). The 10 participants in the highest quartile (Q4) were defined as high IS producers. The other 30 participants in the Q1, Q2, and Q3 were defined as low IS producers (**Figure 1C, 1D**). The high IS producers were all female (n=10; P=0.025) and more likely to be omnivores (n=8; P=0.136). Otherwise, there was no difference in the age, body mass index, blood pressure, eGFR, fasting blood glucose, lipid profiles, and baseline plasma IS concentrations between the 2 groups. The high and low IS producers were different with respect to the principal coordinate analysis of β-diversity of the gut microbiota. A prediction model was constructed based on the individual IS producing capacity as contributed by the gut microbiome features and host genotypes.

Conclusion: We found high variability of IS in the response to OTCT across individuals, suggesting that universal dietary recommendations may have limited utility. High IS producers should avoid consuming foods that contain high levels of tryptophan. Therefore, the OTCT can be used to identify IS-producer phenotypes and may serve as a personalized dietary guidance and optimize food choices. Potential clinical applications for the OTCT require further studies to validate its use in patients with CKD.

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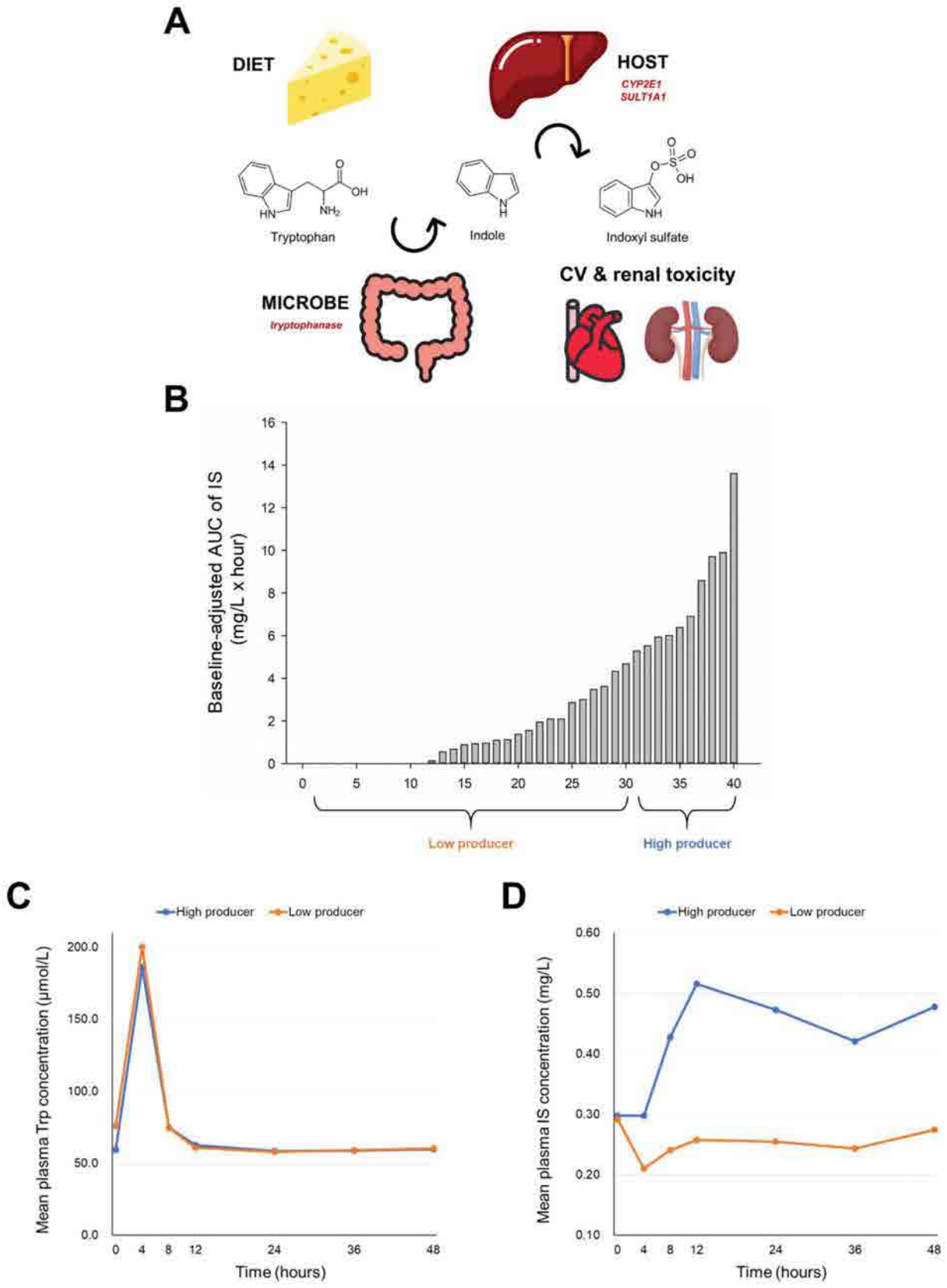

A
DIET
HOST
CYP2E1
SULT1A1
Tryptophan
Indole
Indoxyl sulfate
MICROBE
tryptophanase
CV & renal toxicity
B
Baseline-adjusted AUC of IS (mg/L x hour)
Low producer
High producer
C
High producer
Low producer
Mean plasma Trp concentration (µmol/L)
Time (hours)
D
High producer
Low producer
Mean plasma IS concentration (mg/L)
Time (hours)

Figure 1

MO044

HIGH DIETARY PHOSPHATE INTAKE ENHANCES INTACT FGF23 AND CAUSES ACUTE TUBULAR INJURY WITH SEVERE INFLAMMATION AND FIBROSIS IN UNTREATED MICE

Isabel Vogt[1], Stefanie Walter[1], Anna Catharina Veenstra[1], Tamar Kapanadze[2], Jessica Schmitz[3], Jan Hinrich Bräsen[3], Roland Schmitt[2], Florian Limbourg[2], Dieter Haffner[1], Maren Leifheit-Nestler[1]

[1]Hannover Medical School, Department of Pediatric Kidney, Liver and Metabolic Diseases, Hannover, Germany, [2]Hannover Medical School, Department of Nephrology and Hypertension, Hannover, Germany and [3]Hannover Medical School, Institute of Pathology, Nephropathology Unit, Hannover, Germany

Background and Aims: In early stages of chronic kidney disease (CKD) rising levels of the phosphaturic hormone fibroblast growth factor (FGF) 23 maintain the phosphate homeostasis, whereas in end-stage kidney disease hyperphosphatemia manifests. Both elevated FGF23 and phosphate levels contribute to CKD progression and are associated with an increased mortality in CKD patients. So far, it is unknown whether high inorganic phosphate uptake causes renal injury as well in the absence of CKD. Therefore, we analyzed the effects of a long-term high phosphate diet (HPD) on the renal function in healthy mice.

Method: We studied the effects of a 2% HPD compared to a 0.8% normal phosphate diet (NPD) fed to healthy male C57BL/6 mice. After six month, blood pressure and metabolic serum and urine parameters were measured. The renal function was characterized by histology, flow cytometry and gene expression analysis. Additionally, we investigate the effects of elevated FGF23 and phosphate on mouse proximal tubular cells (mPT) *in vitro*.

Results: Feeding of a HPD for 6 months significantly increased systolic blood pressure (95 vs 79 mmHg; p=0.003), plasma creatinine (0.33±0.01 vs 0.29±0.02 mg/dL; p=0.004), C-term FGF23 (1991±394 vs 309±56 pg/mL; p<0.0001), intact FGF23 (1701±429 vs 191±30 pg/mL; p<0.0001) and urinary phosphate excretion (1732±968 vs 520±123 mg/dL; p=0.0005) compared to NPD controls, whereas serum phosphate (14.3±5.3 vs 13.4±2.9 mg/dL; p=0.68) and parathyroid hormone levels (417±104 vs 544±187 pg/mL; p=0.51) remained unchanged. The HPD caused acute tubular injury in the renal cortex with loss of polarity of proximal tubular epithelial cells and enhanced renal fibrosis and inflammation demonstrated by PAS and Picrosirius red staining. These histological pathologies were associated with a 100-fold increase of KIM-1 and a 7-fold increase of NGAL mRNA expression in the kidneys of HPD mice compared to the NPD group. In HPD mice, flow cytometry analysis showed a reduced storage of $Ly6C^{hi}$ monocytes in the spleen, whereas $Ly6C^{hi}$ monocytes, granulocytes, macrophages, B-cells, and CD4+ T-cells (each p<0.05) were significantly induced in the kidney compared to NPD-fed mice. Histological staining's displayed an accumulation of B- and T-cells in regions of tubular injury in HPD mice. Furthermore, the HPD significantly enhanced the mRNA expression of the chemotactic markers for monocytes *Il34* and *Ccl2* and inflammatory cytokines *Tnfα* and *Il1β*. Whether enhanced phosphaturia directly or HPD-mediated increase of intact FGF23 cause the renal toxicity is currently investigated in mPTs.

Conclusion: Chronic high phosphate load induces kidney injury in the proximal tubules with severe inflammation and fibrosis in healthy mice. Our results suggest that a controlled dietary intake of inorganic phosphate is not only important for CKD patients but also for the general population.

MO045

MITOCHONDRIAL DYSFUNCTION AND MUSCLE ENERGETICS IN CKD PATIENTS

Jorge Gamboa[1], Alp Ikizler[1], Chang Yu[1], Bruce Damon[1], Nancy Brown[1], Theodore Towse[2]

[1]Vanderbilt University Medical Center, Nashville, United States of America and [2]Grand Valley State University, Allendale Charter Township, United States of America

Background and Aims: Patients with chronic kidney disease (CKD) suffer from frailty and sarcopenia. Skeletal muscle mitochondria are important for physical function and could be a target to prevent frailty and sarcopenia.

Method: We tested the hypothesis that mitochondrial function worsens with the progression of CKD. We evaluated the interaction between mitochondrial function and co-existing comorbidities such as impaired physical performance, intermuscular adipose tissue (IMAT) infiltration, inflammation, and oxidative stress. We evaluated in-vivo thigh mitochondrial function using 31-phosphorus magnetic resonance spectroscopy to obtain the phosphocreatine (PCr) recovery constant, a measure of mitochondrial function. We measured physical performance using the six-minute walk test, IMAT infiltration and markers of inflammation in plasma.

Results: Sixty-three participants were studied including controls (n=21), patients with CKD not on maintenance hemodialysis (MHD; n=20), and patients on MHD (n=22). We found a prolonged PCr recovery constant in patients on MHD (53.3 (43.4, 70.1) seconds) and with CKD not on MHD (46.3 (40,0, 49.9) seconds) compared to controls (34.2 (28.8, 43.7) seconds) ($p<0.001$ between groups), Figure 1A-C. Mitochondrial dysfunction was associated with poor physical performance, greater IMAT, and increased markers of inflammation Figure 2A-C.

Conclusion: Mitochondrial function worsens with the progression of CKD and correlates with physical function, IMAT, inflammation, and oxidative stress. These data suggest that therapeutic approaches targeted at mitochondrial dysfunction and dynamics could prevent or treat frailty and sarcopenia in patients CKD.

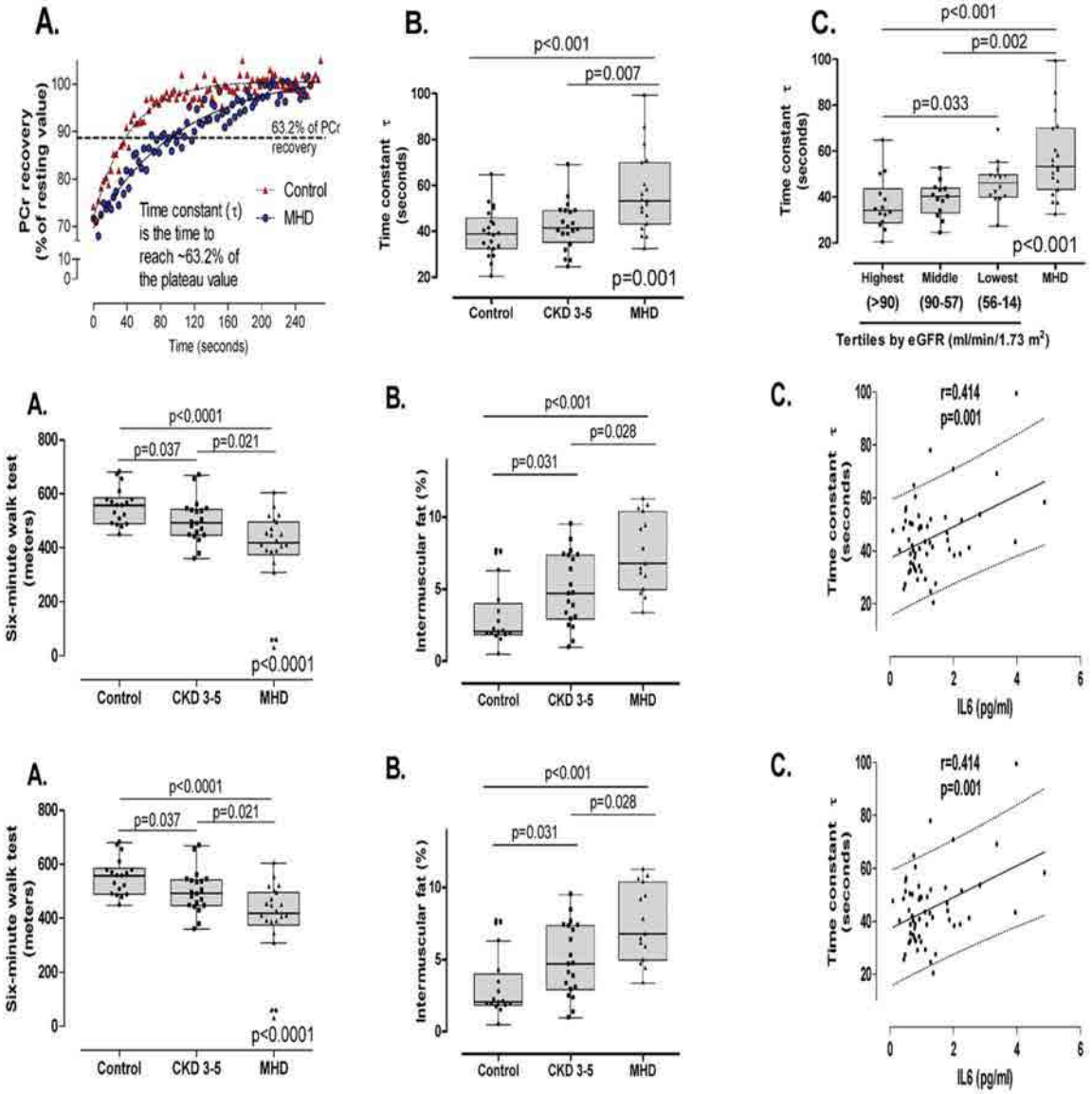


Figure 1 and 2

MO046

MICROBIOTA DERIVED SHORT CHAIN FATTY ACIDS, PROPIONATE AND BUTYRATE, CONTRIBUTE TO MODULATE THE INFLAMMATORY RESPONSE IN CHRONIC KIDNEY DISEASE.

Viviana Corte[1], Ana Cristina Andrade[2], Paula Diaz-Bulnes[1], Nuria Salazar Garzo[3], Jose Joaquin Bande[2], J. Emilio Sanchez-Alvarez[2], Carmen Diaz-Corte[2,4], Carlos Lopez-Larrea[1,4], Beatriz Suarez-Alvarez[1,4]

[1] Instituto de Investigación Biosanitaria del Principado de Asturias (ISPA), Hospital Universitario Central de Asturias (HUCA), Laboratorio de Inmunología Traslacional, Oviedo, Spain, [2]Hospital Universitario Central de Asturias, UGC Nefrología., Oviedo, Spain, [3]Instituto de Investigación Biosanitaria del Principado de Asturias (ISPA), Group Diet, Microbiota and Health, Oviedo, Spain and [4]Red de Investigación Renal REDINREN, Instituto de Salud Carlos III

Background and Aims: Dysbiosis, or changes in the gut microbiota composition, had been related to the developed of several pathologies, such as chronic kidney disease. Until now, multiple studies have focused on the influence of diet on outcomes of patients with CKD. These patients with advanced disease are recommended a restricted intake of vegetable fiber due to the phosphorus and potassium levels, and low proteins to avoid the generation of uremic toxins. It is known that dietary changes lead to alterations in gut microbiota, but also in microbial metabolites production, some of which could be beneficial for the host. A recent and exciting area of research has begun to explore the role of microbiota-derived metabolites in the renal physiology. Short-chain fatty acids (SCFA, acetate, propionate and butyrate) are a type metabolite produced from dietary fiber by gut microbiota that enter in the bloodstream leading to distal effects, such as modulation of the immune cells. SCFAs are essential to maintain the permeability of the intestinal epithelial barrier, the metabolic functions and have potent anti-inflammatory effects. The aim of this study was to identify the SCFAs levels during the progression of CKD and determinate the functional role of these metabolites in the renal inflammation.

Method: SFCAs (acetate, propionate and butyrate) levels were determined using gas chromatography-mass spectrometry in fecal samples collected from patients with different stages of CKD (n=60) and age-matched healthy control (n=20). Moreover, common bacterial families were determined by quantitative PCR. Additionally, the *in-vitro* effect of the three SCFAs was evaluated in the human tubular epithelial cell line HK2 using RNA-seq, specific silencing with siRNAs and histone deacetylases (HDAC) inhibitors. To evaluate the effect in immune cells, monocyte and macrophages were treated with LPS and ATP /Nigericin to induce inflammasome activation.

Results: The SCFAs levels were significantly lower in patients with CKD than in healthy controls, mainly propionate and butyrate. Moreover, these levels progressively decreased with the developed of the disease, showing the patients with stage 5 (CKD5) have the lowest levels that correlates with a lesser abundance of *Clostridium IV* family. According to the renal function, butyrate levels were positively correlated with the glomerular filtration rate and negatively with the blood urea nitrogen and creatinine levels. Surprisingly, high propionate levels correlate with the most elevated serum calcidiol concentrations. Functionally, propionate and butyrate show a similar pattern in the modulation of inflammatory genes in HK2 cells. Most regulated pathways are associated with Inflammatory response (GO:0006954: *IL6, TNF, CCL2, RELB, IRAK2, NFKB1,CCL20*) and immune response (GO:0006955: *CSF2, CXCL3, CD40, IL7R, LIF*). Additionally, both SCFAs regulates the expression of multiple epigenetic enzymes involves in the chromatin remodeling, mainly in histone acetylation. In monocytes/macrophages, propionate and butyrate inhibits the *IL1B, CASP*, and *ASC* gene transcription damaging the IL-1β secretion. We determined that the effect of SCFAs in these *in-vitro* models is mediated by inhibition of HDAC although also change other histone modifications (H3K9me3, H3K27me3) and through the GPR109A receptor.

Conclusion: Our initial results showed that patients with advanced CKD have low levels of SCFAs, and those were correlated with the renal function. Treatment of human renal and immune cells with propionate and butyrate induces profound changes in the chromatin structure, changing the whole-genome gene expression and modulating key pathways in the renal pathology. Increasing the SCFAs levels in those patients could be a potential therapeutic strategy to slow down the disease progression.

MO047

COMPARISON BETWEEN DUAL-ENERGY X-RAY ABSORPTIOMETRY AND BIOELECTRICAL IMPEDANCE FOR BODY COMPOSITION MEASUREMENTS IN ADULTS WITH CHRONIC KIDNEY DISEASE.

Natália Tomborelli Bellafronte[1], Lorena Vega-Piris[2], Paula Garcia Chiarello[3], Guillermina Barril Cuadrado[4]

[1]University of São Paulo, Ribeirão Preto Faculty of Medicine, Post-graduate Program in Health Sciences, Ribeirão Preto, Brazil, [2]Health Research Institute of the Hospital Universitario de la Princesa, Methodology Unit, Madrid, Spain, [3]University of São Paulo, Ribeirão Preto Faculty of Medicine, Health Sciences Department, Ribeirão Preto, Brazil and [4]Hospital Universitario La Princesa, Nephrology Department, Madrid, Spain

Background and Aims: Chronic kidney disease (CKD) patients frequently have an altered body composition driven by metabolic disorders from the uremic syndrome that usually leads to increased protein catabolism, with obesity and muscle impairment being common conditions associated with worse clinical prognosis and high mortality rates. Therefore, with increased mortality and disability rates of CKD patients in the last quarter of a century and the association of a poor body composition with low survival, routine and longitudinal assessment of body composition could improve clinical outcomes. Due to limited availability of reference methods to assess nutritional status, alternative methods are used. In view of the above, our goal was to evaluate the agreement between multifrequency bioelectrical impedance spectroscopy (BIS) and Dual-energy X-ray Absorptiometry (DXA) for assessment of body composition in CKD.

Method: Cross-sectional and prospective analyses by DXA (Hologic, GE®) and BIS (BCM, Fresenius Medical Care®) in whole-body (BISWB) and segmental (BISSEG) protocols were performed in CKD non-dialysis-dependent, hemodialysis and peritoneal dialysis (for at least 3 months), and renal transplantation (for at least 6 months) adult ($18 \leq$ age ≤ 60 years old) patients. Measurements were performed consecutively by the same professional after an 8-hour fast, drainage of the peritoneal dialysate and just after the midweek hemodialysis session. Intraclass correlation coefficient (ICC) and Bland-Altman plots were evaluated for agreement analysis in group and individual levels, respectively; linear regression analysis was performed for bias assessment and development of new equations; ROC curve was constructed for diagnosis of inadequate error tolerance (DXA - BIS $> \pm$ 2kg).

Results: A total of 266 patients were included: 137 men (M) and 129 women (W); 81 were in non-dialysis-dependent treatment, 83 in hemodialysis, 24 in peritoneal dialysis, and 80 had renal transplantation. Total sample had a mean age of 47 $\pm$ 10 years old. CKD was secondary to systemic arterial hypertension in 29% of the total sample, to glomerulonephritis in 25%, to diabetes mellitus in 10%, to polycystic kidney in 7%, to glomerulosclerosis and systemic syndromes in 8%, and to other causes and unknown etiology in 20%. Fourteen patients (4 M and 10 W) were in automated and 9 (4 M and 5 W) in continuous ambulatory PD. KTx was by living donor in 18 (14 M and 4 W) and by deceased donor in 63 (34 M and 29 W) patients. The agreement with DXA was greater for BISWB than BISSEG; for fat mass (FM) (ICC in M = 0.89; ICC in W = 0.93) than for fat free mass (FFM) (ICC in M = 0.57; ICC in W = 0.52). Bland-Altman plots showed high limits of agreement (FFM: from -9.51 to 15.64kg; FM: from -7.71 to 7.32kg) with greater bias for FFM as muscular mass increases and for FM in extremes of body fat. The agreement was lower when using the prospective data (body change analysis) (ICC for FFM in M = 0.20; ICC for FFM in W = 0.49; ICC for FM in M = 0.46; ICC for FM in W = 0.58). The factors that interfered in bias between methods were extra to intracellular water ratio (ECW/ICW), body mass index, fat mass index, waist circumference, resistance and reactance (adjusted r^2 for FFM = 0.90; r^2 for FM = 0.87). FFM had poorer agreement in the last tertile of ECW/ICW sample (ICC in M = 0.69, 0.68 and 0.51; ICC in W = 0.71, 0.74 and 0.38 for first, second and third tertiles, respectively). An ECW/ICW cut-off point of > 0.725 for inadequate error tolerance was determined. New prediction equations for FFM ($r^2 = 0.91$) and FM ($r^2 = 0.89$) presented adequate error tolerance in 55% and 63% in the validation sample compared to 30% and 39% of the original equation, respectively.

Conclusion: For body composition evaluation in CKD, BIS applied using the whole-body protocol, in normal hydration CKD patients is as reliable as DXA; BIS must be used with caution among overhydrated patients with ECW/ICW > 0.725. The newly developed equations are indicated for greater precision.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii149–iii153, 2020

CLINICAL DIABETIC NEPHROPATHY

MO048

MULTICENTRE PROSPECTIVE VALIDATION OF THE URINARY PEPTIDOME-BASED CLASSIFIER CKD273 AS A PREDICTOR OF RENAL FUNCTION DECLINE IN SUBJECTS WITH TYPE 2 DIABETES

Morten Lindhardt[1,2], Nete Tofte[1], Gemma Currie[3], Marie Frimodt-Moeller[1], Heiko Von der Leyen[4], Christian Delles[3], Harald Mischak[5], Peter Rossing[1,6] For the PRIORITY Investigators[7]

[1]Steno Diabetes Center, Copenhagen, Gentofte, Denmark, [2]Holbæk Hospital, Medical department, Holbæk, Denmark, [3]University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom, [4]Hannover Clinical Trial Center GmbH, Hannover, Germany, [5]Mosaiques Diagnostics, Hannover, Germany, [6]Copenhagen University, København, Denmark and [7]European Union Seventh Framework Programme

Background and Aims: In the PRIORITY study, it was recently demonstrated that the urinary peptidome-based classifier CKD273 was associated with increased risk for progression to microalbuminuria. As a prespecified secondary outcome, we **aim** to evaluate the classifier CKD273 as a determinant of relative reductions in eGFR (CKD-EPI) of 30% and 40% from baseline, at one timepoint without requirements of confirmation.

Method: The 'Proteomic prediction and Renin angiotensin aldosterone system Inhibition prevention Of early diabetic nephRopathy In TYpe 2 diabetic patients with normoalbuminuria trial' (PRIORITY) is the first prospective observational study to evaluate the early detection of diabetic kidney disease in subjects with type 2 diabetes (T2D) and normoalbuminuria using the CKD273 classifier. **Setting:** 1775 subjects from 15 European sites with a mean follow-up time of 2.6 years (minimum of 7 days and a maximum of 4.3 years). **Patients:** Subjects with T2D, normoalbuminuria and estimated glomerular filtration rate (eGFR) $\geq$ 45 ml/min/1.73m^2. Participants were stratified into high- or low-risk groups based on their CKD273 score in a urine sample at screening (high-risk defined as score $>$ 0.154).

Results: In total, 12 % (n = 216) of the subjects had a high-risk proteomic pattern. Mean (SD) baseline eGFR was 88 (15) ml/min/1.73m^2 in the low-risk group and 81 (17) ml/min/1.73m^2 in the high-risk group ($p < 0.01$). Baseline median (interquartile range) urinary albumin to creatinine ratio (UACR) was 5 (3-8) mg/g and 7 (4-12) mg/g in the low-risk and high-risk groups, respectively ($p < 0.01$).

A 30 % reduction in eGFR from baseline was seen in 42 (19.4 %) subjects in the high-risk group as compared to 62 (3.9 %) in the low-risk group ($p < 0.0001$). In an unadjusted Cox-model the hazard ratio (HR) for the high-risk group was 5.7, 95 % confidence interval (CI) (3.9 to 8.5; $p<0.0001$). After adjustment for baseline eGFR and UACR, the HR was 5.2, 95 % CI (3.4 to 7.8; $p<0.0001$).

A 40 % reduction in eGFR was seen in 15 (6.9 %) subjects in the high-risk group whereas 22 (1.4 %) in the low-risk group developed this endpoint ($p<0.0001$). In an unadjusted Cox-model the HR for the high-risk group was 5.0, 95 % CI (2.6 to 9.6; $p<0.0001$). After adjustment for baseline eGFR and UACR, the HR was 4.8, 95 % CI (2.4 to 9.7; $p<0.0001$).

Conclusion: In normoalbuminuric subjects with T2D, the urinary proteomic classifier CKD273 predicts renal function decline of 30 % and 40 %, independent of baseline eGFR and albuminuria.

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MO049 **EFFECT OF VITAMIN D ON ENDOTHELIAL FUNCTION IN EARLY DIABETIC NEPHROPATHY**

Himansu Mahapatra[1], Adarsh Kumar[2,3], Bindu Kulshreshtha[4], Anubhuti Chirkara[2]

[1]ABVIMS, Dr. R.M.L. Hospital, New Delhi, India, Nephrology, Delhi, India, [2]ABVIMS, Dr. R.M.L. Hospital, New Delhi, India, Biochemistry, delhi, India, [3]ABVIMS, Dr. R.M.L. Hospital, New Delhi, India, Nephrology, delhi, India and [4]ABVIMS, Dr. R.M.L. Hospital, New Delhi, India, Endocrinology, Delhi, India

Background and Aims: Diabetic Nephropathy is associated with endothelial dysfunction at an early stage. The benefit of Vitamin D supplementation on endothelial function is supported by a few studies in non-diabetic chronic kidney disease (CKD). However, studies on its effect in early DN is scarce. Hence, the present study was planned to assess the effect of vitamin D supplementation on endothelial function by measuring Flow mediated dilation (FMD) in patient of early DN.

Method: A total of 730 Diabetic subjects were screened for early DN based on Inclusion criteria (eGFR $\geq$ 120ml/min/1.73m^2 with unrestricted ACR value eGFR of 60- 120 mL/min/1.73m2 and ACR 30-300mg) and Exclusion criteria (on ACE I or ARB, eGFR<60ml/min/1.73m^2, Hypercalcemia (>11.5mg%), UTI, Pregnancy, Hypertension, HbA1c (>8.0 %), vitamin D supplementation during the last 6 month). Of them 103 included subjects were underwent randomization to receive either Cholecalciferol (54) or matching Placebo (49) in a double blind method. All were subjected to routine investigations, urinary albumin: creatinine (UACR), C reactive protein (CRP), serum 25(OH)vitamin D, intact parathyroid hormone (iPTH) and Flow mediated dilatation at the zero and six months. All subjects were subjected. Comparative results at zero and six months of both groups were compared and analyzed.

Results: There was no significant difference between cholecalciferol and placebo group with respect to CRP, iPTH, 25-hydroxyvitamin D (25(OH) D), UACR, FMD at baseline. Median FMD after 6 month was significantly higher in cholecalciferol as compared to placebo group [Median (IQR): 24 % (21.75-26.0) and 22% (18-24) respectively, p= 0.01]. After 6 month UACR was significantly lower in the cholecalciferol group as compared to placebo group (p= 0.04). Significant association of vitamin D level was observed with CRP level. In 25(OH) D < 20 ng/ml subgroup there was significant decrease in CRP level in comparison to 25(OH) D $\geq$20 ng/ml subgroup (p=0.04).

Conclusion: There was significant improvement in endothelial function as assessed by FMD% following vitamin D supplementation. Vitamin D supplementation given to early diabetic nephropathy patients may have favourable effects on cardiovascular outcome as reflected by improvement in FMD% and decrease in CRP level.

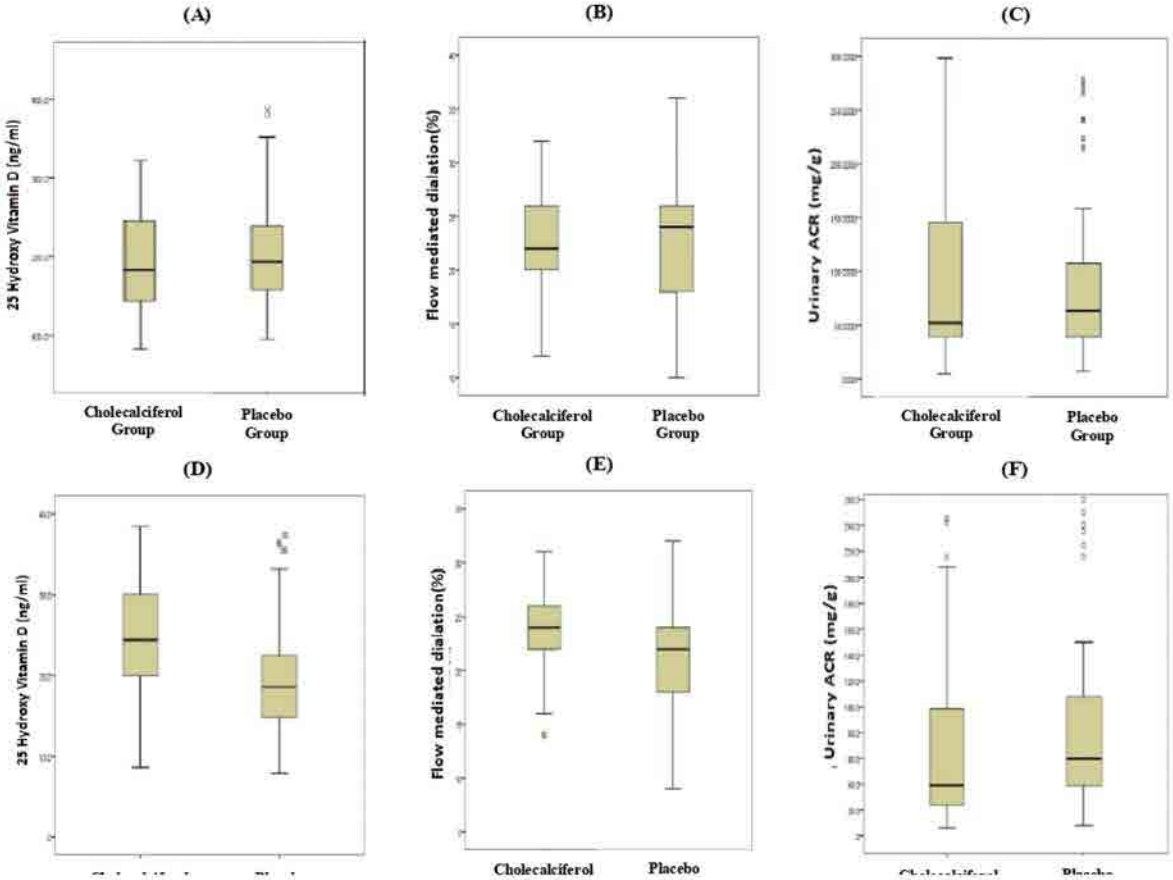


Figure1. Boxplot of baseline parameter (1A to 1C) and 6 month parameter (1D to 1F). FMD and 25 hydroxyvitamin D levels improved in the cholecalceferol-treated but not in placebo group (fig. 1D and 1E). UACR was significantly lower in cholecalceferol-treated group (fig.1F). In the box plot, the whiskers are 1.5 (IQR) from edges of the box, which are the 25th and 75th percentiles, respectively. Data points beyond the

Figure:

MO050

GLYCEMIC CONTROL AND THE RISK OF AKI IN PATIENTS WITH DIABETES AND CKD: PARALLEL POPULATION-BASED COHORT STUDIES IN U.S. AND SWEDEN ROUTINE CARE

Yang Xu[1], Aditya Surapaneni[2], Jim Alkas[1], Alexander Chang[3], Morgan Grams[2], Juan Jesus Carrero[1]

[1]Karolinska Institutet, Medical Epidemiology and Biostatistics, Stockholm, Sweden, [2]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, United States of America and [3]Geisinger Health System, Division of Nephrology, United States of America

Background and Aims: Patients with diabetes and chronic kidney disease (CKD) have increased susceptibility to acute kidney injury (AKI), but the underlying mechanisms are not well known. We here explore the association between glycemic control and risk of AKI.

Method: We created two parallel observational cohort studies of Swedish (SCREAM project, Stockholm, 2006-2011) and U.S. (Geisinger Heath system, Pennsylvania, 1996-2018) adult patients with diabetes mellitus and confirmed CKD stages G3-G5. Glycemic control was evaluated through repeated HbA1c measurements, which were categorized into 5 levels of glycemic control intensity, with HbA1c 6-6.9% as referent category, and continuously using cubic splines. We evaluated the association between baseline and time-varying HbA1c levels with AKI (defined as increase in creatinine >=0.3 mg/d over 48 hours or 1.5x creatinine over 7 days) using Cox proportional hazards regression and, in sensitivity analyses, Fine and Gray competing risk models accounting for death.

Results: In the Swedish cohort, there were 13932 patients with median age 76 years, 51% women, median eGFR 50.8 (Interquartile Range (IQR) 41.4-57.1) ml/min/1.73. In the U.S. cohort, there were 26520 patients with median age 71 years, 55% women and 52.1 (IQR 43.4-57.5) ml/min/1.73 m2. During a median of 2.3 and 3.1 years of follow up, 3172 and 8671 AKI events were recorded in the Swedish and US cohorts, respectively. The adjusted association between baseline HbA1c and AKI was similar in both cohorts, with the lowest risk between 6-6.9% and higher risk at higher levels of HbA1c. Compared to baseline HbA1c 6-6.9%, baseline HbA1c>9% associated with a 1.28 fold (95% CI 1.11-1.47) higher risk of AKI in the Swedish cohort, and a 1.14 (95% CI 1.04-1.25) higher risk in the U.S. cohort. Conversely, baseline HbA1c<6% did not associate with AKI. When using time-varying HbA1c, AKI risk was higher for HbA1c>9% (HR 1.18, 95% CI 1.03-1.37 in Swedish cohort and 1.27, 1.17-1.37 in U.S. cohort); AKI risk was also higher for HbA1c<6% in the U.S. cohort (1.12, 1.04-1.19), but not in the Swedish cohort (1.06, 0.97-1.16)).

Conclusion: Higher A1c was associated with AKI in adults with diabetes and CKD, suggesting that better glycemic control may also reduce risk of AKI.

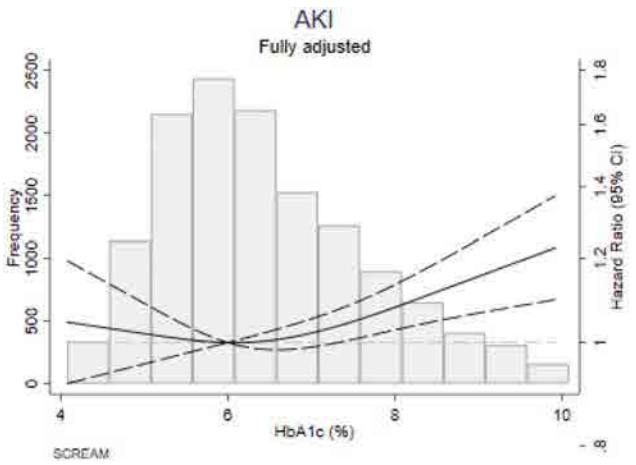


Figure. Multivariable-adjusted associations between baseline HbA1c (continuous variable) and the risk of AKI in two parallel cohorts of adults with diabetes CKD; Abbreviation: ESRD, end-stage renal disease; HbA1c, glycated hemoglobin.

MO051

EFFECTS OF SEMAGLUTIDE ON CHRONIC KIDNEY DISEASE OUTCOMES: A POST HOC POOLED ANALYSIS FROM THE SUSTAIN 6 AND PIONEER 6 TRIALS

Katherine Tuttle[1], David Cherney[2], Samy Hadjadj[3], Thomas Idorn[4], Ofri Mosenzon[5], Vlado Perkovic[6], Søren Rasmussen[4], Benjamin Wolthers[4], Stephen C Bain[7]

[1]University of Washington PMRC, Institute of Translational Health Sciences and Nephrology Division, Spokane, United States of America, [2]Toronto General Hospital, Department of Medicine, Division of Nephrology, Toronto, Canada, [3]University of Nantes, CHU Nantes, L'institut du thorax, INSERM, CNRS, Nantes, France, [4]Novo Nordisk, Søborg, Denmark, [5]Hadassah Hebrew University Hospital, Diabetes Clinical Research Center, Jerusalem, Israel, [6]University of New South Wales, Faculty of Medicine, Sydney, Australia and [7]Swansea University Medical School, Diabetes Clinical Research Cymru, Swansea, United Kingdom

Background and Aims: The SUSTAIN 6 cardiovascular outcomes trial (CVOT) indicated a renal benefit with subcutaneous (s.c.) once-weekly (OW) semaglutide vs placebo. The PIONEER 6 CVOT reported cardiovascular safety with oral semaglutide in a similar cohort using a similar trial design. In the present *post hoc* study, eGFR data from the SUSTAIN 6 and PIONEER 6 trials were pooled to evaluate the potential benefit of semaglutide (s.c. or oral) vs placebo on chronic kidney disease (CKD) outcomes.

Method: Data from 6,480 subjects from SUSTAIN 6 (N=3,297; median follow-up, 2.1 years; mean baseline eGFR, 76 mL/min/1.73 m^2) and PIONEER 6 (N=3,183; median follow-up, 1.3 years; mean baseline eGFR, 74 mL/min/1.73 m^2) were pooled for semaglutide (0.5 mg s.c. OW, 1.0 mg s.c. OW or 14 mg oral once daily) or placebo. We evaluated time to onset of persistent eGFR reduction (thresholds of ≥30%, ≥40%, ≥50% and ≥57% [57% corresponds to a doubling of serum creatinine]) from baseline in the overall pooled population and by baseline CKD subgroups (≥30–<60 mL/min/1.73 m^2, n=1,699; ≥60 mL/min/1.73 m^2, n=4,762; data were missing for 19 subjects). Analyses were performed using a Cox proportional-hazards model with treatment group (semaglutide vs placebo) and CKD subgroup as fixed factors and the interaction between both stratified by trial.

Results: In the overall population, the hazard ratios (HRs) for time to onset of persistent eGFR reductions with semaglutide vs placebo were <1.0, but did not achieve statistical significance. In subjects with baseline eGFR ≥30–<60 mL/min/1.73 m^2, HRs for semaglutide vs placebo were consistently lower compared with the overall population and, in this subgroup, semaglutide significantly reduced the risk of developing a persistent 30% eGFR reduction vs placebo (Figure; p=0.03). Numerically larger effects were seen with increasing eGFR reduction thresholds in this subgroup, with the exception of the 57% eGFR reduction threshold. No statistically different interactions between treatment and CKD subgroup were observed.

Conclusion: The findings of this *post hoc* analysis of pooled data from SUSTAIN 6 and PIONEER 6 on clinically relevant outcomes for CKD support a smaller magnitude of eGFR decline with semaglutide vs placebo, despite relatively short follow-up times. The small number of events at both the 50% and 57% thresholds, and the associated broad confidence intervals, limit the interpretability of the results. In line with previous findings, the data suggest a renal benefit of semaglutide vs placebo in subjects with established CKD. The FLOW trial (ClinicalTrials.gov Identifier: NCT03819153), which is dedicated to exploring CKD outcomes with semaglutide treatment, is ongoing to test this hypothesis in patients with CKD at baseline.

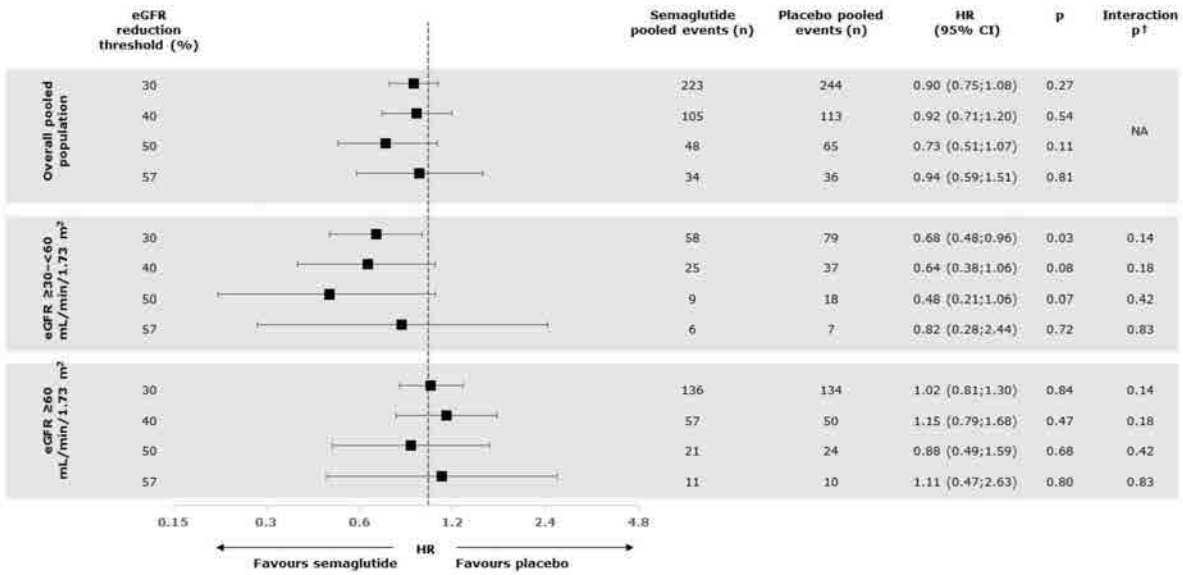


Figure: Semaglutide treatment effect on time to persistent eGFR reduction* across the overall pooled population and chronic kidney disease subgroups: a *post hoc* pooled analysis from the SUSTAIN 6 and PIONEER 6 trials

*Time to 'persistent' reductions in eGFR was defined as the time from randomisation to the first visit in which the value from the subsequent visit was confirmed by fulfilling the same relative reduction from baseline as the value from the previous visit. If no subsequent visit was performed, the confirmation was omitted. †Test for heterogeneity between treatment effects across eGFR subgroups. CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; NA, not applicable.

MO052 BIOPSY PROVEN KIDEY DISEASES IN TYPE 2 DIABETIC PATIENTS WITH IMPAIRED RENAL FUNCTION

Jin Hyuk Paek[1], Ohyun Kwon[1], Yaerim Kim[1], Woo Yeong Park[1], Seungyeup Han[1], Jeongsoo Yoon[2], Kyubok Jin[1]

[1]Keimyung University School of Medicine, Internal Medicine, Daegu, Korea, Rep. of South and [2]Yoon's Internal Medicine Clinic, Daegu, Korea, Rep. of South

Background and Aims: Diabetic nephropathy (DN) is a major microvascular complication of diabetes mellitus (DM) and the most common cause of end stage of renal disease worldwide. The nature of kidney disease in type 2 DM is more complex than type 1 DM. However, the usefulness of kidney biopsy in type 2 DM is still controversial and there are few reports about the biopsy proven kidney disease, especially in patients with impaired renal function.

Method: We retrospectively reviewed 1454 patients who received native kidney biopsy at Keimyung university Dongsan medical center between 2005 and 2018. Among 1454 patients, 92 patients were diagnosed with type 2 DM before kidney biopsy. Fifty-three patients with impaired renal function (estimated glomerular filtration rate < 60 mL/min/1.73 m^2 using Modification of Diet in Renal Disease formula) were finally enrolled in this study. We categorized the pathologic diagnoses as DN, non-diabetic renal disease (NDRD), and NDRD mixed with DN (Mixed).

Results: The mean age at kidney biopsy was 58.4 $\pm$ 11.2 and mean eGFR was 28.6 $\pm$ 14.6 mL/min/1.73 m^2. Nineteen patients (35.8%) had diabetic retinopathy and mean duration of DM before kidney biopsy was 102.1 $\pm$ 82.2 months. Of the 53 patients, there were 28 NDRD (52.8%), 18 DN (34.0%), and 7 Mixed (13.2%). Diabetic retinopathy was more common in DN, following Mixed and NDRD (72.2%, 42.9%, and 10.7%, respectively, $p < 0.001$). Multivariable logistic regression analysis revealed that diabetic retinopathy was significantly associated with DN (OR, 23.672; 95% CI, 4.290-130.609; $p < 0.001$). In multivariable cox proportional hazard models, creatinine level (HR, 1.779; 95% CI, 1.404-2.255; $p < 0.001$) and dipstick albuminuria $\geq$ 2+ (HR, 22.721; 95% CI, 4.670-110.542; $p < 0.001$) were identified as independent prognostic factors for renal survival.

Conclusion: Kidney disease of type 2 diabetic patients were various and clinical parameters could not completely predict. Kidney biopsy is an important tool for the definite diagnosis and the proper treatment of kidney disease in diabetic patients with impaired renal function.

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REVISITING THE BONE IN CKD

MO053 INHIBITION OF SODIUM PHOSPHATE TRANSPORTER NPT2A IMPROVES EXPERIMENTAL VASCULAR CALCIFICATION AND PHOSPHATE HOMEOSTASIS IN RATS

Juergen Klar[1], Giese Anja[1], Alexander Ehrmann[1], Christoph Thiel[1], Bernd Riedl[1], Frank Eitner[1]

[1]*Bayer AG, Wuppertal, Germany*

Background and Aims: A dysregulated phosphate homeostasis is strongly associated with mortality, cardiovascular events and vascular calcification, particularly in patients suffering from CKD. Inhibition of the tubular phosphate transporter Npt2a provides a novel and unique mechanism to address phosphate homeostasis imbalance and vascular calcification.

Method: Npt2a activity was measured in a cell-based assay, using a stable CHO cell line with inducible Npt2a expression. Male Wistar rats were used for all experiments. Healthy rats were treated orally with BAY 767, a potent Npt2a inhibitor developed at Bayer AG to assess urinary phosphate excretion. Vascular calcification was induced by administration of a pan-FGFR inh. (25mg/kg) for 10 days. Calcium content in the aorta was measured as surrogate for vascular calcification. Blood samples were withdrawn at the end of the study to determine the plasma levels of FGF-23, parathyroid hormone and phosphate with commercially available assay systems according to the manufactures protocols (FGF-23 and PTH: ELISA Kit, Immuntopics; phosphate: Pentra400 system).

Results: BAY 767 was identified as potent Npt2a inhibitor, with an IC50 of 2.9/6 nM on rat/ human Npt2a, respectively, selective over Npt2b, Npt2c and Pit-1. Single dose treatments of healthy rats resulted in a significant, dose-dependent increase in urinary phosphate excretion within 16h. In an experimental vascular calcification model, massive vascular calcification and hyperphosphatemia was induced by daily oral administration of a FGFR inh. Simultaneous treatment with the Npt2a inhibitor BAY 767 significantly inhibited vascular calcification in comparison to untreated rats. In this set-up the plasma phosphate level was increased after 10 days up to 3.7 mmol/L in the FGFR inh. treated group compared to 1.9 mmol/L in control animals, whilst treatment with BAY 767 reduced plasma levels to 2.7 mmol/L. In addition, FGF-23 and PTH were also reduced under compound BAY 767 treatment. However, in the same model 2.2% lanthanum carbonate was not beneficial with respect to vascular calcification.

Conclusion: Our results show for the first time that treatment with a Npt2a inhibitor improves vascular calcification by addressing urinary phosphate excretion and phosphate homeostasis in rats.

Npt2a inhibition may provide a new therapeutic principle for patients suffering from disbalanced phosphate homeostasis and vascular calcifications, including CKD patients.

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MO054

VASCULAR CALCIFICATION IMPAIRS BONE MINERALIZATION

Maria Lerche Mace[1], Eva Gravesen[1], Anders Nordholm[1,2], Soeren Egstrand[1,2], Marya Morevati[1], Geert Behets[4], Patrick D'Haese[4], Klaus Olgaard[1,5], Ewa Lewin[2]

[1]Rigshospitalet, Nephrology, Copenhagen, Denmark, [2]Herlev Hospital, Nephrology, Herlev, Denmark, [4]University of Antwerp, Laboratory of Pathophysiology, Wilrijk, Belgium and [5]University of Copenhagen, Clinical Medicine, Copenhagen, Denmark

Background and Aims: Several studies report an association between low BMD and vascular calcification (VC) in the general population and in CKD patients. Development of VC in CKD is a cell regulated process where the vascular smooth muscle cell alters phenotype to a bone-like secretory cell. Our group has previously demonstrated the expression of Wnt inhibitors in VC and so we ask if the presence of VC affects bone metabolism.

Method: A novel model of isogenic aorta transplantation (ATx) was developed and used in the study. Severe uremic vascular calcifications were induced in inbred Dark Aguti (DA) rats by 5/6 nephrectomy, high phosphate diet and calcitriol treatment. After 14 weeks the calcified abdominal aorta of the uremic rat was transplanted into a normal DA rat (uremic ATx, n=16). A normal aorta was transplanted into a normal DA rat as sham group (normal ATx, n=9) and age-matched normal rats were used as one more control group (control, n=6). Rats were sacrificed 4 weeks after ATx and plasma biochemistry, bone and vessels were analyzed. Data are presented as mean±SEM or median [range]. Statistical significance *p<0.5,**p<0.01,*** p<0.001.

Results: The uremic donor rat suffered from severe kidney disease with disturbed mineral balance and its aorta had a high calcium content of 15.7±0.8 µg Ca/mg vs. none in the normal aorta. Uremic ATx, normal ATx and control rats had same plasma levels of creatinine, Ca^{2+}, phosphate, PTH, FGF23 and sclerostin. The uremic ATx had significant lower bone mineral density (BMD) compared to normal ATx and control rats (1576±5 vs. 1592±5* & 1613±6* mg/cc). The impact on bone mineralization was also detected in the bone histomorphometry analysis, where the uremic ATx had less osteoid compared to normal ATx (median 3% [0,3%;8%] vs. 5% [2%;8%]*). Moreover, the uremic ATx had fewer osteoblasts and more osteoclasts. The effect on bone was supported by substantial gene analysis of several genes related to bone remodeling, mineralization and Wnt signaling. The uremic ATx rats had significant changes in mRNA levels of several genes in bone compared to normal ATX and control rats such as increased alkaline phosphatase (3.26±0.29 vs. 1.56±0.32*** & 0.86±0.12***), decreased osteoblast marker osteocalcin (0.54±0.06 vs. 0.92±0.14* & 1.19±0.06***) and increased osteoclast marker cathepsin K (2.36±0.24 vs. 1.19±0.23** & 1.01±0.07***). In addition, we found upregulation of the bone mineralization inhibitors osteopontin (1.46±0.18 vs. 0.69±0.17** & 0.49±0.06**) and progressive ankylosis protein homolog (8.10±0.60 vs. 3.21±0.74** & 2.39±0.48**) as well as collagen I (9.30 [2.73;14.81] vs. 2.30 [0.31;19.33]* & 2.78 [1.63;7.52]***). The inhibitor of bone formation sclerostin was significant increased (2.90 [1.54;13,29] vs. 1,23 [0.32;3.20]** & 0.93 [0.39;2,19]**) along with a slight downregulation of bone stimulator BMP2 (3.18±0.15 vs. 4.06±0.30* & 3.98±0.44*. Finally, the Wnt signaling pathway was affected by upregulation of β-catenin (3.15±0.25 vs. 1.28±0.26*** & 1.03±0.13***) and the downstream gene Snail1 (3.73±0.33 vs. 1.54±0.45*** & 1.04±0.12***).

Conclusion: These novel findings indicate the existence of a tissue crosstalk between vessels and bone. The presence of vascular calcification lowers BMD, decreases the amount of osteoid and affects several pathways in bone.

MO055

STABLE CALCIUM ISOTOPES: A NOVEL BIOMARKER OF BONE MINERAL CONTENT IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Rukshana Shroff[1], Alex Heuser[2], Alex Lalayiannis[1], Aysun Karabay Bayazit[3], Augustina Jankauskiene[4], JUSTINE BACCHETTA[5], Varvara Askiti[6], Claus Schmitt[7], Andromachi Mitsioni[6], Nicola Crabtree[8], Mary Fewtrell[1], Lorenzo Biassoni[1], Dagmar-Christiane Fischer[9], Anton Eisenhauer[2]

[1]Great Ormond Street Hospital for Children and UCL Institute for Child Health, London, United Kingdom, [2]Geomar Helmholtz Centre for Ocean Research Kiel, Kiel, Germany, [3]Cukurova University, Adana, Turkey, [4]Clinic of Pediatrics, Vilnius University, Vilnius, Lithuania, [5]Hôpital Femme Mère Enfant, Hospices Civils de Lyon, Bron, Lyon, France, [6]"P. & A. Kyriakou" Childrens' Hospital, Athens, Greece, [7]Center for Pediatrics and Adolescent Medicine, Heidelberg, Germany, [8]Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom and [9]Rostock University Medical Hospital, Rostock, Germany

Background and Aims: In CKD dysregulated calcium (Ca) homeostasis is common and causally associated with reduced bone mineral density (BMD) and vascular calcification. Currently available radiological measures and biomarkers do not allow accurate evaluation of BMD.

The aim of our study was to determine the sensitivity and specificity of stable Ca isotopes in determining bone mineral content.

Method: We measured stable Ca isotopes ^{44}Ca and ^{42}Ca by plasma-ionization mass-spectrometry in blood and urine. The relationship between bone Ca gain and loss is calculated using a compartment model based on Ca kinetics, and expressed as $\delta^{44/42}Ca_{\cdot}$ Ca absorption from bones increases $\delta^{44/42}Ca_{Blood}$ and $\delta^{44/42}Ca_{Urine}$, and resorption decreases these fractions.

104 children in CKD4-5 and on dialysis (CKD4-5D), 40 matched controls and 100 adults underwent Ca isotope measurement, bone biomarkers, dual energy x-ray absorptiometry (DXA) and tibial peripheral quantitative CT scan (pQCT), an accurate measure of cortical BMD.

Results: In healthy children the $\delta^{44/42}Ca_{Blood}$ and $\delta^{44/42}Ca_{Urine}$ were higher than in adults ($p<0.0001$), reflecting avid Ca uptake during bone formation. Since urinary Ca excretion is impaired in CKD, $\delta^{44/42}Ca_{Blood}$ was higher and $\delta^{44/42}Ca_{Urine}$ lower in children with CKD4-5D compared to controls ($p<0.001$ for both); Figure 1.

In CKD2-5D $\delta^{44/42}Ca_{Blood}$ positively correlated with cholecalciferol ($p=0.01$) and alfacalcidol ($p=0.002$) doses, implying increased bone Ca uptake when Ca bioavailability is increased. $\delta^{44/42}Ca_{Blood}$ positively correlated with biomarkers of bone formation (alkaline phosphatase, $p=0.05$) and negatively with bone resorption markers (PTH, $p=0.013$; TRAP5b, $p<0.001$ and CTX, $p=0.006$). $\delta^{44/42}Ca_{Blood}$ positively correlated with tibial cortical BMD-Z-score ($p=0.006$, $R^2=0.39$), and DXA hip BMD-Z-score ($p=0.02$). On multivariable linear regression analysis significant and independent predictors of tibial cortical BMD-Z-score were $\delta^{44/42}Ca_{Blood}$ ($\beta=0.68$, $p=0.006$) and PTH (β-0.39, $p=0.04$), together predicting 67% of the variability in BMD.

Conclusion: Ca isotope ratios provide a novel, non-invasive method of assessing bone mineralization. Further studies are in progress to define optimal levels of $\delta^{44/42}Ca_{Blood}$ that can guide safe and effective treatment to prevent Ca deficiency or overload.

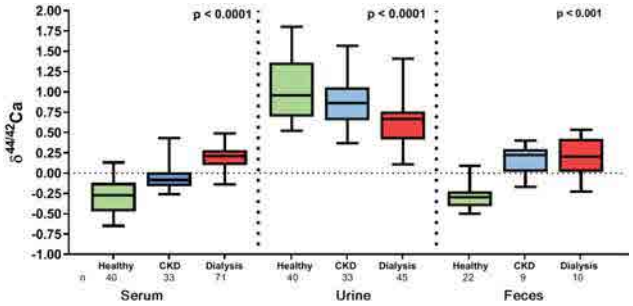


Figure 1 – Stable Ca isotope fractions in serum, urine and feces in CKD4-5 and dialysis patients

MO056 **MODIFICATION OF P16, P21 AND NRF2 EXPRESSION IN A MODEL OF UREMIC VASCULAR CALCIFICATION**

JONAS LAGET[1], SAM HOBSON[2], BERNARD JOVER[3], KAREN MUYOR[1], Flore Duranton[1], Karolina Kublickiene[5], ANNE DOMINIQUE LAJOIX[6], Peter Stenvinkel[5], Angel Argiles Ciscart[1], Nathalie Gayrard[1]

[1]RD NEPHROLOGIE EA7288 BC2M, MONTPELLIER, France, [2]Karolinska University Hospital, Division of Renal Medicine, Department of Clinical Science, Technology and Intervention, Stockholm, Sweden, [3]INSERM, U1046 PHYMEDEXP, MONTPELLIER, France, [5]Karolinska University Hospital, Division of Renal Medicine, Department of Clinical Science, Technology and Intervention, Stockholm, Sweden and [6]MONTPELLIER UNIVERSITY, EA7288 BC2M, MONTPELLIER, France

Background and Aims: Vascular calcification (VC) is a consequence of ageing that confers development of future cardiovascular events. Accumulation of senescent cells can lead to structural and functional abnormalities in vessel wall towards increased stiffness, reduced compliance and impaired contractile and dilatory capacity. Thus, accumulation of senescent cells in the arterial wall could also contribute to the pathophysiology of VC. To test this hypothesis, the presence of cellular markers of senescence, p16, p21 and NRF2, was assessed in aorta from rat model of VC associated with chronic kidney disease (CKD).

Method: Six-week-old Sprague-Dawley rats underwent 5/6th subtotal nephrectomy (SNx, n=6) or no surgery (Control, n=1). After 8 weeks of renal failure, the regular chow was supplemented with high phosphate (1.2%) and vitamin D (1 µg/day, 5 days per week) for 1 or 4 weeks to initiate vascular calcification (SNx-VC group). At the end of the protocol (Figure 1), blood pressure was measured, and thoracic aorta was taken for determination of calcification by Von Kossa staining, and protein and gene expressions of p16, p21, and NRF2 by immunostaining and qPCR, respectively.

Results: After 4 weeks of dietary intervention, SNx rats showed an increase in pulse pressure (88±15mmHg *vs* 35 mmHg for the control). Marked VC was also observed in these animals, 17% of calcified area vs <1 % in the control rat. Calcification was focal giving strong and no calcified areas on the same aorta. Expressions of p16, p21and NRF2 proteins were enhanced at the site of calcification in the SNx-VC 4-week (4W) group whereas it was unchanged in aortic media without calcification compared to the control rat (Figure 2). In SNx-VC 1-week (1W) rats, no change in pulse pressure or vascular calcification was observed without obvious changes for staining patterns of selected markers. Using qPCR we found p16 gene expression to be higher in the most calcified aortas (4W) (fold-change = 4.32 *vs* 1W) and p21 gene expression to be slightly increased (fold-change = 0.53 *vs* 1W). NRF2 gene expression was enhanced in 1W group compared to control, but decreased in the most calcified samples (4W).

Conclusion: This pilot study suggests that uraemia-induced cellular senescence accompanies VCs, as suggested by the modified expression of p16 or NRF2 genes. Our observations deserve exploration in larger studies using additional senescence markers for validation. If so, cellular senescence kinetics will be evaluated in order to test whether senolytics compounds could be a therapeutic option to arrest VC in CKD.

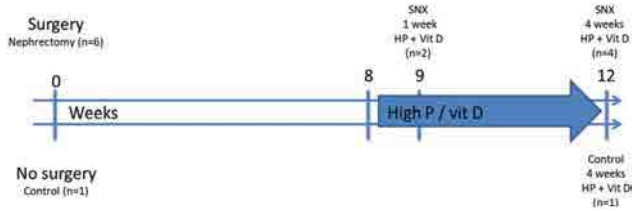


Figure 1. Study design

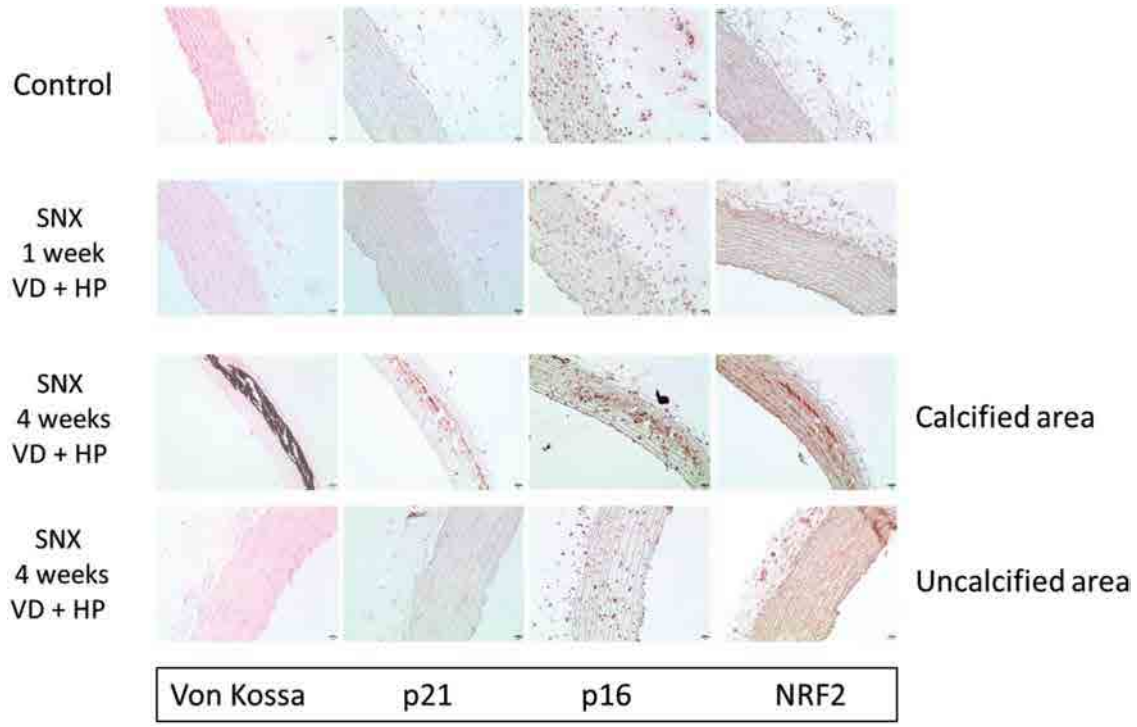


Figure 2. Representative images of Von kossa staining and immunostaining of p16, p21 and NRF2 proteins in the different groups of rats.

MO057 **HYPOXIA AS INDUCER OF FIBROBLAST GROWTH FACTOR 23 IN OSTEOCYTES**

Josephine Bonnemaijer[1,2], Pieter Koolwijk[2], Nathalie Bravenboer[3], Huib Van Essen[3], Marc Vervloet[1]

[1]Amsterdam University Medical Centers, Nephrology, Amsterdam, Netherlands, [2]Amsterdam University Medical Centers, Physiology (cardiovascular), Amsterdam, Netherlands and [3]Amsterdam University Medical Centers, Clinical Chemistry, Amsterdam, Netherlands

Background and Aims: Cardiovascular disease accounts for a major proportion of deaths among chronic kidney disease (CKD) patients. Fibroblast Growth Factor 23 (FGF23), a key regulator in phosphate homeostasis and mainly produced by osteocytes, is associated with CKD progression and cardiovascular mortality. FGF23 is involved in the development of left ventricular hypertrophy that can lead to congestive heart failure. Dysfunction of the heart causes tissue malperfusion, for instance in bones, inducing the hypoxia-inducible signaling pathway. Recently, the hypoxia-inducible factor-1α (HIF-1α) has been suggested as inducer of FGF23. Therefore, we investigated whether hypoxia in osteocytes induces FGF23 production mediated by the stabilization of HIFs.

Method: Human sarcoma osteogenic cells (SaOS2 cell line) and primary human osteocytes were cultured and exposed to hypoxic conditions (1% and 5% O_2) and normoxic condition (20% O_2) for 24 hours. qPCR was performed to investigate the expression of HIFs and FGF23 mRNA in these cells. HIFs protein expression was also evaluated by Western Blot analysis.

Results: Our data show that HIF-1α, and not HIF-2α, protein increases in SaOS2 cells and primary osteocytes under hypoxic conditions as compared to normoxic condition. In addition, we found that FGF23 mRNA expression is elevated in SaOS2 cells in these hypoxic conditions compared to normoxic condition (Fig.1). This increase was significant in SaOS2 cells exposed to 1% O_2 ($p < 0.05$). Preliminary data of primary osteocytes show that FGF23 mRNA is not expressed in hypoxic conditions compared with normoxic conditions (Fig.1).

Conclusion: HIF-1α protein was increased in both SaOS2 cells and primary osteocytes exposed to 1% O_2. Hypoxic conditions upregulated FGF23 mRNA in SaOS2 cells. Taken together, these findings suggest that bone malperfusion upregulates FGF23 by stabilizing HIF-1α. This could then close a vicious circle where FGF23 induces cardiovascular disease, and circulatory failure upregulates FGF23.

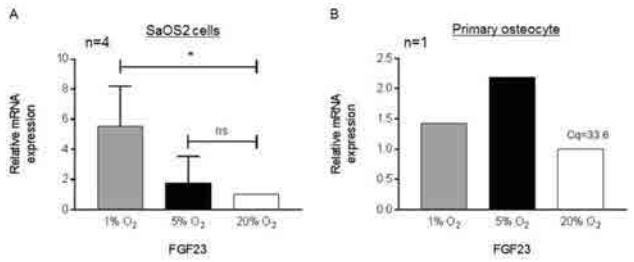


Figure 1: Relative FGF23 mRNA expression in SaOS2 cells and primary osteocytes

MO058

INHIBITION OF OSTEOCLAST DIFFERENTIATION BY 1.25-D AND THE CALCIMIMETIC KP2326 REVEALS 1.25-D RESISTANCE IN ADVANCED CKD

Julie Bernardor[1,2,3], Sacha Flammier[1,2], Bruno Ranchin[2], Segolene Gaillard[4], Diane Platel[1], Olivier Peyruchaud[1], Irma Machuca-Gayet[1], Justine Bacchetta[1,2,5,6]

[1]INSERM, UMR 1033, Faculté de Médecine Lyon Est, Université Claude Bernard Lyon1, Lyon, France, [2]Hôpital Femme Mère Enfant, Hospices Civils de Lyon, Centre de Référence des Maladies Rénales Rares, Lyon, France, [3]Unité de Nice Sophia Antipolis, Faculté de Médecine, Nice, France, [4]INSERM CIC 1407, CNRS UMR 5558, Service de Pharmacotoxicologie Clinique, Hospices Civils de Lyon, Bron, France, [5]Hôpital Femme Mère Enfant, Hospices Civils de Lyon, Centre de Référence des Maladies Rares du Calcium et du Phosphate, Bron, France and [6]Université Claude Bernard Lyon 1, Faculté de Médecine Lyon Est, Lyon, France

Background and Aims: Active vitamin D analogs and calcimimetics are cornerstones for managing secondary hyperparathyroidism (SHPT) in chronic kidney disease (CKD). Their direct effects on bone cells remain to be determined.

Method: Peripheral blood mononuclear cells (PBMCs) of 19 pediatric CKD patients and 6 healthy donors (HD) were differentiated into osteoclasts in presence of M-CSF and RANKL. Effect of combined or single treatment with active vitamin D (1.25-D) and/or the calcimimetic KP2326 were evaluated onto osteoclast differentiation and osteoclast mediated bone resorption.

Results: 1.25-D inhibited osteoclastic differentiation, a significant resistance to 1.25-D was observed when CKD worsens. A significant albeit less important inhibitory effect of KP2326 on osteoclastic differentiation was also found both in cells derived from HD and CKD patients, through an activation of the Erk pathway. This inhibitory effect was not modified by CKD stage. Combinatorial treatment with 1.25-D and KP2326 did not result in synergistic effects. Last, KP2326 significantly inhibited human osteoclast-mediated bone resorption.

Conclusion: Both 1.25-D and KP2326 inhibit osteoclastic differentiation, however to a different extent. Whilst 1.25-D has no significant effect on bone resorption, KP2326 inhibits bone resorption. Recent data showed that calcimimetics also have a direct anabolic effect on bone, through the stimulation of osteoblastic differentiation and mineralization in human mesenchymal stem cells *in vitro*. All these results provide a strong rationale for a global positive effect of calcimimetics on bone remodeling. Calcimimetics also significantly decrease FGF23 levels. In the setting of global systematic deleterious effects of high FGF23 levels in CKD, and keeping in mind that active vitamin D analogs stimulate FGF 23 production, all these data could favor the use of decreased doses of 1.25-D with low-doses of calcimimetics in SHPT in dialysis, the combination of these two therapies already being proposed in the 2017 K-DIGO guidelines.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii160–iii160, 2020

THE HYPERTENSION SPECTRUM IN CKD: PATHOPHYSIOLOGY AND RISK

MO059

CONTRIBUTION OF OPIOID RECEPTOR SIGNALING IN PODOCYTES TOWARDS THE DEVELOPMENT OF SALT-SENSITIVE HYPERTENSION AND KIDNEY INJURY

Daria Golosova[1], Vladislav Levchenko[1], Christine Klemens[1], Oleg Palygin[1], Alexander Staruschenko[1]

[1]*Medical College of Wisconsin, Physiology, Milwuakee, United States of America*

Background and Aims: The global increase in opioid use requires practitioners to be aware of the side effects and contraindications of these medications in order to avoid complications, especially in patients with organ dysfunction such as cardiovascular disease and chronic kidney disease. It has been reported that opioid use is strongly associated with predictors of poor cardiovascular outcomes such as increased albuminuria and reduced GFR. Opioids work by binding to kappa-, mu- and delta-opioid receptors (ORs). We hypothesize that stimulation of ORs modulates calcium flux in podocytes ultimately leading to cell apoptosis, development of albuminuria, glomeruli damage and progression of hypertension.

Method: To test this hypothesis, we applied specific OR agonists to: 1) *in vitro* - immortalized cultured human podocytes (hPod), 2) *ex vivo* - freshly isolated human and rat glomeruli; and 3) *in vivo* - Dahl salt-sensitive (SS) rats. Calcium response in the podocytes was analyzed via ratiometric confocal fluorescent microscopy using calcium fluorescent dyes. For chronic studies Dahl SS rats were fed a high salt (HS; 8%) NaCl diet for 14 days with or without a daily *i.v.* bolus infusion of BRL52537, a potent and selective kappa-OR agonist.

Results: The hPods displayed a fast increase in fluorescence following an addition of BRL52537 (EC_{50} = 162 ± 2 μM) in a 2 mM calcium solution. A pre-application of kappa-OR antagonist (NorBNI) disrupted the effect of BRL52537 on calcium flux. The effect of BRL52537 on calcium in podocytes was completely abolished when we used the calcium-free solution or a pre-application of SAR7334 (a TRPC6 channel inhibitor), which revealed that calcium flux is mediated by activation of TRPC6 channels rather than other plasma membrane channels or depletion of intracellular calcium stores. Immunofluorescent analysis of human kidney validated kappa-OR protein expression in podocytes. Podocytes of the freshly isolated human glomeruli also revealed robust increases in fluorescent intensity following a single application of BRL52537, which was abolished by a pre-application of SAR7334. Effect of kappa-OR agonist was specific since application of Damgo (mu-OR agonist) or DPDPE (delta-OR agonist) had either no or minimal effect in normotensive rats. Chronic studies in Dahl SS rats showed that in BRL-treated group animals had elevation of microalbuminuria (13 ± 3 vs. 3 ± 1 Alb/Cre at day 7 of HS), higher mean arterial pressures (179 ± 15 mmHg vs. 151 ± 11 mmHg), and nephrinuria (50,232 ± 22,254 vs. 15,230 ± 4,647 a.u./Cre) compared to control rats. Glomeruli isolated from the hypertensive opioid treated rats had a significantly higher level of basal calcium (245 ± 23 vs. 139 ± 9 nM) in podocytes compared to non-treated group. Additionally, acute application of BRL52537 to podocytes of hypertensive animals resulted in a sustained increase in total $[Ca^{2+}]_i$ influx.

Conclusion: Our data establish that stimulation of kappa-ORs are specifically involved in increasing of intracellular calcium in podocytes through the TRPC6 pathway, which causes calcium overload and cellular damage. Observed increase in the calcium flux in podocytes most likely further contribute to the kidney injury and progression of salt-induced hypertension.

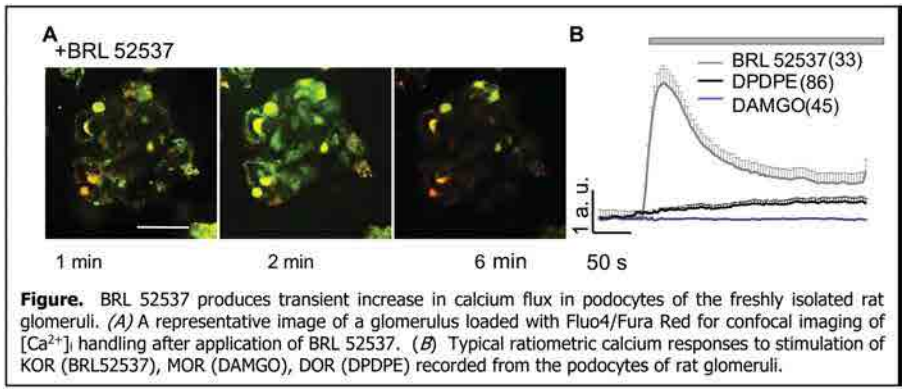


Figure. BRL 52537 produces transient increase in calcium flux in podocytes of the freshly isolated rat glomeruli. *(A)* A representative image of a glomerulus loaded with Fluo4/Fura Red for confocal imaging of $[Ca^{2+}]_i$ handling after application of BRL 52537. (*B*) Typical ratiometric calcium responses to stimulation of KOR (BRL52537), MOR (DAMGO), DOR (DPDPE) recorded from the podocytes of rat glomeruli.

Figure:

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NEPHROPATHOLOGY INSIGHTS

MO060

ACUTE KIDNEY INJURY PROMOTES DEVELOPMENT OF A PAPILLARY RENAL CELL ADENOMA-CARCINOMA SEQUENCE FROM RENAL PROGENITORS

Anna Julie Peired[1], Marco Allinovi[1,2], Giulia Antonelli[1], Maria Lucia Angelotti[1], Francesco Guzzi[1], Paola Romagnani[1,3]

[1]University of Florence, Department of Biomedical, Experimental and Clinical Sciences "Mario Serio", Florence, Italy, [2]Careggi University Hospital, Nephrology, Dialysis and Transplantation Unit, Florence, Italy and [3]Meyer Children's University Hospital, Nephrology and Dialysis Unit, Florence, Italy

Background and Aims: Renal cell carcinoma (RCC) accounts for 2% of all cancers, with about 190,000 new cases per year worldwide. Risk factors for RCC include obesity, diabetes, hypertension and genetic factors, but the majority of cancers occur in apparent absence of clear risk factors. Acute tissue injury (AKI) causes DNA damage and repair processes involving increased cell mitosis and polyploidization, leading to cell function alterations that may potentially drive cancer development. We proposed to verify whether AKI plays a role in RCC development, and to identify the cellular origin of RCC.

Method: We used the following techniques: 1. observational, retrospective clinical trial to identify a possible association of AKI with RCC. 2. Experimental AKI induction in wild-type mice to study tumor development over 36 weeks. 3. Analysis of TCGA Research Network dataset on human papillary RCC (pRCC) molecular characterization, focusing on AKI-driven pathways. 4. Development of mouse models in which the intracellular domain of Notch 1 (NICD1), a molecule modulated during AKI, is expressed constitutively by all Pax8+ tubular epithelial cells (Pax8/NICD1) or only by Pax2+ renal progenitors (Pax2/NICD1) upon induction in adult mice. The mice were sacrificed at 36 weeks or 4 weeks after AKI. 5. Clonal analysis of tumoral lesions with Confetti reporter. 6. Examination of single cell RNA sequencing (RNAseq) data from pRCC patients.

Results: We observed that an AKI episode is a major risk factor for pRCC development and recurrence in patients. Wild-type mice subjected to AKI developed pRCC over time in an adenoma-carcinoma sequence, corroborating our human findings. Among AKI-related pathways, Notch1 overexpression in human pRCC associated with worse outcome, prompting us to generate Notch1-overexpressing mice. At 36 weeks o at 4 weeks following AKI, Pax8/NICD1 mice presented a significant decline of renal excretory function as well as type 2 pRCCs. Confetti lineage tracing showed that most of the pRCCs were monoclonal or biclonal, suggesting that they could originate from a local stem cell/progenitor population. Pax2/NICD1 mice presented type 2 pRCCs, and lineage tracing identified single Pax2+ tubular progenitors as the source of pRCCs. Single cell RNAseq analysis confirmed that the molecular signature of the pRCC cell of origin matched the one of human tubular progenitors.

Conclusion: This study expose the link between AKI and pRCC development in patients, with important clinical implications. In mice, AKI promotes long-term development of type 2 papillary tumors by activating the AKI-associated Notch1 pathway. Additionally, pRCC originates from clonal proliferation of renal progenitors in a classical adenoma-carcinoma sequence leading to invasive pRCC growth and metastatization in mice.

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MO061

PLASMINOGEN DEFIENCY DOES NOT PROTECT MICE FROM SODIUM RETENTION IN EXPERIMENTAL NEPHROTIC SYNDROME

Mengyun Xiao[1], Bernhard Nikolaus Bohnert[1], Matthias Woern[1], Edward Plow[2], Tobias B. Huber[3], Florian Grahammer[3], Ferruh Artunc[1]

[1]University Hospital Tübingen, Internal Medicine IV, Renal Division, Tuebingen, Germany, [2]Cleveland Clinic, Lerner Research, Columbus, United States of America and [3]University Hospital Hamburg-Eppendorf, Internal Medicine III, Hamburg, Germany

Background and Aims: Sodium retention and edema formation are the hallmarks of nephrotic syndrome and thought to be mediated by proteolytic activation of the epithelial sodium channel (ENaC) by aberrantly filtered serine proteases. Plasmin is highly abundant in nephrotic urine and has been proposed to be the principal serine protease responsible for ENaC activation in nephrotic syndrome. However, there is not enough evidence to demonstrate the essential role of plasmin in mediating sodium retention in an experimental nephrotic model.

Method: We investigated sodium retention and edema formation in a mouse model of nephrotic syndrome based on an inducible podocyte-specific podocin knockout (Bl6-Nphs2$^{tm3.1Antc\ or\ \Delta ipod}$ * Tg(Nphs1-rtTA*3G^{8Jhm})* Tg(tetO-cre)^{1Jaw}). To generate an inducible podocin knockout with plasminogen deficient model (Nphs2$^{\Delta ipod}$ * *Plg*$^{-/-}$, hereafter referred to as *Plg*$^{-/-}$), plasminogen deficient mice (Bl6-Plg$^{tm1Jld\ or\ -/-}$) were intercrossed with Nphs2$^{\Delta ipod}$ mice. Nephrotic syndrome was induced after oral doxycycline treatment for 14 days. Body weight, urinary protein, urinary sodium excretion, as well as urinary plasmin activity were daily determined 14 days after end of induction. To determine if sodium retention can be prevented by serine protease inhibitor aprotinin in *Plg*$^{+/+}$ and *Plg*$^{-/-}$ mice after induction of nephrotic syndrome, sustained-release pellets containing aprotinin (2 mg per day) or placebo pellets were implanted to either *Plg*$^{+/+}$ or *Plg*$^{-/-}$ mice (n=4 per group).

Results: Uninduced *Plg*$^{+/+}$ (n=6-13) and *Plg*$^{-/-}$ mice (n=6-14) had normal kidney function and sodium handling. After end of doxycycline induction, there was no significant differencein proteinuria increase between *Plg*$^{+/+}$ (from 2 ± 0 to 161 ± 16 mg/mg creatinine, $p<0.05$) and *Plg*$^{-/-}$ mice (from 9 ± 8 to 146 ± 44 mg/mg creatinine, $p<0.05$) leading to similar hypoalbuminemia. In urine samples from *Plg*$^{+/+}$ mice, Western blot revealed urinary excretion of plasminogen/plasmin which was completely absent in *Plg*$^{-/-}$ mice. Accordingly, urinary plasmin activity was only detectable in *Plg*$^{+/+}$ mice using a chromogenic substrate. After onset of proteinuria, amiloride-sensitive natriuresis was increased compared to uninduced mice indicating ENaC activation. While urinary sodium excretion dropped in both genotypes indicating sodium retention (from 193 ± 16 to 16 ± 6 µmol/24h in *Plg*$^{+/+}$ mice, $p<0.05$; from 229 ± 11 to 26 ± 7 µmol/24h in *Plg*$^{-/-}$ mice, $p<0.05$). As a consequence, body weight maximum increased in both genotypes 21 ± 1% in *Plg*$^{+/+}$ and 17 ± 2% in *Plg*$^{-/-}$ mice (p=0.616) and was paralleled by development of ascites. Urinary amidolytic activity were completely prevented by the presence of aprotinin, as well as sodium retention and ascites in both *Plg*$^{+/+}$ and *Plg*$^{-/-}$ mice.

Conclusion: This study shows for the first time that mice lacking urinary plasmin are not protected from ENaC-mediated sodium retention in experimental nephrotic syndrome, however it can be prevented by aprotinin. These findings point to an essential role of other hitherto unknown serine proteases excreted in nephrotic urine.

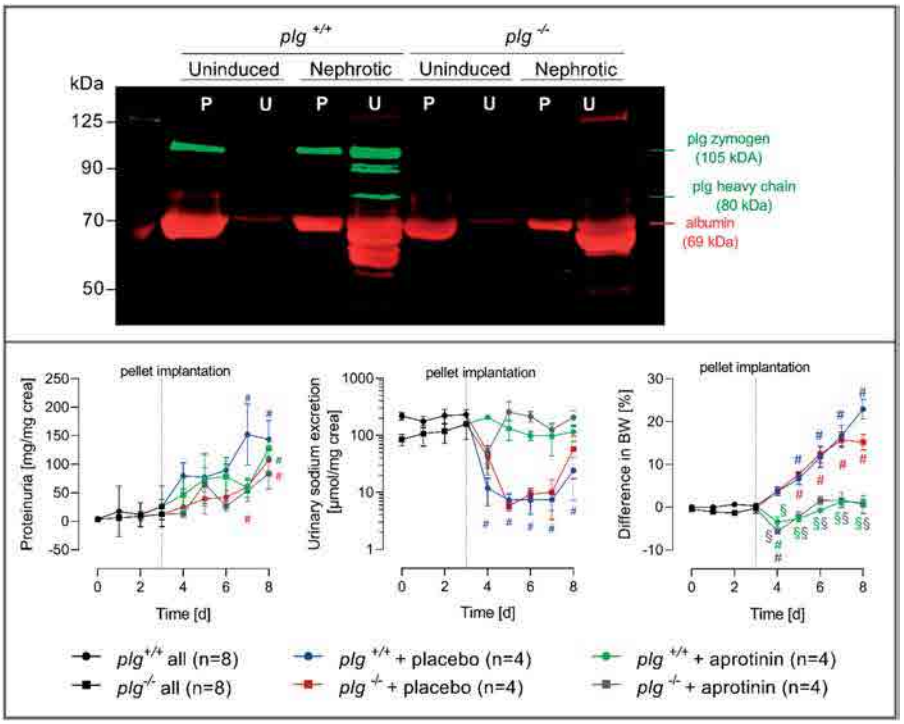


Figure:

MO062

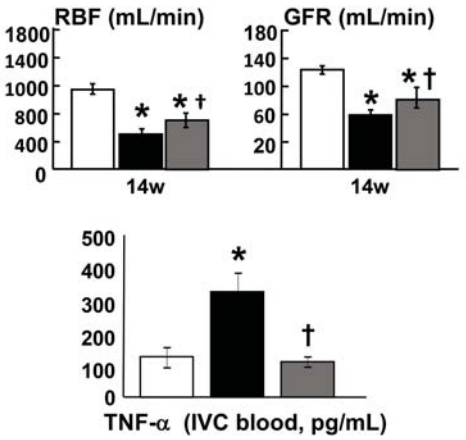
CHRONIC KIDNEY DISEASE, INFLAMMATION, AND HEART FAILURE WITH PRESERVED EJECTION FRACTION: A RENAL-CARDIO AXIS?

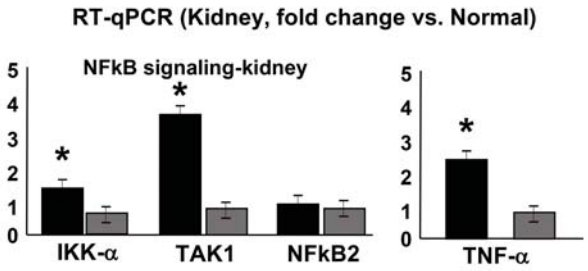
Alejandro Chade[1], Maxx Williams[2], Jason Engel[2], Gene Bidwell[3]

[1]University of Mississippi Medical Center, Physiology and Biophysics; Medicine; Radiology, Jackson, United States of America, [2]University of Mississippi Medical Center, Physiology and Biophysics, Jackson, United States of America and [3]University of Mississippi Medical Center, Neurology; Cell and Molecular Biology, Jackson, United States of America

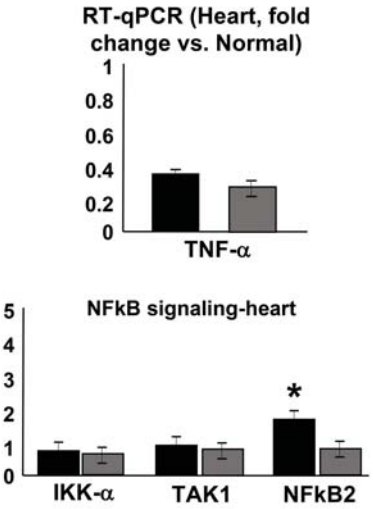
Background and Aims : Inflammation contributes to progressive renal dysfunction and increases cardiovascular mortality of patients with chronic kidney disease (CKD). The association of CKD and heart failure with preserved ejection fraction (HFpEF) is observed in up to 50%, suggesting the possibility of a shared pathophysiology. CKD and HFpEF are commonly associated with inflammation. Using a novel swine model of CKD and HFpEF, we propose that a renal-cardio inflammatory axis drives diastolic dysfunction and HFpEF in CKD and that targeting renal inflammation will improve cardiac health and reduce cardiovascular risk.

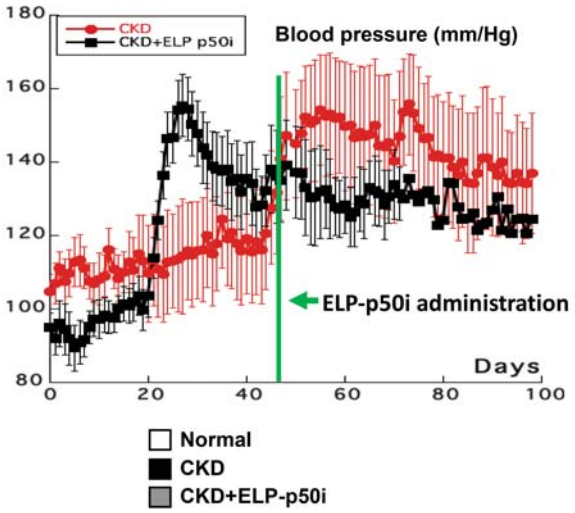
Methods : We developed a biopolymer-fused peptide of nuclear-factor kappa (NFk)B (ELP-p50i) that we show it blocks its activity *in vitro* and *in vivo*. NFkB is a key pro-

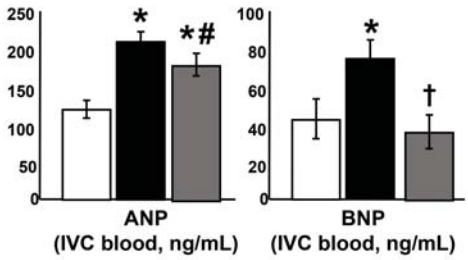




Echocardiographic parameters	Normal	CKD	CKD+ELP-p50i
Morphology			
LV wall thickness (cm)	*0.7*	*1.45*	*0.76*
LV dimension (diastole, cm)	6.8	5.41	5.33
LV dimension (systole, cm)	4.03	3.6	2.76
Left atrial diameter (cm)	*4.8*	*6.6*	*4.6*
Functional			
Ejection fraction (EF, %)	>50%	>50%	>50%
E/A	*1.42*	*1*	*1.13*
E/e'	6.7	7.7	7.78







* p<0.05 vs. normal
† p<0.05 vs CKD; #p=0.07 vs. CKD

Figure

inflammatory transcription factor that is upregulated in CKD. To test our hypothesis, we induced CKD in 10 pigs via bilateral renovascular disease and dyslipidemia. Pigs were observed for 6 weeks, renal hemodynamics quantified (multi-detector CT), then randomized to single intra-renal ELP-p50i or placebo (n=5 each), and studies repeated 8 weeks later accompanied by echocardiographic assessment. Blood pressure was continuously measured (telemetry). Blood was collected to measure circulating TNF-α and biomarkers of HF (ANP, BNP). Furthermore, kidneys and hearts were used to quantify expression of factors involved in NFkB signaling.

Results : CKD led to a significant loss of renal function, accompanied by left ventricular hypertrophy and diastolic dysfunction with pEF, increased renal mRNA expression of TNF-α and canonical and non-canonical mediators of NFkB signaling, and elevated systemic TNF-α, ANP, and BNP, indicating renal and cardiac dysfunction. Most of these changes were improved after intra-renal ELP-p50i, although cardiac inflammatory signaling was unchanged (Figure) suggesting the kidney as a source of inflammation that can target the heart in CKD.

Conclusion : We show that a renal anti-inflammatory strategy via targeted inhibition of renal NFkB improves renal and cardiac function in CKD, suggesting an inflammatory renal-cardio axis. The translational pathological features of CKD and HFpEF combined with the predictive power of the model may contribute to advance the field towards new treatments targeting renal inflammation to reduce cardiovascular risk in CKD.

MO063

CHRONIC INTERSTITIAL NEPHRITIS IN AGRICULTURAL COMMUNITIES IS A TOXIN-INDUCED PROXIMAL TUBULAR NEPHROPATHY

Benjamin Vervaet[1], Cynthia Nast[2], Channa Jayasumana[3], Gerd Schreurs[1], Frank Roels[4], Chula Herath[5], Nika Kojc[6], Vahid Samaee[7], Sonali Rodrigo[5], Swarnalata Gowrishankar[8], Christiane Mousson[9], Rajeewa Dassanayake[10], Carlos Orantes[11], Vincent Vuiblet[12], Claire Rigothier[13], Patrick D'Haese[1], Marc De Broe[1]

[1]University of Antwerp, Laboratory of Pathophysiology, Antwerp, Belgium, [2]Cedars-Sinai Medical Center, Los Angeles, United States of America, [3]Rajatrata University of Sri Lanka, Faculty of Medicine, Anuradhapura, Sri Lanka, [4]Ghent University, Department of Pathology, Ghent, Belgium, [5]Sri Jayewardenepura General Hospital, Department of Nephrology, Colombo, Sri Lanka, [6]University of Ljubljana, Institute of Pathology, Faculty of Medicine, Ljubljana, Slovenia, [7]University of Antwerp, Electron Microscopy for Materials Science (EMAT), Antwerp, Belgium, [8]Apollo Hospitals, Department of Pathology, Hyderabad, India, [9]Centre Hospitalier Universitaire de Dijon, Department of Nephrology, Dijon, France, [10]General Hospital, Renal Unit, Polonnaruwa, Belgium, [11]Ministry of Health of El Salvador, National Institute of Health, San Salvador, El Salvador, [12]Centre Hospitalier Universitaire de Reims, Departments of Nephrology and Renal Pathology, Reims, France and [13]Centre Hospitalier Universitaire de Bordeaux, Service Néphrologie, Transplantation, Dialyse et Aphérèses, Bordeaux, France

Background and Aims: 30 years after the detection of CINAC, there is no consensus on its etiology. Heat stress/dehydration and toxic exposure are the two most likely etiologies. There are no diagnostic criteria that can directly identify CINAC patients.

Method: Renal biopsies (RB) (18 Sri Lanka, 10 El Salvador, 1 India, 3 France) of patients with CINAC (CKD2-3) were examined by light (LM) and electron microscopy (EM) in comparison to RB of normal kidneys at implantation and 6 and 12 months of calcineurin inhibitor (CNI) therapy, transplant patients on CNI with indication biopsies (n=24), proteinuric nephropathies (n=15), light chain disease (n=4), cases on nephrotoxic drugs (lomustine, clomiphene, lithium, tenofovir, cisplatinum) and CKD of various causes (n=20). A rat study was conducted comparing histopathology of heat stress/dehydration with cyclosporine nephrotoxicity.

Results: In addition to previously described histopathological changes, there was a unique constellation of proximal tubular cell (PTC) findings: cellular/tubular atrophy, cell fragment shedding, weak to non-proliferative capacity of the PTC and dysmorphic lysosomes increased in size and number with a light-medium electron-dense matrix containing dispersed dark electron-dense non-membrane bound "aggregates". Identical renal lesions were observed in 55-80% of renal transplant protocol biopsies taken after 6 and 12 months of calcineurin inhibitor (CNI) therapy and in indication biopsies, in implantation biopsies the prevalence was 6%. Several cases of nephrotoxic drugs (lomustine, clomiphene, lithium) and a subset of patients with light chain disease, all conditions that can be linked to CNI, presented the same lesion. Control RBs (n=66) of normal kidney, toxic nephropathies (tenofovir, cisplatinum), and overt proteinuric patients of different etiology to some extent could demonstrate the tubular cell changes observed by LM, but not or very rarely those that were observed by EM. Rats treated with cyclosporine for 4 weeks developed similar PTC lysosomal alterations, absent in a dehydration group.

Conclusion: A sensitive constellation of renal PTC lesions was detected associated with CINAC and CNI nephrotoxicity in several countries, suggesting a common new paradigm where CINAC patients are experiencing a tubulotoxic mechanism similar to CNI nephrotoxicity, the latter also being known as a direct or suggested indirect effect of pesticides.

MO064

TISSUE-RESIDENT B CELLS DETERMINE SUSCEPTIBILITY TO URINARY TRACT INFECTION BY ORCHESTRATING MACROPHAGE POLARISATION

Ondrej Suchanek[1,2,3,4], Sathi Wijeyesinghe[5], John Ferdinand[1,2], Zewen K. Tuong[1,2], Anita Chandra[6], Simon Clare[4], Rachael Bashford-Rogers[7], Trevor Lawley[4], Klaus Okkenhaug[6], David Masopust[5], Menna Clatworthy[1,2,3]

[1]MRC Laboratory of Molecular Biology, Molecular Immunity Unit, Cambridge, United Kingdom, [2]University of Cambridge, Department of Medicine, Cambridge, United Kingdom, [3]Addenbrooke's Hospital, Department of Nephrology, Cambridge, United Kingdom, [4]Wellcome Sanger Institute, Hinxton, United Kingdom, [5]University of Minnesota, Department of Microbiology and Immunology, Centre for Immunology, Minneapolis, United States of America, [6]University of Cambridge, Department Of Pathology, Cambridge, United Kingdom and [7]Wellcome Centre for Human Genetics, Oxford, United Kingdom

Background: Urinary tract infection (UTI) is an important clinical problem. More than half of women and 1 in 10 men will be affected during their lifetime. Many of these affect the lower urinary tract but recurrent pyelonephritis can lead to scarring and chronic kidney disease. There is an increasing appreciation that tissue-resident immune cells, such as macrophages, play an important role in defence against infection, but only little is known about B lymphocytes in this context. Here we sought to address the question of whether B cells reside in the kidney and bladder in homeostasis and to determine their phenotype and contribution to local organ immunity.

Methods and Results: Using intravenous labelling and parabiosis, we identified a population of bona-fide self-renewing, tissue-resident B cells that included non-naïve and innate-like CD5+ B-1 cells, in murine kidneys and urinary bladder (but also in liver and lung). The size and phenotype of this B cell subset was influenced by genetic background, age, and microbiome, with an expanded population evident after co-housing with pet-store mice. Although kidney B cells had less diverse *Igh* repertoire compared to blood, their seeding was largely independent of their B-cell receptor specificity. In human kidneys we found a similar enrichment for non-naïve B cells compared to blood and spleen.

Using two strains of genetically modified mice with higher ($PI3K\delta^{E1020K\text{-}B}$) or lower (μMT-) numbers of tissue-resident B cells, we tested the function of these cells during UTI. Surprisingly, the number of tissue-resident B cells inversely correlated with bacterial clearance. We found that these B cells were spatially co-localised with kidney macrophages and skewed their polarization towards an anti-inflammatory M2 phenotype, leading to reduced anti-microbial responses. This effect was, at least in part, driven via IL-10.

Conclusion: In conclusion, our data identify a critical role for tissue-resident B cells in modulating local immunity in the urinary tract, determining the inflammatory 'set-point' of resident and recruited myeloid cells, with important clinical implications for the use of B-cell depleting therapies and conditions such as infection, transplant rejection, fibrosis or autoimmunity.

Graphical Abstract:

EXPERIMENTAL AKI

MO065

TUBULAR EPITHELIAL CELL POLYPLOIDIZATION IS REQUIRED TO SURVIVE AKI BUT PROMOTES CKD DEVELOPMENT

Letizia De Chiara[1], Elena Lazzeri[1], Maria Lucia Angelotti[1], Carolina Conte[1], Anna Julie Peired[1], Giulia Antonelli[1], Maria Elena Melica[1], Benedetta Mazzinghi[2], Laura Lasagni[1], Paola Romagnani[1,2]

[1]University of Florence, Department of Experimental and Clinical Biomedical Sciences "Mario Serio", Firenze, Italy and [2]Meyer Children's University Hospital, Nephrology and Dialysis Unit, Firenze, Italy

Background and Aims: Acute kidney injury (AKI) is a global health concern. If not lethal in the acute phase, AKI is considered reversible based on the capacity of surviving tubular cells (TECs) to re-enter cell cycle. However, even mild AKI episodes carry a substantial risk of developing chronic kidney disease (CKD). The pathophysiological basis for this phenomenon remains unclear. Recently, we demonstrated that tubular epithelial cells (TECs) can undergo endoreplication-mediated hypertrophy after AKI. Endoreplications are incomplete cell cycles that lead to the formation of polyploid cells. As polyploid cells can provide increased cell function without restoring tissue integrity, we hypothesized that this mechanism is essential to survive AKI but it can be potentially maladaptive.

Method: To address this hypothesis, we employed a series of *in vitro* and *in vivo* transgenic models based on the Fluorescence Ubiquitin Cell Cycle Indicator (FUCCI) technology to monitor cell cycle phasing in combination with YAP1 overexpression or downregulation. In the *in vivo* models, YAP1 overexpressing mice and YAP1 knock-out mice were subjected to unilateral ischemia reperfusion injury (IRI) or glycerol-induced rhabdomyolysis to induce AKI. Polyploid cells have been then characterized by microarray analysis, cell sorting, super-resolution STED microscopy and transmission electron microscopy.

Results: *In vitro*, human renal tubular cells undergo polyploidization. The fraction of polyploid cells significantly decreases when YAP1 nuclear translocation is blocked, suggesting a possible involvement of YAP1 in regulating TEC polyploidization. After AKI in mice, the inhibition of YAP1 significantly reduces the number of polyploid cells and worsens kidney function resulting in a dramatic decrease of mouse survival. In contrast, YAP1 overexpression leads to an increase in the number of polyploid cells up to 20% of all TECs, further confirming the role of YAP1 in controlling TEC polyploidization. In YAP1 overexpressing mice, electron microscopy and STED analysis revealed the presence of both mononucleated and binucleated polyploid cells. Strikingly, these mice appear to be more prone to develop tubulointerstitial fibrosis acquiring a marked senescent phenotype along with significant decline in renal function thus suggesting an association between polyploidization and CKD development. Indeed, isolation of polyploid cells proved that these cells actively transcribe and secrete pro-fibrotic and senescent factors confirming their role in CKD progression.

Conclusion: These data suggest that: 1) polyploidization after AKI is required to preserve renal function in the acute phase of damage and it is essential for survival 2) polyploid cells are pro-fibrotic and senescent leading in the long run to the progression of AKI to CKD.

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MO066 GASDERMIND MUTATION IS PROTECTIVE AGAINST RENAL ISCHEMIA REPERFUSION INJURY

Natasha Rogers[1,2], Jennifer Li[1], Stephen Alexander[3,4]

[1]The Westmead Institute for Medical Research, Westmead, Australia, [2]Westmead Hospital, Renal and Transplant Unit, Westmead, Australia, [3]The Children's Hospital at Westmead, Pediatrics and Child Health, Westmead, Australia and [4]Kids Research Institute, Westmead, Australia

Background and Aims: Ischemia reperfusion injury (IRI) is an important contributor to acute kidney injury (AKI) and manifests as delayed graft function following kidney transplantation. Limiting the damage of IRI has implications on graft outcomes and has driven further exploration of the underlying pathophysiology. We hypothesize that pyroptosis, a pro-inflammatory form of cell death, has an important role in IRI and AKI. The pyroptosis pathway converges to the cleavage and release of N-terminal of the Gasdermin-D protein, leading to pore formation in the cell membrane and cell death. We examined the effects of Gasdermin-D mutation on inflammation in acute kidney injury.

Method: Male C57BL/6 mice were exposed to ethyl-*N*-nitrosourea mutagenesis, leading to a loss-of-function, single nucleotide polymorphism (isoleucine to asparagine mutation, I105N) in the Gasdermin-D gene. Age- and gender-matched littermate control wild-type, heterozygous and homozygous Gasdermin-D^{I105N} mice were subjected to bilateral renal IRI (36°C, 22mins) and sacrificed 24-hours post-reperfusion for analysis of renal function, histology and biomolecular phenotyping. To delineate if the GasderminD mutation in renal parenchymal or hematopoietic cells were key drivers of IRI, we generated chimeric mice with whole body irradiation and infusion of syngeneic donor bone marrow. Following 8 weeks of engraftment, bilateral renal IRI was performed with analysis at 24 h reperfusion.

Results: Homozygote and heterozygote Gasdermin-D^{I105N} mice were protected from renal IRI in a gene dose-dependent manner when compared to wild-type, with lower mean serum creatinine (15.7, 48.1 and 85.5μmol/L respectively, $p<0.001$), less histological tubular injury and cell death (1.8, 3.6 and 5.1 TUNEL+ cells/hpf, $p<0.01$) and significantly decreased expression of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, RANTES). Homozygote GasderminD^{I105N} chimeric mice (reconstituted with wild-type donor bone marrow) were more susceptible to IRI, and serum creatinine was similar to that of wild-type chimeric control mice, indicating that hematopoietic cells rather than parenchymal cells, are likely predominant drivers of injury. Similarly, adoptive transfer of CpG-activated CD11c+ dendritic cells into homozygous Gasdermin-D^{I105N} mice augmented renal injury compared to GpC-treated cells.

Conclusion: GasderminD^{I105N} mice were protected from IRI and demonstrates the importance of the pyroptosis pathway on acute kidney injury. Manipulation of GasderminD is potentially an attractive target to mitigate inflammation and cellular death following injury.

MO067

PHASE-SPECIFIC IRF4 AND IRF8 REGULATION/ EXPRESSION OF MONONUCLEAR PHAGOCYTES DURING ISCHEMIC ACUTE KIDNEY INJURY/DISEASE

Na Li[1,2], Stefanie Steiger[2], Chenyu Li[2], Zhihua Zheng[1], Hans-Joachim Anders[2], Julia Lichtnekert[2]

[1]The Seventh Affiliated Hospital, Sun Yat-sen University,, Division of Nephrology, shenzhen, P.R. China and [2]Medical Clinic and Polyclinic IV, University Hospital Munich, Ludwig Maximilian University of Munich, Division of Nephrology, munich, Germany

Background: Ischemic acute tubular necrosis is a common cause of acute kidney disease (AKD) and subsequent chronic kidney disease (CKD). The different phases of AKD involve a greater functional diversity of mononuclear phagocytes (MPCs) including resident and infiltrating macrophages and conventional dendritic cells (cDCs). In addition, hematopoietic transcription factors such as IRF4 and IRF8 play an important role in immune cell maturation and polarization that contribute to tissue inflammation and remodeling. However, their role on MPCs polarization and function during AKD are not well understood. Hence, we hypothesized that the dynamically altered MPC subsets contribute to the progression of AKD, accompanied with varied expression of IRF4 and IRF8.

Methods: AKD was induced by transient unilateral renal pedicle clamping in C57BL/6N mice. After 1, 3, and 7 days kidneys, renal lymph nodes and spleens were collected. Flow cytometry was performed to identify different MPC subsets. GFR was measured and mRNA expression of inflammatory, anti-inflammatory transcription factors determined via RT-PCR. For *in vitro* experiments, bone marrow-derived macrophages and cDCs, tubular epithelial cells (TECs), renal and splenic resident $CD11b^+$ immune cells isolated from naïve mice were stimulated with LPS or cultured under hypoxic condition for 3 and 10 hours. Bone marrow-derived monocytes were differentiated into macrophages or cDCs, and stimulated with LPS for 3 and 10 hours. After stimulation, cells were harvested for mRNA analysis via RT-PCR.

Results: We identified four renal phenotypically distinct MPC subsets with diverse expression patterns of CD11b/CD11c during the different phases of post-ischemic AKD. During the early (day 1) and late injury phase (day 3), the number of infiltrating $CD11b^{hi}CD11c^{low}$ R2 and $CD11b^{hi}CD11c^{hi}$ R3 macrophage-like subsets increased, along with a significant GFR decline compared with sham-operated mice (see Figure). During the repair phase (day 7), the number of $CD11b^{low}CD11c^{low}$ R1 (resident macrophage-like MPCs) and $CD11b^{low}CD11c^{hi}$ R4 (infiltrating cDC-like MPCs) subsets significantly increased (see Figure). Both resident macrophage-like (R1) and cDC-like (R4) MPCs significantly upregulated the expression of IRF8, whereas cDCs-like (R4) MPCs were also positive for IRF4 during the repair phase. This pattern of MPCs was consistent in spleen and renal lymph node. *In vitro* stimulation of renal and splenic $CD11b^+$ cells from naïve mice with LPS or under hypoxic condition induced a significant upregulation of IRF4 and IRF8 compared to untreated cells. This was also observed in bone marrow-derived macrophages and cDCs but not in TECs.

Conclusions: Our data indicate that infiltrating macrophage-like and cDC-like MPCs appear in high numbers during the early and late injury phase. Furthermore, both resident macrophage-like and cDC-like MPCs are predominately present during the late injury and recovery phase in AKD with altered IRF4 and IRF8 expression pattern. Further studies are needed to unravel a potential role of IRF4 and IRF8 during the progression of AKD and CKD by e.g. using fate mapping approaches.

MO068

A KIDNEY-ON-THE-CHIP APPROACH USING PRIMARY HUMAN TUBULAR CELLS IN A 3D CO-CULTURE SYSTEM

Gregor J. Wilken[1], Julian Aurelio Marschner[1], Paola Romagnani[2], Hans-Joachim Anders[1]

[1]Division of Nephrology,, Department of Medicine 4, University Hospital of LMU Munich, Germany, München, Germany and [2]Excellence Centre for Research, Transfer and High Education for the Development of DE NOVO Therapies (DENOTHE), Department of Clinical and Experimental Biomedical Sciences, University of Florence, Florence, Italy

Background and Aims: Conventional 2D mono-culture i*n vitro* models using immortalized cell lines are still widely used in experimental nephrology, although their value is limited by poor translatability and predictive value for the *in vivo* or even human situation. The implementation of more sophisticated *in vitro* assays as routine cell culture systems is often limited by complex protocols and long lasting procedures. We aimed to establish and validate a relatively easy-to-use but yet (patho-) physiologically relevant cell culture assay that mimics key aspects of the *in vivo* situation of renal tubules, including a leak-thight epithelium with a luminal and baso-lateral side, interstitial matrix, a peri-tubular capillary and circulating blood cells inside its lumen.

Method: We utilized the 3-lane OrganoPlate® system (Mimetas, Leiden, Netherlands) as a scaffold. After infusing a collagen I matrix in the middle channel (C2), primary human renal progenitor cells are seeded into the upper channel (C1), adhering to the C2-matrix. The plate is put on a perfusion rocker (Mimetas), that facilitates continuous gravity-triggered bi-directional perfusion of C1. Within 48h the cells form a leak-tight tubular structure with a continuous lumen. Next, human endothelial cells are seeded into the bottom channel (C3), which adhered to the opposite site of the C2-matrix and – upon continuous perfusion – formed a vessel-like structure with a continuous lumen, as well. Finally, primary human white blood cells were isolated and seeded into C3 (see figure).

Results: Establishing the whole tubule-on-the-chip as described above takes on average three days. We investigated its operational life span by monitoring the barrier integrity of the tubular structure in C1 using a fluorescence-labeled dextran (150 kDa). Over a course of 5 days the tubular integrity did not decline, suggesting that the co-culture system remains stable and functional for at least 5 days. In accordance with other studies, the primary human tubular cells constituting the 3D tubule-on-the-chip expressed higher levels of functionally relevant proteins, e..g the tight-junction protein ZO-1 and the sodium-potassium-pump Na-K-ATPase, compared to standard 2D settings without perfusion. This emphasizes, that even primary cells show a physiologically reduced phenotype in standard 2D settings, which possibly impedes the identification and representative quantification of physiologically and hence also patho-physiologically relevant mechanisms *in vitro*. To study the interaction of cells in the tubule-on-the-chip, we investigated the recruitment of immune cells from C3 (vessel) across C2 (interstitium) to C1 (renal tubule), which - *in vivo* - represents a detrimental mechanism of action in intrarenal forms of AKI. Under baseline conditions the immune cells inserted into C3 did not leave their compartment. Upon damaging the tubular cells in C1 with extracellular histones, neutrophils and monocytes left C3 (extravasation), migrated through C2 and could be found in close contact with epithelial cells of C1. This serves as a proof of principle, that the tubule-on-the-chip is applicable to study complex cell-cell and cell-substrate interactions, such as chemokine-mediate immune cell homing. Measuring lactate dehydrogenase release for a number of known nephrotoxic agents revealed, that tubular cells forming a 3D-structure while kept under perfusion show significantly different responses to the same dose compared to standard 2D conditions, suggesting that dose-response studies using target cells out of their tissues context can be misleading when extrapolating results from *in vitro* to *in vivo*.

Conclusion: The results of this study suggest, that sophisticated 3D co-culture models of a renal tubule including an interstitial compartment, a peri-tubluar capillary and circulating immune cells are feasible and potentially suited to allow for in depth mechanistic studies *in vitro*.

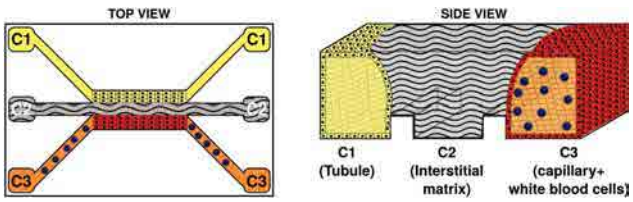


Figure:

MO069

HIF-1A C-TERMINAL TRANSCRIPTIONAL ACTIVATION DOMAIN MEDIATED KLF5 SIGNALING DRIVES AKI TO CKD PROGRESSION

Zuolin Li[1], Jia-ling Ji[2], Linli Lv[1], Yan Yang[1], Tao-tao Tang[1], Bin Wang[1], Bicheng Liu[1]

[1]Institute of Nephrology, Southeast University School of Medicine, Department of Nephrology, Zhong Da Hospital, Nanjing, P.R. China and [2]2nd affiliated hospital of Nanjing Medical University, Department of pediatric nephrology, Nanjing, P.R. China

Background and Aims: Acute kidney injury (AKI) is increasingly recognized as a major risk factor for progression to CKD. However, the mechanisms governing AKI to CKD progression are poorly understood. Hypoxia is a key player in the pathophysiology of the AKI to CKD transition. Thus, we aimed to investigate the exact mechanisms of AKI to CKD progression mediated by hypoxia.

Method: Mild ischemic injury and severe ischemic injury (AKI-to-CKD transition) were established by clamping renal pedicle for 30 and 40 minutes, respectively. Meanwhile, the mice model of AKI-to-CKD transition was treated with HIF-1α inhibitor, PX-478. In vitro, PHD inhibition and combined PHD with FIH inhibition mimic the HIF-1α activation caused by mild or severe hypoxia, respectively. Besides the human proximal tubular epithelial cell line HK-2, tubular cells were isolated from mice for primary culture. KLF5 knockdown, FIH and HIF-1α C-terminal transcriptional activation domain (C-TAD) overexpression in tubular cells were achieved by Lentiviral transfection. Immunocoprecipitation was used to explore the relationship between the HIF-1α and FIH-1. Luciferase reporter assay was used to investigate whether KLF5 was regulated transcriptionally by HIF-1α C-TAD. To explore the roles of FIH-1 and HIF-1α C-TAD in vivo, FIH-1 and HIF-1α C-TAD overexpression (Lentivirus-mediated) was given after severe ischemic injury or mild ischemic injury via tail vein injection, respectively.

Results: AKI to CKD progression was highly associated with the time-course expression of tubular HIF-1α in severe ischemia/reperfusion injury. Interestingly, ameliorated AKI-to-CKD transition was observed by treating PX-478, which destabilized HIF-1α. In vitro, fibrogenesis could be induced by combined PHD with FIH inhibitor treatment in TEC. More interestingly, alleviated fibrogenesis could be achieved by knockdown of KLF5 and overexpression of FIH, respectively, while HIF-1α C-TAD overexpression promoted fibrogenesis in tubular cells. Immunocoprecipitation results indicated that HIF-1α and FIH-1 are interactive. Furthermore, we demonstrated that KLF5 could be regulated transcriptionally by HIF-1α C-TAD by luciferase reporter assay. In vivo, AKI to CKD progression was ameliorated significantly when mice model of AKI-to-CKD transition intervened with FIH-1 overexpression (Lentivirus-mediated). However, treatment of HIF-1α C-TAD (Lentivirus-mediated) in mild ischemic injury model could promote progression of CKD significantly.

Conclusion: FIH-1 mediated HIF-1α C-TAD activation was the key mechanism of AKI to CKD transition by transcriptionally regulating the KLF5 pathway in tubules. Blockade of FIH-1 mediated HIF-1α C-TAD in tubules may serve as a novel therapeutic approach to ameliorate AKI to CKD progression.

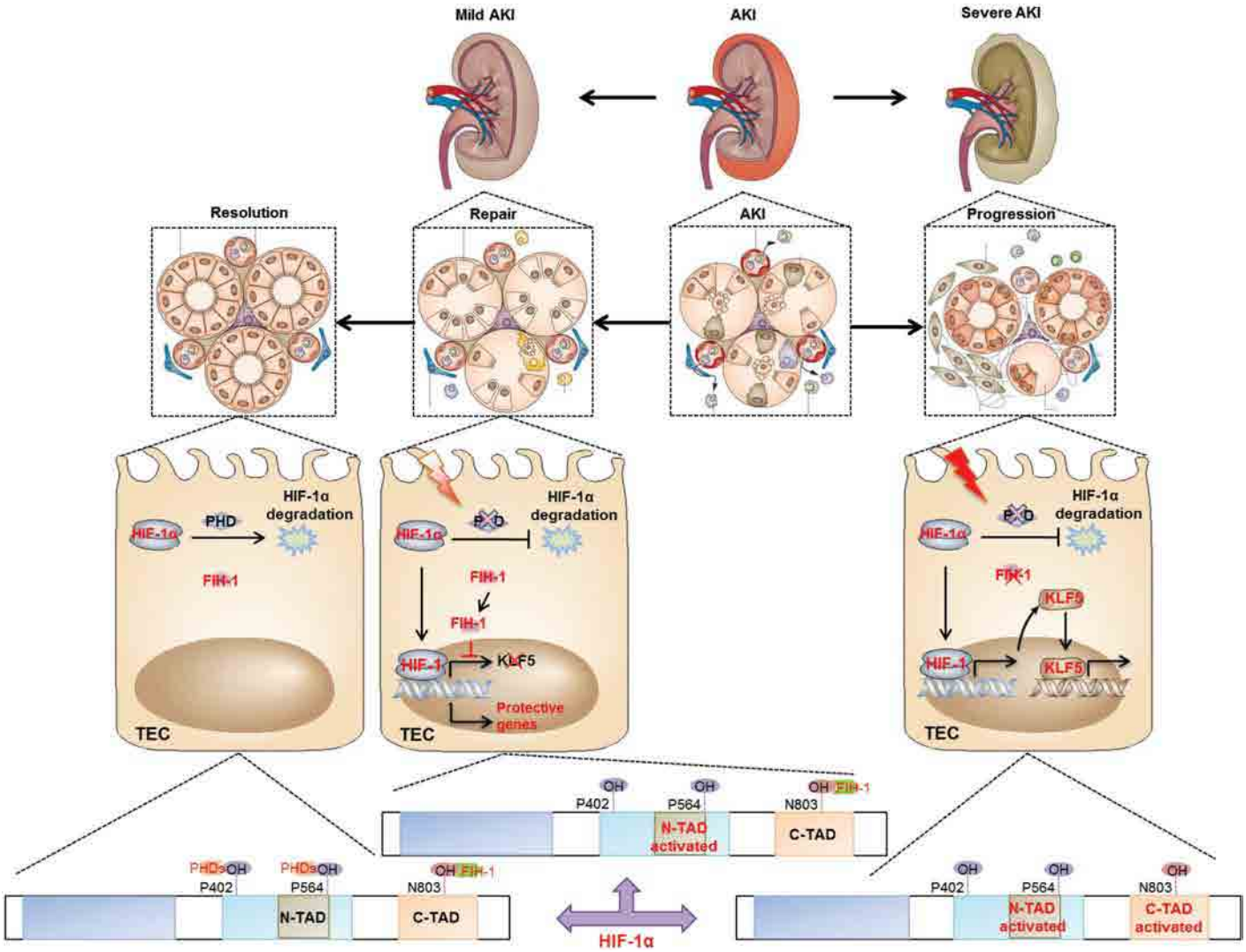


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Nephrology Dialysis Transplantation 35 (Supplement 3): iii000–iii000, 2020

CKD EPIDEMIOLOGY

MO070

APPROPRIATE INTERVAL BETWEEN TWO EGFR MEASUREMENTS FOR THE EVALUATION OF THE ASSOCIATION OF EGFR SLOPE WITH INCIDENCE OF RENAL EVENTS.

Maiko Kokubu[1], MASARU MATSUI[1], Takayuki Uemura[1], Kazuhiko Tsuruya[2]

[1]*Nara Prefecture General Medical Center, Department of Nephrology, NARA, Japan and* [2]*Nara Medical University, Division of Nephrology, NARA, Japan*

Background and Aims: In recent years, growing evidence has shown the prognostic utility of eGFR slope for the risk of end-staging renal disease (ESRD). Previous observational studies have assessed the association between renal events and eGFR slopes estimated by two measurements of eGFR but had great differences in the interval between two eGFR measurements. In this study, we thus aimed to determine the appropriate interval between two eGFR measurements to evaluate the association of eGFR slope with incidence of renal events.

Method: This is a retrospective cohort study in 203 chronic kidney disease (CKD) patients who visited Nara Prefecture General Medical Center, Japan between 1 January 2013 and 31 December 2016 and in whom two or more than two measurements of eGFR levels were confirmed in medical records. eGFR slopes were estimated by using two measurements of eGFR at baseline and 0.5, 1, 1.5, 2, or 3 years. We excluded patients with acute kidney injury, urologic malignancies, nephrotic syndrome with steroid treatment or collagen diseases. Outcome was renal events defined as a composite of ESRD and eGFR decline of $>$ 30%. C statistics were used to evaluate the association between eGFR slope and incidence of renal events.

Results: The median (interquartile range) age of study participants was 67 (56-77) years and 71 (37%) were male. The median (interquartile range) levels of baseline eGFR were 34 (21-48) mL/min/1.73m2 and diabetes was present in 80 (39%) participants. During the median follow-up period of 38 months, renal events occurred in 52 participants. Medial levels of eGFR slopes0.5, 1, 1,5, 2 and 3yr were -7.8, -3.6, -2.9, -0.9, -1.5 mL/min/1.73m2, respectively. C-statistics of eGFR slopes0.5, 1, 1,5, 2 and 3yr for renal events were 0.622, 0.691, 0.797, 0.858, 0.806, respectively (shown in Figure 1), and that of eGFR slope1.5yr was significantly higher than that of eGFR slope0.5yr and eGFR slope1yr ($p<0.001$ and $p=0.001$, respectively). In stratified analysis, eGFR slope1.5yr had higher prognostic ability of renal events in patients with versus without diabetes, advanced CKD and proteinuria. C-statistics of renal events when considering baseline eGFR alone was 0.853 but combination use of baseline eGFR and eGFR slope1.5yr significantly increased c-statistics, to 0.913 ($p=0.01$).

Conclusion: eGFR slope for high prognostic ability of renal events may be needed to be calculated by at least 1.5-year interval between two eGFR measurements.

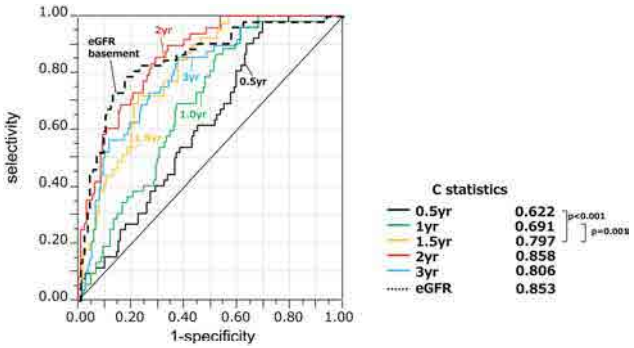


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MO071

EXTERNAL VALIDATION OF ISCHEMIC STROKE RISK PREDICTION MODELS IN ATRIAL FIBRILLATION PATIENTS WITH CHRONIC KIDNEY DISEASE: THE STOCKHOLM CREATININE MEASUREMENTS (SCREAM) PROJECT

Y De Jong[1,2], Edouard Fu[1], Juan Jesus Carrero[3], Friedo W. Dekker[1], Merel Van Diepen[1], Gurbey Ocak[1,4]

[1]Leiden University Medical Center (LUMC), Clinical Epidemiology, Leiden, Netherlands, [2]Leiden University Medical Center (LUMC), Internal Medicine, Leiden, Netherlands, [3]Karolinska Institute, Medical Epidemiology and Biostatistics (MEB), Sweden and [4]St. Antonius Hospital, Internal Medicine, Nieuwegein, Netherlands

Background and Aims: Ischemic stroke (IS) is a leading cause of morbidity and mortality world-wide.

Patients with chronic kidney disease (CKD) have an increased ischemic stroke risk. Stroke risk scores, including the CHA_2DS_2-VASc, $CHADS_2$, ATRIA, GARFIELD, AFI and the modified-$CHADS_2$, have been developed to identify patients with an increased stroke risk in patients with atrial fibrillation (AF) allowing for personalization of anticoagulant prescription. In the original articles, these risk scores had reasonable predictive abilities. However, the predictive performances of these stroke risk in patients with CKD is unclear. Therefore, the aim of this study was to validate existing stroke risk scores in patients with AF and different stages of CKD.

Method: The study included subjects with newly-diagnosed AF from the SCREAM (Stockholm CREAtinine Measurements) database, a healthcare utilization cohort of residents from Stockholm, Sweden, during 2007-2011. The performance of prediction models were compared across eGFR strata: normal (KDIGO classification G1-2; eGFR >60) mild (G3; eGFR 30-60) and advanced (G4-5; eGFR <30, not on dialysis) CKD. Model discrimination was evaluated through c-statistics, and calibration by plotting predicted probabilities and observed frequencies for IS.

Results: A total of 36.004 subjects with AF and known eGFR were identified. During a median follow up of 1.91 years, 2572 (7.1%) suffered an ischemic stroke. The incidence rate of stroke increased across lower eGFR strata: from 6.3% in patients with eGFR>60 to 10.4% and 7.3% in patients with eGFR 30-60 and <30. Predictive performance of the stroke risk models was moderate-to-good in patients normal eGFR, but worsened with lower eGFR strata: C-statistics ranged from 0.68 to 0.77 for patients with normal (G1-2) eGFR, 0.58 to 0.72 for mild (G3) CKD, and 0.53 to 0.70 for patients with advanced (G4-5) CKD (Table). The modified-$CHADS_2$ showed the best predictive performance in all CKD groups. Calibration plots (Figure 1) showed that the predicted risk was higher than the observed risk for almost all stroke risk models, independent of CKD status. The modified-$CHADS_2$ showed slightly higher predicted risks than the observed risks (Figure) and has the most accurate ability (almost equal observed and predicted risks) in CKD patients.

Conclusion: The predictive performance of models for IS in a large cohort of AF patients decreased with decreasing kidney function. Predictions became less accurate in the clinically more relevant final stages of CKD. Therefore, most commonly used stroke risk models may not be useful for guiding individual decision-making in patients with CKD. The modified-$CHADS_2$ score showed good and consistent discrimination and calibration, in AF patients normal eGFR, as well as in mild and advanced CKD, and would therefore be the preferred option for use in clinical practice in AF patients with CKD.

Table: Discrimination of included models C-statistic with 95% CI, stratified per KDIGO-CKD stage.

CKD stage	Normal (G1-2)	Mild CKD (G3)	Advanced CKD (G4-5)
Total / strokes (%)	26 249/1 625 (6.3)	8.625/866 (10.4)	1.130/82 (7.3)
CHA_2DS_2-VASc	0.68 (0.67-0.70)	0.58 (0.55-0.60)	0.55 (0.48-0.62)
$CHADS_2$	0.69 (0.68-0.70)	0.61 (0.59-0.63)	0.58 (0.52-0.64)
ATRIA	0.73 (0.72-0.74)	0.65 (0.63-0.67)	0.61 (0.55-0.68)
Garfield	0.75 (0.73-0.76)	0.68 (0.66-0.70)	0.68 (0.62-0.75)
AFI	0.67 (0.65-0.68)	0.58 (0.56-0.59)	0.53 (0.48-0.58)
Modified-$CHADS_2$	0.77 (0.75-0.78)	0.72 (0.70-0.73)	0.70 (0.64-0.76)

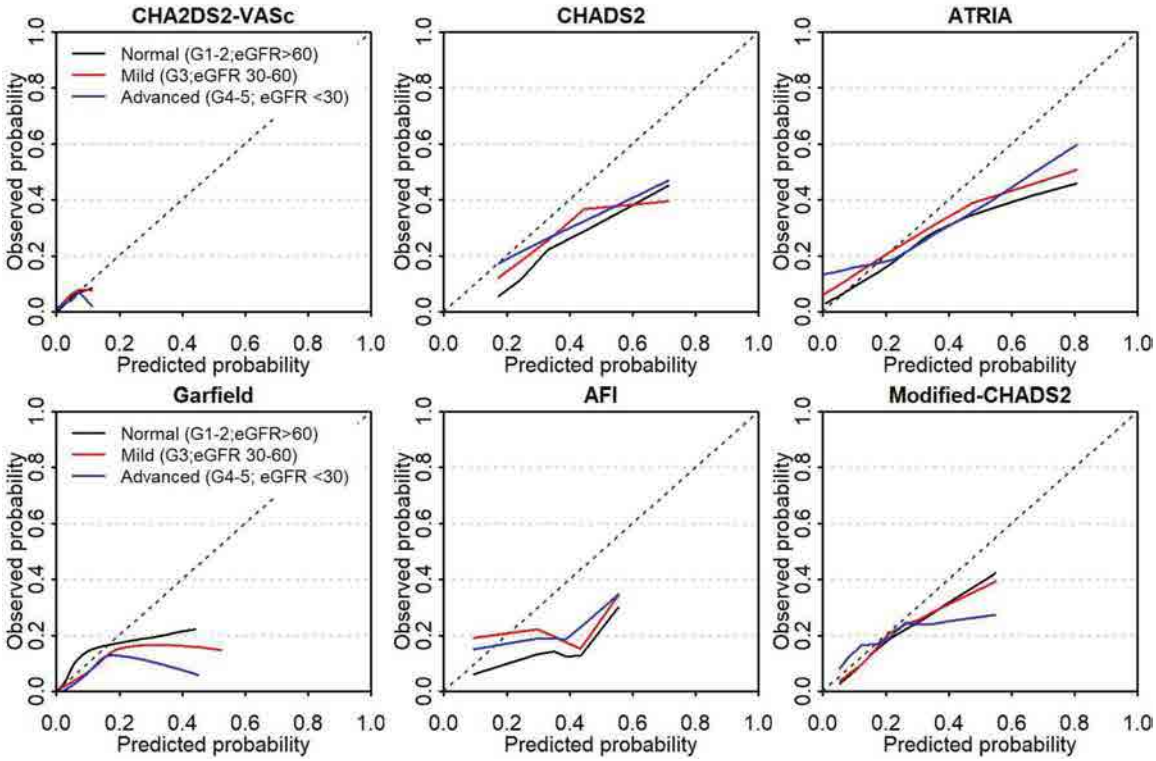


Figure 1: calibration plots of included prediction models for ischemic stroke.

MO072

LONGITUDINAL SERUM BICARBONATE MEASUREMENTS AND RISK OF CHRONIC KIDNEY DISEASE PROGRESSION AND MORTALITY: INSIGHTS FROM THE CKD-REIN COHORT

Mathilde Prezelin-Reydit[1,2], Christian Combe[3], Jerome Harambat[4,5], Ziad Massy[6], Marie Metzger[7], Céline Lange[7], Oriane Lambert[7], Benedicte Stengel[7], Karen Leffondré[2]

[1]Aurad Aquitaine, Gradignan, France, [2]INSERM U1219-Bordeaux Population Health, Biostatistic team, Bordeaux, France, [3]Hospital Center University De Bordeaux, Nephrology, Transplantation, Dialysis, Bordeaux, France, [4]Hospital Center University De Bordeaux, Pediatry and Nephrology, Bordeaux, France, [5]INSERM U1219-Bordeaux Population Health, LEHA team, Bordeaux, France, [6]Ambroise Paré Hospital (AP-HP), Boulogne-Billancourt, France and [7]CESP, University of Paris-Saclay, Inserm UMRS 1018, Villejuif, France

Background and Aims: Metabolic acidosis is a common complication of CKD and may contribute to CKD progression. However, the association between serum bicarbonate and CKD progression has not yet been investigated using longitudinal measurements.

Method: We used data from CKD-REIN, a prospective cohort study conducted in 40 representative French nephrology clinics which included 3033 patients with CKD stages 3 to 5 between 2013 and 2016. Patients who had no serum bicarbonate or no creatinine measure at within 6 months of their inclusion date in the CKD-REIN study were excluded. All serum bicarbonate measurements were taken into account, from inclusion to the occurrence of renal replacement therapy (RRT), death, or end of follow-up, whichever came first. We used a shared random-effect model for the joint analysis of individual trajectories of serum bicarbonate and the hazard of the composite outcome (RRT or death before RRT) and each specific event separately. Hazard ratio were adjusted (aHR) for age, sex, primary kidney disease, metabolic syndrome, cardiovascular disease, proteinuria (< 30, 30-300, > 300 mg/day), and the CKD-EPI estimated glomerular filtration rate (eGFR) at baseline.

Results: A total of 2977 patients (65.4% men, median age 69 years) were included. At baseline, the median eGFR was 31.8 mL/min/1.73m^2 and the median bicarbonate concentration was 25 mmol/L. During a median follow-up of 4.5 years, 615 patients received RRT and 378 died before RRT. At any time of follow-up, a decrease of 1 mmol/l of the current level of serum bicarbonate was associated with a significantly increased hazard of RRT or death before RRT (aHR 1.05, 95%CI 1.02-1.08). The estimated effect was stronger on death before RRT (aHR 1.05, 95% CI 1.00-1.09) than on RRT (aHR 1.02, 95% CI 0.99-1.06).

Conclusion: A lower current level of serum bicarbonate is associated with an increased mortality in patients with CKD stage 3 to 5.

MO073

ACCELERATION OF KIDNEY FUNCTION DECLINE AFTER INCIDENT HOSPITALIZATION WITH CARDIOVASCULAR DISEASE: THE STOCKHOLM CREATININE MEASUREMENTS (SCREAM) PROJECT

Junichi Ishigami[1], Marco Trevisan[2], Lars Lund[3], Tomas Jernberg[3,4], Josef Coresh[1], Kunihiro Matsushita[1], Juan Jesus Carrero[2]

[1]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, United States of America, [2]Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden, [3]Karolinska Institutet, Karolinska University Hospital, Department of Medicine, Unit of Cardiology, Heart and Vascular Theme, Stockholm, Sweden and [4]Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Stockholm, Sweden

Background and Aims: The cardiorenal syndrome refers to a bidirectional relationship between the kidney and the heart. However, epidemiological evidence of cardiovascular disease (CVD) as a risk factor for chronic kidney disease (CKD) progression is actually scarce. We here quantified slopes of kidney function decline before and after the incidence of major CVD.

Method: We examined the slopes of estimated glomerular filtration rate (eGFR) decline in the 2 years before vs. after an incident hospitalization with heart failure (HF) (n=20,420), coronary heart disease (CHD) (n=18,152), or stroke (n=1,808) using data from a complete laboratory data collection in Stockholm, Sweden between 2006 and 2011. We used mixed-effect models with unstructured residual correlation matrix and stratified by index eGFR (≥60, 30-59, <30 ml/min/1.73m^2).

Results: Overall, patients who had HF were older, and had more comorbidities (e.g., diabetes, hypertension) and lower eGFR compared to those who had CHD or stroke. Incident hospitalization with HF and CHD, but not stroke, was significantly associated with a subsequent accelerated decline in eGFR, with a faster eGFR decline and greater slope change after HF than CHD. In the overall population, the pre-event vs. post-event eGFR slopes (ml/min/1.73m^2 per year) were -1.67 (-1.77 to -1.57) vs. -2.76 (-2.82 to -2.71), with a Δslope of -1.09 (-1.16 to -1.02) for HF; -1.09 (-1.20 to -0.98) vs. -1.87 (-1.92 to -1.81), with a Δslope of -0.78 (-0.85 to -0.70) for CHD; and -1.00 (-1.37 to -0.63) vs. -0.99 (-1.19 to -0.78), with a Δslope of 0.02 (-0.24 to 0.27) for stroke (**Figure 1A**). The accelerated declines in eGFR after HF and CHD were consistent across the spectrum of eGFR, although pre-event eGFR slopes were steeper in lower eGFR (e.g., pre-event eGFR slope for HF -0.64 (-0.76 to -0.53) for eGFR ≥60, -1.43 (-1.57 to -1.30) for eGFR 30-59, and -2.42 (-2.71 to -2.12) for eGFR <30 ml/min/1.73m^2) (**Figure B-D**).

Conclusion: Incident hospitalization with cardiac diseases (i.e., HF and CHD) was significantly associated with a subsequent acceleration of eGFR decline.

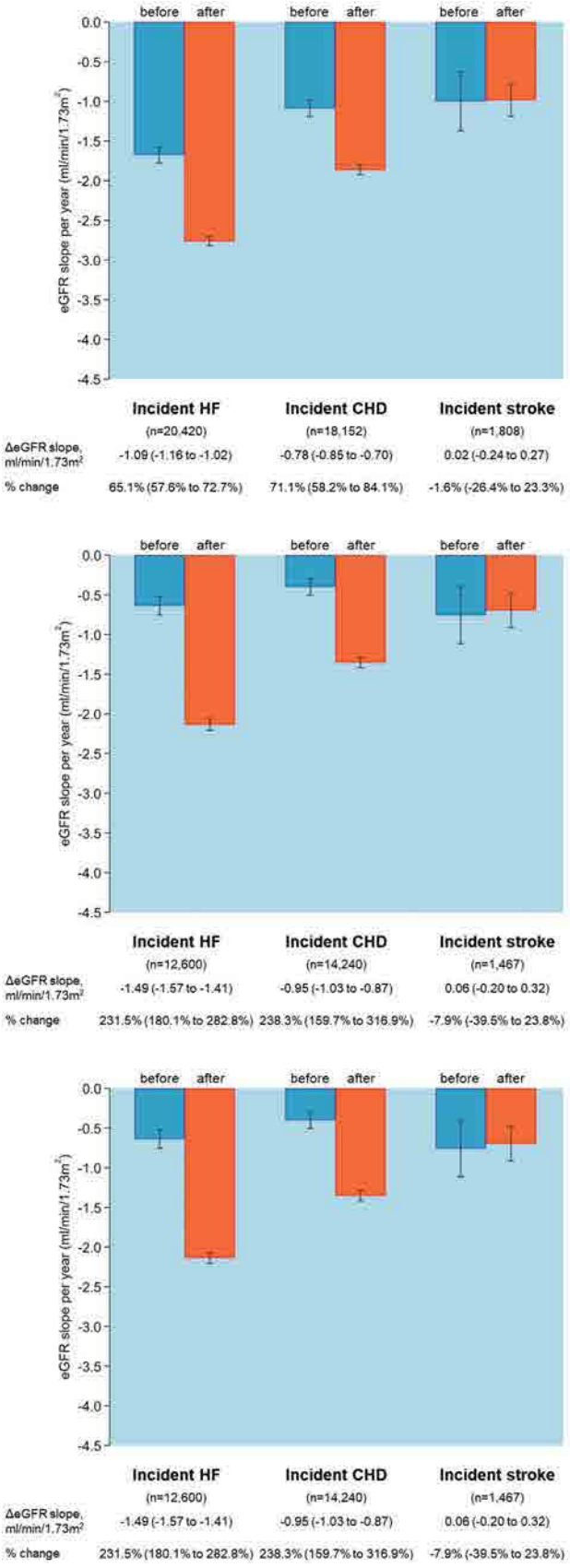


Figure: Individual slopes of eGFR decline before and after incident hospitalization with CVD. The model was adjusted for age and sex.

MO074 **RENAL FUNCTION DECLINE IN OLDER MEN AND WOMEN WITH ADVANCED CKD - RESULTS FROM THE EQUAL STUDY**

Nicholas Chesnaye[1], Friedo W. Dekker[2], Marie Evans[3], Fergus Caskey[4], Claudia Torino[5], Maurizio Postorino[5], Maciej Szymczak[6], Chava Ramspek[2], Christiane Drechsler[7], Christoph Wanner[7], Kitty J Jager[1]

[1]ERA-EDTA Registry, Dept of Medical Informatics, Amsterdam, Netherlands, [2]Leiden University Medical Center (LUMC), Department of Clinical Epidemiology, Leiden, Netherlands, [3]Karolinska Institutet and Karolinska University hospital, Department of Clinical Intervention and technology (CLINTEC), Stockholm, Sweden, [4]University of Bristol, Population Health Sciences, Bristol, United Kingdom, [5]CNR-IFC, Clinical Epidemiology and Pathophysiology of Renal Diseases and Hypertension & G.O.M., Reggio Calabria, Italy, [6]Wroclaw Medical University Library, Dept of Nephrology and Transplantation Medicine, Wrocław, Poland and [7]University Hospital Würzburg, Division of Nephrology, Würzburg, Germany

Background and Aims: Understanding the mechanisms underlying the differences in renal decline between men and women may improve sex-specific clinical monitoring and management. To this end, we aimed to compare the slope of renal function decline in older men and women in CKD 4-5, taking into account informative censoring related to the sex-specific risks of mortality and dialysis initiation.

Method: The EQUAL study is an observational prospective cohort study in stage 4-5 CKD patients ≥65 years not on dialysis. Data on clinical and demographic patient characteristics were collected between April 2012 to December 2018. eGFR was calculated using the CKD-EPI equation. Linear mixed models were used to model the eGFR trajectory by sex, and joint models were applied to deal with informative censoring.

Results: We included 7801 eGFR measurements in 1682 patients over 2911 years of follow-up. Renal function declined 14.0% (95% CI 12.9%-15.1%) on average each year. Renal function declined faster in men (16.2% per year, 95% CI 15.9%-17.1%) compared with women (9.6% per year, 95% CI 6.3%-12.1%), which remained largely unchanged after accounting for various mediators, and for informative censoring due to mortality and dialysis initiation. We identified effect modification by diabetes, with faster declines in renal function found especially in women with diabetes.

Conclusion: In conclusion, renal function declines faster in men compared with women, which remained similar after adjustment for mediators, and despite a higher risk of informative censoring in men. We demonstrate a disproportional negative impact of diabetes specifically in women.

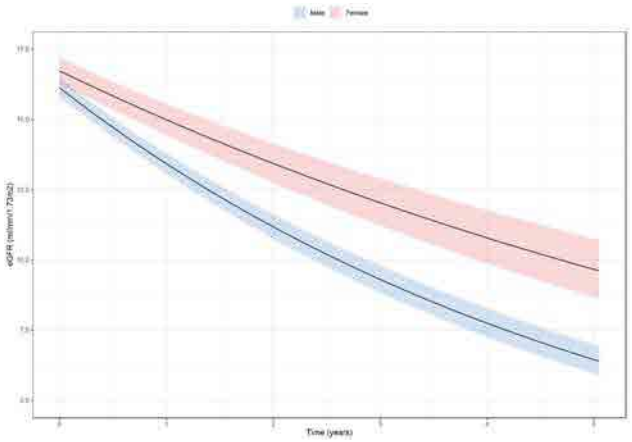


Figure:

Nephrology Dialysis Transplantation 35 (Supplement 3): iii177–iii181, 2020

PAEDIATRIC NEPHROLOGY

MO075 **DNA METHYLATION AND RESPONSE TO STEROIDS IN CHILDREN WITH NEPHROTIC SYNDROME**

Samantha Hayward[1,2,3], Matthew Suderman[4], Agnieszka Bierzynska[1], Gavin I Welsh[1], Moin A. Saleem[1]

[1]University of Bristol, Bristol Medical School: Translational Health Sciences, Bristol, United Kingdom, [2]UK Renal Registry, Learning and Research Building, Bristol, United Kingdom, [3]North Bristol NHS Trust, Renal Medicine, Bristol, United Kingdom and [4]University of Bristol, Bristol Population Health Science Institute, Bristol, United Kingdom

Background and Aims: Historically, paediatric patients with nephrotic syndrome (NS) have been crudely categorised by their response to steroids: steroid resistant (SRNS), steroid sensitive (SSNS) and secondary SRNS. However, growing evidence that these categories do not correspond to single diseases has led to a demand that they be re-defined based on biological mechanisms involved in the disease process. Indeed, next generation sequencing has identified causative mutations in up to 30% of paediatric NS patients ('monogenic' NS); however, specific disease mechanisms in the remaining patients remain unknown.

We propose that the remaining phenotype variation in NS may be explained by DNA methylation, the reversible but heritable addition of methyl groups to DNA that change how the underlying DNA sequence is interpreted.

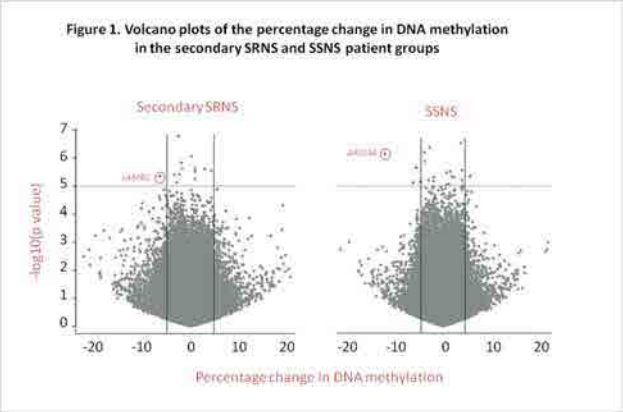


Figure:

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MO076

LONGITUDINAL CHANGES AND OUTCOME OF HIGH BLOOD PRESSURE IN EUROPEAN CHILDREN ON RENAL REPLACEMENT THERAPY

Enrico Vidal[1], Marjolein Bonthuis[2], Kitty J Jager[3], Jerome Harambat[4]

[1]University of Udine, Division of Pediatrics, Department of Medicine, Udine, Italy, [2]ESPN/ERA-EDTA Registry, Amsterdam UMC, University of Amsterdam, Department of Medical Informatics, Amsterdam, Netherlands, [3]ESPN/ERA-EDTA Registry, Amsterdam UMC, University of Amsterdam, Department of Medical Informatics and [4]Bordeaux University Hospital, Pediatric Nephrology Unit, Bordeaux, France

Background and Aims: Few studies have focused on trends of hypertension (HTN) and status of blood pressure (BP) control over time in children on renal replacement therapy (RRT). In this study, we aimed to evaluate the 5-year trend in BP antihypertensive medications (AHs) use, as well as the association between HTN and mortality among RRT patients enrolled within the ESPN/ERA-EDTA Registry.

Method: 25.223 BP measurements from 5.032 patients who started RRT before 20 years of age, between 2007-2016, were included. Mixed models were used to analyse trends of BP, the JointPoint regression to assess prevalence of uncontrolled HTN (uHTN) over time, and multivariable Cox proportional hazard models to evaluate association of BP with mortality.

Results: Mean systolic BP (SBP) at RRT initiation was 1.66(±0.15), 1.05(±0.15) and 1.09(±0.08) SDS in HD, PD and transplanted (Tx) patients, respectively, while it was 1.41(±0.19), 1.12(±0.18), and 0.79(±0.06) SDS in the corresponding RRT categories after 5 years. Patients on HD showed a significant decrease in the prevalence of uHTN over time (57.1% at dialysis start vs 41.4% after 5 years; annual percentage change [APC] -4%; 95% CI: -5.7;-2.2; $p<0.05$), coupled with a significant reduction in AHs use (APC -3.5%; 95% CI: -6.7;-0.2). PD patients showed a similar reduction in uHTN prevalence (APC -4.9%; 95% CI: -7.2;-2.6; $p<0.05$), but a significant increase in AHs use (APC +3.6%; 95% CI: 0.6;6.6; $p<0.05$). After 5 years, Tx patients showed a significant reduction in both prevalence of uHTN (APC -4.8%; 95% CI: -7.8;-1.7; $p<0.05$) and use of AHs (APC -2.2%; 95% CI: -4.1;-0.3%; $p<0.05$). Having uHTN was not associated with mortality (HR 0.95; 95% CI: 0.68-1.33).

Conclusion: A more adequate control of BP over time seemed to be obtained in children on RRT. Findings in PD patients suggest that this requires a progressive increase in the use of AHs.

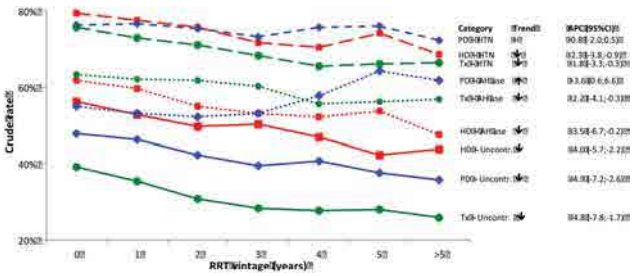


Figure: Prevalence of HTN and AH use according to dialysis vintage. Rates are adjusted by age, gender, PRD, Country GDP (PPP).

MO077

TEN YEAR TRENDS IN PAEDIATRIC RENAL REPLACEMENT THERAPY IN EUROPE: DATA FROM THE ESPN/ERA-EDTA REGISTRY

Marjolein Bonthuis[1], Jerome Harambat[2], Enrico Vidal[3], Kitty J Jager[4]

[1]ESPN/ERA-EDTA Registry, Amsterdam UMC, University of Amsterdam, Department of Medical Informatics, Amsterdam public Health research institute, Amsterdam, Netherlands, [2]Bordeaux University Hospital, Pediatric Nephrology Unit, Bordeaux, France, [3]University of Udine, Division of Pediatrics, Department of Medicine, Udine, Italy and [4]ESPN/ERA-EDTA Registry, Amsterdam UMC, University of Amsterdam, Department of Medical Informatics, Amsterdam public Health research institute, Amsterdam, Netherlands

Background and Aims: The ESPN/ERA-EDTA Registry includes data on children with end-stage kidney disease receiving renal replacement therapy (RRT) in Europe for 10 consecutive years. We examined time trends in incidence, prevalence and patient survival for paediatric RRT in Europe.

Method: We included all children aged < 15 years starting RRT in 22 European countries from 2007 to 2016. General population statistics were derived from Eurostat. Incidence and prevalence were expressed per million age related population (pmarp) and time trends were studied with Joinpoint regression. We analyzed patient survival using Cox regression.

Results: The incidence of children commencing RRT < 15 years remained stable over the past ten years, varying between 5.5 pmarp to 6.5 pmarp. The incidence by treatment modality did not change over time: 2.0 to 3.0 pmarp for haemodialysis (HD) and peritoneal dialysis (PD) and 1.0 pmarp for transplantation. Overall prevalence rose by 2% annually (95% CI: 1.5-2.3%) from 29.5 pmarp in 2007 to 35.6 pmarp in 2016.

The increase in prevalence was observed in all age categories, but was strongest among children older than 5 years at RRT initiation. The prevalence of patients on all treatment modalities increased during the study period: from 4.5 to 5.4 pmarp for HD, from 4.9 pmarp to 6.0 pmarp for PD and from 19.6 to 23.9 pmarp for transplantation (Figure).

Four-year adjusted patient survival on RRT was around 96% and similar for those initiating from 2007-2009 and from 2010-2012 (adjusted HR: 0.97, 95% CI: 0.69-1.36).

Conclusion: Over the past decade we found a stable incidence and an increasing prevalence of European children on RRT. Four-year patient survival was good, and did not change over time. These data are important to inform patients and healthcare providers and to aid health policy makers on future resource planning of pediatric RRT in Europe.

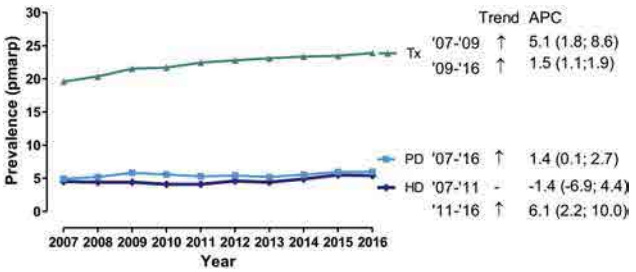


Figure: Prevalence of RRT (pmarp) by treatment modality and year.

MO078

HEMODIAFILTRATION MAINTAINS A SUSTAINED IMPROVEMENT IN BP COMPARED TO CONVENTIONAL HEMODIALYSIS IN CHILDREN - THE HDF, HEART AND HEIGHT (3H) STUDY

Francesca De Zan[1], Aysun Karabay Bayazit[2], Karolis Azukaitis[3], Nur Canpolat[4], Sevcan Bakkaloglu[5], Saoussen Krid[6], Mieczysław Litwin[7], Fabio Paglialonga[8], Charlotte Samaille[9], Mohan Shenoy[10], Manish Sinha[11], Brankica Spasojevic[12], Claus Schmitt[13], Franz Schaefer[13], Enrico Vidal[14], Rukshana Shroff[15]

[1]University Hospital of Padova, Nephrology, Dialysis and Transplant Unit, Department of Woman's and Child's Health, Padova, Italy, [2]Cukurova University, Adana, Turkey, [3]Vilnius University, Clinic of Pediatrics, Vilnius, Lithuania, [4]Cerrahpasa School of Medicine, Istanbul, Turkey, [5]Gazi University Hospital, Ankara, Turkey, [6]Hôpital Necker-Enfants Malades, Paris, France, [7]Children's Memorial Health Institute, Warsaw, Poland, [8]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [9]Hôpital Jeanne De Flandre, Lille Cedex, France, [10]Royal Manchester Children's Hospital, Manchester, United Kingdom, [11]Evelina Children's Hospital, London, United Kingdom, [12]University Children's Hospital, Belgrade, Serbia, [13]Center for Pediatrics and Adolescent Medicine, Heidelberg, Germany, [14]University of Udine, Division of Pediatrics, Department of Medicine, Udine, Italy and [15]Great Ormond Street Hospital for Children NHS Foundation Trust, and University College London Institute of Child Health, London, United Kingdom

Background and Aims: Hypertension is prevalent in children on dialysis and associated with left ventricular hypertrophy, cardiovascular disease and mortality. We studied the effect of different dialysis modalities (conventional hemodialysis [HD] vs hemodiafiltration [HDF]) on BP and risk factors affecting the evolution of BP over a one-year follow-up.

Method: This is a post-hoc analysis of the "3H - HDF-Hearts-Height" dataset, a multicenter, non-randomized, parallel-arm intervention study. The time–averaged 24-h mean arterial pressure (MAP) was used for the analyses and hypertension defined as 24-h MAP standard deviation score exceeding the 95th percentile.

Results: All 133 children who completed 12 months follow-up in the 3H study were included in this post - hoc analysis. 78 (74%) were on HD and 55 (77%) on HDF. At baseline MAP-SDS was > 95th percentile in 64 (82%) of children on HD and 23 (41.8%) patients on HDF, but these data are skewed by a high percentage of prevalent dialysis patients in the study. 43 (55%) of HD patients and 23 (42%) of HDF patients were on antihypertensive medications, and uncontrolled hypertension (BP>95th centile on medications) was present in 38 (88%) of HD patients and 6 (25%) of HDF patients. In the stepwise logistic regression at baseline, independent risk factors for hypertension were gender (OR 2.29; 95%CI 1.06–4.96; p=0.04) and inter-dialytic weight gain at baseline (OR 1.3; 95%CI 1.1–1.55; p=0.004). Over the one-year study period, MAP-SDS increased by 39% in HD patients and 12% in HDF patients (p< 0.001) (Figure). Significant risk factors for hypertension over time were dialysis modality (OR for HD compared to HDF 7.65; 95% CI 3.23 – 18.12; p< 0.001), inter-dialytic weight gain (OR 1.21; 95% CI 1.05 – 1.39; p=0.007), and dialysate sodium (for 1 mmol/L increase in dialysate sodium MAP-SDS increased by 1.1mmHg ; 95% CI 1.01 – 1.21; p=0.04).

Conclusion: Children on HD compared to HDF had a 7.6-fold higher 24-hr MAP-SDS and a sustained increase in BP over the one-year study period. Higher inter-dialytic weight gain and higher dialysate sodium levels were associated with a higher MAP-SDS in both groups.

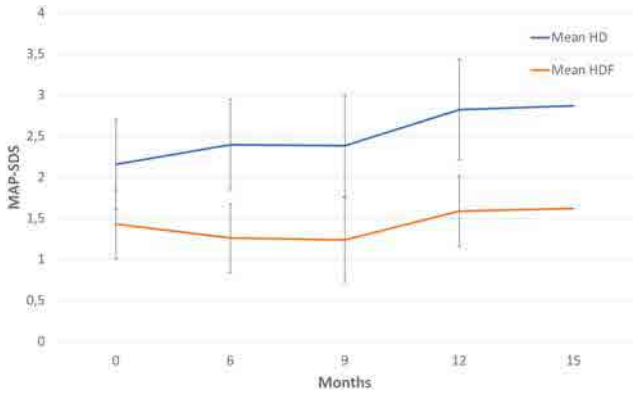


Figure:

MO079 **SECURITY OF THERAPEUTIC APHERESIS IN PEDIATRICS. PROSPECTIVE STUDY DURING 2018 IN 171 APHERESIS SESSSIONS**

Víctor López Baez[1], Pedro Arango Sancho[1], Yolanda Calzada Baños[2], Elena Codina Sampera[2], Ana Vinuesa Jaca[2], Lina Hernández Zúñiga[2], Álvaro Madrid Aris[2]

[1]Hospital Sant Joan de Déu, Nefrología Pediátrica, Esplugues de Lobregat, Spain and [2]Hospital Sant Joan de Déu, Nefrología Pediátrica, Esplugues de Lobregat, Spain

Background and Aims: Identify hypocalcemia and hemodynamic disorders related to apheresis in pediatrics either complications in vascular access or related to anticoagulation and adverse reactions with replacement fluid.

Method: Prospective and descriptive study of 171 sessions for therapeutic apheresis in pediatrics during 2018. Inclusion criteria was based on the 2016 Clinical-Practice-of-Therapeutic-Apheresis-guidelines(ASFA). The apheresis technique was selected also based on the 2016 ASFA Guidelines and the expertise in our center.

Results: The 171 sessions were distributed as follows: 73% were immunoadsorption(IA), 12% were cytoapheresis, 10.5% were LDL-apheresis and 4.5% therapeutic plasma exchange(TPE). The average age was 9 years and 58% were women. 50, 33 and 17% were due to Nephrological, Neurological and Digestive pathology respectively. 83% of the nephrological indications correspond to a category I of the ASFA Guidelines, as well as 25% of the neurological indications and all indications of Digestive pathology correspond to a category II. 58, 25 and 17% used temporary catheter, permanent catheter and needles respectively. Only one patient is accidentally removed from the temporary jugular catheter and it has not been related to vascular access or by the apheresis technique itself. Sixty-six percent had individual anticoagulation with citrate/calcium plus heparin and the remaining 33%, only once. Any case of bleeding related to catheter or others. Only 3 sessions of IA in the hypocalcemia objective, being symptomatic in only one of them. Of all 8 sessions of TPE, we performed 6 with frozen fresh plasma as replacement fluid with no adverse reactions.

Conclusion: The apheresis techniques in pediatrics had been presented with few complications in our center, none derived from vascular access, anticoagulation, infections or adverse effects due to use of replacement fluid. The training of medical and nursing staff is essential to identify risk situations. The use of protocols and international guidelines ensure safety in pediatrics.

Technical Details (171 sessions)				
	TPE	LDL	IA	GC*
Number of sessions (%)	8(4,5)	18(10,5)	124(73)	21(12)
Intervals (days)	2	3	3	15
Duration (hours)	1-2	1-3	1-3	1
Vascular access	HD-C	HD-C	HD-C	PiN**
Replacement fluids	Alb/FFP	-	-	-
Anticoagulation	Hep/Cit	Hep/Cit	Hep/Cit	Hep/Cit

* GC: Granulocyteapheresis
** PiN: Peripheral insertion needle SUPERCATH® (18G)



IDICATION	Disease (TA modality)	ªR
Nephrology (50%)	FSGS (IP/LDL/IA)	I-1B
	nonHLA-AMR (IA)	I-1B
	Dense deposit disease (IA)	-
Neurology (33%)	Guillain-Barré (IA)	I-1A
	Neuromyelitis óptica spectrum disorders AQ4 (IA)	II-1B
	Juvenile amyotrophic lateral sclerosis (TPE)	-
	Acute desseminated encephalomyelitis anti-MOG (TPE)	II-2C
Gastroenterology (17%)	Ulcerative colitis (Cytapheresis)	II-1B

ªR: Grading recomendations ASFA 2016

COMPLICATION	Nº of Sessions	
Hypotension	0/171	
Hypocalcemia	Asymptomatic	2/171
	Symptomatic	1/171
Replacement Fluids	0/8	
Vascular Access	Infecctions	0/171
	Extracción accidental	1/171
Anticoagulation	0/171	

Figure:

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10.1093/ndt/gfaa141

CARDIOVASCULAR AND RENAL PROTECTION - EFFECTS OF SGLT2 INHIBITORS AND GLP-1 RECEPTOR AGONISTS IN PEOPLE WITH CKD AND TYPE 2 DIABETES

TO001

EFFECTS OF THE BET-INHIBITOR APABETALONE ON CARDIOVASCULAR EVENTS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND ACUTE CORONARY SYNDROME, ACCORDING TO PRESENCE OR ABSENCE OF CHRONIC KIDNEY DISEASE. A BETONMACE TRIAL REPORT.

Kam Kalantar-Zadeh[1], Kausik K Ray[2], Stephen J Nicholls[3], Henry N Ginsburg[4], Kevin A Buhr[5], Jan Johansson[6], Ewelina Kulikowski[7], Peter P Toth[8], Michael Sweeney[9], Gregory G Schwartz[10]

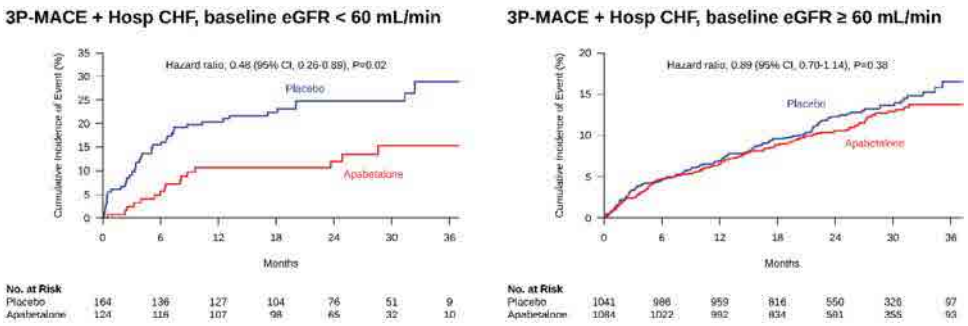
[1]Division of Nephrology and Hypertension, University of California Irvine , [2]Imperial Centre for Cardiovascular Disease Prevention, Imperial College, London, UK; , London, United Kingdom, [3]MonashHeart, Monash University, Melbourne, Australia, [4]Columbia University, New York, United States of America, [5]University of Wisconsin, Statistical Data Analysis Center, University of Wisconsin, Madison, United States of America, [6], Resverlogix Corp, San Francisco, United States of America, [7]Resverlogix Corp., Research, Calgary, Canada, [8]University of Illinois College of Medicine, Department of Family and Community Medicine, Peoria, United States of America, [9]Resverlogix Corp. and [10]VA Denver Aurora, Division of Cardiology

Background and Aims: Patients with type 2 diabetes (T2D) and acute coronary syndrome (ACS) are at high risk for recurrent cardiovascular (CV) events, particularly in the presence of chronic kidney disease (CKD). Apabetalone (APB) is a novel inhibitor of bromodomain and extraterminal (BET) proteins. Its cardiovascular efficacy and safety were evaluated in a phase 3 trial, BETonMACE.

Method: BETonMACE was a randomized, double-blind, comparison of effects of ABP or placebo (PBO) on major adverse CV events (MACE) defined as CV-death, non-fatal myocardial infarct or stroke, in 2425 pts with T2D and recent ACS. Here we report MACE plus CHF hospitalization in subjects with or without CKD Stage 3.

Results: Baseline characteristics: median age 62 years, 25.6% female, 87.6% white, 90% high intensity statin use, mean LDL-C 70.3 and HDL-C 33.3 mg/dl, median HbA1c 7.3%, and 11% with CKD Stage 3. Overall in the trial, MACE plus CHF hospitalization occurred in 139 (11.5%) patients with ABP and 173 (14.3%) with PBO (HR 0.78, 95% CI 0.63-0.98). In the subgroup with CKD, MACE plus CHF hospitalization occurred in 16 (12.9%) on APB and 41 (25%) on PBO (HR 0.48, 95% CI 0.26-0.89). In the subgroup without CKD, MACE plus CHF hospitalization occurred in 123 (11.3%) and 132 (12.7%) with APB or PBO, respectively (HR 0.89, 95% CI 0.70-1.

Conclusion: Patients with T2D, ACS, and Stage 3 CKD have a very high risk of subsequent MACE plus CHF hospitalization. The BET protein inhibitor ABP may reduce this risk.



Figures:

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TO002

REDUCTION IN THE RATE OF EGFR DECLINE WITH SEMAGLUTIDE VS PLACEBO: A POST HOC POOLED ANALYSIS OF SUSTAIN 6 AND PIONEER 6

Katherine Tuttle[1], David Cherney[2], Samy Hadjadj[3], Thomas Idorn[4], Ofri Mosenzon[5], Vlado Perkovic[6], Søren Rasmussen[4], Benjamin Wolthers[4], Stephen C Bain[7]

[1]University of Washington PMRC, Institute of Translational Health Sciences and Nephrology Division, Spokane, United States of America, [2]Toronto General Hospital, Department of Medicine, Division of Nephrology, Toronto, Canada, [3]University of Nantes, CHU Nantes, L'institut du thorax, INSERM, CNRS, Nantes, France, [4]Novo Nordisk, Søborg, Denmark, [5]Hadassah Hebrew University Hospital, Diabetes Clinical Research Center, Jerusalem, Israel, [6]University of New South Wales, Faculty of Medicine, Sydney, Australia and [7]Swansea University Medical School, Diabetes Research Unit Cymru, Swansea, United Kingdom

Background and Aims:

The SUSTAIN 6 cardiovascular outcomes trial (CVOT) indicated that once-weekly (OW) subcutaneous (s.c.) semaglutide may have beneficial effects on kidney function. SUSTAIN 6 and the more recent PIONEER 6 CVOT (oral semaglutide) had similar designs and subject populations; both evaluated the effects of semaglutide compared with placebo on important macro- and microvascular outcomes. This *post hoc* analysis of pooled data from the two trials evaluated the effects of semaglutide vs placebo on kidney function, assessed by estimated glomerular filtration rate (eGFR) slope.

Method:

Data for 6,480 subjects from SUSTAIN 6 (OW s.c. semaglutide 0.5 and 1.0 mg or placebo, n=3,297; median follow-up 2.1 years) and PIONEER 6 (oral semaglutide once-daily 14 mg or placebo, n=3,183; median follow-up 1.3 years) were pooled into two groups: semaglutide and placebo. Annual change in eGFR was compared between semaglutide and placebo in patients with eGFR data at baseline, both overall and by baseline eGFR subgroup ($\geq$30–<60 or $\geq$60 mL/min/1.73 m^2). Data were analysed using a linear random regression model with individual intercept and time slope. Estimated treatment difference (ETD) between annual rates of eGFR slope (from baseline to timepoint of interest) was calculated at Year 1 and Year 2 (Year 2 data predominantly from SUSTAIN 6); interaction p-values indicated differences between subgroups.

Results:

In the overall treatment population, the annual rate of eGFR change was 0.60 mL/min/1.73 m^2 (95% confidence interval [CI]: 0.31;0.90; p<0.0001) lower with semaglutide vs placebo in Year 1. In the subgroup with an eGFR $\geq$60 mL/min/1.73 m^2 at baseline, the ETD for semaglutide vs placebo at Year 1 was 0.48 mL/min/1.73 m^2/year (95% CI: 0.13;0.82). Whereas, at Year 1, the subgroup with eGFR $\geq$30–<60 mL/min/1.73 m^2 had an ETD of 1.07 mL/min/1.73 m^2/year (95% CI: 0.46;1.68) (Table). Accordingly, a numerically larger difference in ETD was observed in the eGFR $\geq$30–<60 mL/min/1.73 m^2 vs the eGFR $\geq$60 mL/min/1.73 m^2 subgroup (not statistically significant; $p_{interaction}$=0.21).

Conclusion:

Semaglutide was associated with a significantly smaller decline in renal function compared with placebo in subjects across stages of impaired kidney function at baseline. Although benefits were observed in the overall population, the findings indicate that the primary benefit may be observed in those with established chronic kidney disease.

Table:

Annual eGFR change with semaglutide or placebo and ETD between semaglutide and placebo in pooled SUSTAIN 6 and PIONEER 6 trials

	Semaglutide	Placebo
Overall number of subjects contributing to analysis	3,232	3,231
Annual eGFR change [95% CI], mL/min/1.73 m^2/year	–0.95 [–1.16;–0.74]	–1.55 [–1.77;–1.34]
ETD [95% CI], mL/min/1.73 m^2	Yr 1: 0.60 [0.31;0.90] Yr 2: 1.21 [0.62;1.80]***	
Baseline eGFR subgroups		
$\geq$60 mL/min/1.73 m^2, n	2,375	2,374
Mean baseline eGFR, mL/min/1.73 m^2	85.5	85.8
Annual eGFR change [95% CI], mL/min/1.73 m^2/year	–1.15 [–1.40;–0.91]	–1.63 [–1.87;–1.38]
ETD [95% CI], mL/min/1.73 m^2	Yr 1: 0.48 [0.13;0.82] Yr 2: 0.95 [0.27;1.64]*	
$\geq$30–<60 mL/min/1.73 m^2, n	779	777
Mean baseline eGFR, mL/min/1.73 m^2	47.4	46.9
Annual eGFR change [95% CI], mL/min/1.73 m^2/year	–0.29 [–0.73;0.14]	–1.36 [–1.80;–0.92]
ETD [95% CI], mL/min/1.73 m^2	Yr 1: 1.07 [0.46;1.68] Yr 2: 2.14 [0.92;3.36]**	
p-value for treatment by subgroup interaction (Year 2)	0.21	

*p<0.01;

**p<0.001;

***p<0.0001. eGFR was calculated using the CKD-EPI equation. Data were analysed using a linear random effects regression model with individual intercept and time slope and for subgroups interaction between time slope and subgroups. ETD calculated for semaglutide–placebo. Statistical significance of ETD tested at Year 2. CI, confidence interval; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; ETD, estimated treatment difference; n, number of subjects contributing to the analysis; Yr, year.

COGNITIVE IMPAIRMENT IN CKD

TO003

CROSSTALK OF UREMIC TOXINS AND INFLAMMASOME IN CHRONIC KIDNEY DISEASE-RELATED COGNITIVE IMPAIRMENT

LUNG-CHIH LI[1], WEI-YU CHEN[2], Jin Po Chen[1], Wen-Chin Lee[2], JENG-LIN YANG[2]

1Kaohsiung Chang-Gung Memorial Hospital, Nephrology, Kaohsiung, Taiwan, R.O.C. and 2Kaohsiung Chang-Gung Memorial Hospital, Institute for Translational Research in Biomedicine, Kaohsiung, Taiwan, R.O.C.

Background and Aims: Chronic kidney disease (CKD) is getting prevalent and causes big burden to the health care systems worldwide. CKD-associated cognitive impairment (CI) not only influences the behave function, but also results in longer hospitalization and higher risk of mortality. Inflammation is an important pathogenesis of CKD and plays a crucial role in progression of CKD. In this study, we hypothesized that accumulated uremic toxins, especially indoxyl sulfate (IS) and P-cresyl sulfate (PCS) induce neuroinflammation via activation of NLRP3 inflammasome in the brain tissue of CKD animals. This study aims to delineate the crosstalk between uremic toxins and inflammation in CKD-induced CI.

Method: Eight-week-old male C57B6 wildtype and NLRP3 knockout mice received sham and 5/6 nephrectomy to mimic CKD status. AST-120 (Kremezin), a spherical carbon adsorbent, was given orally to mice to neutralize the accumulated uremic toxins. The Y-maze and Morris water maze (MWM) testes were applied to evaluate cognitive function, including the spatial, short-term and long-term memory in shame, CKD, and AST-120 treated CKD mice. HPLC was used to examine the concentration of IS and PCS in the serum and brain tissues. Western blot and immunohistochemistry stain were used to identify the protein expression of target molecules in the brain tissue.

Results: CKD mice showed impaired spatial, short-term and long-term memory; however, 10% AST-120 attenuated CKD-induced memory impairment (Figure 1). IS, but not PCS, elevated in the brain tissues, especially in the frontal cortex and hippocampus. AST-120 reduced CKD-induced IS elevation in the brain tissue, and also ameliorated NLRP3 inflammasome activation in the astrocytes in the frontal and hippocampus. Finally, NLRP3 deficiency reversed the CKD-induced memory impairment (Figure 2).

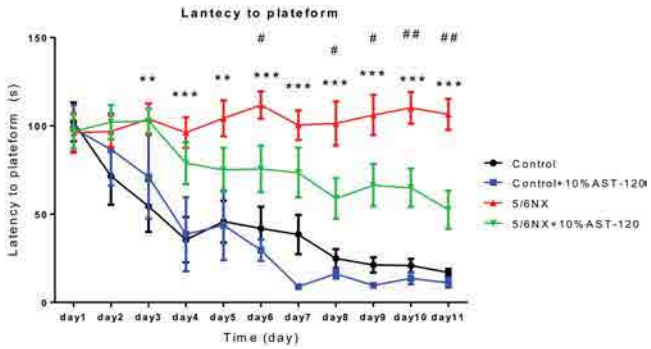


Figure 1. MWM test in sham and 5/6Nx mice in the presence or absence of AST-120. C57BL/6 mice at 8 weeks old received sham or 5/6Nx with or without AST-120 treatment received water maze test 8 weeks after the surgery. Mice were tested daily and the time to the escape platform and the escape latency to reach the platform was recorded. AST-120 (green) partially improved 5/6Nx-induced memory impairment (red). **P<0.01, ***P<0.001 vs control, # P<0.05, ## P<0.01vs 5/6Nx.

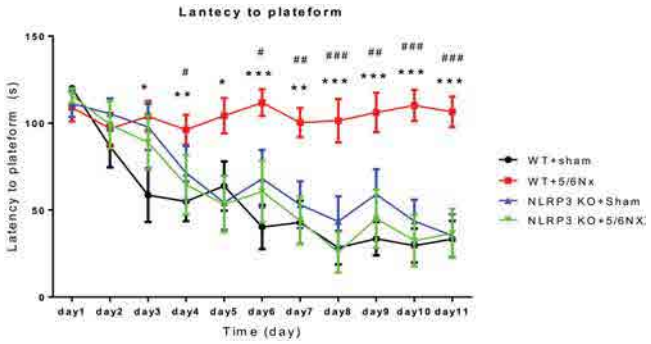


Figure 2. MWM test in wild type and NLRP3 knockout mice (KO) with and without 5/6Nx. KO of NLRP3 (green) reversed 5/6Nx-induced short-term memory impairment (red). *P<0.05, **P<0.01, ***P<0.001 vs WT+sham, #P<0.05, ##P<0.01, ###P<0.001 vs WT+5/6Nx.

Conclusion: IS is the major uremic toxin that causes CI in CKD mice via activating NLRP3 inflammasome pathway in the brain tissue. However, AST-120 effectively ameliorates CKD-induced CI.

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TO004 IMPACT OF RENAL TRANSPLANT ON COGNITIVE FUNCTION AMONG ESRD PATIENTS ON DIALYSIS

Anupma Kaul[1], Dharmendra Bhaduria[1], Narayan Prasad[1], Amit Gupta[1]

1Sanjay Gandhi Post Graduate Institute of Medical Sciences, Nephrology, Lucknow, India

Background and Aims: Kidney transplantation can help in mitigating neuropsychological (NP) impairments in end-stage renal disease (ESRD). Evidences have shown mixed responses on the the nature of cognitive function in patients who have undergone renal transplantation.Present study looked into the factors impacting cognitive domains and impact post transplant.

Method: 43 patients who were stable ESRD on thrice a week hemodialysis were investigated 6 months pre and post transplant using a battery of neurophysiological testing assessing attention–concentration, psychomotor ability and memory.

Formal kinetic modelling of dialysis delivery ensured adequate renal replacement therapy. Transplant function was assessed on regular interval and following a stable graft function and on stable doses of immunosuppressive medication 6 months post transplant were reassessed

Results: Within-subject comparisons showed statistically significant improvement in memory performance after kidney transplant. Other NP measures (attention– concentration and psychomotor abilities) showed non-significant improvements. Normative comparisons showed NP impairments on dialysis, which were not apparent after transplant

Conclusion: These data demonstrate improvements in cognition following kidney TX and emphasize the reversibility of the memory problems evidenced in dialysis

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EXPERIMENTAL TRANSPLANTATION

TO005

OPERATIONAL TOLERANCE IN KIDNEY TRANSPLANT RECIPIENTS: TOMOGRAM TRANSCRIPTOMIC STUDY

Ondrej Viklicky[1], Jiri Klema[2], Petra Mrazova[3], Daniel Abramowicz[4], Marc Abramowicz[5], Annick Massart[4], Petra Hruba[3], TOMOGRAM Study Group[3,4]

[1]Institute for Clinical and Experimental Medicine, Dept. of Nephrology, Prague, [2]Czech Technical University, Department of Computer Science, Prague, Czech Republic, [3]Institute for Clinical and Experimental Medicine, Transplant Laboratory, Prague, Czech Republic, [4]Antwerp University Hospital and Antwerp University, Antwerp, Belgium and [5]Université Libre de Bruxelles, Department of Medical Genetics, Hôpital Erasme, Brussels, Belgium

Background and Aims: TOMOGRAM, multicenter study founded by DESCARTES ERA/EDTA WG, aims to identify transcriptomic and genomic signatures of operational tolerance (OT) in recently identified cohort of OT kidney transplant recipients.

Method: RNA sequencing of peripheral blood was evaluated in 15 OT patients recently identified by TOMOGRAM consortium in 8 European countries, 23 stable patients ($\geq$ 15 years on immunosuppression, STA), 14 CABMR patients ($\geq$ 1 year, CR), 14 non-transplant CNI-treated patients and 14 healthy controls (HC). Differential expression was performed using DESEq2 and gene annotation analysis using Enrichr. Besides immunosuppression unadjusted model, robust negative-binomial regression model was created to adjust for immunosuppression intake. The models was trained on homogeneous group of STA patients.

Results: Using model unadjusted for immunosuppression, no differences in transcriptomic profiles between OT, STA and HC groups were identified. Nine transcripts were upregulated and 2 downregulated in OT compared CR group. The number of deregulated transcripts substantially increased when the model was adjusted for immunosuppression. Gene annotation analysis of top ranked deregulated 1109 transcripts (FC>2, adjusted p value <0.0001) showed deregulation of biological processes related to interferon-γ-mediated signaling pathway ($p=1.4*10^{-5}$), response to cytokine ($p=1.5*10^{-5}$), type I interferon signaling pathway (p=0.00036), regulation of I-kappaB kinase/NF-kappaB signaling (p=0.0021), cytokine-mediated signaling pathway (p=0.019) and neutrophil mediated immunity (p=0.033). While interferon-γ-mediated and type I interferon signaling were related to transcripts increased in CR, neutrophils associated transcripts were increased in OT. Analysis of cell types transcripts showed enrichment of CD19 B cells ($p=1.6*10^{-9}$) in CR, while CD56NK cells ($p=2.5*10^{-11}$) and CD8 T cells ($p=1.6*10^{-11}$) transcripts predominated in OT. To reveal probability of operational tolerance inside STA group, 13 transcripts able to discriminate OT and CR cohorts with high AUC (>0.89) were used in PCA analysis (ADGRG3, ATG2A, GDPD5, IL16, MX2, SLA2, PRKD2, SLIRP, GNLY, SRCAP, ARGHAP9, IGHM, CD5). The high probability of OT signature was found in a single STA patient.

Conclusion: Contrary to previous reports which pointed out towards naïve B cell signatures, unique OT patients exhibit other specific immunosuppression-independent transcriptomic profiles.

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TO006

NON-INVASIVE DIAGNOSIS OF BK VIRUS-ASSOCIATED NEPHROPATHY USING URINARY PROTEOMICS IN KIDNEY ALLOGRAFT PATIENTS

Martin Pejchinovski[1], David Marx[2], Jochen Metzger[1], Jérôme Olagne[2,3], Sophie Caillard[2], Bruno Moulin[2], William Mullen[4], Harald Mischak[1,4], Maarten Naesens[5], Dany Anglicheau[6], Pierre Marquet[7], Wilfried Gwinner[8]

[1]Mosaiques Diagnostics GmbH, Clinical Proteomics, Hannover, Germany, [2]University Hospital of Strasbourg, Department of Nephrology and Transplantation, Strasbourg, France, [3]University Hospital of Strasbourg, Department of Pathology, Strasbourg, France, [4]University of Glasgow, Proteomics and systems medicine, Glasgow, United Kingdom, [5]University Hospitals Leuven, Department of Nephrology and Renal Transplantation, Leuven, Belgium, [6]Necker hospital,AP-HP, Department of Nephrology and Renal Transplantation and INSERM U1151, Paris, France, [7]Université de Limoges, CHU Limoges, U1248 INSERM, Limoges, France and [8]Hannover Medical School, Department of Nephrology, Hannover, Germany

Background and Aims: BK virus-associated nephropathy (BKvN) is an important complication occurring after kidney transplantation. Its treatment mainly relies on lowering immune suppression. BKvN's histological aspect can mimic T cell-mediated rejection (TCMR) and other inflammatory conditions featuring tubulitis and interstitial infiltrate. At present, the screening strategy consists of measuring urinary and blood viral loads of BKv. Upon rising BK viremia, BKvN diagnosis is established by a graft biopsy. Biopsies are invasive and are not suitable for repeated screening. Therefore, the aim of this case-control study was to establish a urinary proteome-based test for BKvN diagnosis.

Method: Urine was obtained from 700 allograft recipients prior to either protocol or „for cause" biopsies during the first year of post-transplantation surveillance. Aside from normal biopsy findings (N=294), the histological diagnoses included BKvN (N=50), IFTA II-III (N=145), glomerulonephritis (N=17) and T cell-mediated, antibody-mediated, mixed or borderline rejection episodes (N=194). From all patients, relevant clinical and demographic data including Banff classification scores, HLA mismatches and the presence of donor-specific antibodies was collected at the date of sample collection and in further clinical follow-up. BKvN cases were defined as having SV40-positive immunostaining on allograft biopsy. BKvN patients were considered as cases and all other recipients were considered as controls. Patient's urinary peptide profiles were generated using capillary electrophoresis coupled to mass spectrometry consisting of 9430 different peptides in the mass range of 0.8 to 20 kDa.

Results: The CE-MS peptide profiles of randomly selected 30 BKvN cases and 307 kidney allograft controls (one sample per patient) were statistically analyzed to identify the most discriminative peptide markers for BKvN. In total, there were 117 peptides detected to have significantly different urinary excretion rates between both patient groups after false discovery rate adjustment for multiple testing. Thirty-two of these peptides were selected by cross-validated variable selection to establish a Support Vector Machine-based multi-marker model. Applying the 32-peptide marker model to an independent validation cohort consisting of 20 BKvN cases and 343 controls resulted in an area under the receiver operating characteristic curve of 0.86 and a 95% confidence interval from 0.82 to 0.89 with the p-value below 0.0001 and sensitivities and specificities for BKvN diagnosis of 85 and 76 %, respectively. Most notably, distribution of the classification values (figure 1) in the different patient groups of the validation set indicated specificities of the peptide marker model for TCMR/borderline of 85% (17 of 20 true negative classifications) and for viruria/viremia of 73% (8 of 11 true negative classifications)

Conclusion: In conclusion, the established urinary peptide marker model might serve as a non-invasive diagnostic test for BKvN and its differentiation from TCMR and states of isolated viruria or viremia.

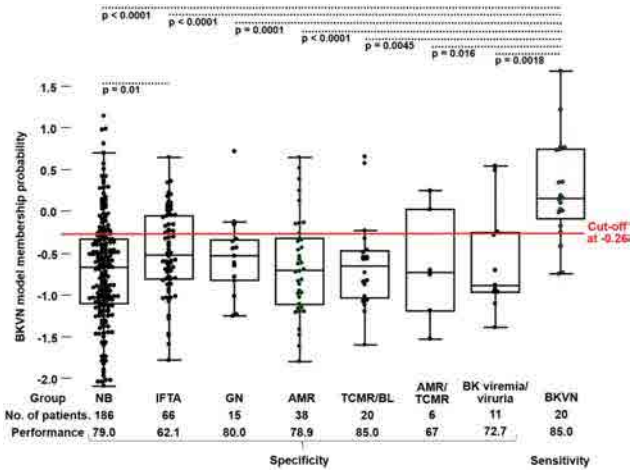


Figure 1: Distribution of numerical classification values by the BKVN peptide marker model composed of 32 naturally occurring urinary peptides in the different patient subgroups of the kidney allograft validation cohort. P-values for rank sum differences between the groups were obtained by the Mann-Whitney test after a positive Kruskal-Wallis test. Abbreviations: AMR, antibody-mediated rejection; BKVN, BK virus nephropathy; BL, borderline; GN, glomerulonephritis; IFTA, interstitial fibrosis/tubular atrophy; NB, normal biopsy; TCMR, T cell-mediated rejection.

TO007

PLASMA EXTRACELLULAR VESICLES MEDIATE ENDOTHELIAL TO MESENCHYMAL TRANSITION AND TUBULAR SENESCENCE IN RENAL ANTIBODY MEDIATED REJECTION BY COMPLEMENT ACTIVATION

ROSSANA FRANZIN[1,2], Alessandra Stasi[1], Fabio Sallustio[1], Chiara Divella[1], Guido Merlotti[2], Marco Quaglia[2], Claudia Curci[1], Giovanni Stallone[3], Vincenzo Cantaluppi[1], Loreto Gesualdo[1], Giuseppe Castellano[3]

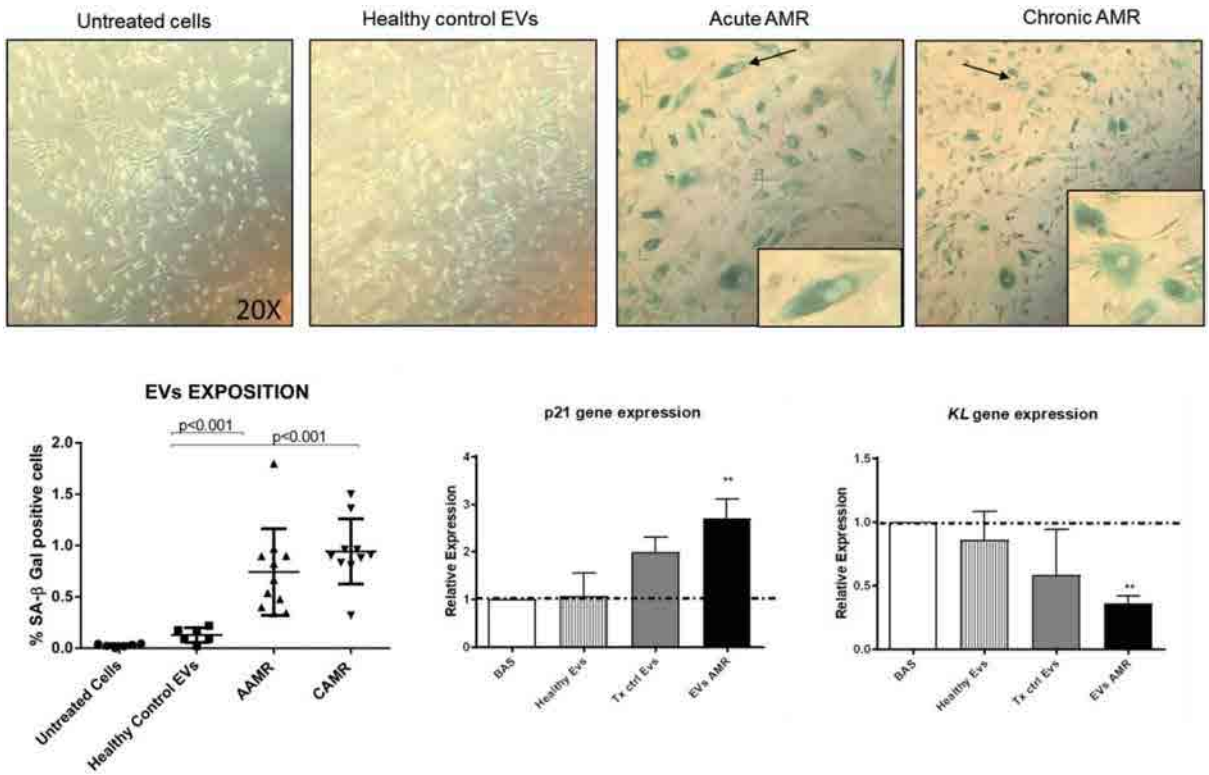
[1]Bari, Department of Emergency and Organ Transplantation, Nephrology Unit, Bari, Italy, [2]University of Piemonte Orientale, Department of Translational Medicine, Novara, Italy and [3]University of Foggia, DEPARTMENT OF MEDICAL AND SURGICAL SCIENCES

Background and Aims: EVs (Extracellular vesicles) are circulating microparticles able to mediate cell-to cell communication by carrying proteins, DNA, RNA or antibodies on their surface. EV are emerging as pivotal in renal Antibody-mediated rejection (AMR), one of the major causes of transplant failure associated to a massive complement activation. AMR is characterized by endothelial to mesenchymal transition (EndMT) and the occurrence of tubular accelerated senescence process, known as graft "Inflammaging". However, the potential role of EVs in accelerating the renal aging and graft fibrosis after AMR is not well understood.

Method: Plasma EVs were isolated from 10 Acute AMR (AAMR), 10 Chronic AMR (CAMR) patients, 5 stable graft transplanted patients and 5 healthy volunteers. EVs were isolated by ultracentrifugation at 100.000 g for 1h at 4°C, quantified by Nanoparticle Tracking Analysis (Nanosight, NTA EV/ml) and characterized by FACS (Attune Nxt). RPTEC and endothelial cell culture were incubated with EVs (5e+4 EVs/cells target for 24h. MTT test was performed to assess cell viability. Cellular senescence was investigated by qPCR for p21, p53, Klotho and CYP1B1 and SA-β-gal staining were performed. To assess EndMT analysis for CD31, VE-cadherin, Vimentin, Collagen I was performed by FACS. mRNA level of C3 and CFH were also measured by qPCR and C4d deposits were evaluated in endothelial cell colture by IF. Renal biopsies were then analyzed for inflammaging (p16INK4a) and EndMT markers (CD31/αSMA) by IHC and IF.

Results: The Nanosight analysis showed significant differences in the amount of-EVs count per ml of plasma in AMR patients compared to healthy subjects. EVs appeared to be significantly augmented in acute AMR, in a higher manner than chronic AMR (NTA, p=0.0154). By cytofluorimetric analysis, the endothelial markers CD31 and VE-cadherin appeared to be significantly increased compared of healthy control, indicating a predominant endothelial EV origin ($p<0.05$). Furthermore, an increase for CD3, CD4, CD8, CD40 and CD40L lymphocyte/monocytes markers was found. In vitro, the exposure of RPTEC and endothelial cells to AMR-derived EVs did not induce the loss of cell proliferation. However, AMR-derived EVs induced senescence in RPTEC, as observed by increase in SA-β-gal positive cells, upregulation of p21, p53, CYP1B1 and downregulated KL gene expression ($p<0.05$). EVs induced the EndMT as observed by FACS with the downregulation of CD31, VE-cadherin (CD144) and increase of Vimentin and Collagen I (p=0.025). To evaluate the contribution of EVs to local complement activation, C3 and CFH qPCR analysis were performed. EVs from AMR patients induced a significant increase in C3 gene expression with concomitant downregulation in CFH in RPTEC. EV exposition induced the classical and lectin pathway activation in endothelial culture medium, and C4d deposition. These data support the hypothesis that circulating EVs can amplify local complement activation in systemic endothelial and tubular cells during AMR, therefore leading to accelerated senescence and fibrosis as later effects. Finally, renal AMR biopsies showed significant tubular senescence as indicated by p16 expression; p16 was significantly upregulated in Chronic compared with Acute AMR biopsies ($p<0.05$). The AMR biopsies showed positivity for EndMT, as indicated by CD31 decrease and interstitial αSMA upregulation ($p<0.05$).

Conclusion: These results suggest a putative role for circulating AMR derived-EVs in inducing the tubular inflammaging by local complement activation and early fibrosis by EndMT. The EVs cargo characterization that is ongoing might highlight novel targets for therapeutic intervention.



Figure

TO008

COMPARATIVE TRANSCRIPTOME AND CO-EXPRESSION NETWORK ANALYSIS REVEALED A POTENTIAL ROLE OF C1QB AND INTERFERON TYPE 1 PATHWAY IN CIRCULATING IMMUNE CELLS OF KIDNEY TRANSPLANTS PATIENTS WITH CHRONIC ANTIBODY MEDIATED REJECTION.

Gloria Santoro[1], Simona Granata[1], Paola Pontrelli[2], Mattia Rossi[1], Giovanni Gambaro[1], Giuseppe Grandaliano[3], Gianluigi Zaza[1]

[1]University of Verona, Renal Unit, Department of medicine, Verona, Italy, [2]University of Bari, Nephrology, Dialysis and Transplantation, Department of Emergency and Organ Transplantation, Bari, Italy and [3]Università Cattolica del Sacro Cuore, Renal Unit, Rome, Italy

Background and Aims: Chronic antibody-mediated rejection (CAMR) is a multifactorial pathological condition that can affect more that 40-50% of kidney allografts. Its clinical evolution is often silent, and this can delay its diagnosis. Although many advances in understanding the biological mechanisms underlying its onset/development, at the moment, no reliable non-invasive diagnostic biomarkers are available in clinic.

Method: We enrolled 29 patients with biopsy-proven CAMR, 29 stable transplant recipients (controls). Subsequently, the microarray profile of mRNA isolated from peripheral blood mononuclear cells (PBMCs) from 10 randomly selected CAMR patients and 10 controls was evaluated by Agilent technology. For the bioinformatics analysis we employed several statistical algorithms (including ANOVA and Kruskal-Wallis tests adjusted for multiple-tests) and a Weighted Gene Correlation Network Analysis (WGCNA) to select genes biologically associated in co-expressed networks.

Results: 935 genes resulted differentially expressed between the two study groups, demonstrating the large biological impact of this pathological condition on circulating immune-inflammatory cells. After WGCNA co-expression analysis, a group of genes (enclosed in a single co-expression module, 13 genes) resulted highly discriminating CAMR *versus* controls ($p<.5.2$ e-7, FDR<1%). This module included: Interferon-induced transmembrane proteins (IFITM) 2, 3, 4, confirming previous results by our group. However, the top discriminative gene was C1QB (Complement component 1, q subcomponent, B chain, $p<000.1$), a key element involved in the classical complement pathway. ELISA confirmed the microarray results on the entire patients' cohort.

Conclusion: Our study confirmed the role of the type 1 interferon pathway in CAMR and underlined its capability to promote C1QB expression. These effects could contribute to better define the role of innate immunity in CAMR. Finally, C1QB, if validated in a large cohort of patients, could represent a new valuable molecular diagnostic biomarker for this complication.

TO009

THE POTENTIAL OF DONOR-DERIVED CELL-FREE DNA AS A BIOMARKER FOR REJECTION IN KIDNEY TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Veerle Wijtvliet[1], Philip Plaeke[1,2], Steven Abrams[3,4], Niel Hens[4,5], Els Gielis[1], Rachel Hellemans[1,6], Benedicte De Winter[1], Daniel Abramowicz[1,6], Kristien Ledeganck[1]

[1]University of Antwerp, Laboratory of Experimental Medicine and Paediatrics and member of the Infla-Med Centre of Excellence, Antwerp, Belgium, [2]Antwerp University Hospital, Department of Abdominal Surgery, Antwerp, Belgium, [3]University of Antwerp, Global Health Institute, Department of Epidemiology and Social Medicine, Antwerp, Belgium, [4]Hasselt University, Center for Statistics, I-BioStat, Data Science Institute, Diepenbeek, Belgium, [5]University of Antwerp, Centre for Health Economics Research and Modelling Infectious Diseases and Centre for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, Antwerp, Belgium and [6]Antwerp University Hospital, Department of Nephrology and Hypertension, Antwerp, Belgium

Background and Aims: Donor-derived cell-free DNA (dd-cfDNA) is actively studied as a non-invasive biomarker for the diagnosis of kidney allograft rejection, with conflicting results being reported. Therefore, we conducted a systematic review and meta-analysis to provide a clear overview of the potential value of dd-cfDNA to diagnose kidney rejection, and specifically antibody-mediated rejection (ABMR).

Method: A systematic literature search was performed in Pubmed, Web of Science, and the Cochrane library using the search terms: "cell free DNA AND kidney transplantation". We included studies that 1) described dd-cfDNA fractions in blood of kidney allograft recipients; and 2) were published as English original research papers between January 1, 1994 and November 26, 2019. The methodological quality was assessed by the Methodological Index for Non-Randomized Studies (MINORS). Out of 287 hits, 55 duplicates were removed. 232 remaining abstracts were screened, leaving 36 articles for full-text review, of which 11 were included in a systematic review and data from 7 articles were synthesized in a meta-analysis. A weighted median of medians (WMM) (median with 95% confidence interval (CI) in squared brackets) was computed as a pooled estimate for the median dd-cfDNA fractions in different groups of patients. A meta-analysis was prespecified to be performed among following patient groups: 1) ABMR patients; 2) T-cell-mediated rejection (TCMR) patients; 3) stable patients; 4) patients without rejection at indication biopsy. The pooled ABMR group consisted of patient groups with pure ABMR and/or mixed ABMR/TCMR. Weighted median differences of medians (WMDM) were estimated for pairwise comparisons among the aforementioned groups, according to the approach proposed by McGrath et al. (2019).

Results: A large heterogeneity was observed between the selected studies in 1) study design; 2) inclusion criteria (consecutively transplanted patients versus patients with an acute kidney event); 3) statistical reporting (mean ± SD versus median with IQR or min-max); and 4) the definition of study groups. This made the results of the selected studies only partially comparable or suitable for further meta-analysis. Three studies calculated the fraction of dd-cfDNA in stable patients, resulting in a WMM of 0.29% [0.26-0.45]. In the ABMR group, a remarkably higher WMM (2.5% [1.4-2.9]) was observed, when combining the data from five separate studies. Four of those five studies also described dd-cfDNA levels in TCMR patients and patients without rejection at indication biopsy, resulting in a WMM of 0.27% [0.26-2.69] and 0.57% [0.3-0.67], respectively. As presented in Figure 1, median dd-cfDNA fractions were significantly higher in patients with ABMR vs. patients without rejection at indication biopsy (Figure 1A). As compared to patients with TCMR, a tendency to higher median dd-cfDNA fractions was observed in patients with ABMR (Figure 1B). Patients with TCMR had no higher median dd-cfDNA fractions than patients without rejection at indication biopsy.

Conclusion: Despite the large heterogeneity between the selected studies, our results point towards higher median dd-cfDNA fractions in patients with ABMR vs. patients without rejection at indication biopsy. Furthermore, a tendency to lower median dd-cfDNA fractions was noted in patients with TCMR compared to ABMR. dd-cfDNA might be useful in the diagnosis of ABMR if confirmed in further studies.

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EXTRACORPOREAL TREATMENT OF ESKD

TO010 A NEW IMMUN-TOXICOLOGICAL TEST TO DETECT POLYSULFONE HYPERSENSITIVITY IN HEMODIALYSIS PATIENTS

Joachim Beige[1], Ralph Wendt[2], Despina Rüssmann[3], Karl-Peter Ringel[4]

[1]KfH Kuratorium für Dialyse und Nierentransplantation e.V., Leipzig, Germany, [2]Hospital St. Georg, Nephrology, Leipzig, Germany, [3]KfH Kuratorium für Dialyse und Nierentransplantation e.V., KfH-Hauptverwaltung, Neu-Isenburg, Germany and [4]Rilab Laboratory, Germany

Background and Aims: Incompatibility of dialysis procedure due to hypersensitivity against dialyzer material which currently is mainly based on polysulfone and derivatives can not be assessed by routine laboratory tests. Although the frequency of such symptoms is suspected to be low (below 2%) such resembles an important clinical problem because dialysis procedures are frequently accompanied by symptoms of non-tolerability with reasons not being entirely clear while circulatory reasons are suspected to play a major role.

Method: To enlighten the role of polysulfone hypersensitivity, we adapted known standardized material immune-toxicological tests (lymphocyte transformation test, basophil degranulation test) to the specific conditions of dialysis and polysulfone material sensitivity. We developed a method of polysulfone micronisation and measured humoral immune response of isolated patient́s lymphocytes when incubated with polysulfone dispersion.

Results: 39 samples from 103 patients with suspected polysulfone hypersensitivity showed positive results for type 1 (n=19), type 4 (n=18) or both type (n=2) reactions. There were no significant differences in the level of stimulation measured for DI, SI and lymphogenesis before and after dialysis (average delta -0.4; -0.28; - 1.74, p = 0.71; 0.34; 0.37) and with different dialyzer materials (Tab. 1). Patients with pos. type 4 results (LTT and lymphogenesis) showed highly correlated results in either LTT or lymphogenesis test (Fig. 1, R=0.87, $p<0.0001$). 8 out of 8 samples from patients with repeated test on different PS showed positive results on either PS. One patient tested positive on PS showed no hypersensitivity with another non-PS (PMMA) material.

Conclusion: This is the first methodological report showing plausible in-vitro results of patients samples concerning polysulfone intolerance. On the first superficial view, a "false-negative" rate of 60% looks rather disappointing, because all samples derived from patients with suspicion of PS hypersensitivity. However, due to the clinical variability of intolerance symptoms and the high prevalence of any problems after HD initiation, mainly of circulatory origin after initiating extracorporeal circuit, this rate may obviously express the true frequency of isolated PS material hypersensitivity in suspected patients. Alternative pathophysiological pathways of material sensitivity like complement activation, remain to be elucidated and incorporated into a comprehensive future testing panel. Further clinical and laboratory research is needed to define true polysulfone hypersensitivity and to enlighten the field of hypothetic subclinical material incompatibility in patients with impaired dialysis tolerability.

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TO011

HEALTH UTILITY BUT NOT UREMIC TOXINS ARE ASSOCIATED WITH ONE YEAR MORTALITY IN HD PATIENTS

Wim Van Biesen[1], Amaryllis Van Craenenbroeck[2], Daniel Abramowicz[3], Holvoet Els[4], Veys Nic[4], Griet Glorieux[4], Marie Madeleine Couttenye[5], Sunny Eloot[4]

[1]Ghent University Hospital, Gent, Belgium, [2]Hospital Gasthuisberg Leuven, Renal Division, Leuven, Belgium, [3]University Hospital Antwerp, Nephrology, Edegem, Belgium, [4]Ghent University Hospital, Renal Division, Gent, Belgium and [5]University Hospital Antwerp, Renal Division, Antwerp, Belgium

Background and Aims: Patient centred care is progressively gaining importance. Standardized outcomes should take into account patient relevant outcomes, such as mortality and quality of life. It is unknown whether the health utility index EQ5D, an objective assessment of quality of life, is associated with mortality in haemodialysis patients. Serum concentrations of different uremic toxins have been associated with survival. We intended to explore whether EQ5D rather than concentrations of representative uraemic toxins (UT) was associated with mortality.

Method: Prospective longitudinal multicentric cohort study of all haemodialysis patients at 5 representative dialysis centres in Flanders. Total and free concentrations of representative uraemic toxins indoxyl sulfate (IxS), p-cresyl sulfate (pCS), p-cresyl glucuronide (pCG), indole acetic acid (IAA), 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid (CMPF), hippuric acid (HA) and uric acid (UA) were determined at baseline. Mini Nutritional Assessment (MNA) and EQ5D were assessed by dedicated nurses. Mortality was assessed from administrative or medical records. A Cox regression model was built, both fixed and as conditional forward including clinical parameters, MNA, EQ5D and serum concentrations of the different uraemic toxins.

Results: 216 prevalent patients (62%male, age 67.2 ± 15.7) all on high flux haemodialysis were included. Over the observation period, 59 patients (27%) died. Health utility as assessed by EQ5D was 0.69±0.28; perceived health by visual analogue scale (VAS) (0-100) was 59.6±18.6. Adjusting for age, gender and MNA score, free but not total concentrations of IxS, pCS and IAA and EQ5D score were associated with overall survival in the forced entry model. However, neither in the fixed entry, the forward or backward model were serum concentrations of uraemic toxins retained, and only age, gender, BMI, EQ5D and VAS were consistently associated with survival.

Conclusion: Measures of health utility, such as EQ5D, and quality of life, such as a simple VAS score, are more predictive of survival in patients on regular haemodialysis than serum concentrations of a panel of relevant uraemic toxins. Health utility and QoL are thus not only directly relevant to patients, but also indirectly through an association with improved survival.

The concept of dialysis adequacy has been challenged over the last decade, mainly because it was focusing on small solute clearance. Different authors reported that concentrations of middle molecular and protein bound solutes were more representative. In our study, free but not total solute concentrations were associated with survival. However, adjusting additionally for health utility and/or health perception and/or assessment of nutritional status abolishes this association. Studies assessing interventions to enhance solute removal should not only include solute concentrations as outcome, but also consider EQ5D, VAS and nutritional status as important outcomes to enhance patient centeredness of their findings.

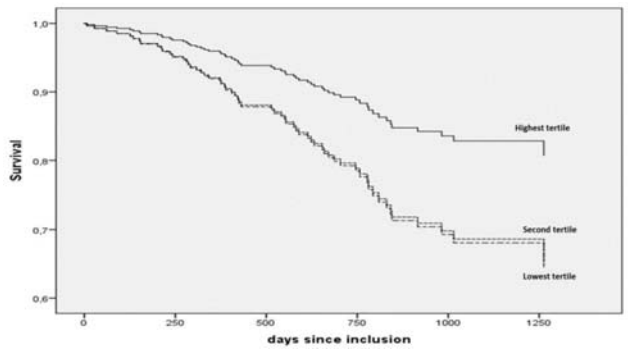


Figure: Survival in function of tertiles of EQ5D score, adjusted for age, gender, BMI and relevant uraemic toxins

TO012

HOW DIFFERENT IS THE CLEARANCE OF LARGE MIDDLE MOLECULES AND INFLAMMATORY MARKERS FROM EXPANDED HEMODIALYSIS THERAPY COMPARED TO ONLINE HEMODIAFILTRATION?

Fernando Hadad Arrascue[1], Lars-Göran Nilsson[2], Angelito Bernardo[3], Angela Rivera[3], Lourdes Guardiola Belmonte,[1], Florentina Rosique[4], Alberto Andreu Muñoz[4], Antonio Perez Perez[4], Juan Cabezuelo-Romero[5]

[1]Clínicas de Diálisis RTS, Nephrology, Murcia, Spain, [2]Baxter International, Lund, Sweden, [3]Baxter Healthcare Corporation, Deerfield, United States of America, [4]Hospital General Universitario Reina Sofía, Murcia, Spain and [5]Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain

Background and Aims: Expanded hemodialysis (HDx) with a medium cut-off dialyzer, Theranova® 500, can achieve a middle molecule clearance but its efficacy or comparison with HDF is still unknown. It is still unknown on how large middle molecules and inflammation markers are affected over time with a medium cut-off dialyzer. This study compared the purifying effectiveness of Theranova® 500 dialyzer with respect to online Hemodiafiltration (OL-HDF).

Method: Sixty-three patients who were already receiving HDF were evaluated and 43 were randomized by residual renal function. Twenty-one patients received treatment with HDx using Theranova® 500 and 22 patients remained in HDF in post-dilution mode, using a high-flux dialyzer, Polyflux® 170H, for up to 24 weeks. The dialysis time and the adequacy parameters for both arms were the same. Large middle molecules were measured (kappa immunoglobulin free light chains [κ-FLC], lambda immunoglobulin free light chains [λ-FLC], chitinase-3-like protein 1 [YKL-40], fibroblast growth factor 23 [FGF-23] and serum beta-2 microglobulin [β2M]), ; and inflammatory markers (high sensitivity C-reactive protein [hs-CRP], pentraxin - 3 [PTX-3], interleukin-6 [IL-6], interleukin-10 [IL-10]) at 12 weeks of treatment; and its change from baseline to weeks 12 and 24 in mid-week pre-dialysis. The method of measurement was the immunoassay. Siemens immunoassay was used for FLCs.

Results: HDx with Theranova® 500 demonstrated comparable results to OL-HDF with convective volume 24.4±3.2 L in terms of reduction rate (RR) of middle molecules (κ-FLC, λ-FLC, FGF-23 and β2M) at 12 weeks of treatment. HDx demonstrated similar performance to HDF in mid-week pre-dialysis plasma levels of middle molecules from baseline, at 12 and 24 weeks of treatment. Greater RR of YKL-40 at 12 weeks of treatment was seen in HDx group when compared to HDF (58.1% vs 42.4%; $p \leq 0.0001$), and there was a difference in the pre-dialysis β2M change from Baseline values between the groups (-0.60 for HDx arm and +3.28 for HDF arm, p=0.46). HDx with Theranova® 500 demonstrated comparable results to HDF in terms of reduction rate (RR) of inflammatory markers (hs-CRP, PTX-3, IL-6 and IL-10) at 12 weeks of treatment.

There were no differences in the parameters of adequacy of dialysis between both arms. Both treatments were effective in maintaining pre-dialysis albumin and fibrinogen levels throughout the study. There were no significant adverse events related to the safety of Theranova.

Conclusion: HDx with Theranova® 500 is an emergent, effective and safe hemodialysis therapy that showed a purifying efficacy at least comparable to OL-HDF.

TO013

ADSORPTION THERAPY AND SEPTIC SHOCK: A RETROSPECTIVE STUDY COMPARING COUPLED PLASMA FILTRATION-ADSORPTION AND CYTOSORB.

Vittorio Di Maso[1], Domenico Grecò[1], Martina Cozzi[1], Elisa Bedina[1], Ugo Gerini[1], Elisa Olivo[1], Sabina Leonardi[1], Fabiola Giudici[2], Giorgio Berlot[3], Francesco Bianco[1]

[1]ASUGI Trieste, Internal Medicine - Nephrology and Dialysis Unit, Trieste, Italy, [2]University of Padua, Epidemiologyy and Public Health, Departemnt of Cardiac, Thoracic, Vascular Science - Unit of Biostatistics, Padova, Italy and [3]ASUGI Trieste, Perioperative Medicine, Intensive care and Emergency, Trieste, Italy

Background and Aims: Septic shock is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Excessive release of cytokines and other inflammatory mediators is a key mechanism and cytokines adsorption therapies are applied in this context to restore a balanced immune homeostasis. Different adsorption techniques are available but there are no studies comparing these different adsorption approaches. The aim of this retrospective observational study was to compare Coupled Plasma Filtration Adsorption (CPFA) and CytoSorb™ in terms of hemodynamic and clinical response, mortality and renal function recovery.

Method: A retrospective observational study was designed enrolling all patients admitted to ICU with a diagnosis of septic shock treated with blood adsorption, either CPFA or CytoSorb™, from January 2015 to December 2017. Primary endpoints of the study were the assessment of changes in NE dosage, MAP values, SOFA score and PCT levels before and after blood adsorption. Secondary endpoints ICU length of stay (LOS), mortality at 30, 60 and 90 days from adsorption initiation; renal outcome at 30 and 90 days from adsorption initiation.

Results: The study included 28 patients (14 CPFA, 14 Cytosorb™). Adsorption treatment was associated with a significant (p=0.03) improvement in hemodynamics with a Norepinephrine/Mean Arterial Pressure ratio (NE/MAP) of 0.64 (0.14-2.6) pre-treatment vs 0.11 (0.0-0.32) post-treatment regardless of the applied technique. Furthermore, a significant ($p<0.001$) procalcitonin (PCT) post treatment reduction was demonstrated with a comparable effect in the two groups (p=0.32) (Fig.1). No difference has been found in SOFA score changes (p=0.06) and again without any difference between groups (p=0.17). Overall Survival (OS) rate at 30 days was comparable between groups being 64.3% in CPFA and 78.6% in CytoSorb™ group (p=0.34). Finally, a complete recovery of kidney function at 30 and 90 days has been obtained in respectively 90% and 100% of survived patients without any difference between groups (p=1.00) (Fig.2).

Conclusion: These data confirmed the effectiveness of adsorption in terms of short-term clinical improvement independently from the applied technique, supporting the role of both these adjunctive therapies in septic shock treatment. CPFA and Cytosorb™ have comparable effects in terms of hemodynamic improvement, clinical outcome, mortality and recovery of kidney function from septic shock AKI.

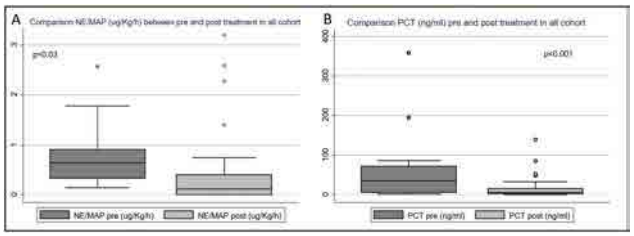


Figure 1: Variation of clinical parameters before and after adsorption therapy. Panel A: NE/MAP was significantly reduced after the adsorption therapy. **Panel B:** PCT was significantly lower after the adsorption therapy.

Kidney function before hospital admission	CPFA (n=14)	CytoSorb™ (n=14)	p-value
Normal Kidney Function	12 (85.7%)	11 (78.6%)	
Chronic Kidney Disease	1 (7.1%)	2 (14.3%)	0.99
Chronic Hemodialysis (CH)	1 (7.1%)	1 (7.1%)	
Kidney function in survivors at 30 days	CPFA (n=8)[a]	CytoSorb™ (n=10)[b]	
Recovered Kidney Function	7 (87.5%)	9 (90%)	0.99
Persistent Acute Kidney Injury	1 (12.5%)	1(10%)	
Kidney Function in survivors at 90 days	CPFA (n=7)[c]	CytoSorb™ (n=9)[d]	
Recovered Kidney Function	7 (100%)	9 (100%)	1.00
Persistent Acute Kidney Injury	0 (0%)	0 (0%)	

[a] 5 patients died and 1 patient CH; [b] 3 patients died and 1 patient CH
[c] 6 patients died and 1 patient CH; [d] 4 patients died and 1 patient CH

Figure 2: Kidney function recovery in patients treated with adsorption. Recovery of kidney function is defined by the return of eGFR values at the levels registered before hospital admission.

TO014 **COMPARISON BETWEEN HIGH FLUX-HD AND OL-HDF ON SURVIVAL AND ADEQUACY: TEN YEARS EXPERIENCE.**

Vincenzo Terlizzi[1], Bernardo Lucca[2], Chiara Manenti[2], Paola Gaggia[2], Roberto Zubani[1,2], Massimo Sandrini[2], Ezio Movilli[2], Francesco Scolari[1,2]

[1]Università degli Studi di Brescia - Facoltà di Medicina e Chirurgia -, Brescia, Italy and [2]U.O. Nefrologia - ASST Spedali Civili di Brescia

Background and Aims: Four RCTs have been published that compared on-line HDF (Ol-HDF) with HD. However, to date, an indisputable answer in determining whether patients treated with Ol-HDF had a better survival than those treated with high-flux HD (Hf-HD) has not been reached. The aim of our study was to retrospectively evaluate the impact of the dialysis modality (Hf-HD, Ol-HDF or acetate-free biofiltration AFB) on patient survival and dialysis adequacy.

Methods: We retrospectively evaluated all the incident patients that started dialysis due to uremia from 01-01-2008 to 31-12-2018 at the U.O. Nephrology ASST Spedali Civili of Brescia. Exclusion criteria were: duration of dialysis treatment less than 3 months, and previous dialytic treatment or kidney transplantation. The dialysis modality performed (Hf-HD vs Ol-HDF), the modality of infusion (pre-dilution or post-dilution) and mean total convective volume (replacement fluid volume + ultrafiltration) during last year's dialysis session in Ol-HDF were analyzed for each patient.

Results: During observation 677 patients started HD treatment. 70 patients were excluded due to less than 3 months HD treatment. 607 patients (male 390, 64%) were analyzed. 467 pts (77%) were treated with Hf-HD, 103 pts (17%) with Ol-HDF, 36 pts (6%) with AFB. Median duration of HD treatment was 2.6 years (IQR 1.3; 4.7). Ol-HDF was performed in post-dilution mode in 60% of cases (total convective volume 25±4 L); pre-dilution mode was used in 40% of the cases (total convective volume 51±18 L). Patients in the Ol-HDF group were significantly younger than those in Hf-HD and AFB groups (respectively 59±15 years vs 71±15 vs 78±9, p <0.05), and had less diabetes, hypertension and ischemic heart disease (p<0.05) while presenting similar prevalence of cirrhosis (p=0.93) and peripheral vascular disease (p=0.09). Adequacy indices were similar between groups (eKt/V 1.39±0.02 vs 1.41±0.01 vs 1.44±0.04, p=0.47) as well as the protein intake (PCRn 0.92±0.01 vs 0.93±0.01 vs 0.90±0.03 g/Kg/d, p=0.69) and residual renal function (1.5±0.3 vs 1.6±0.1 vs 0.8±0.4 ml/min, p=0.20). Patients on Ol-HDF more frequently had an AV fistula (71% vs 58% vs 59%, p<0.05). At the end of follow-up, 12% of patients had undergone kidney transplantation, 42% continued dialytic treatment while 43% died. Univariate analysis showed a better survival for Ol-HDF patients (Figure 1) (p <0.05). This benefit was confirmed in multivariate analysis (Figure 2) showing that older age, cirrhosis and ischemic heart disease negatively affect survival, while a high protein intake, use of an AV fistula and Ol-HDF (HR 0.43[0.30-0.61]) are protective.

Conclusions: The use of Ol-HDF is associated with better survival compared to Hf-HD. This is confirmed after adjustment for demographic and comorbidities of the patients, characterizing Ol-HDF as an independent predictor of better survival.

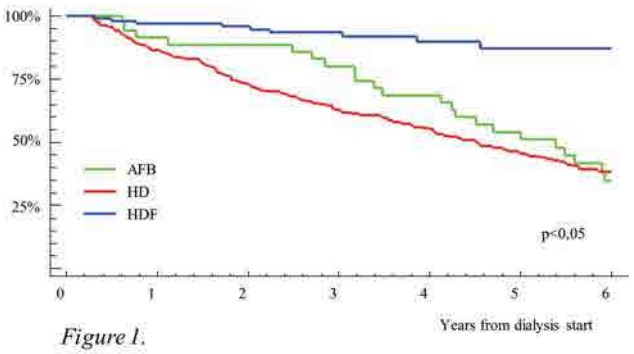


Figure 1.

	HR	Lower limit	Upper Limit	p
PCRn	**0,33**	0,22	0,48	<0.05
Age	**1,03**	1,02	1,04	<0.05
Cirrhosis	**1,60**	1,26	2,03	<0.05
HDF	**0,43**	0,30	0,61	<0.05
AV Fistula	**0,64**	0,55	0,75	<0.05
Coronary artery disease	**1,69**	1,42	2,00	<0.05

Figure 2.

	HR	Lower limit	Upper Limit	p
PCRn	**0,33**	0,22	0,48	<0.05
Age	**1,03**	1,02	1,04	<0.05
Cirrhosis	**1,60**	1,26	2,03	<0.05
HDF	**0,43**	0,30	0,61	<0.05
AV Fistula	**0,64**	0,55	0,75	<0.05
Coronary artery disease	**1,69**	1,42	2,00	<0.05

Figure 2.

Figure:

TO015

INTRADIALYTIC ON-LINE MULTICOMPONENT TOTAL REMOVED SOLUTE MONITORING IN SPENT DIALYSATE BY A NOVEL MINIATURIZED OPTICAL SENSOR

Annika Adoberg[1], Joosep Paats[2], Jürgen Arund[2], Liisi Leis[1], Kristjan Pilt[2], Ivo Fridolin[2], Merike Luman[1,2]

[1]North Estonia Medical Centre, Nephrology Centre, Tallinn, Estonia and [2]Tallinn University of Technology, Department of Health Technologies, Tallinn, Estonia

Background and Aims: Urea is the most commonly exploited marker of dialysis adequacy. Plenty of other uremic retention solutes with a deleterious effect on morbidity and mortality of uremic patients accumulate in ESKD patients [1]. Commonly, the uremic solutes are divided into three physicochemical types [2] with the representative markers urea, uric acid (UA),indoxyl sulfate (IS), and β2-Microglobulin (B2M). Optical monitoring of the uremic marker molecules has been proposed [3]. Despite being cumbersome as a clinical routine, direct dialysis quantification from total dialysate collection (TDC) is as the 'gold standard' for measuring the total amount of uremic solutes removed [4]. A robust and compact optical on-line dialysis monitoring device is a step closer to automatic assessment of removal of uremic toxins in dialysis.

The aim of this study was to evaluate intradialytic on-line multicomponent Total Removed Solute (TRS) monitoring in the spent dialysate by a novel miniaturized optical sensor during hemodialysis (HD) and hemodiafiltration (HDF) with different settings.

Method: Ten ESKD patients (6 male and 4 female, 60.2±16.8 years) on chronic HDF were enrolled into the study (fistula N=9, graft N=1). For each patient 5 midweek dialysis sessions (length 240min, HD: N=1, Qb=200ml/min, Qd=300ml/min, 1,5m^2; HDF: N=4, Qb≥300ml/min, Qd≥500ml/min, Vsubst≥15l, 1,8m^2 and 2,2m^2) were included. Spent dialysate from the drain was monitored on-line by a miniaturized sensor prototype (Optofluid Technologies OÜ, Estonia). For the reference, the samples from the spent dialysate drain tube of the HD machine were taken as 7, 60, 120 and 180min after the start and at the end of the session (240min). The concentrations of urea and B2M in dialysate were determined in the clinical laboratory. Concentration of IS and UA was determined utilizing the HPLC. TRS values were calculated using the tank weight and the lab or optical tank solute concentrations. t-test was used to determine significant differences between the methods (P≤0.05).

Results: The laboratory and optical TRS values were 489±112mM and 512±87mM for urea (R2=0.870), 4232±712μM and 4331±756μM for UA (R2=0.985), 230±47mg and 231±40mg for B2M (R2=0.906), 606±339μM and 616±321μM for IS (R2=0.969) (Fig. 1), being not statistically different for any uremic solutes. The reason for higher correlation for UA and IS is direct measurements of UA and IS by the optical sensor whereas urea and B2M are estimated indirectly.

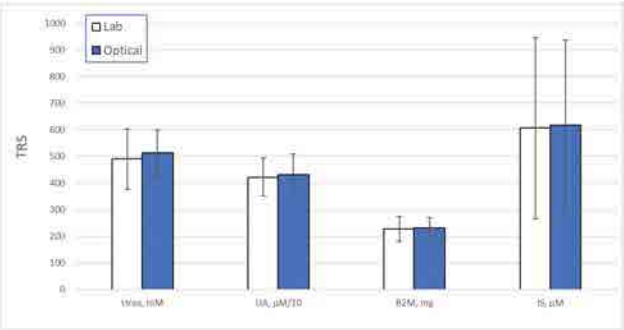


Figure 1. Laboratory and optical TRS values.

Conclusion: Novel miniaturized optical sensor successfully carried out intradialytic on-line multicomponent TRS monitoring for the uremic solutes urea, UA, B2M and IS in the spent dialysate.

OUTCOME AFTER AKI

TO016 MAJOR ADVERSE CARDIOVASCULAR OUTCOMES FOLLOWING ACUTE KIDNEY INJURY: AN OBSERVATIONAL COHORT STUDY

Samira Bell[1], Moneeza Siddiqui[1], Nicosha De Souza[1], Ewan Pearson[1], Colin Palmer[1]

[1]*University of Dundee, Division of Population Health and Genomics, Dundee, United Kingdom*

Background and Aims: Acute kidney injury (AKI) is associated with adverse long term outcomes such as increased mortality. It is unclear however whether the increased mortality is due to cardiovascular events. The aim of this study was to examine major adverse cardiovascular events (MACE) following AKI in a population cohort in Scotland (GoDARTS) specifically examining a "low risk" younger age group without previous cardiovascular events.

Method: An observational cohort study of people in Tayside & Fife (Scotland, UK) recruited into GoDARTS from December 1998 to July 2017 was performed. Data were linked between the following datasets: population demography files, Scottish Morbidity Record of hospital admissions (SMR01); biochemical laboratory results, medicines dispensed by community pharmacies, the Scottish Care Initiative-Diabetes Collaboration (SCI-DC), the Scottish Renal Registry (SRR) and Scottish death registry data held by the Scottish General Records Office (GRO). AKI was defined using the creatinine based Kidney Disease Improving Global Outcomes (KDIGO) definition. MACE events were defined as hospitalisations or death due to myocardial infarction, ischaemic stroke, or coronary artery disease using International Classification of Diseases codes. Follow-up began at the time of first AKI occurrence for cases, and first recorded creatinine measurement for controls. Analyses were restricted to those who were 45 years or younger at the start of follow-up and who had no history of MACE. Survival analyses were performed using cox models adjusted for sex, age, CKD stage at baseline, Scottish index for multiple deprivation, medication use and diabetes. A forward step-wise method was used for variable selection. Analyses stratified by type 2 status were also performed.

Results: Data were available for 18,163 individuals in GoDARTS of which 15,884 individuals had creatinine measurements which could be used to classify whether an AKI event occurred. Of these, 6534 had at least one AKI event and 8807 never had an event. AKI was associated with more than two-fold increase in risk of MACE, independent of age, sex, type 2 diabetes, deprivation, anti-hypertensives, prior MACE and baseline renal function, HR 2.10 (1.90, 2.26), $p<0.0001$. On limiting the cohort to individuals under 45 years with no prior MACE this association persists, HR 1.95 (1.49, 2.55), $p<0.0001$. When stratified by diabetes status using the same model the effect persisted in both groups. In low risk non-diabetics, the hazards of MACE were 2.59 times higher for AKI cases (95%CI:1.28,5.24 $p<0.0001$), while in low risk diabetics the hazards were 1.83 times higher for AKI cases (95%CI:1.27,2.44 $p<0.0001$).

Conclusion: AKI is associated with significantly increased risk of prospective MACE with a two-fold increase when adjusted for age, prior MACE, baseline renal function, type 2 diabetes, deprivation and blood pressure. In a low-risk group (relatively younger and with no prior MACE), this risk persists. It is unclear whether AKI leads to CV events or AKI is more likely in this population but this finding highlights that cardiovascular risk reduction in patients following AKI is vital.

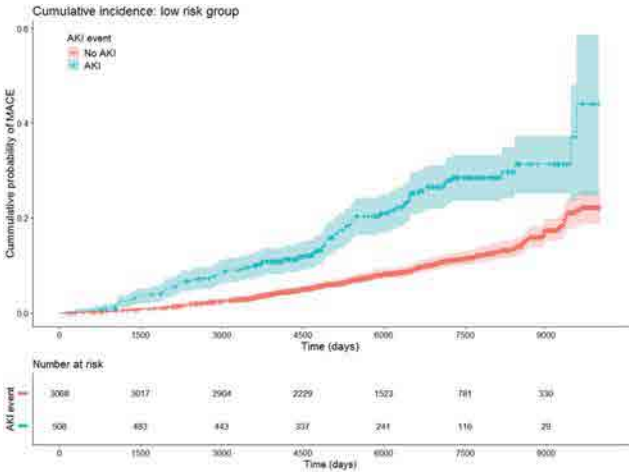


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TO017

CLINICAL CHARACTERISTICS AND INDEPENDENT PREDICTORS OF CHECK POINT INHIBITORS-ASSOCIATED AKI: WHAT DO WE KNOW?

Mónica Bolufer[1], Clara Garcia Carro[1], Roxana Bury[1], Eva Muñoz[2], Enriqueta Felip[2], Alejandra Gabaldon[3], Maria Jose Carreras[4], Daniel Seron Micas[1], María José Soler[5]

[1]Vall Hebron Hospital, Nephrology, Barcelona, Spain, [2]Vall Hebron, Oncology, Barcelona, Spain, [3]Vall Hebron, Pathological anatomy, Barcelona, Spain, [4]Vall Hebron, Pharmacy, Barcelona, Spain and [5]Vall DHebron, Nephrology/PI17/00257, Spain

Background and Aims: Checkpoint inhibitors (CPI) are used to treat solid organ malignancies. CPI–associated acute renal injury (AKI) is an adverse effect of these therapies and its incidence is 13-29%. Clinical data on this complication is scarce. The aim of our study is to define clinical characteristics and risk factors of CPI-associated AKI.

Method: Clinical and demographic data of all patients receiving immunotherapy between March 2018 and May 2019 at our center were evaluated. Patients were divided into two groups depending on the development of AKI during the study period. AKI was defined according to AKIN classification. We compared clinical and demographic characteristics between these two groups and patients who developed mild AKI and severe AKI.

Results: During the study period, 821 patients received CPIs. Mean age 62.03±12.06 years and 486(59.2%) men. Malignancies were lung in 249 (30.3%), urogenital tract in 168 (20.5%), melanoma in 89 (10.8%) and others in 315 patients (38.4%). 446(54.3%) patients received anti-PD1, 230(28%) anti-PDL1, 13 (1.6%) anti-CTLA4, 36 (4.4%) received other drug and 96(11.7%) were treated with both anti-CTLA4 and anti-PD1 or anti.PDL1. Baseline creatinine was 0.85±0.30 mg/dL and 188 (22.9%) patients presented creatinine>1 mg/dL before starting CPI.

125 patients (15.2%) developed AKI during the study period, 85(68%) men and mean age 65.1±10.7 years. Baseline creatinine of these patients 0.97±0.45 mg/dL and 44 (35.2%) presented basal creatinine>1mg/dL. Mean creatinine at the diagnosis of AKI 2.27±1.34 mg/dL and two patients required haemodialysis. Leukocyturia was present in 21 patients(16.8%) and haematuria in 12 (9.6%). 5 patients presented AKI secondary to obstructive uropathy. Mean time from CPI initiation to AKI was 5.6±5.8 months. Of those 125 patients, 23 (18.4%) were referred to Nephrology and 9 (7.2%) underwent kidney biopsy. 1 patient presented endocapillar proliferative non-CPI related glomerulonephritis and 8 (6.4%) acute tubule-interstitial nephritis (ATIN). 23 (18.4%) patients were treated with corticosteroids. Mean creatinine at 6 months after AKI was 1.04±0.34 mg/dL (data from 45 patients) and 40 patients (data from 45 patients) showed complete recovery of kidney function at 6 months. Patients who developed a severe AKI stage 2 or 3 were more frequently women (41.8% vs 24.3%, p=0.03), had lower basal creatinine (0.86±0.25 vs 1.06±0.54 mg/dL, p=0.0130), showed and increased latency from CPI initiation to AKI (6.9±6 vs 4.5±5.5 months, p=0.0267) and presented worse recovery of kidney function at 6 months than patients with AKI stage 1(creatinine 6 months 1.18±0.40 mg/dL, p=0.0398 and complete recovery of kidney function at 6 months 70.5% vs 93.3%, p=0.0353). There was no association between the severity of AKI and type of CPI and type of malignance.

When comparing patients who developed AKI with patients whit patient who did not, patients with AKI were older (65.1±10.7 vs 62.03±12.06 years old, p=0.0017), more frequently men (68% vs 57.9%), p=0.0296) and presented higher baseline creatinine (0.97±0.45 vs 0.85±0.30 mg/dL, p<0.0001), as well as more frequently a baseline creatinine > 1 mg/dL (35.2% vs 20.7%, p=0.0004). Type of CPI and type of malignance were not associated with the presence of AKI. Older age (OR 1.020, CI 95% 1.002-1.038) and baseline creatinine (OR 3.293, CI 95% 1.678-6.461) were identified as independent predictors of AKI development in our CPI treated patients

Conclusion: CPI-associated AKI incidence in our centre is 15.2%. Of them, 44% developed severe AKI. Only 18.4% were referred to a nephrologist and kidney biopsy performed in 7.2%. ATIN was the most common diagnosis. 18.4% received corticosteroids. Older age and higher baseline creatinine were identified as independent predictors for AKI development in patients with cancer CPI-treated. Patients developing a severe AKI showed worse kidney function at 6 months.

TO018

ACUTE KIDNEY INJURY IDENTIFICATION: USE OF ELECTRONIC AKI ALERTS VERSUS ELECTRONIC HEALTH RECORDS IN HOSPITAL EPISODE STATISTICS

Manuela Savino[1], Anna Casula[1], Esther Wong[1], Nitin Kolhe[3], James Medcalf[1,5], Dorothea Nitsch[6,7,8]

[1]UK Renal Registry, Bristol, United Kingdom, [3]Royal Derby Hospital, United Kingdom, [5]Leicester General Hospital, United Kingdom, [7]London School of Hygiene & Tropical Medicine, United Kingdom and [8]Royal Free London NHS Foundation Trust, United Kingdom

Background and Aims: Acute kidney injury (AKI) refers to an abrupt decline in the glomerular filtration rate (GFR) which may be associated with significant morbidity and mortality. Since April 2015, an automated real-time electronic alert system for AKI has been introduced and progressively implemented in England, with alert data being sent to the UK Renal Registry (UKRR) for collection into a master patient index (MPI). Historically, the only way to routinely measure AKI incidence in hospital was to analyse the Hospital Episode Statistics (HES). The introduction of the MPI allows for the first time a comparison between warning-test score defined AKI and clinical coding. This project aims to determine whether episodes of AKI identified in the UKRR MPI correspond to coded diagnoses on the discharge record held in HES.

Method: The UKRR MPI of all AKI electronic alerts (AKI stages 1, 2 and 3) in patients ≥18 years of age, between 01/01/2017 and 31/12/2017 were linked to HES data to identify a hospitalised AKI population. Descriptive analyses were conducted to describe the demographics and to investigate whether those with electronic AKI alert also had an International Classification of Diseases (ICD)-10 code for AKI (N17) in HES.

Results: From 01/01/2017 to 31/12/2017, 301,504 hospitalised adults received an AKI electronic alert. AKI severity was positively associated with the percentage of AKI alerts which were coded in HES. There was also a significant variation in HES coding between hospitals, but generally, variation was most pronounced for AKI stage 1, with a mean of 48.2% [SD 14], versus AKI stage 3, with a mean of 83.3 % [SD 7.3] (figures 1, 2 and 3). There was an inverse trend with age in that younger adults AKI staging warning scores were less often coded in HES and this was true for all the three AKI stages (33% of AKI episodes coded in HES for people aged 18-29 versus 64% for people ≥ 85 years old) (Table 1).

Conclusion: In 2017, earlier stages AKI warning scores were poorly coded in HES. There was also high degree of inter-hospital variability, particularly for AKI warning score 1, reflecting potentially poor clinical recognition and documentation in medical record and subsequent clinical coding. AKI warning scores were poorly captured in HES for younger adults in comparison to those of older age; reasons for which need to be identified. Use of HES to identify cases of AKI is likely to underestimate the incidence of AKI, especially for AKI stage 1, though a high proportion of the most severe cases will be captured.

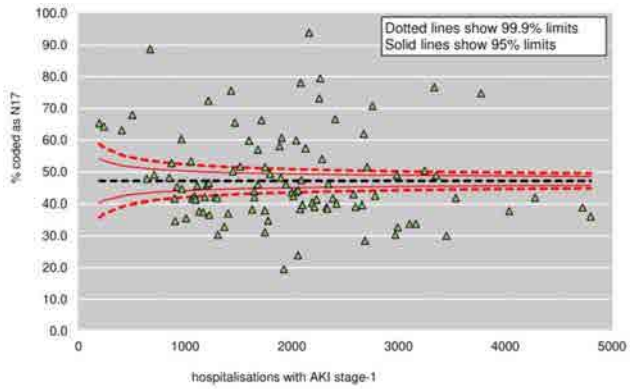


Figure 1: Percentage of peak AKI stage 1 electronic alerts in 2017 validated in HES using code N17, by hospital

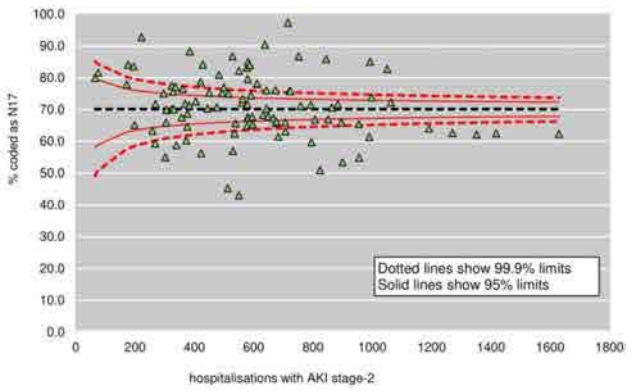


Figure 2: Percentage of peak AKI stage 2 electronic alerts in 2017 validated in HES using code N17, by hospital

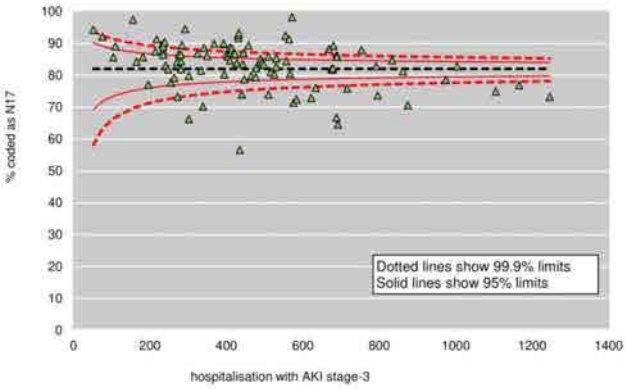


Figure 3: Percentage of peak AKI stage 3 electronic alerts in 2017 validated in HES using code N17, by hospital

TO019

PROGNOSTIC VALUE OF ACUTE KIDNEY INJURY AND HEMOCONCENTRATION DURING ACUTE HEART FAILURE

Yannis Lombardi[1,2], Franck Boccara[2], Kadiatou Baldet[3], Stéphane Ederhy[2], Pascal Nhan[2], Quentin Riller[4], Marion Chauvet-Droit[2], Marie-Liesse Jean[2], Saroumadi Adavane-Scheuble[2], Loris Azoyan[5], Ariel Cohen[2]

[1]Assistance Publique - Hôpitaux de Paris, Nephrology resident, Paris, France, [2]Assistance Publique - Hôpitaux de Paris, Hôpital Saint-Antoine, Department of Cardiology, Paris, France, [3]Centre Hospitalier Universitaire de Dijon Bourgogne, Department of Nephrology, Dijon, France, [4]Assistance Publique - Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Department of Internal Medicine, Paris, France and [5]Assistance Publique - Hôpitaux de Paris, Hôpital Tenon, Department of Internal Medicine, Paris, France

Background and Aims: Acute kidney injury (AKI) occurring after diuretic treatment initiation for acute heart failure (AHF) is a common phenomenon, with an incidence estimated between 20 and 50% of AHF hospitalizations. Previous studies found that persistent AKI is associated with poor prognosis. Treatment-induced hemoconcentration is associated with improved prognosis, but several definitions previously used are not suited for clinical practice. Transient AKI, with or without hemoconcentration, is of unsettled prognosis. We aim to determine the independent prognostic value of transient AKI, persistent AKI and hemoconcentration in the context of AHF hospitalization, using practical definitions.

Method: Data were obtained from the Greater Paris University Hospitals (GPUH) Clinical Data Warehouse. Patients hospitalized for AHF in various GPUH units were included. AHF hospitalization was defined as hospitalization with at least one AHF ICD-10 code and at least one recorded furosemide administration. Bumetanide is rarely used in GPUH hospitals hence it was not considered. AKI in a period of 14 days following first furosemide administration was defined based on KDIGO guidelines. Hemoconcentration was defined as an increase in serum proteins $\geq$ 5 g/l during the same period. Multivariate logistic regression was performed to determine which characteristics were predictive of AKI. Cox regression of 100 days all-cause mortality using multiple confounders was performed to determine the prognostic value of transient AKI ($<$ 14 days), persistent AKI ($\geq$ 14 days) and hemoconcentration. Patients with AKI upon hospital entry were excluded from regression analyses. AKI and hemoconcentration were treated as time-dependent covariates to adjust for immortality bias.

Results: Five hundred seventy nine patients were included. Among them, 529 had no AKI upon hospital entry and 513 had at least one recorded serum proteins and creatinine value following furosemide initiation. Median follow-up was 114 days. AKI in a period of 14 days following furosemide initiation occurred in 234 patients (40.4%). At baseline, patients in the AKI group more frequently suffered from chronic kidney disease or presented with clinical and echocardiographic signs of right heart failure. Independent predictors of AKI were arterial hypertension upon furosemide initiation (adjusted OR 1.86 [1.08 – 3.22]), elevated serum creatinine upon furosemide initiation (adjusted OR 1.07 [1.01 – 1.14] per 10 µmol/l increase) and initial intravenous administration of furosemide (adjusted OR 2.42 [1.39 – 4.29]). Death during follow-up occurred in 35% of patients in the AKI group compared to 21% in the non-AKI group ($p < 0.001$). In multivariate analysis, persistent AKI was independently associated with increased mortality in a period of 100 days following furosemide initiation (adjusted HR 2.31 [1.07 – 4.99]). Transient AKI was not significantly associated with mortality (adjusted HR 0.64 [0.34 – 1.19]). Hemoconcentration was independently associated with decreased mortality (adjusted HR 0.46 [0.27 – 0.79]).

Conclusion: After furosemide initiation during hospitalization for AHF, persistent AKI ($\geq$ 14 days) was independently associated with increased 100 days mortality. Hemoconcentration, using a definition suited for clinical practice ($\geq$ 5 g/l increase in serum proteins), was independently associated with decreased 100 days mortality. No significant association was found between mortality and transient AKI ($<$ 14 days). Those findings show that laboratory tests at a limited cost – serum proteins and creatinine – are helpful to evaluate treatment response and mortality risk during AHF. Prospective randomized controlled trials are needed to establish diuretic strategies based on both AKI and hemoconcentration.

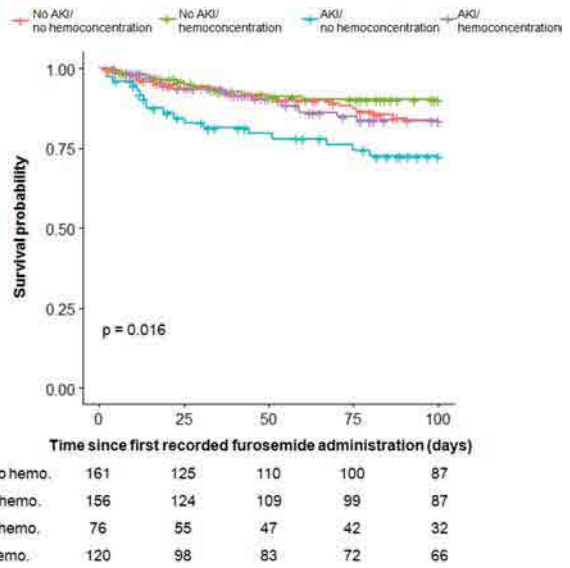


Figure. Kaplan-Meier curves of 100 days survival following the first in-hospital furosemide administration in the context of acute heart failure.

TO020

POTENTIAL INTERPRETATIONS OF CRITERIA FOR AKI BY AUTOMATED DECISION SUPPORT ALGORITHMS: IMPACT ON AKI INCIDENCE

Jill Vanmassenhove[1], Johan Steen[1], Johan Decruyenaere[2], Dominique Benoit[2], Eric Adriaan J. Hoste[2], Wim Van Biesen[1]

[1]Ghent University Hospital, Renal Division, Gent, Belgium and [2]Ghent University Hospital, Intensive Care Unit, Gent, Belgium

Background and Aims: The reported incidence of Acute Kidney Injury (AKI) at the intensive care unit (ICU) is variable. Although the Kidney Disease Improving Global Outcome (K-DIGO) improved harmonisation of this definition, there is remaining variability in the actual implementation of this AKI definition, with variable interpretation of the urinary output (UO) criterion, and of the baseline serum creatinine (Screa) criterion. This hampers progress of our understanding of the clinical concept AKI and leads to confusion and unclarity when interpreting models to predict AKI or associated outcomes. With the advent of big data and artificial intelligence based decision algorithms, this problem will only become more of interest, as the user will not know what exactly the construct AKI in the application used means and represents. Therefore, we intended to explore the impact of different interpretations of the Screa and the UO criterium as presented in the K-DIGO definition on the incidence of AKI stage 2.

Method: We included all patients of an electronic health data system applied in a tertiary ICU between 2013 and 2017. Sequential Organ Failure Assessment (SOFA) score was calculated, and gender, age, weight and mortality at ICU and in hospital were extracted. All serum creatinine (sCrea) values during ICU stay and hospitalisation were extracted, as were UO data, with their time stamps. In addition, all available Screa data up to 1 year before ICU admission were retrieved from a dataset external to the ICU. AKI was defined according to KDIGO stage 2, using different possible interpretations of the Screa and/or the UO criterion. For the evolution of Screa as compared to a baseline value, we sued either a value directly available to ICU staff (def 1), a presumed eGFR of 75ml/min (def 2), the first available value after admission to ICU (def 3), the lowest value during the current hospitalisation before ICU admission (def 4), the lowest value before the hospitalisation episode as found in an external dataset (def 5). For the UO criterion, we also applied two criteria in line with K-DIGO stage 2: a UO below 6ml/kg during a 12 hour block (def 6) or a UO below 0.5ml/kg/hour during each of 12 consecutive one hour intervals (def 7). Def 8 identified patients who did not comply with any of the definitions (1-7), so who had no AKI according to any definition. Definition 9 and 10 identified patients who complied with at least one out of the Screa criteria 1-5 (def 9) or out of the UO criteria (def 10). Definition 11 identified patients who complied both with at least one Screa and one UO criterium.

Results: Our dataset included 16433 ICU admissions (34.7% female, age 60.7±16.4 years). Overall, 8.1% of patients died at ICU, and another 5.2% during their hospitalisation. The SOFA score at admission was 6.9±4.1. The incidence of AKI according to the stage 2 definition of K-DIGO varied according to the interpretation of the diagnostic criteria from 4.3% when baseline creatinine was defined as the first ICU value, to 35.3% when the UO criterium was interpreted as a UO below 6ml/kg over a 12 hour block (fig). Only half of patients (53.7%) did not comply with any of the definitions (def 8), 10.9% and 19.7% complied with one of the Screa (def 9) OR one of the UO criteria (def 10) respectively, and 15.7% complied with both (def 11). There was substantial reclassification across the different definitions.

Conclusion: Unclarity on the actual interpretation of the Screa and UO criteria used in the K-DIGO definition of AKI leads to substantial differences in incidence of AKI, and also with substantial reclassification according to different definitions. This is especially concerning in an era of big data and automated decision support, as clinicians might not know which construct of AKI is actually being represented.

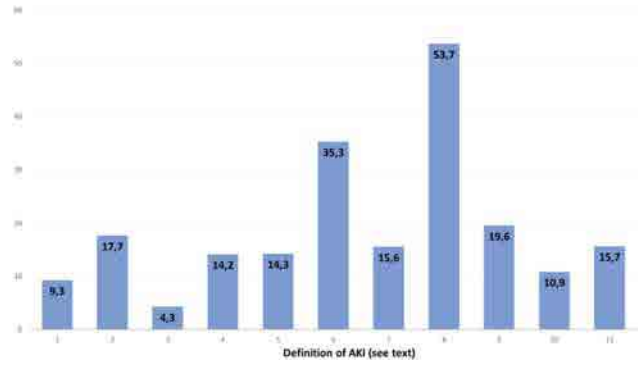


Figure:

TO021

LONG-TERM OUTCOMES OF COMMUNITY- VERSUS HOSPITAL-AQUIRED ACUTE KIDNEY INJURY: A RETROSPECTIVE ANALYSIS OF A LARGE COHORT IN A GERMAN TERTIARY CARE CENTER.

Dmytro Khadzhynov[1], Danilo Schmidt[1], Kai-Uwe Eckardt[1], Kai M. Schmidt-Ott[1]

[1]*Charite Universitaetsmedizin Berlin, Department of Nephrology and internal Intensive Care Medicine, Berlin, Germany*

Background and Aims: This study compared epidemiology, short- and long-term outcomes for patients with community-acquired (CA) and hospital-acquired (HA) acute kidney injury (AKI).

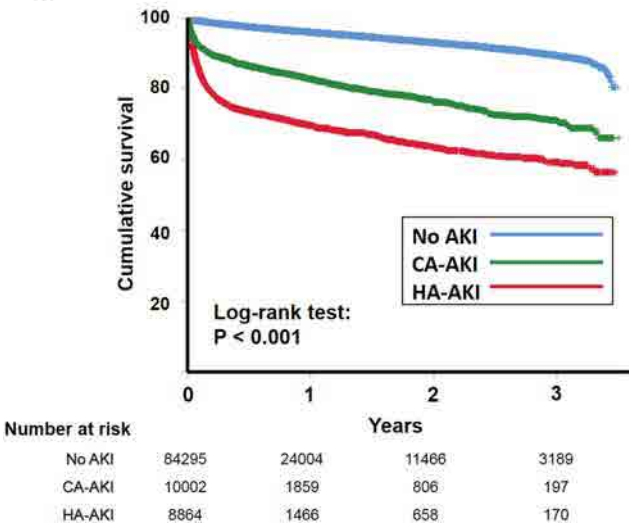
Method: We retrospectively analyzed all episodes of AKI over a period of 3.5 years (2014–2017) on the basis of routinely obtained serum creatinine measurements in 103,161 patients whose creatinine had been measured at least twice and who had been in the hospital for at least two days. We used the "Kidney Disease: Improving Global Outcomes" (KDIGO) criteria for AKI and analyzed the first hospital admission. A total of 103161 were admitted in hospital and fulfilled the inclusion criteria. Average observation period per patient was 248 days.

Results: The incidence of CA-AKI among included hospital admissions was 9.7% compared with an incidence of 8.6% of HA-AKI, giving an overall AKI incidence of 18,3%. Patients with CA-AKI were younger than patients with HAAKI (64 vs 66,2y) and had significantly less comorbidities, including preexisting cardiac failure, ischemic heart disease, hypertension, diabetes. Patients with CA-AKI were more likely to have stage 1 AKI (69,3 vs 58,4%, $p<0.001$) and had significantly shorter lengths of hospital stay than patients with HA-AKI (14 vs 24d, $p<0.001$).

Those with CA-AKI had better survival than patients with HA-AKI (Figure 1; $p<0.001$). Patiens with CA-AKI were less likely dialysis dependent before discharge (1,9 vs 4,8% in HA-AKI; $p<0.001$) Patients with HA-AKI received more often administrative coding of AKI (29,3% vs 26,5% in CA-AKI patients; $p<0.001$)

Conclusion: Patients with CA-AKI sustain less severe AKI than patients with HA-AKI, accordigly showing better short- and long-term outcomes. However, patiens with CA-AKI are at risk of inadequate clinical perception of AKI.

Figure 1



Number at risk				
No AKI	84295	24004	11466	3189
CA-AKI	10002	1859	806	197
HA-AKI	8864	1466	658	170

Figure 1. Patients survival

Nephrology Dialysis Transplantation 35 (Supplement 3): iii203–iii217, 2020
10.1093/ndt/gfaa143

MODERATED POSTER SESSION 1

P0013 **MAP KINASES-REGULATED PROTEINS IN SIGNALING PATHWAYS OF VASOPRESSIN IN KIDNEY COLLECTING DUCT**

Hyo-Ju Jang[1], Hyun Jun Jung[2], Si-Yoon Han[1], Hyo-Jung Choi[1], Eui-Jung Park[1], Hye-Jeong Park[1], Tae-Hwan Kwon[1]

[1]School of Medicine Kyungpook National University, Department of Biochemistry and Cell Biology, Daegu, Korea, Rep. of South and [2]Johns Hopkins University School of Medicine, Division of Nephrology Department of Medicine, Baltimore, United States of America

Background and Aims: Activation of G protein-coupled vasopressin V2 receptor (V2R) is critical in water and electrolyte transport in the kidney collecting duct (CD) cells. Stimulation of V2R affects several downstream pathways, including PKA, PI3K/AKT, Wnt, and Ca^{2+}/calmodulin. Previous studies have shown that MAP kinases are also involved as an apparent downstream signaling pathway of V2R. However, the role of MAP kinases and their substrate proteins in the vasopressin signaling, including the regulation of AQP2 expression and phosphorylation, are unclear. In the present study, substrates of MAP kinases were identified using bioinformatic analyses, and they were mapped on the downstream signaling pathways of V2R. Tripartite motif-containing protein 28 (TRIM28) was identified as a substrate of ERK1 as well as a vasopressin-responsive protein *via* bioinformatic tools. We further evaluated whether TRIM28 plays a role in vasopressin-mediated regulation of AQP2 in the kidney CD.

Method: To identify comprehensive substrates of MAP kinases in the kidney CD, we investigated 1) the expression of MAP kinases in CD cells by use of databases based on high-throughput profiles of transcriptome and proteome (http://hpcwebapps.cit.nih.gov/ESBL/Database/index.html); and 2) MAP kinases substrates expressed in the CD cells by use of protein phosphorylation databases (PhosphoNetworks and RegPhos 2.0). The identified substrates were mapped on the downstream signaling of V2R. Cellular and subcellular localization of selected substrate protein (TRIM28) was examined by immunohistochemistry. The role of TRIM28 in vasopressin-mediated AQP2 regulation was examined by quantitative real-time PCR (qRT-PCR) and semiquantitative immunoblotting after RNA interference of TRIM28 in mpkCCDc11 cells.

Results: Immunoblotting of mpkCCDc11 cells revealed that both p-ERK1/2 and pS261-AQP2 expression was decreased in response to dDAVP (10^{-9} M) stimulation. *In silico* analyses demonstrated that five MAP kinases (ERK1, ERK2, ERK3, JNK2, and MAPK p38 alpha) were identified as the MAP kinases expressed in kidney CD cells. Based on several protein kinase-substrates databases, 189 proteins were identified as the substrates of the five MAP kinases. In particular, sequential data mining revealed TRIM28, as the substrate of ERK1, has the only one phosphorylation site which was down-regulated by vasopressin stimulation. Since TRIM28 is a transcription cofactor and also a ubiquitin-protein E3 ligase, we examined whether TRIM28 is involved in the regulation of AQP2 expression as a mediator of MAP kinases action. Immunofluorescence labeling of mouse and rat kidneys revealed that TRIM28 was exclusively expressed in the nuclei of the tubular epithelial cells, including CD cells. dDAVP-induced AQP2 mRNA and protein up-regulation was significantly attenuated in mpkCCDc11 cells with siRNA-mediated knockdown of TRIM28.

Conclusion: We identify MAP kinase substrates in the kidney CD, which are mapped on the downstream signaling pathways of V2R. TRIM28 is identified as a substrate of MAP kinases that involves in vasopressin signaling pathways. TRIM28 is likely to play a role in the regulation of AQP2 expression, particularly in the AQP2 transcription.

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P0029

GLUCOSYLCERAMIDE SYNTHASE INHIBITION PRESERVES MITOCHONDRIAL FUNCTION AND REDUCES REACTIVE OXYGEN DAMAGE IN THE JCK MOUSE MODEL OF POLYCYSTIC KIDNEY DISEASE

Tyler Picariello[1], Kelly Rogers[1], Laurie Smith[1], Christina Bracken[2], Nickolay Bukanov[3], Oxana Ibraghimov-Beskrovnaya[1], Thomas Natoli[1]

[1]Sanofi-Genzyme, Rare and Neurological Disease Research, Framingham, United States of America, [2]Twentyeight-Seven Therapeutics, Watertown, United States of America and [3]Janssen Research and Development, Boston, United States of America

Background and Aims: Polycystic kidney disease (PKD) is characterized by the formation and progressive growth of renal cysts ultimately leading to end-stage renal disease (ESRD). Previous work has shown that treatment of PKD mouse models with a glucosylceramide synthase inhibitor (GCSi) inhibits glycosphingolipid metabolism and blocks disease progression. Clinical trials to determine the efficacy of GCSi treatment for ADPKD are currently ongoing.

ADPKD patient kidneys, as well as kidneys from *in vivo* mouse models of PKD, display defects in mitochondrial morphology and function, leading to reactive oxygen species (ROS) generation. Functional defects include decreased fatty acid oxidation and increased glycolysis that can promote cellular proliferation. To determine if glucosylceramide synthase inhibition ameliorates mitochondrial dysfunction, we assessed the impact of GCSi treatment on mitochondrial formation and function in the *jck* mouse model of PKD.

Method: Twenty-six-day old WT or *jck* mice were treated with vehicle or 60 mg/kg GCSi (Genz667161) in feed for 38 days prior to tissue harvest. Kidney mRNA expression was measured using RT-PCR. Kidney protein levels were measured by western blot. Mitochondrial DNA content was measured using real-time PCR. Oxidized DNA was detected by immunohistochemistry using anti-8OHdG antibodies. Oxidized proteins were measured using the Oxyblot system (manufacturer).

Results: Reduced cystogenesis following GCSi treatment was associated with preserved mitochondrial number in *jck* mice as evidenced by increased levels of mitochondrial DNA, increased mitochondrial proteins (Tom20, VDAC, SirT3, and MT-Co1), and elevated mRNA expression (*Nd3*, *Cox3*, and *Atp8*). Stabilization of mitochondrial number was accompanied by activation of pathways that promote mitochondrial biogenesis, including increased PGC1α protein and *Ppargc1a* and *Tfam1*. Downregulation of several antioxidant genes (*Gpx6*, *Gstk1*, *Prdx3*, and *Sod2*) were observed in untreated *jck* samples. Consistent with this, levels of oxidized DNA and oxidized proteins were increased in untreated *jck* samples. Treatment with GCSi partially reversed the downregulation of antioxidant genes and decreased the levels of oxidized DNA and proteins to near WT levels in *jck* tissues.

We then compared the *jck* model to tissues derived from ADPKD patients. Western blots demonstrate a reduction in electron transport chain (CxI-CxV) and mitochondrial outer-membrane markers in both untreated *jck* and ADPKD samples compared to controls. Similarly, the mitochondrial genes *Nd1*, *Nd2*, *Cox2*, and *Atp6* were reduced in untreated *jck* kidneys and ADPKD samples relative to controls. As previously mentioned, we observed a generalized loss of antioxidant gene expression in untreated *jck* kidneys. Consistent with this, there were increased levels of both oxidized DNA and oxidized protein in untreated *jck* samples; this increase in DNA and protein oxidation was mirrored in ADPKD patient samples.

Conclusion: Mitochondrial number and function were reduced in both untreated *jck* mouse kidneys and human ADPKD samples. Increased oxidative stress, as evidenced by increased levels of oxidized DNA and proteins, is evident in both *jck* and ADPKD tissues. *In vivo* treatment with a GCSi effectively reversed the observed increase in oxidative stress and inhibited disease progression in the *jck* model of ADPKD. Our data demonstrate that reduced kidney cyst growth following GCSi treatment is associated with preserved mitochondrial formation and function.

P0030 **MIR-182 INHIBITS KIDNEY FIBROSIS BY REGULATING TGF-B1/SMAD3 PATHWAY IN ADPKD**

Liping Sun[1,1], Xinzhou Zhang[1]

[1]*Key Renal Laboratory of Shenzhen, Department of Nephrology, Shenzhen, P.R. China*

Background and Aims: The aim of the present study was to investigate the molecular mechanism of miR-182 in kidney fibrosis in polycystic kidney disease (PKD).

Method: We measured the expression of miR-182 in kidney tissue of autosomal dominant polycystic kidney disease (ADPKD). Additionally, we investigated the relationship between miR-182 and fibrotic protein by transfecting miR-182 mimics and miR-182 inhibitor into polycystic kidney cyst-lined epithelial cells, respectively. Furthermore, we observed the interaction between TGF-β1 and miR-182 and fibrinogen factors of cyst-lined epithelial cells after TGF-β1 intervention, and measured the expression of Smad2, 3 protein.

Results: (1) MiR-182 was positively correlated with fibrosis of cyst-lined epithelial cells; (2) TGF-β1 could induce fibrosis of cyst-lined epithelial cells; (3) the expression of miR-182 had an remarkably impact on the fibrosis induced by TGF-β1, but had little effect on the expression of TGF-β1; (4) the expression of Smad3 protein in TGF-β1 induce- cyst-lined epithelial cells were increased.

Conclusion: TGF-β and miR-182 promoting the fibrosis of polycystic kidney cyst - lined epithelial cells may be mediated by the TGF-β/Smad3 signaling pathway, of which Smad3 was an important regulator.

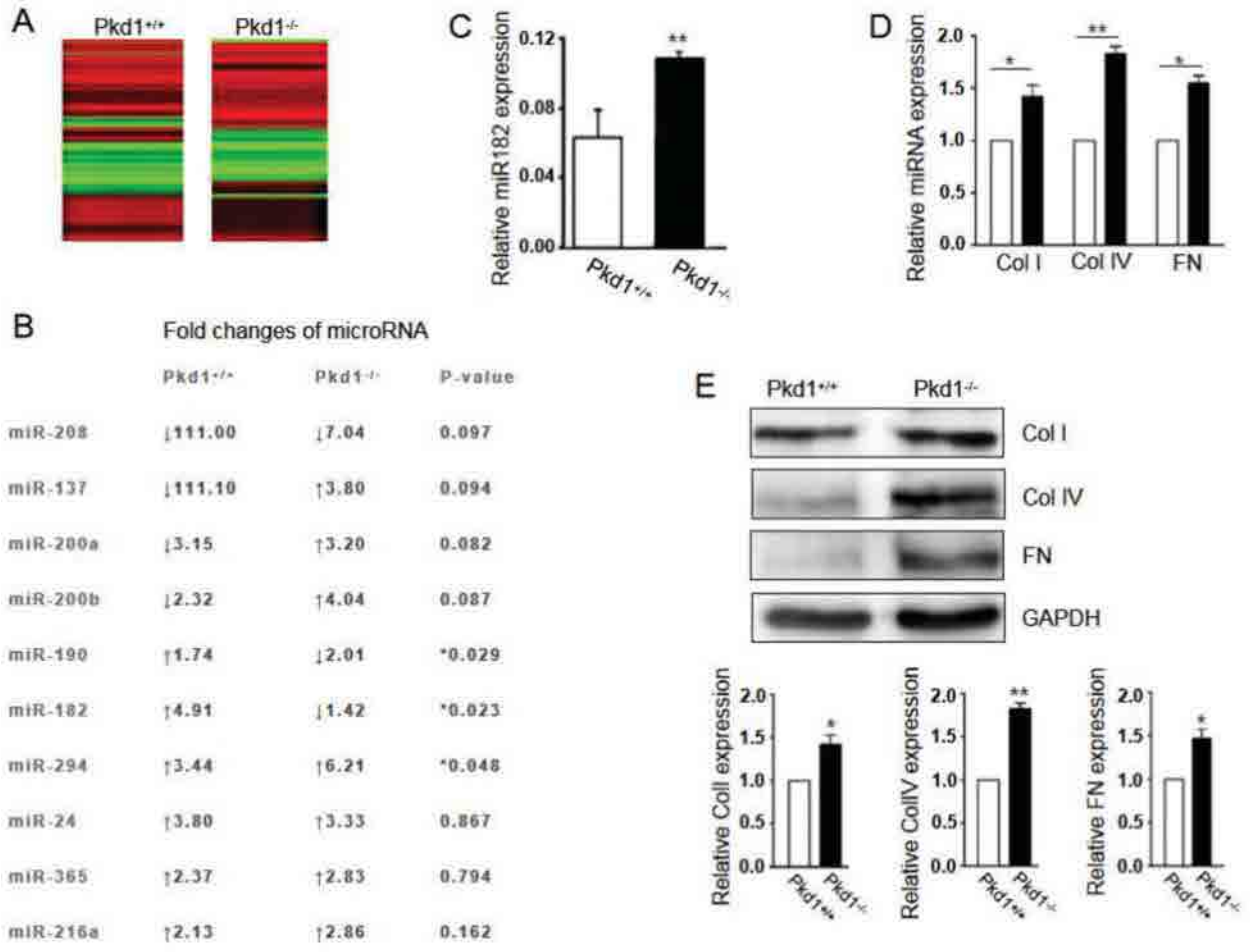


Figure 1

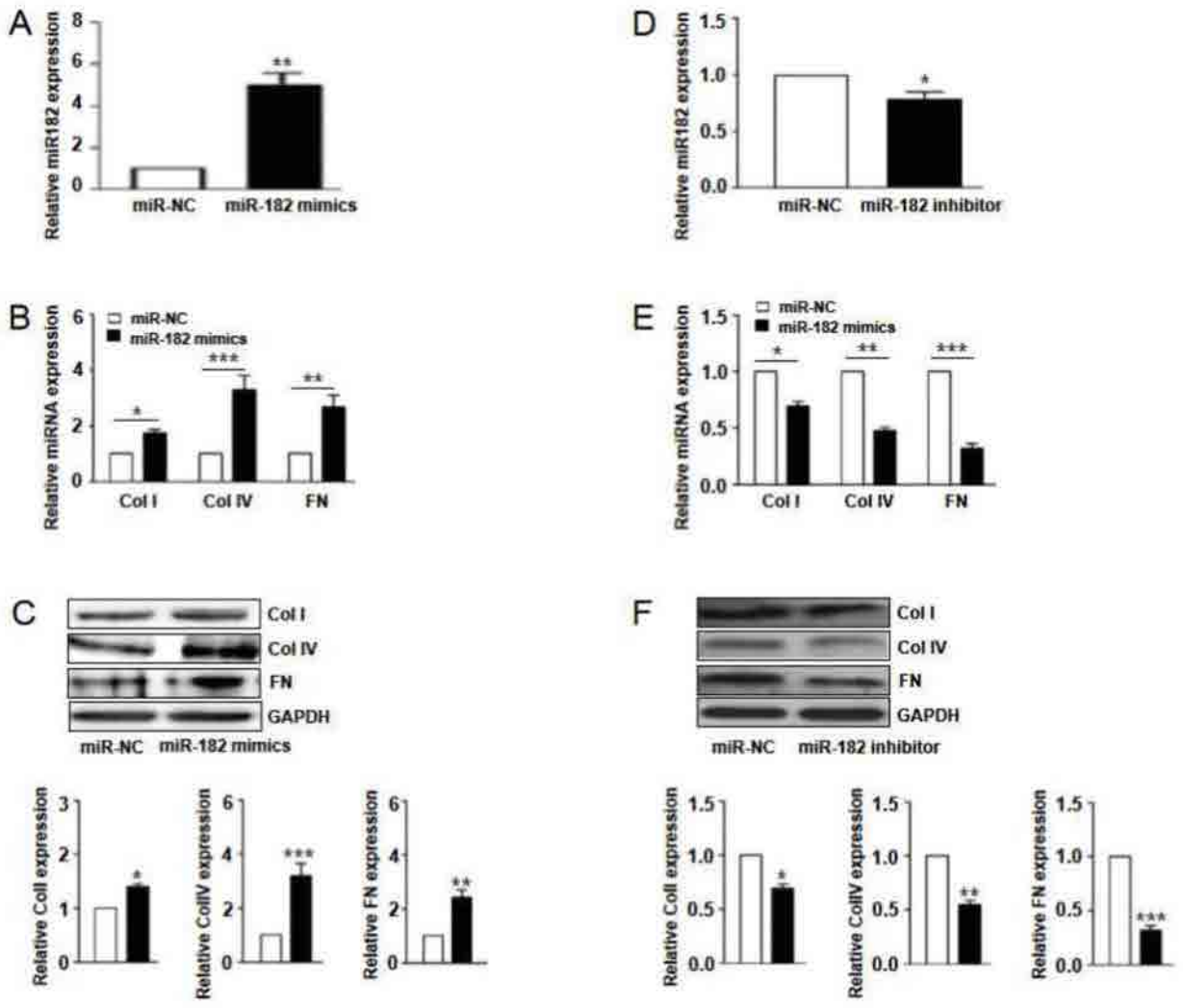

A
Relative miR182 expression
miR-NC
miR-182 mimics
D
Relative miR182 expression
miR-NC
miR-182 inhibitor
B
miR-NC
miR-182 mimics
Relative miRNA expression
Col I
Col IV
FN
E
miR-NC
miR-182 mimics
Relative miRNA expression
Col I
Col IV
FN
C
Col I
Col IV
FN
GAPDH
miR-NC
miR-182 mimics
Relative ColI expression
Relative ColIV expression
Relative FN expression
F
Col I
Col IV
FN
GAPDH
miR-NC
miR-182 inhibitor
Relative ColI expression
Relative ColIV expression
Relative FN expression

Figure 2

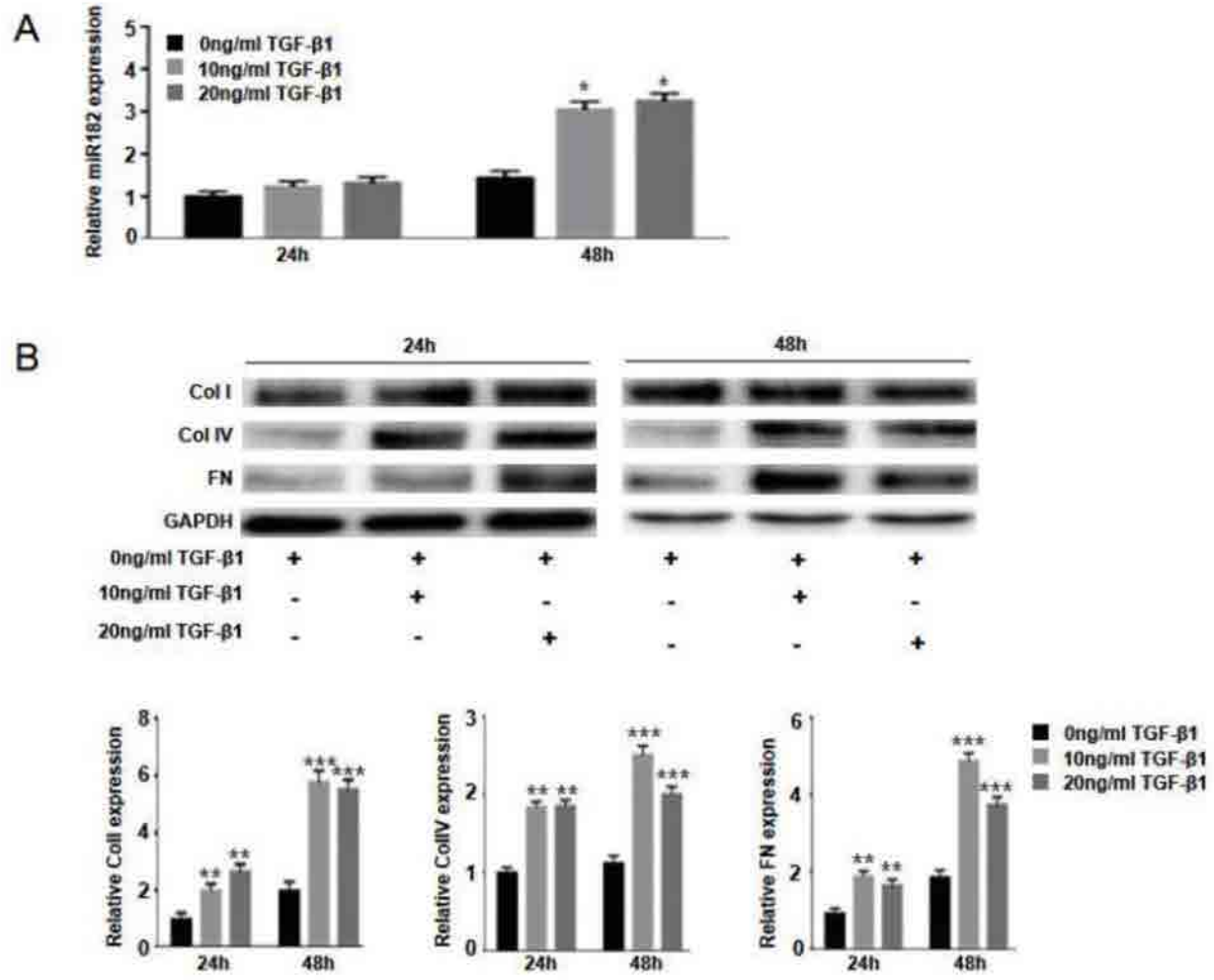

A
Relative miR182 expression
0ng/ml TGF-β1
10ng/ml TGF-β1
20ng/ml TGF-β1
24h
48h
B
24h
48h
Col I
Col IV
FN
GAPDH
0ng/ml TGF-β1
10ng/ml TGF-β1
20ng/ml TGF-β1
Relative ColI expression
Relative ColIV expression
Relative FN expression

Figure 3

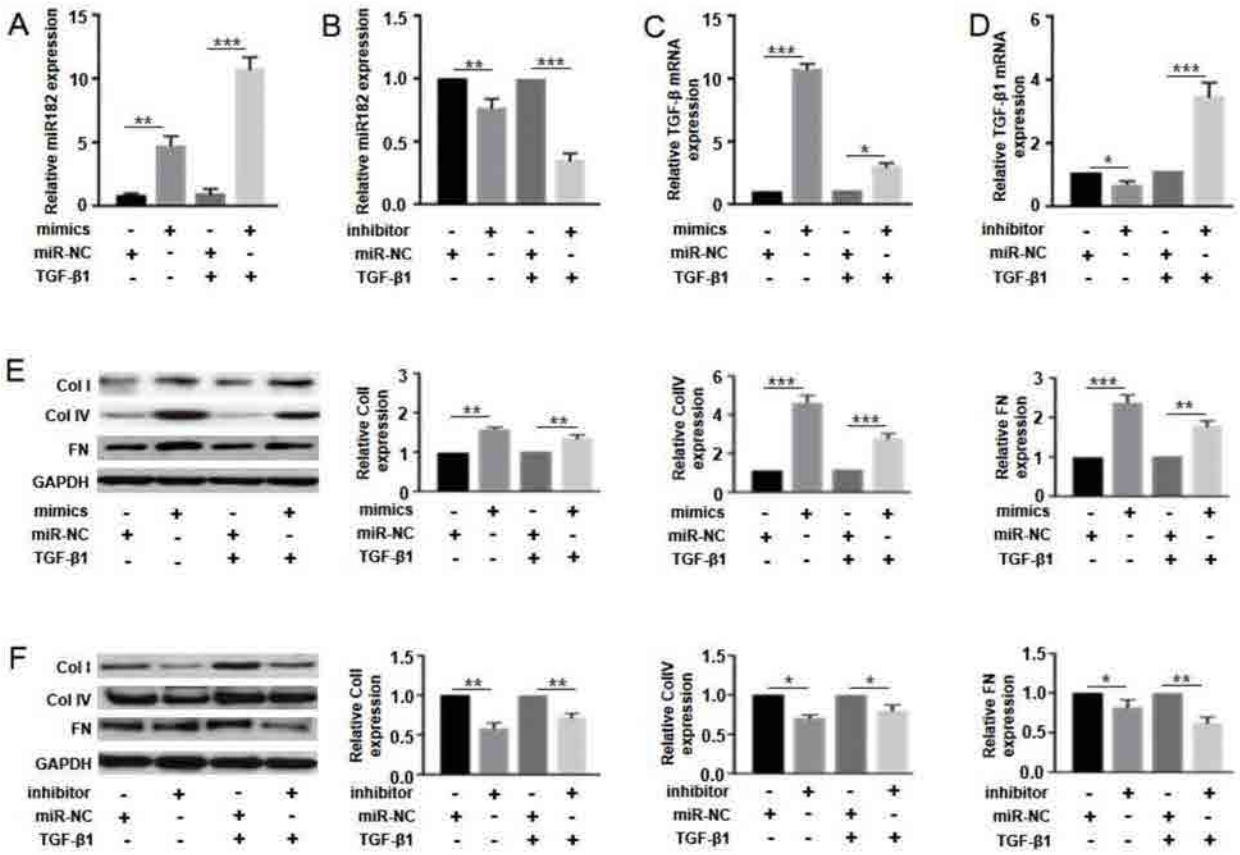

A
Relative miR182 expression
mimics
miR-NC
TGF-β1
B
Relative miR182 expression
inhibitor
miR-NC
TGF-β1
C
Relative TGF-β mRNA expression
mimics
miR-NC
TGF-β1
D
Relative TGF-β1 mRNA expression
inhibitor
miR-NC
TGF-β1
E
Col I
Col IV
FN
GAPDH
mimics
miR-NC
TGF-β1
Relative ColI expression
Relative ColIV expression
Relative FN expression
F
Col I
Col IV
FN
GAPDH
inhibitor
miR-NC
TGF-β1
Relative ColI expression
Relative ColIV expression
Relative FN expression

Figure 4

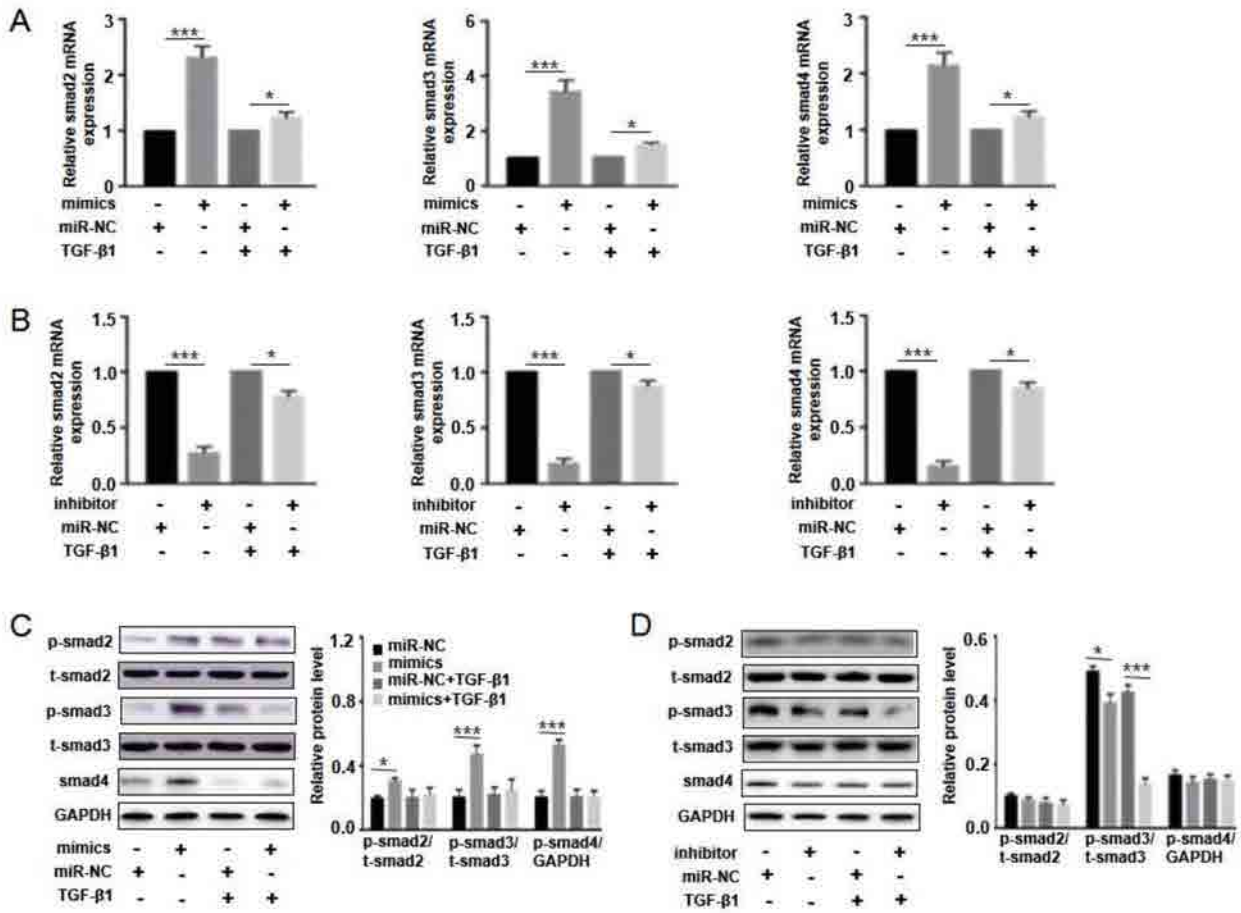

A
Relative smad2 mRNA expression
Relative smad3 mRNA expression
Relative smad4 mRNA expression
mimics
miR-NC
TGF-β1
B
Relative smad2 mRNA expression
Relative smad3 mRNA expression
Relative smad4 mRNA expression
inhibitor
miR-NC
TGF-β1
C
p-smad2
t-smad2
p-smad3
t-smad3
smad4
GAPDH
mimics
miR-NC
TGF-β1
Relative protein level
miR-NC
mimics
miR-NC+TGF-β1
mimics+TGF-β1
p-smad2/ t-smad2
p-smad3/ t-smad3
p-smad4/ GAPDH
D
p-smad2
t-smad2
p-smad3
t-smad3
smad4
GAPDH
inhibitor
miR-NC
TGF-β1
Relative protein level
p-smad2/ t-smad2
p-smad3/ t-smad3
p-smad4/ GAPDH

Figure 5

P0511 ENHANCER AND SUPER-ENHANCER DYNAMICS IN REPAIR AFTER ISCHEMIC ACUTE KIDNEY INJURY

Julia Wilflingseder[1,2,3], Michaela Willi[2], Hye Kyung Lee[2], Hannes Olauson[1,4], Jakub Jankowsky[3], Takaharu Ichimura[1], Reinhold Erben[3], M Todd Valerius[1], Lothar Hennighausen[2], Joseph Vincent Bonventre[1]

[1]Brigham and Women's Hospital, Harvard Medical School, Renal Division, Boston, United States of America, [2]National Institute of Diabestes, Digestive and Kidney Disease, NIH, Laboratory of Genetics and Physiology, Bethesda, United States of America, [3]University of Veterinary Medicine, Physiology, Vienna, Austria and [4]Karolinska Institutet, Division of Renal Medicine, Department of Clinical Sciences, Intervetion and Technology, Stockholm, Sweden

Background and Aims: The endogenous repair process of the mammalian kidney allows rapid recovery after acute kidney injury (AKI) through robust proliferation of tubular epithelial cells. There is currently limited understanding of which transcriptional regulators activate these repair programs and how transcriptional dysregulation leads to maladaptive repair. Here we investigate the existence of enhancer dynamics in the regenerating mouse kidney.

Method: RNA-seq and ChIP-seq (H3K27ac, H3K4m3, BRD4, POL2 and selected transcription factors) were performed on samples from repairing kidney cortex 2 days after ischemia/reperfusion injury (IRI) to identify activated genes, transcription factors, enhancer and super-enhancers associated with kidney repair. Further we investigated the role of super-enhancer activation in kidney repair through pharmacological BET inhibition using the small molecule JQ1 in vitro and in acute kidney injury models in vivo.

Results: Response to kidney injury leads to genome-wide alteration in enhancer repertoire in-vivo. We identified 16,781 enhancer sites (H3K27ac and BRD4 positive, H3K4me3 negative binding) active in SHAM and IRI samples; 6,512 lost and 9,774 gained after IRI. The lost and gained enhancer sites can be annotated to 62% and 63% of down- and up-regulated transcripts at day 2 after kidney injury, respectively. Super-enhancer analysis revealed 164 lost and 216 gained super-enhancer sites at IRI day 2. 385 super-enhancers maintain activity before and after injury. ChIP-seq profiles of selected transcription factors based on motif analysis show specific binding at corresponding enhancer sites. We observed lost enhancer binding of HNF4A and GR mainly at kidney related enhancer elements. In contrast, STAT3 showed increased binding at injury induces enhancer elements. No dynamic was observed for STAT5. Both transcription factor groups show corresponding mRNA changes after injury. Pharmacological inhibition of enhancer and super-enhancer activity by BRD4 inhibition (JQ1: 50mg/kg/day) before IRI leads to suppression of 40% of injury-induced transcripts associated with cell cycle regulation and significantly increased mortality between days 2 and 3 after AKI.

Conclusion: This is the first demonstration of enhancer and super-enhancer function in the repairing kidney. In addition, our data call attention to potential caveats for use of small molecule inhibitors of BET proteins that are currently being tested in clinical trials in cancer patients who are at risk for AKI. Our analyses of enhancer dynamics after kidney injury in vivo have the potential to identify new targets for therapeutic intervention.

P0512

SKLB023 ATTENUATED LIPOPOLYSACCHARIDE-INDUCED ACUTE KIDNEY INJURY VIA INHIBITION OF NF-KAPPPAB AND MAPKS PATHWAYS

Qian Ren[1], Liang Ma[1], Ping Fu[1]

[1]*Division of Nephrology, Kidney Research Institute, West China Hospital of Sichuan University, Chengdu, P.R. China*

Background and Aims: Excessive nitric oxide (NO) production by the activation of inducible nitric oxide synthase (iNOS) during sepsis was considered to contribute to acute kidney injury (AKI) and selective inhibition of iNOS activity may be a promising strategy for the treatment of sepsis-induced AKI. The novel small molecule compound (Z)-N-(3-Chlorophenyl)-2-(4-((2,4-dioxothiazolidin-5-ylidene) methyl) phenoxy) acet-amide (SKLB023) as a selective iNOS inhibitor was designed, synthesized by our lab and exhibited therapeutic potential in arthritis and non-alcoholic steatohepatitis models with potent anti-inflammatory effects. This study aimed to evaluate whether SKLB023 as a drug candidate could offer renal protective effect against sepsis-induced AKI.

Method: 21 C57BL6 mice (20-22g, 6-8 weeks old) were randomly divided into three groups: control, model, SKLB023 pretreatment. AKI was induced by a single injection of 10mg/kg LPS, and SKLB023 was orally administrated at the dose of 50 mg/kg for three consecutive days and one hour before LPS injection. All mice were sacrificed 16h after LPS injection and blood and kidney tissues were collected for further evaluation. LPS-induced renal dysfunction was assessed by measurement of blood creatinine and urea nitrogen (BUN) as well as histopathological changes. Moreover, the kidney mRNA and protein expression of neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule 1(KIM-1), newly identified kidney injury markers, were tested by polymerase chain reaction (PCR) and western blot. To explore underlying mechanisms, the renal expression of inflammatory cytokine genes IL-1β, IL-6, mcp-1 and proteins iNOS, COX-2, IL-1β, TNF-α, IL-6, HMGB1 in were measured. The total expression of nuclear factor-kappa B (NF-κB), IκBα and MAPKs proteins (ERK1/2, p38 MAPK) and their corresponding phosphoproteins (p-NF-κB, p-IκBα, p-ERK1/2, p-P38 MAPK) in mice kidneys were subsequently analyzed by western blot.

Results: 16hours following LPS challenge, mice developed AKI as evidenced by elevated creatinine and BUN levels and corresponding pathological changes. Additionally, kidney expression of NGAL and KIM-1 were remarkably increased after LPS injection. SKLB023 pretreatment, however, alleviated LPS-induced renal dysfunction. Moreover, the excessive production of inflammatory cytokines during sepsis was significantly suppressed by SKLB023. Further observation from PCR and immunoblot results indicated that SKLB023 attenuated the activity of NF-kB and the phosphorylation of ERK1/2 and p38 MAPK in septic AKI mice.

Conclusion: These data demonstrated that SKLB023 exhibited renoprotective effect in LPS-induced AKI, which was associated with its anti-inflammatory activities by inhibiting the NF-kappaB and MAPK signaling pathways

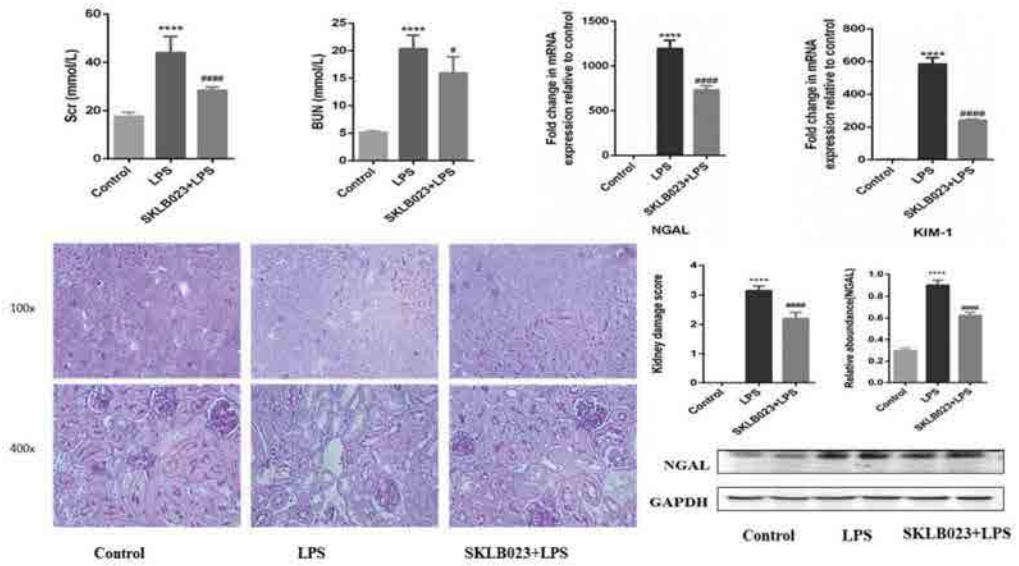


Figure 1. SKLB023 pretreatment alleviated LPS-induced septic AKI

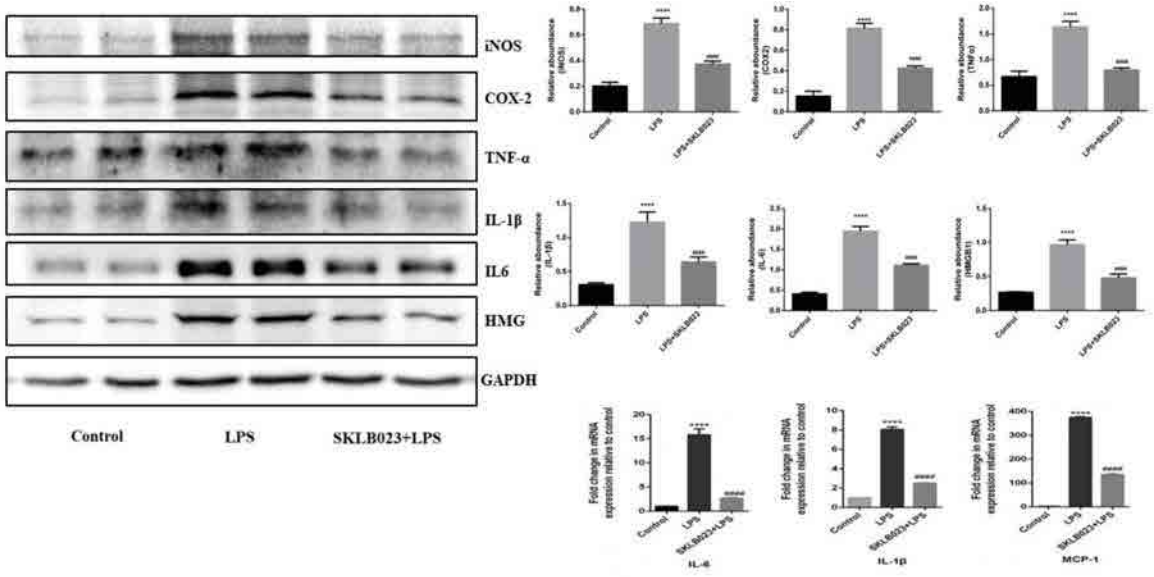


Figure 2. SKLB023 pretreatment alleviated renal inflammation in LPS-induced septic AKI

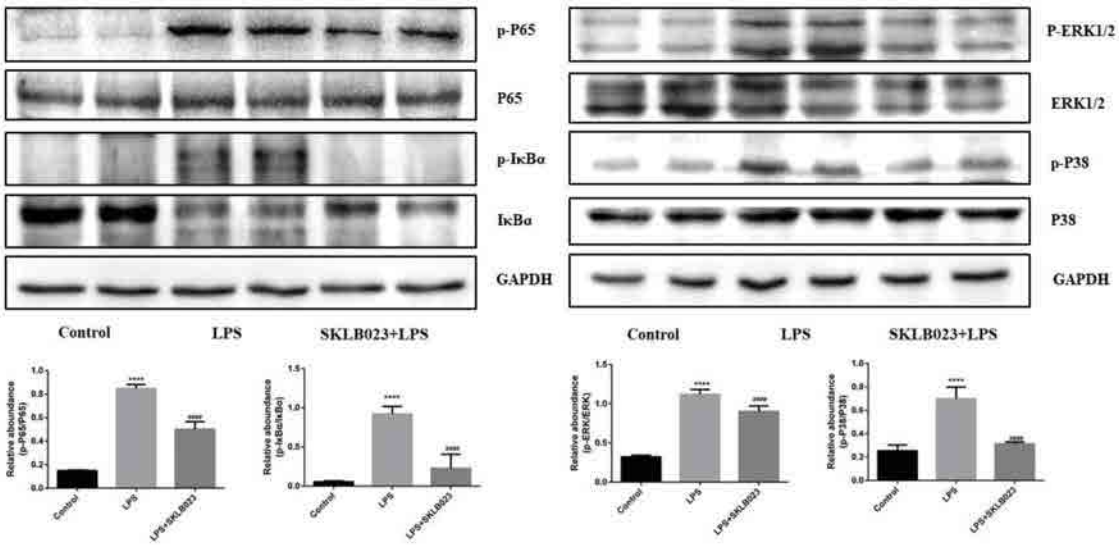


Figure 3. SKLB023 suppressed the activation of NF-κB and MAPK pathways in PS-induced septic AKI mice

P0513 **NECROINFLAMMATION VERSUS CRYSTAL CLOTS AS THERAPEUTIC TARGET IN CHOLESTEROL CRYSTAL EMBOLISM-RELATED KIDNEY INFARCT**

Chongxu Shi[1]

[1]*Medizinische Klinik und Poliklinik IV Klinikum der Universitaet Muenchen, Nephrologisches Zentrum, Munich, Germany*

Background and Aims: Cholesterol crystal embolism (CCE) is usually a consequence of the rupture of atheromatous plaques in patients with advanced atherosclerosis. We hypothesized that necroinflammation contributes to CCE-related kidney injury/disease (AKI/AKD).

Method: Injection of cholesterol crystal (CC) into C56BL/6 WT mice kidney via the left kidney artery induced vascular obstruction, kidney infarction, and GFR loss (measured by transcutaneous monitoring of sinistrin clearance in awake and unrestricted mice). GFR recovered to baseline at 2 weeks despite persistent kidney injury and scarring, probably because the non-injected right kidney developed compensatory hypertrophy. To study the role of necroinflammation in this process, we injected CC to either Mlkl-/- mice or WT mice pre-treated with PBS, the necroptosis inhibitor Nec-1s or the NLRP3 inhibitor MCC950 30 min before CC injection.

Results: At 24h, Nec-1s, MCC950 treatment had significantly reduced infarct size, kidney injury, neutrophil infiltration, and vascular injury compared to PBS control group. Reduced infarct size, e.g. with Nec-1s persistented until day 14. CC injection into Mlkl-/- mice gave the same results. However, none of these interventions had an effect on GFR loss, i.e. AKI because they did not affect crystal clot formation in the arteria afferent to glomerular perfusion. In contrast, anticoagulant treatment prevented infarcts and GFR loss.

Conclusion: In this new model of unilateral CCE-induced AKI/AKD global kidney function recovers within 14 d, presumably due to adaptive responses in the contralateral kidney as the post-infarct tissue injury persists and leads to kidney atrophy. As both the NLRP3 inflammasome as well as necroptosis are involved in kidney infarct formation, we conclude on necroinflammation as the central mechanism of CCE-induced AKI/AKD. However, what defines AKI is renal function. We found that crystal clot formation is upstream of kidney infarction but independent of necroinflammation. We conclude, despite necroinflammation is central in kidney infarct formation, crystal clots are the better therapeutic target to prevent CCE-related AKI.

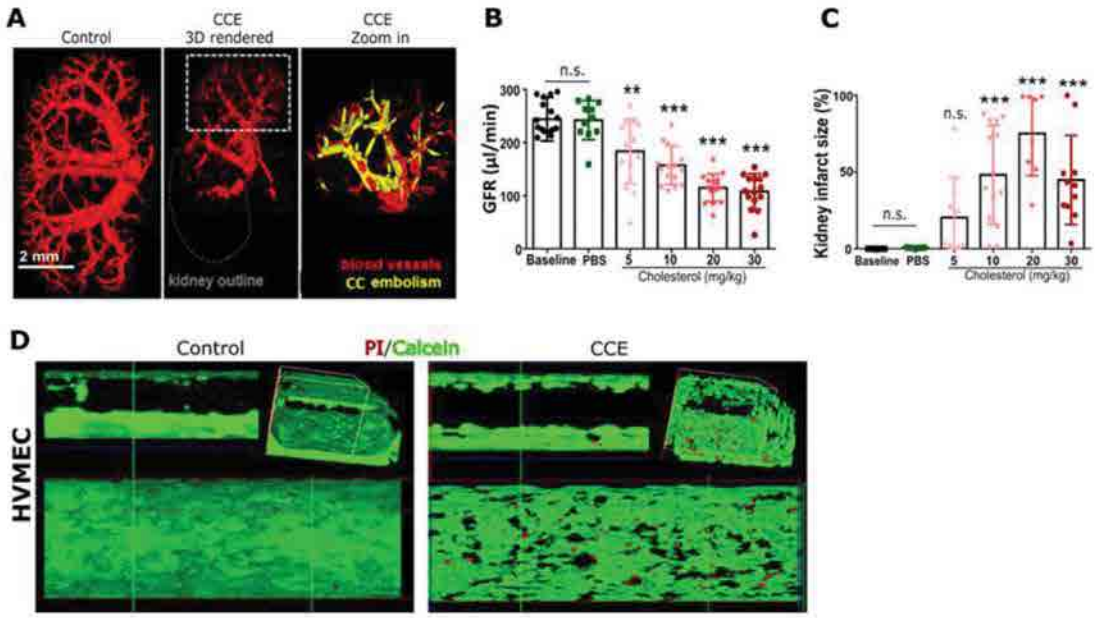


Figure:

P0514

USP30 INHIBITOR ATTENUATES PROGRESSIVE FIBROSIS IN ISCHEMIA INDUCED CHRONIC KIDNEY DISEASE (CKD), EVEN AFTER DELAYED TREATMENT INITIATION AFTER INJURY

David Bedford[1], Jamie Wright[1], Song Rong[2], Paul Thompson[1], Nelli Shushakova[2], Sonja Schmidt[2], Faikah Gueler[2], Judit Molnar[1]

[1]Mission Therapeutics, Cambridge, United Kingdom and [2]Phenos GmbH, Hannover, Germany

Background and Aims: Much literature evidence points towards an essential role of mitochondrial quality control mechanisms in acute kidney injury progression. Renal ischemic-reperfusion injury (IRI) results in metabolic adaptation of proximal tubule epithelial cells, a site of high mitochondrial turnover (1). Moreover, exacerbation of renal injury has been demonstrated following IRI in both PTEN-induced kinase 1 (PINK1) knockout and Parkin knockout mice (2). The identification of a single point mutation (m.547A>T) within the mitochondrial genome of a large pedigree of patients with maternally-inherited tubulointerstitial kidney disease, highlights the importance of mitochondrial integrity in human renal pathophysiology (3).

USP30 is a mitochondrial associated deubiquitylating enzyme that acts on the mitochondrial import receptor subunit TOM20 to repress PINK1/Parkin-mediated mitophagy and modulate mitochondrial protein transport (4,5). Within kidney, USP30 expression is predominantly tubular and accordingly, USP30 inhibition may provide a mechanism to protect against IRI. MTX008 is a selective small molecule inhibitor of USP30. Prophylactic administration of MTX008 15 mg/kg (p.o.) BID has shown robust and reproducible efficacy in a mouse model of IRI-induced kidney fibrosis (6). Here we present data showing that dosing MTX008 15 mg/kg (p.o.) BID in a therapeutic paradigm, also results in efficacy in the same IRI-induced kidney fibrosis model.

Method: On Day 0 (zero) C57BL/6 mice were anaesthetized, and their left renal pedicle was clamped transiently for 45 min, causing circulatory arrest in the kidney with consecutive IRI. Mice were then administered either vehicle or MTX008 15 mg/kg (p.o.) BID for 21 days, with first treatment starting five hours following IRI surgery (i.e. therapeutics dosing). Mice were monitored and kidneys harvested at Day +21. Kidney sections were quantitatively assessed for relative cellular morphology, fibrosis and macrophage infiltration using blinded histological scoring methods.

Results: Body weight was similar between groups and remained constant throughout the observation periods. Masson trichrome staining revealed significantly less tubular atrophy in MTX008 treated animals on Day +21. Similarly, fibronectin expression and macrophage infiltration in the cortex was also significantly reduced in MTX008 treated mice on Day +21.

Conclusion: MTX008, a novel selective small molecule inhibitor of USP30 has shown efficacy in a model of IR-induced CKD when dosed therapeutically. Initiating treatment after the establishment of IRI has shown significant benefits towards reduced progression to CKD with less tubular atrophy and renal fibrosis. Mission Therapeutics is investigating MTX008 in a variety of preclinical renal injury models with a view to developing this novel molecule towards the clinic. Therapeutic dosing opens a new and attractive opportunity for the treatment of AKI and sets our UPS30 inhibitor apart from other molecules currently in development.

P0515 **BRD4 PROTEIN REGULATES THE RESPONSES TO HYPOXIA TRIGGERED IN THE EXPERIMENAL RENAL DAMAGE.**

Paula Diaz-Bulnes[1,2], Ramon M Rodriguez[1,2], Viviana Corte[1], Elisenda Banon[2,3], Marta Lazo[2,3], Maria Jose Ramirez[2,3], Carlos Lopez-Larrea[1,2], Beatriz Suarez-Alvarez[1,2]

[1]Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Hospital Universitario Central de Asturias (HUCA), Laboratorio de Inmunología Traslacional, Oviedo, Spain, [2]Red de Investigación Renal (REDINREN), Instituto de Salud Carlos III and [3]Fundació Clínic per la Recerca Biomèdica (FCRB), Laboratori Experimental de Nefrologia i Trasplantament (LENIT), Barcelona, Spain

Background and Aims: Renal hypoxia is not only one of the most common causes of acute kidney injury, but also a critical mediator in the transition to chronic kidney disease. When the kidney is exposed to an insufficient supply of oxygen to meet demand, some adaptive mechanisms are triggered by the cells to maintain homeostasis. Induction of HIF-1α transcription factor and activation of unfolded protein response (UPR) pathway, as consequence of ER dysfunction, are both essential to mediate the cell survival. The UPR pathway is regulated by three major protein sensors (IRE1α, PERK and ATF6) which under ER stress initiate the activation of the XBP1, ATF4 and ATF6 transcription factors, respectively. However, inappropriate activation of these mechanisms could lead to the enhanced transcription of genes involved in key processes in renal damage (inflammation, cell death or autophagy). On the other hand, BRD4 is an epigenetic reader that recognizes acetylated lysine residues on histone and other proteins, and mediates the binding of transcription factors to the transcriptional machinery. Our aim was to investigate whether BRD4-mediated epigenetic mechanisms could modulate the response to hypoxia triggered in acute renal damage.

Method: Tubular epithelial cell line, HK2, was cultured with thapsigargin (Tg) or in hypoxia chamber (1% O_2, 5% CO_2). In addition, these cells were treated with specific BET proteins inhibitors (JQ1, I-BET762) and with small interfering RNAs (siRNA BRD4, p300), or were subjected to knockdown of ATF4 and XBP1 by CRISPR/cas9 technology. Transcriptional changes were analyzed in each condition by RNA-sequencing. The binding of BRD4 to target genes and recruitment of the transcriptional machinery was analyzed by chromatin immunoprecipitation (ChIP) with specific antibodies against BRD4, RNA PolII, AcH3 and AcH4. Effect of JQ1 inhibitor was assayed in an ischemia/reperfusion injury (IRI) model, and analysis of gene expression, inflammatory cell infiltration, and epigenetic remodeling was carried out by quantitative PCR, IHQ and ChIP assay, respectively.

Results: Treatment of HK2 cells with BETs inhibitors, previously cultured with Tg or under hypoxia conditions, inhibits the gene expression of the GPR78 ER chaperon, and the XBP1 and ATF4 transcription factors modulating the downstream signaling pathways. Meanwhile, ATF6 expression remains unchanged. Gene silencing with siRNA and ChIP assays reveal that under activation of the UPR pathway or hypoxia, BRD4 recognizes acetylated histones in the GPR78, ATF4 and XBP1 promoters, recruits the pTEF-b complex and activates RNA-pol II allowing the gene transcription. Additionally, inhibition of BRD4 impairs the HIF-1α stabilization, downregulating the expression of hypoxia-induced genes. Results from whole-genome gene expression assays after stable knockdown of XBP1 and ATF4 reveal that most (86%) of the UPR genes regulated by BET proteins are dependent of XBP1 and only 32% by ATF4. Moreover, almost all genes regulated by ATF4 are also XBP1-dependent. This result may be due to the fact that ATF4 regulates IRE1α expression and thus modulates the XBP1 mRNA splicing. Administration of JQ1 in an IRI model supports that blockage of BRD4 ameliorates the renal damage (reducing BUN and creatinine levels) due to a decreased UPR activation and expression of HIF-1α target genes. As consequence, the expression of inflammatory genes and the inflammatory cell infiltration is diminished.

Conclusion: Our results show that BRD4 protein regulates two key processes, induction of HIF-1α transcription factor and UPR pathway activation triggered by renal hypoxia. Pharmacological inhibition of BET proteins reduces the activation these pathways, ameliorating renal damage and avoiding its progression.

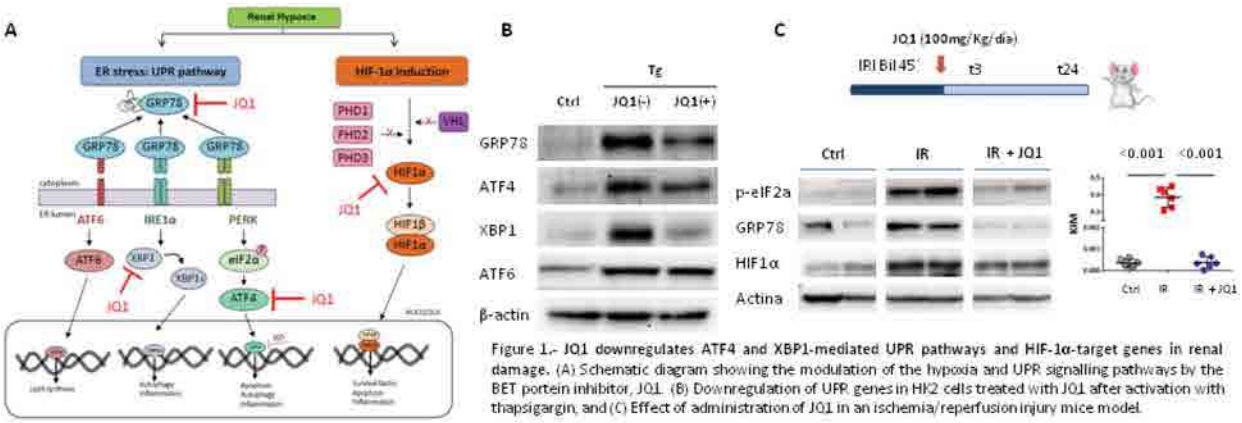


Figure 1.- JQ1 downregulates ATF4 and XBP1-mediated UPR pathways and HIF-1α-target genes in renal damage. (A) Schematic diagram showing the modulation of the hypoxia and UPR signalling pathways by the BET portein inhibitor, JQ1. (B) Downregulation of UPR genes in HK2 cells treated with JQ1 after activation with thapsigargin, and (C) Effect of administration of JQ1 in an ischemia/reperfusion injury mice model.

Figure:

P0516 **DCR2 PROMOTES RENAL FIBROSIS BY ACCELERATING TUBULAR CELL SENESCENCE AFTER ISCHEMIA REPERFUSION INJURY**

Jia Chen[1], Yani He[1]

[1]*Daping Hosipital, Army medical university, Nephrology, Chongqing, P.R. China*

Background and Aims: Cell senescence of renal tubular epithelial cells (RTECs), which is involved in renal fibrosis, is a key event in the progression of acute kidney injury (AKI). However, the underlying mechanism remains unclear. This study aims to investigate the role and mechanism of decoy receptor 2 (DcR2) in renal fibrosis and cell senescence of RTECs.

Method: $^{KSP\text{-}cre}DcR2^{f/f}$ mouse (Tubular DcR2 KO) and Ischemia-Reperfusion (I/R) Injury models were constructed. The models were divided into moderated (ischemia 20min) and severe (ischemia 35min) injury. The expression of renal DcR2, senescent markers (P16, P21, SA-β-gal) and senescent phenotype (IL-6, TGF-β1) were detected. Furthermore, wild type (WT) mice and $^{KSP\text{-}cre}DcR2^{f/f}$ mice were used to compare the degree of renal tissue and functional damage and the senescence of renal tubular cells after I/R injury. In vitro, knockdown and overexpression experiments were performed by transfected DcR2 siRNA or overexpressed adenovirus in hypoxia-reoxygenation stimulated mouse primary RTEC. The cell senescence and phenotype markers were further detected.

Results: The levels of Scr, BUN and urinary DcR2 and renal injury scores were significantly increased in I/R group at the early stage (1d) of renal injury compared with sham group. Renal fibrosis was observed in the later stage (21-42d) in severe injury. DcR2 was mainly expressed in renal tubules, and the percentage of tubular DcR2 was increased after I/R injury. DcR2 was co-expressed with P16 and SA-β-gal, and urinary DcR2 levels were related to senescent makers, suggesting that DcR2 was associated with cell senescence. The renal function and renal injury scores were lower in $^{KSP\text{-}cre}DcR2^{f/f}$ mice than that of WT after renal reperfusion. And the area of renal fibrosis was significantly decreased in $^{KSP\text{-}cre}DcR2^{f/f}$ mice compared with WT, indicating DcR2 inhibited renal fibrosis. Furthermore, the expression of senescent phenotype were suppressed in tubular DcR2 KO mice after I/R injury, suggesting that DcR2 could promote the senescence of renal tubule cells.

Conclusion: DcR2 promotes renal fibrosis by accelerating tubular cell senescence after ischemia-reperfusion Injury, suggesting that DcR2 may be a potential intervention target during the progression of AKI.

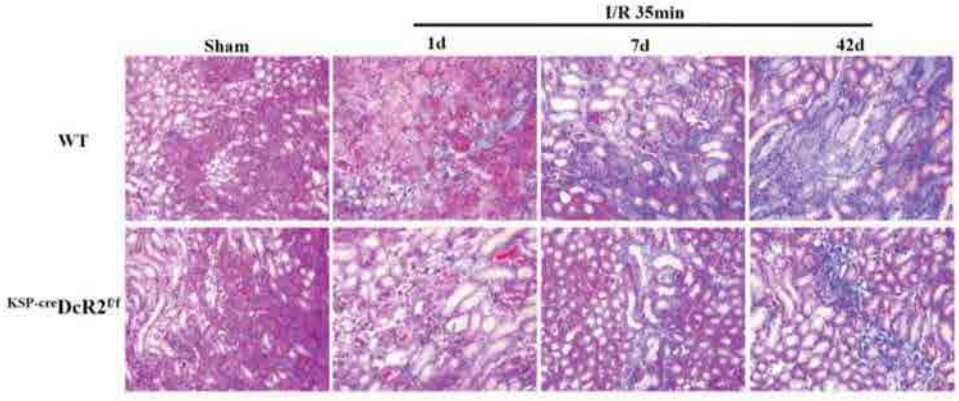


Figure:

P0517

RENAL STEM CELLS (ARPCS) AS A NEPHROPROTECTIVE APPROACH DURING CISPLATIN-INDUCED ACUTE KIDNEY INJURY: A DEFENSE MECHANISM BY EXTRACELLULAR VESICLES CARRYING THE CYP1B1 GENE

ROSSANA FRANZIN[1,2], Fabio Sallustio[1,3], Claudia Curci[4], Simona Simone[1], Angela Picerno[1], Giuseppe Depalma[5], Giuseppe Castellano[6], Anna Gallone[4], Giovanni Battista Pertosa[1], Loreto Gesualdo[1]

[1]University of BARI, Department of Emergency and Organ Transplantation, Nephrology Unit, Italy, [2]University of Piemonte Orientale, Department of Translational Medicine, [3]University of BARI, Interdisciplinary Department of Medicine, [4]University of BARI, Department of basic medical sciences, neurosciences and sense organs, [5]Experimental oncology and biobank management unit, Giovanni Paolo II / I.R.C .C .S. Cancer Institute, Bari and [6]University of Foggia, Department Medical Science

Background and Aims: Cisplatin, is a nonspecific cytotoxic agent that primarily interferes with cellular DNA replication and the cell cycle, nevertheless it lacks tumor selectivity and acts also in normal cells. The most serious adverse reaction of cisplatin is Acute Kidney Injury (AKI), limiting its use and efficacy in chemotherapy. Cisplatin nephrotoxicity is observed in more than 30% of older patients, however the mechanism of nephrotoxicity remains unclear and specific preventive measures are not available. Today, there is an urgent need for specific nephroprotective strategies to be used during cisplatin chemotherapy. Recently, we found that tubular stem/progenitor cells (tARPC) are able to protect the tubular epithelial (RPTEC) from cisplatin induced injury, preserving their proliferation and inhibiting apoptosis. The aim of this study was to identify the molecular mechanisms involved in tARPC-mediated resistance to cisplatin.

Method: Co-cultures of RPTEC cells and tARPCs were exposed to cisplatin (2.5 μM) for 6 h and then kept in culture for 96 h. Gene expression profile was obtained from tARPCs and RPTECs by Agilent SurePrint G3 Human Gene Expression Microarrays. Genespring and R software were used for the analysis. Gene expression data were validated by Real-time PCR. Extracellular vesicles were isolated from cell culture supernatant by miRCURY Exosome Cell/Urine/CSF Kit (Qiagen) and RNA contained in extracellular vesicles was purified, analyzed in quality by Bioanalyzer (RNA nano) and evaluated by qPCR. The BrdU assay and caspase 3 were used to measure proliferation and apoptosis levels. Immunohistochemical expression of activated caspase-3 was used as a marker of apoptosis in RPTECs.

Results: By a whole-genome gene expression analysis, we found 107 genes specifically modulated by RPTECs in response to cisplatin and, among these, 30 genes induced by ARPCs following the cisplatin damage. In particular, we found a strong upregulation of the CYP1B1 gene (false discovery rate corrected p value <0.05; fold change=4,1). The qPCR confirmed the increase in CYP1B1 levels in the co-cultures with respect to the respective basal conditions ($p<0.05$). Interestingly, the CYP1B1 mRNA was also enveloped in Extracellular Vesicles released in the cell co-culture media by tARPC and RPTEC after cisplatin exposition. The *CYP1B*1 gene encodes a member of the cytochrome P450 superfamily of enzymes and the produced enzyme metabolizes procarcinogens, such as polycyclic aromatic hydrocarbons. CYP1B1 has been shown to be active within tumors and is also capable of metabolizing a structurally diverse range of anticancer drugs. It is responsible for the resistance to docetaxel, cisplatin, tamoxifen and nucleoside analogues. CYP1B1 is involved in the detoxification of the body by various exogenous toxic agents, including cisplatin. We found that *CYP1B1* gene was expressed at low levels in RPTECs and in cisplatin-damaged RPTECs. Moreover, 96 h days after 2.5 μM exposure to cisplatin, RPTECs reduced the proliferation and underwent in apoptosis, as showed by caspase 3. However, in co-culture with ARPCs, ARPC cellular and extracellular vesicles CYP1B1 gene expression significantly increased, the apoptotic process was stopped and RPTECs increased their proliferation rate.

These data support the hypothesis that ARPCs are sensor of cisplatin damaged-RPTEC and confers cisplatin resistance by transferring CYP1B1 gene in extracellular vesicles.

Conclusion: This is the first evidence of a cisplatin-induced overexpression of CYP1b1 in renal epithelial cells as a defense mechanism against cisplatin toxicity. This is consistent with our previous data showing that renal progenitors are resistant to cisplatin. The findings may have biological and clinical significance in terms of their implications in cellular communications and potential use of CYP1B1 as biomarkers for AKI induced by cisplatin or as protective agent.

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10.1093/ndt/gfaa143

MODERATED POSTER SESSION 2

P0650

URINE PEPTIDOME ANALYSIS IN HEART FAILURE, CHRONIC KIDNEY DISEASE AND CARDIORENAL SYNDROME TOWARDS THE DEFINITION OF DISEASE-SPECIFIC MARKERS.

Eleni Petra[1], Tianlin He[2], Agnieszka Latosinska[3], Rafael Stroggilos[4], Harald Mischak[3], Antonia Vlahou[4]

[1]Institute for Molecular Cardiovascular Research (IMCAR, RWTH Aachen, Germany) and Biomedical Research Foundation Academy of Athens (BRFAA), Biotechnology, Athens, Greece, [2]Institute for Molecular Cardiovascular Research (IMCAR, RWTH Aachen, Germany) and Mosaiques Diagnostics GmbH , Hannover, Germany, [3]Mosaiques Diagnostics GmbH, Hannover, Germany and [4]Biomedical Research Foundation Academy of Athens (BRFAA), Biotechnology, Athens, Greece

Background and Aims: The cardiorenal syndrome (CRS) reflects the complex interplay between kidney and heart diseases, but its molecular basis remains poorly understood. Multiple studies have demonstrated the association of urinary biomarkers with both heart and kidney diseases. However, their relevance and involvement in CRS have not been investigated yet. To address this gap, a study was designed with the aim to compare urinary biomarkers specific for heart failure (HF) and chronic kidney disease (CKD) with peptides representing CRS, with the ultimate target to connect these findings towards a better understanding of CRS pathophysiology.

Method: A total of 3.463 urinary peptidomic datasets from patients with HF, CKD, or with both HF and CKD (CRS) as well as patients with no apparent diseases (controls) were retrieved and analyzed from the urinary peptidomics database (Latosinska A et al., Electrophoresis 2019; 40: 2294-2308). Following the matching for age, gender, heart and kidney function, differences in the abundance of urinary peptides were investigated in a cohort comprised of 390 patients with HF, 257 patients with CKD, 392 patients with CRS and 356 controls. The non-parametric Mann-Whitney U test was applied, followed by correction for multiple testing using the Benjamini-Hochberg method. To map the peptides to the protein precursor, the alignment tool Geneious (www.geneious.com) was applied, while the PeptideRanker (http://distilldeep.ucd.ie/PeptideRanker/) was used to predict probability of peptide being bioactive.

Results: The multiple pair-wise comparisons resulted in the identification of numerous differentially abundant peptides ($p<0.05$) between the studied conditions, including among others 176 HF-specific, 146 CKD-specific and 35 CRS-specific peptides. Among the HF-specific peptides, the majority (n=94, 53.4%) originated from collagen type I, II and III. In the case of CKD-specific peptides, 24 (16.43%) originated from alpha-1-antitrypsin, 19 (13.0%) from b2-microglobulin and 15 (10.27%) from collagen type I. For the CRS specific peptides, fragments of Ig lambda-2 chain C regions (n=4, 11.42%), collagen type III (n=4, 11.42%), secreted and transmembrane protein 1 (n=3, 8.57%) and gelsolin (n=1, 2.85%) were identified (figure: 1). Of the 176 HF-specific peptides, 94 (53.40%) were predicted as bioactive, including, among others, fragments of collagen types I (n=43, 45.74%) and III (n=21, 22.34%). In the former, peptides with the higher bioactivity scores were aligned close to the N terminus of the precursor protein, whereas in the latter, peptides were in close proximity to both N and C termini. Along the same lines, 32 (21.91%) of the 146 CKD-specific peptides were predicted as bioactive, including peptides from collagen types I and III with the highest score, as well as fragments from collagen type V and the C terminus of the b2-microglobulin and alpha-1-antitrypsin proteins. No CRS-specific peptides could be predicted as bioactive.

Conclusion: Specific urinary peptides significantly associated with CRS, but not with HF or CKD, could be identified. These data indicate that on a molecular level, CRS is not merely the result of a combination of HF and CKD, but may represent a distinct pathology, defined via specific proteomic changes. It is expected that interpretation of these findings in the context of existing literature as well as *in vitro* activity assays will help to understand their biological relevance in CRS.

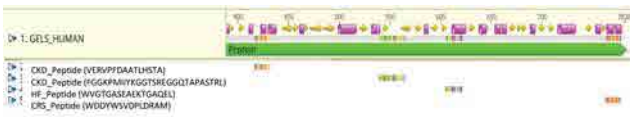


Figure: Specific peptides are associated with distinct pathologies. As example, peptides significantly associated with CKD, HR, or CRS derived from Gelsolin are depicted. The data indicate potential activation of distinct proteases specific for the different pathologies.

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P0954 **EFFECTS OF INTRADIALYTIC EXERCISE FOR ADVANCED-AGED PATIENTS UNDERGOING HEMODIALYSIS: A RANDOMIZED CONTROLLED TRIAL.**

HIROKI YABE[1], Kenichi Kono[2], Yumiko Ishikawa[3], Hisanori Azekura[4]

[1]School of Rehabilitation Sciences, Seirei Christopher University, Department of Rehabilitation, Hamamatsu, Japan, [2]International University of Health and Welfare School of Health Sciences at Narita, Department of Physical Therapy, Narita, Japan, [3]Sanaru sun clinic, Department of Nursing, Hamamatsu, Japan and [4]Sanaru sun clinic, Department of Nephrology, Hamamatsu, Japan

Background and Aims: Exercise therapy, a treatment for poor physical function in patients undergoing dialysis, has shown some evidence of effectiveness. Some meta-analysis indicated the effectiveness of exercise interventions on exercise tolerance, muscle strength, and quality of life. However, most studies assessing the effects of exercise in patients undergoing hemodialysis have involved middle-aged patients; few data for advanced-age patients undergoing hemodialysis are available. The concept of exercise intervention for young to middle-aged patients undergoing hemodialysis is not entirely applicable to older patients, and whether exercise training improves physical function in older patients undergoing hemodialysis remains unclear. Therefore, the present randomized controlled trial (RCT) was performed to verify the effectiveness of exercise therapy in advanced-age patients undergoing hemodialysis.

Method: In this single-center, prospective, parallel RCT, all patients were randomly assigned to either the exercise or control group. The inclusion criteria were an age of $\geq$70 years and no acute or chronic medical conditions that would preclude assessment of the outcome measures or the performance of exercise. Ethical approval was provided by Seirei Christopher University.

Patients randomized to the exercise group were offered 6 months of exercise training three times a week. The training program involved both resistance and aerobic training exercises. Four types of resistance exercises were performed using an elastic tube. The exercise intensity was adjusted by the tube stiffness to achieve a target a Borg score of 13 to 15 for fatigue. The aerobic exercise program consisted of ergometer cycling for 20 minutes. The exercise intensity was adjusted to a target Borg score of 13. The leg extremity muscle strength (LES), Short Physical Performance Battery (SPPB) score, and 10-m walk speed were evaluated before and after 6 months of training.

The group effect was analyzed by analysis of covariance (ANCOVA) using the change in scores (Δ, post minus pre) as the dependent variable and baseline value of the dependent variable in the model as a covariate. Additional covariates for the ANCOVA models were identified by comparison of group means at baseline. The effect size (ES) was calculated as the change in the exercise group minus the change in the control group divided by the pooled standard deviation, corrected for sample size.

Results: Among the 101 randomly assigned patients, 17 (16.8%) were unavailable for follow-up testing. As a result, 84 patients (44 in the exercise group and 40 in the control group) were included in the analysis. The group comparison revealed no differences in any baseline characteristics between the two groups. Statistically significant increases in the ΔSPPB score were found in the exercise group (0.7 ± 2.1) as compared with the control group (-0.4 ± 2.0), with a moderate ES of 0.57. The ΔLES and Δ10-m walk speed were not significantly different between the groups, and the ES was 0.18 and 0.00, respectively.

Conclusion: The purpose of this RCT was to verify the effectiveness of exercise therapy in advanced-age patients undergoing hemodialysis. After 6 months of aerobic and resistance intradialytic training, we observed statistically significant increases in the ΔSPPB score in the exercise group as compared with the control group, with a moderate ES of 0.57. Exercise therapy improves physical function in older patients undergoing dialysis, and the effectiveness may differ from that in middle-aged patients; however, this change is clinically important in older patients.

P1311 **IMPORTANCE OF FISTULA POSITION FOR DETECTING STENOSIS WITH VASCULAR ACCESS BLOOD FLOW MEASUREMENT**

Csaba Rikker[1], Edina Juhász[1], Renáta Gáspár[1], Maria Haraszti[1], Bálint Rikker[1], Ildikó Vizi[2]

[1]FMC, Péterfy I. Dialysis Center, Budapest, Hungary and [2]Affidea Hungary Kft., Budapest, Hungary

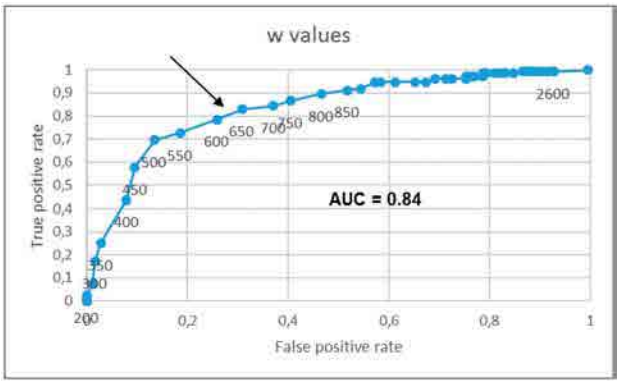
Background and Aims: Surveillance of vascular access function in patients on chronic hemodialysis (HD) by measuring the access blood flow rate (Qa) is a widely accepted method for early detection of dysfunction. Qa threshold can be lower in the more distal accesses than in the more proximal accesses. However, cut-off values of Qa in different access positions have not yet been established. The aim of our study is to determine the critical values of Qa indicative of stenosis in different access sites.

Method: Between July 2012 and July 2019, we performed 5798 Qa measurements of native arteriovenous fistulas (AVFs) (wrist [w]: 2932, forearm [fa]: 2035 and elbow/upper arm [e/ua]: 731) in 242 chronic HD patients using Fresenius 5008 and 5008 S blood temperature monitors (BTMs) at the beginning of HD sessions. As reference we performed 512 colour duplex ultrasonographies (CDUSs) and 205 angiographies (ANGs). CDUS was performed as surveillance method independently from the BTM, or at the presence of low Qa and/or clinical signs of access failure. ANG was performed only in CDUS positive cases or at clinical signs of access failure. We performed percutaneous transluminal angioplasty (PTA) in 174 cases and stent implantation in 2 cases. New AVFs were created in 25 cases. The results were evaluated retrospectively according to access positions using Receiver Operating Characteristic (ROC) curve analysis.

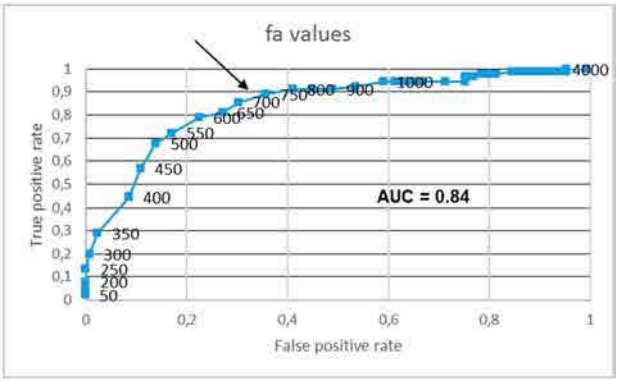
Results: The number of true positive (TP), true negative (TN), false positive (FP), false negative (FN) cases, sensitivity (SENS) and specificity (SPEC) in different AVF sites and Qas are summarised in table below.

Qa mL/min	sum	w <650	fa<700	e/ua<800
TP	212	112	77	23
TN	264	123	90	51
FP	107	55	39	13
FN	43	23	13	7
SENS	0,83	0,83	0,86	0,77
SPEC	0,71	0,69	0,70	0,80

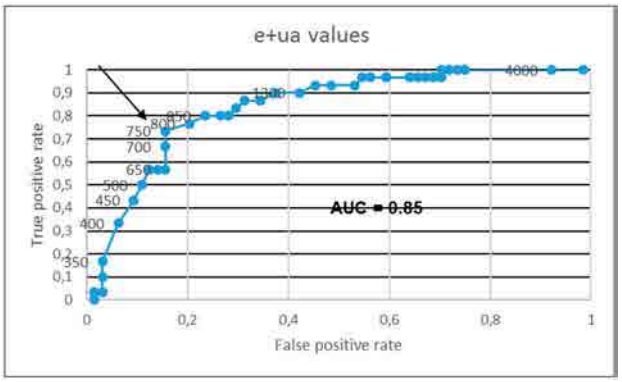
Conclusion: In order to prevent the fistula occlusion, the cut-off Qas can be different in various access positions. Based on our results we suggest 600-650 mL/min for w AVFs, 650-700 mL/min for fa AVFs and 750-800 mL/min for e/ua AVFs as cut-off values.



Figures:



Figures:



Figures:

P1312

EFFECT OF KIDNEY TRANSPLANTATION RATE ON THE ARTERIOVENOUS FISTULA RATE IN PREVALENT HEMODIALYSIS PATIENTS: ANALYSIS OF DATA FROM THE CATALAN RENAL REGISTRY (1997-2017)

Ramon Roca-Tey[1,1,1], Jordi Comas[2], Jaume Tort[2]

[1]Hospital de Mollet, Nephrology, Mollet del Vallès, Spain and [2]Health Department of Catalonia, Registre de Malalts Renals de Catalunya (RMRC), Organització Catalana de Trasplantaments (OCATT), Barcelona, Spain

Background: Kidney transplantation (KT) is considered to be the best option of renal replacement therapy (RRT) for most end-stage renal disease (ESRD) patients (pts). Furthermore, arteriovenous fistula (AVF) is considered to be the best vascular access (VA) for most hemodialysis (HD) pts.

Aims: To analyze the effect of KT rate on the AVF rate in prevalent HD pts. In addition, the likelihood of receiving a kidney graft (KG) over time according to the first VA used to start HD program was also evaluated

Method: Data from the Catalan Registry of ESRD pts treated with either KT or HD were examined for a 20-year period

Results: The functioning KG rate increased progressively from 40.5% (n=2211) in 1997 to 57.0% (n=6149) in 2017 and, conversely, the AVF rate in prevalent HD patients decreased progressively from 86.0% (n=2609) to 63.2% (n=2546) during the same period (for both comparisons, $p < 0.001$).

The characteristics of all prevalent HD pts dialyzed in 1997 (n=3104) vs 2017 (n=4205) were different regarding age 62.6±15.3 vs 70.3±14.2 yr, diabetic nephropathy (DN) 13.2% vs 21.8% and cardiovascular disease (CD) 67.6% vs 75.8% (for all comparisons, $p<0.001$). On December 31, 2017 (maximum KT rate), the characteristics of KG recipients were different compared with prevalent HD pts dialyzed through either an AVF or a tunneled catheter (n=1145): age 57.4±14.5 vs 69.9±13.8 vs 72.0±14.6 yr, DN 9.5% vs 21.7% vs 22.5%, CD 38.6% vs 74.3% vs 83.7% (for all comparisons, $p<0.001$).

By analyzing the likelihood of prevalent pts performing HD through an AVF, we saw it was lower in pts with DN (OR: 0.86; 95% CI: 0.79-0.94, p=0.001) and it decreased progressively as they got older (reference >74 yr): <44 yr (OR:1.55, 95% CI: 1.41-1.70, $p<0.001$), 45-64 yr (OR: 1.47, 95% CI: 1.38-1.56, $p<0.001$) and 65-74 yr (OR: 1.22, 95% CI: 1.17-1.28, $p<0.001$). This probability was higher in males (OR: 1.84, 95% CI: 1.73-1.95, $p<0.001$), pts with polycystic kidney disease (OR: 1.54, 95% CI: 1.35-1.77, $p<0.001$) and pts without CD (OR: 1.32; 95% CI: 1.27-1.38, $p<0.001$) and it increased according to the time on RRT (reference < 1 month): >12 m (OR: 2.39, 95% CI: 2.17-2.64, $p<0.001$). In addition, this likelihood decreased progressively as the percentage of patients with a functioning KG increased (reference >55%): 40-45% (OR: 3.26, 95% CI: 3.05-3.48, $p<0.001$), 45-50% (OR: 1.82, 95% CI: 1.73-1.92, $p<0.001$) and 50-55% (OR: 1.27, 95% CI: 1.21-1.33, $p<0.001$).

The rate of prevalent HD pts waitlisted for KT and dialyzed through AVF decreased progressively from 94.5% (639/676, 1997) to 77.9% (491/630, 2017). In parallel, but always remaining at a lower level, the rate of prevalent HD patients not waitlisted for KT and dialyzed through AVF also decreased progressively from 83.6% (1970/2357) to 60.5% (2055/3399) during the same period (for all comparisons, $p<0.001$). Considering the prevalent HD pts during the period 2014-2017 (n=4029), significant differences were observed between HD pts waitlisted (n=630, 15.6%) and not-waitlisted (n=3399, 84.4%) for KT regarding age (58.2±12.9 vs 72.8±13.1 yr), DN (16.2% vs 23.0%), CD (59.5% vs 80.5%) and distribution of AVF (77.9% vs 60.5%) or tunneled catheter (16.5% vs 30.6%) (for all comparisons, $p<0.001$).

During the period 2012-2014, incident pts starting HD through an AVF (n=1026) had a significant higher likelihood of receiving a KG over time (HR: 1.68, 95% CI: 1.41-2.00, $p<0.001$) in comparison to pts who initiated HD through a catheter (n=1408).

Conclusion: 1) The fall of prevalent HD pts with AVF over time could be associated with a progressive worsening of their clinical profiles along with the increasing rate of KG recipients. 2) In addition to some demographic and clinical characteristics of prevalent HD pts, the annual KT rate was also a determining factor in their AVF rate. 3) Starting HD program through an AVF was independently associated with a greater likelihood of receiving a KG over time as compared to starting HD through a catheter.

P1313 **CHANGES IN VASCULAR ACCESS AND HEALTH-RELATED QUALITY OF LIFE**

Chen Chen[1], Yue Jiao[2], Anke Winter[1], John Larkin[2], Len A Usvyat[2], Manuela Stauss-Grabo[1], Franklin Maddux[3]

[1]Fresenius Medical Care Deutschland GmbH, EMEA Medical Office, Bad Homburg, Germany, [2]Fresenius Medical Care, Global Medical Office, Waltham, United States of America and [3]Fresenius Medical Care AG & Co. KGaA, Global Medical Office, Bad Homburg, Germany

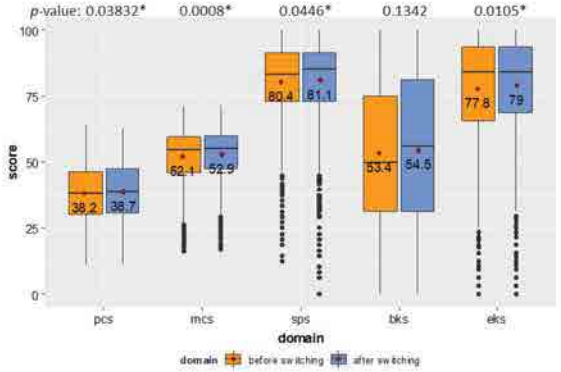
Background and Aims: The patient's reported perception of their health-related quality of life (HRQOL) are important patient-centered metrics that associate with outcomes in hemodialysis (HD) populations. Patients using an arteriovenous (AV) access (fistula or graft) tend to report better HRQOL compared with those dialyzing via a catheter (Wasse et al. 2007; Moura et al. 2014). However, these differences might be due to distinct characteristics of patients who have an AV access placed, or not. For example, catheter-dependent patients are typically older and have more comorbidities than those with an AV access. We considered a different way to evaluate the impact of vascular access on HRQOL in HD patients by assessing whether a change from a catheter to an AV access, and vice versa, associates with changes in HRQOL.

Method: We used data from adult in-center HD patients (age ≥18 years) treated at a large dialysis organization in the United States from 2016-2017. Patients who had one vascular access conversion and used the corresponding access for at least 12 months before and after the conversion were included in the analysis. HRQOL was assessed by Kidney Disease Quality of Life (KDQOL-36) surveys (0-100 scale) performed over the 12 months preceding and following the change. We computed the mean score for each of the five KDQOL domains in each time period and compared the score differences between pre- and post-access change using Student's t-tests for each conversion type.

Results: A total of 1088 HD patients (mean age 59.2 years, 52.6% male, and 59.3% white race) switched from a catheter to an AV access and 3427 patients (mean age 61.8 years, 47.8% male, and 50.7% white race) switched from an AV access to a catheter over the analysis period. After conversion from a catheter to an AV access, patients reported significantly higher physical component summary (+0.5, $p<0.05$), mental component summary (+0.8, $p<0.001$), symptoms and problems of kidney disease (+0.7, $p<0.05$), and effects of kidney disease (+1.2, $p<0.05$) scores (Figure 1). No significant difference was observed for four out of the five domains following the change from an AV access to a catheter, except for physical component summary, where the score dropped by 1.2 points ($p<0.01$) (Figure 2).

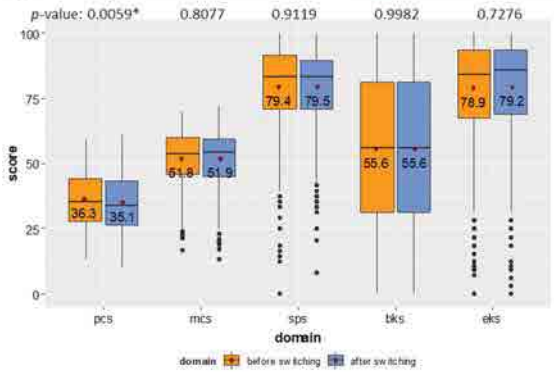
Conclusion: Our results suggest switching from a catheter to an AV access may associate with patients perceiving an improved physical and mental HRQOL. In contrast, changing from an AV access to a catheter might associate with a diminished perception of physical HRQOL. Albeit distinctions in HRQOL are statistically significant, absolute differences were below two points and the clinical meaning needs to be assessed in further adjusted analyses considering the underlying reasons for vascular access conversions. Nonetheless, these findings may be of importance to provide more patient focused care.

Figure 1. KDQOL scores before and after conversion from a catheter to an AV access



pcs = physical component summary; mcs = mental component summary; sps = symptoms and problems of kidney disease score; bks = burden of kidney disease score; eks = effects of kidney disease score

Figure 2. KDQOL scores before and after conversion from an AV access to a catheter



pcs = physical component summary; mcs = mental component summary; sps = symptoms and problems of kidney disease score; bks = burden of kidney disease score; eks = effects of kidney disease score

Figure:

P1314 TEN YEAR EXPERIENCE ON VASCULAR ASSESS PLACEMENT BY NEPHROLOGIST

Himansu Mahapatra[1], Lalit Pursnani[2], Muthukumar B[2], Neeraj Inamdar[2], Adarsh Kumar[2], Kushal DP[2], Renju Binoy[2], Navjot Kaur[2], Mansi Singh[2], Anamika Kumari[2], Chandra Krishnan[2]

[1]ABVIMS, Dr. R.M.L. Hospital, New Delhi, India, Nephrology, New Delhi, India and [2]ABVIMS, Dr. Ram Manohar Lohia Hospital, Nephrology, New Delhi, India

Background and Aims: Across the globe, vascular assess placement for haemodialysis is performed by Anaesthesiologist, Nephrologist, Radiologist, and surgeons depending on the experts availability of that locality. Patient care should not suffer because of lack of round the clock surgical and radiological expertise. We would like to share our ten year experience of vascular assess placement and their outcomes which were performed in the Department of Nephrology.

Method: A total 11429 vascular assess procedures have been carried out during 2009 to 2019. There were 781 AVF, cuffed 476 and non-cuffed 10172 (Internal Juglar 5375, Subclavian 2042 and femoral 2755) catheter insertions were performed. For construction of AVF, Pre-procedure ultrasound Doppler was performed to see both the anatomy of vein and artery. Radiocephalic and brachiocephalic AVF construction were done by side to side arteriovenous anastomosis using 6-0 Prolene double ended needle under strict asepsis. Insertion complications (bleeding and air-embolism), procedure time, patency, blood flow, and post-procedure complications (hematoma) were recorded. Follow up was done on 10th and 30th day of post surgical period. Of 476 Permcath, 58 were placed without valve guided peel away sheath catheters and rest with valve guided peel away sheath catheters in right internal jugular vein.

Results: Of 781 AVF, 557 (71.3%) were males and mean age 42.7±15.1 years. Of them, diabetes 330 (42.25%) and non-diabetes 451 (57.74%) were, Basic disease were DM 134 (16.15%), HTN 115 (14.72%), CGN 121 (15.49%), CTIN 124 (15.87%), Unknown 173 (22.15%) and others 114 (14.59%) were respectively. Common sites of AVF site were were left radiocephalic 319 (40.84%), left brachiocephalic 321 (41.1%) and both side brachiobasilic 141 (18%). Pre procedure ultrasound doppler findings were arterial diameter 2.79±0.96, venous diameter 2.75±0.86, arterial pulse wave velocity 57.93±19.49, diameter. The average duration of the procedure was 70 min without any intra operative complication. Five patients developed post-operative bleeding required re-exploration. The average duration between the construction of the fistula and the day of successful cannulation was 37 days. After six weeks venous diameter were 5.06±1.58 having blood blow of 766.17±536.36 ml/min. Successful cannulation could be done in 418 (53.52%) patients and another 363 (46.47%) patients did not have satisfactory thrill even after the stipulated time of maturation were declared failed AV fistulas. Other common complications observed were stenosis 351 (44.94%), edema 140 (17.92%), ischemia 124 (15.87%), thrombosis 124 (15.87%), infections 109 (13.95%) and aneursyms 112 (14.34%) respectively

The technical success rate of catheter placement were 98% without any major insertion or post-procedure complications. Average procedural time was 20 minutes. Mal position of Permcath was seen in 38 (7.9%) patients, catheter thrombosis 45 (9.4 %) patients.

Conclusion: It is quite safe for nephrologists to perform surgical procedures required for vascular access for dialysis. The valve-guided tunnelled catheter insertion and side to side anastomosis AVF construction may be adopted as a routine practice by the Nephrologists.

P1315

PREDICTABILITY OF SONOGRAPHICALLY DETERMINED IMMEDIATE POST-OPERATIVE BLOODFLOW AND VEIN DIAMETER ON PRIMARY RADIOCEPHALIC FISTULA SHORT AND LONGTERM OUTCOMES.

Claude Renaud[1,2], Desmond Ooi[3], Chuo Ren Leong[3]

[1]Khoo Teck Puat Hospital, Medicine, Singapore, Singapore, [2]National University of Singapore, Medicine, Singapore, Singapore and [3]Khoo Teck Puat Hospital, General Surgery, Singapore, Singapore

Background and Aims: Vascular access (VA) guidelines recommend radio-cephalic (RC) over upper arm autogenous arteriovenous fistulas (AVF) as first line VA for hemodialysis in end stage renal disease (ESRD) patients. RCAVFs generally have inferior maturation and patency rates predicated on a lower feeding arterial blood flow (BF) and outflow vein calibre (VC). However studies on postoperative BF and VC as predictors of AVF outcomes, so far are confounded by their focus on early outcomes only, heterogeneity of AVFs studied, variable timing of assessment and use of non-standardised outcome definitions. Our aim was therefore to assess the accuracy and influence of immediate post-operative BF and VC on both early and longterm outcomes in a homogenous cohort of primary RCAVFs using standardised definitions and outcome measures as mandated by VA guidelines.

Method: This was a prospective study conducted in multi-ethnic Asian ESRD patients who had their primary RCAVFs created between October 2013 and October 2014 under regional anesthesia at Khoo Teck Puat hospital Singapore. All AVFs were assessed immediately after surgery for brachial artery BF and outflow VC using doppler ultrasound. A 10MHz linear probe and GE Logic e R7 machine were used exclusively by a single operator. Receiver operating characteristic (ROC) curves were generated to determine the optimal BF and VC cut-off for AVF maturation. Maturation was defined as BF>600mL/min, VC>6mm and vein depth <6mm at 6 weeks post-op. An area under the curve (AUC)> 0.7 was considered clinically significant. Kaplan–Meier analysis was used to evaluate the AVF primary and secondary patency based on best BF and VC cut-offs. Cox regression statistics was used to determine AVF hazard factors.

Results: Fifty-seven primary RCAVFs were created and included in the study. The baseline characteristics are shown in Table 1. Sonography- based non-assisted maturation at 6 weeks was 56%. ROC identified 410 mL/min and 42mm as the best BF and VC cut-off respectively to most accurately predict 6-week maturation. The sensitivity, specificity, positive predictive value and negative predictive value were 75%, 61%, 44% and 86% for BF at 410 mL/min and 69%, 61%, 41% and 83% for VC at 42mm respectively. Survival analysis (Fig. 1 and 2) showed that AVFs with VC≥42 mm compared to <42mm had significantly greater 6 months, 1-year, 2-year and 4-year primary and secondary patency rates. There was no significant difference in patency rates between AVFs with BF≥410 and <410mL/min. Cox proportional regression hazard analysis showed that diabetes (HR 2.26, CI 1.02-4.99, p= 0.04) and maturation (HR 0.47, 95% CJ 0.24-0.89, p=0.02) as significant contributed to the variability of primary patency. Only VC (HR 0.28, 95% CI 0.13-0.063, p=0.002) impacted significantly towards secondary patency.

Variable,	Value
n=57	
Age (years), median (IQR)	58(13)
Male gender	39(69)
Chinese, n(%)	29 (50)
Diabetes, n(%)	42 (74)
Ischemic heart disease, n(%)	14(24)
Obesity (BMI>30 kg/m²), n(%)	15(31)
Smoker, n(%)	17(30)
On antiplatelets, n(%)	38(67)
Pre-hemodialysis, n(%)	20(35)
Follow up (months), median(IQR)	49(38)

IQR, interquartile range

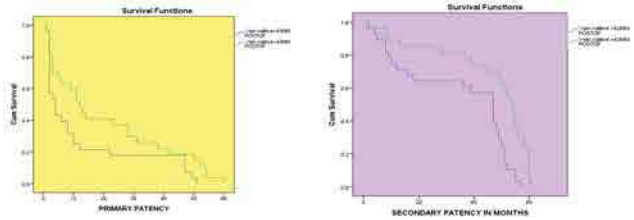


Fig.1–Kaplan-Meier curve showing primary and secondary patency of RC AVFs with vein calbre <42 or >42mm

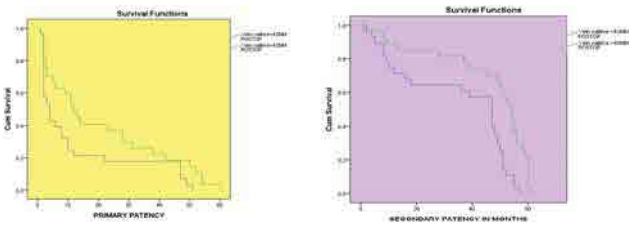


Fig.2 –Kaplan-Meier curve showing primary and secondary patency of RC AVFs with flow <410 or >410 mL/min

Conclusion: An immediate post-op BF≥410mL/min and VC≥42mm can predict early RCAVF outcome in the form of nonassisted maturation, but only VC accurately impact on longterm AVF survival. VA surveillance efforts should therefore target RCAVFs with post-op VC <42mm for timely intervention and maintenance of longterm patency.

P1316 PREDICTORS OF ARTERIO-VENOUS FISTULA FAILURE: A POST-HOC ANALYSIS OF THE FAVOURED STUDY

Yong Pey See[1], Andrea Viecelli[2], David Voss[3], Trevor Mori[4], Peter Kerr[5], Peta-Anne Paul-Brent[2], Yeoungjee Cho[2], David W Johnson[2], Carmel Hawley[2], Elaine M Pascoe[2]

[1]Tan Tock Seng Hospital, Renal Medicine, Singapore, Singapore, [2]Princess Alexandra Hospital, Brisbane, Nephrology, Brisbane, Australia, [3]7Middlemore Renal Department, Counties-Manukau Health, Auckland, Auckland, New Zealand, [4]Medical School, University of Western Australia, Perth, Australia and [5]8Department of Nephrology, Monash Medical Centre, Melbourne, Australia

Background and Aims: An autologous arteriovenous fistula (AVF) is the preferred haemodialysis vascular access but successful creation is hampered by high rates of AVF failure. This study aimed to evaluate patient and surgical factors associated with AVF failure to improve vascular access selection and outcomes.

Method: This is a post-hoc analysis of all participants of FAVOURED, a multi-centre, double-blind, multinational, randomized placebo-controlled trial evaluating the effect of fish oil and/or aspirin in preventing AVF failure in patients receiving haemodialysis. The primary outcome of AVF failure was a composite of fistula thrombosis and/or abandonment and/or cannulation failure at 12 months post AVF creation and secondary outcomes included individual outcome components. Patient data (demographics, comorbidities, medications and laboratory data) and surgical factors (surgical expertise, anaesthetic, intraoperative heparin use) were examined using multivariable logistic regression analyses to evaluate associations with AVF failure.

Results: Of 536 participants, 253 patients (47%) experienced AVF failure during the study period. The mean age was 55 $\pm$ 14.4 years, 64% were male, 45% were diabetic and 4% had peripheral vascular disease. Factors associated with AVF failure included female sex (odds ratio [OR] 1.78, 95% confidence interval [CI] 1.20-2.67), lower diastolic blood pressure (DBP; OR for higher DBP 0.98, 95% CI 0.97-0.99), presence of central venous catheter (OR 1.50, 95% CI 1.02-2.20, p=0.04) and aspirin requirement (OR 1.61, 95% CI 1.01-2.57).

Conclusion: Female sex, requirement for aspirin therapy, requiring haemodialysis via a central venous catheter and lower diastolic blood pressure were factors associated with higher odds of AVF failure. These associations have potential implications for vascular access planning and warrant further studies.

P1317

THE PREVALENCE OF CENTRAL VENOUS CATHETERS AND LOWER ARM ARTERIOVENOUS FISTULAS DEPENDS ON DIFFERENT VASCULAR ACCESS MANAGEMENT POLICIES: A MULTICENTER ITALIAN STUDY

Pietro Finocchiaro[1], Antonino Alberti[2], Rocco Tripepi[3], Maria Carmela Versace[3], Maurizio Garozzo[4], Filippo Milone[4], Giovanni Giorgio Battaglia[4], Sandra La Rosa[5], Rosario Maccarrone[6], Antonio Granata[6], Concetto Sessa[7], Barbara Pocorobba[7], Salvatore Musso[7], Davide Bolignano[8], Dario Pazzano[1], Pietro Volpe[2], Francesca Mallamaci[1]

[1]Grande Ospedale Metropolitano, Nephrology, Dialysis and Transplant Unit, Reggio Calabria, Italy, [2]Grande Ospedale Metropolitano, Vascular Surgery, Reggio Calabria, Italy, [3]National Research Council, Insitute of Clinical Physiology, Reggio Calabria, Italy, [4]Azienda Sanitaria Provinciale di Catania, P.O. S.Marta e S.Venera, Catania, Italy, [5]Presidio Ospedaliero Sciacca, Ospedale Giovanni Paolo II Via Pompei, Agrigento, Italy, [6]Presidio Ospedaliero Agrigento, Ospedale San Giovanni di Dio, Contrada Consolida, Agrigento, Agrigento, Italy, [7]Osedale Maggiore, UOC Nephrology and Dialysis, Modica, Italy and [8]-University "Magna Graecia" of Catanzaro, Department of Medical and Surgical Sciences, CATANZARO, Italy

Background and Aims: According to local resources, different vascular access (VA) procedures are employed in every country. In Italy, high variability exists in VA management among different dialysis units. In 2018, the DOPPS 5 study showed a declining prevalence of lower arm arteriovenous fistulas (AVF) in Europe with an increasing tendency of making upper arm AVFs and placing central venous catheters (CVCs). Accordingly, an Italian Survey in 2013 confirmed an increasing trend in CVCs use among different Italian regions.

Hence, we made an epidemiologic, multicenter study to evaluate a possible relation between this trend and the variability of local VA management policies.

Method: VA data from 236 patients of prevalent patients were collected from five dialysis centers in the South of Italy. The prevalence of the various types of VAs was analyzed in relation to the following different VA surgery policies adopted in the participant centers:

The vascular surgeon makes all VAs and the nephrologist has a coordinator role (Center A).

The nephrologist manages most VA procedures with the vascular surgeon support being requested only for some upper arm fistulas and more invasive surgery (Centers B – C).

The nephrologist manages all VA procedures and the vascular surgeon support is rarely requested (Centers D – E).

Results: Age of patients was comparable among all centers while dialysis vintage was higher in center A ($P<0.001$). The prevalence of lower arm AVFs was significantly reduced In Center A (50.6%) and the prevalence of CVCs (25.8%) was significantly increased as compared to the Centers D-E. On the contrary the Centers D-E had the highest prevalence of lower arm AVF (70.8%) and the lowest of CVCs (12.3%), with a statistically significant difference as compared to Center A (Table 1). Conversely, no differences were noticed when comparing data from Centers B-C vs. Center A and vs. Centers D-E, although the prevalence of lower arm AVFs was slightly higher, but the difference was not significant, and that of CVCs was slightly lower as compared to Center A ,fully supported by the vascular surgeon (Figure 1).

Conclusion: The reduced tendency of lower arm fistulas and the increasing prevalence of CVCs showed by the DOPPS 5 study might not be applicable to all Italian regions. In our study of 5 dialysis units in the South of Italy, the stability of the nephrologist's surgical activity probably played a crucial role in explaining the observed decreased use of CVCs with a steadily high prevalence (over 70%) of the lower arm fistulas, regardless of aging.

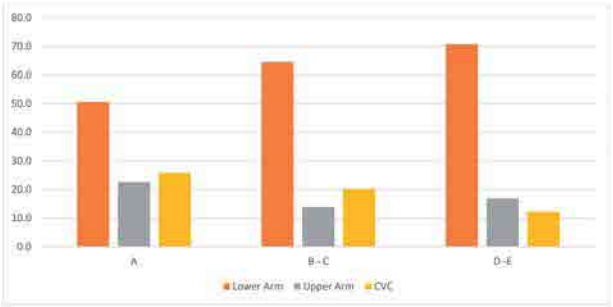


Figure:

P1371

HEART FAILURE HOSPITALISATIONS IN THE PIVOTAL TRIAL OF IV IRON IN HAEMODIALYSIS PATIENTS: A PRE-SPECIFIED SECONDARY ANALYSIS

Pardeep Jhund[1], Mark Petrie[1], Michele Robertson[2], Patrick Mark[1], Michael Macdonald[1], Eugene Connolly[1], Claire White[3], Chante Reid[3], Stefan D. Anker[4], Sunil Bhandari[5], Kenneth Farrington[6], Philip A. Kalra[7], Charles R.V. Tomson[8], David Wheeler[9], Ian Ford[2], John McMurray[10], Iain Macdougall[11]

[1]University of Glasgow, BHF Cardiovascular Research Centre, United Kingdom, [2]University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom, [3]King's College Hospital, Department of Renal Medicine, United Kingdom, [4]German Center for Cardiovascular Research, Department of Cardiology, Berlin, , [5]Hull Royal Infirmary, Renal Unit, United Kingdom, [6]Lister Hospital, Renal Unit, United Kingdom, [7]Salford Royal NHS Foundation Trust, Renal Unit, Salford, United Kingdom, [8]Newcastle Freeman Hospital, Renal Unit, High Heaton, United Kingdom, [9]University College London, Department of Renal Medicine, London, United Kingdom, [10]University of Glasgow, BHF Cardiovascular Research Centre, Glasgow, United Kingdom and [11]King's College Hospital, Department of Renal Medicine, London, United Kingdom

Background and Aims: Heart failure (HF) is a common and potentially deadly complication in patients receiving haemodialysis which is difficult to diagnose and treat. The impact of a proactive high-dose strategy compared to a reactive low-dose strategy of IV iron administration was investigated in the PIVOTAL randomised trial in incident haemodialysis patients, with fatal HF and HF hospitalisation being components of the composite primary cardiovascular endpoint as well as a pre-specified key secondary event.

The aim of this analysis was to examine the effect of a proactive high-dose strategy compared to a reactive lower dose strategy on HF events in patients recruited to PIVOTAL.

Method: As with the primary composite cardiovascular endpoint, HF hospitalisations in PIVOTAL were recorded prospectively via an electronic database, and events were then adjudicated by a blinded Endpoint Adjudication Committee. The time-to-event analyses of the primary, secondary and post hoc outcomes were performed in the intention-to-treat population using Cox proportional hazards regression, with treatment group as the only explanatory variable. The Kaplan–Meier method was used to estimate event rates. Both fatal and non-fatal HF events were analysed as time to first event, and a recurrent event analysis was also performed for non-fatal events.

Results: Overall, 2141 participants were followed for a median of 2.1 years. A first fatal or non-fatal HF event occurred in 51 of 1093 patients (4.7%) in the high-dose iron group and in 70 of 1048 patients (6.7%) in the low-dose iron group (hazard ratio 0.66, 95% confidence interval 0.46 to 0.94; P<0.001) (Figure). There was a total of 63 HF events (including first and recurrent events) in the high-dose iron group and 98 in the low-dose iron group, giving a rate ratio of 0.59 (0.40-0.87); p=0.0084. A history of HF and diabetes were independent predictors of a heart failure event.

Conclusion: Compared with a low-dose regimen, high-dose intravenous iron decreased the occurrence of first and recurrent heart failure events in incident patients undergoing haemodialysis, with large relative and absolute risk reductions.

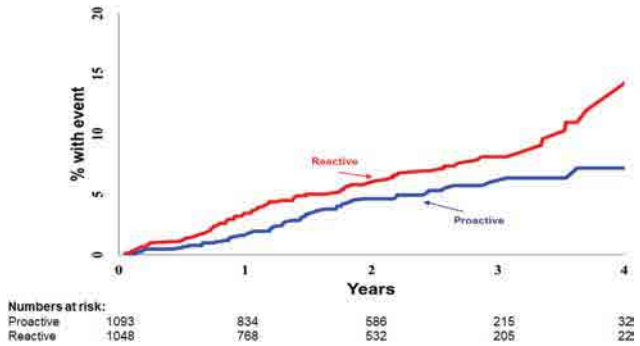


Figure:

MODERATED POSTER SESSION 3

P0667 FIBROBLAST GROWTH FACTOR 21 PROMOTES AND PREDICTS VASCULAR CALCIFICATION IN HAEMODIALYSIS PATIENTS

Liqiong Jiang[1], Bin Wang[2], Bicheng Liu[3]

[1]the Affiliated Suzhou Hospital of Nanjing Medical University, Nephrology, suzhou, P.R. China, [2]Zhong Da Hospital, Southeast University School of Medicine, Institute of Nephrology, Nanjing, P.R. China and [3]Zhong Da Hospital, Southeast University School of Medicine, Zhong Da Hospital, Southeast University School of Medicine, Nanjing, P.R. China

Background and Aims: Cardiovascular disease (CVD) is the leading cause of death in hemodialysis (HD) patients. Vascular calcification (VC) is dramatically accelerated and strongly associated with CVD events and mortality in HD patients. This study aimed to achieve 4 objectives using a population-based retrospective cohort of HD patients: (1)quantify the correlation between FGF21 and VC; (2)determine whether FGF21 is a novel risk factor for VC; (3)examine the predictive effect of FGF21 on VC; (4)explore the underlying mechanism of FGF21 in promoting VC, especially focused on the EndMT process, in cultured human aortic endothelial cells (HAECs).

Method: 802 HD patients were screened, at last 388 HD patients were eligible in the study. Serum FGF21 levels were assessed by ELISA kits. Chest radiographies of HD patients taken by multislice computed tomography were used to measure TACS. HD patients were divided into two groups : low TACS group (< median of TACS) and high TACS group (≧median of TACS). Univariate analyses were performed to compare the differences between two groups. Categorical data were compared using the Chi-square test. Stepwise multivariate linear regression analyses were employed to evaluate variables independently associated with TACS. The ROC curves were performed to calculate the AUC and compare the prognostic value of every independently associated factor or united factor to VC. Additionally HAECs was pretreated with FGF21 in the presence or absence of PTH. The formation of calcium deposits was analysed by Alizarin Red staining (ARS). PCR for the measurement of mRNA of CD31, RUNX2 and FSP1 to evaluate endothelial-to-mesenchymal transition (EndMT) of HAECs.

Results: Prevalence of VC was 70.1% in this study. Serum FGF21 levels of HD patients were 11-fold higher than controls (median 217 vs. 20 pg/ml). HD patients in the high TACS group had older age, higher FGF21, higher FGF23, longer dialysis vintage, higher incidence of hypertension and higher incidence of CVD (all $P<0.05$) compared with those in the low TACS group. Ln (FGF21) was positively related with Ln (TACs+1) ($r=0.295$). ROC curves showed that the AUC of FGF21 for predicting TAC was 0.63 ($P<0.01$), while FGF21 combined with other independent associated factors like age, calcium and PTH, the AUC markedly increased (AUC=0.84) with optimal sensitivity (82%) and specificity (71%). ARS showed that calcium deposition was observed in cultured HAECs stimulated by PTH alone and even aggravated by PTH+FGF21; however, no calcium deposition was observed in HAECs stimulated by FGF21 alone. Compared with the control, reduced expression of CD31(endothelial cell marker) mRNA in parallel with increased expression of RUNX2(osteoblast marker) mRNA and FSP1(mesenchymal cell marker) mRNA was observed in HAECs stimulated by PTH. However, FGF21 alone had no significant effect on the EndMT process. Notably, stimulation of PTH+FGF21 in HAECs aggravated the effect of PTH alone on EndMT.

Conclusion: This study is the first to show that serum FGF21 levels were significantly and independently correlated with VC in HD patients. Furthermore, FGF21 combined with PTH, calcium and age can significantly predict VC in HD patients. Additionally FGF21 aggravated the effect of PTH on calcium deposition and EndMT in HAECs. Taken together, our in vivo and in vitro results indicated that FGF21 was a novel predictor and promoter of VC in HD patients.

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P0869

EXOGENOUS OSTEOGENIC FACTOR 1 ADMINISTRATION ATTENUATED VASCULAR CALCIFICATION AND IMPROVED BONE DISORDERS IN CHRONIC UREMIC RATS

Chien-Te Lee[1], Hwee-Yeong Ng[2], Wen-Lin Chen[1], Yuai-Ting Lee[2]

[1]Kaohsiung Chang Gung Memorial Hospital, Medicine, Kaohsiung, Taiwan, R.O.C. and [2]Kaohsiung Chang Gung Memorial Hospital, Medicine, Nephrology, Kaohsiung, Taiwan, R.O.C.

Background and Aims: Hyperphosphatemia and secondary hyperparathyroidism are frequent complications in chronic kidney disease (CKD) which both contribute to increased morbidity and mortality in CKD. Osteogenic factor-1 (OP-1) is an important member of BMPs subfamily and its effects on CKD-associated mineral and bone disorders (MBD) is controversial. The study examined whether exogenous OP-1 administration can modulate disturbed CKD-MBD in adenine-induced chronic uremic rats

Method: Chronic renal failure was induced in adult male SD rats by feeding adenine-containing diet. After adenine diet feeding 3 weeks, animals were injected with OP-1 (5μg/kg/day) intraperitoneally for 2 weeks. The serum and urine phosphorus levels and associated mineral parameters, including fibroblast growth factor 23(FGF-23), DKK-1 and sclerostin were measured. Vascular calcification was assessed by immunohistochemistry staining on aortic tissue. Bony structure was evaluated by microCT (Bruker-microCT, Kontich, Belgium).

Results: A significant decrease of body weight and deteriorated renal function was observed in adenine and OP-1 treatment groups during study period and serum creatinine levels were similar (5.23 ±1.1 mg/dL vs. 5.4 ±1.2 mg/dL, $p>0.05$). Animals in OP-1 group had lower serum phosphorous (18.7±5.1 vs. 29.0±9.6 mg/dL, $p<0.05$) and intact parathyroid hormone levels (2906.1±1206.9 vs. 4669.7±2505.9 pg/dL, $p<0.05$) compared to adenine group. Decreased urine phosphorous excretion was noted in both groups without significant difference. Levels of serum FGF-23, sclerostin and DKK-1 were significantly lower in OP-1 treatment group (all $p< 0.05$). OP-1 administration diminished the staining of RUNX2 (59.1±3% of adenine-treated group), alkaline-phosphatase (49.4±5.7%), β-caterin (39.3±1.8%), BMP2 (43.2%±6.7%), and BMP7 (51.9±10%, all $p <0.05$). MicroCT revealed that bone mineral density was increased by OP-1 treatment (0.46±0.1 *vs*.0.39±0.06 g/cm^3). Total volume was increased but bone volume was not changed. OP-1 administration did not affect trabecular thickness and trabecular number.

Conclusion: Our data indicated administration of exogenous OP-1 improved hyperparathyroidism and attenuated vascular calcification. OP-1 treatment was also associated with beneficial effects on bony structure in animals with renal failure.

P0870

THE ACTIVATION OF KYNURENIC SYSTEM IN BONE TISSUE AS A NEW REGULATOR OF OSTEOBLASTOGENESIS IN RATS WITH EXPERIMENTAL CHRONIC KIDNEY DISEASE DURING LP533401 THERAPY.

Dariusz Pawlak[1], Adrian Mor[1], Bartlomiej Kalaska[1], Tomasz Domaniewski[2], Beata Sieklucka[1], Anna Pawlak[3], Marta Zieminska[2], Krystyna Pawlak[2]

[1]Medical University of Bialystok, Pharmacodynamics, Bialystok, Poland, [2]Medical University of Bialystok, Monitored Pharmacotherapy, Bialystok, Poland and [3]Medical University of Bialystok, Internal Medicine and Metabolic Diseases, Bialystok, Poland

Background and Aims: Abnormalities in bone metabolism represent the most complex disorder accompanying a chronic kidney disease (CKD) development. Serotonin – one of the tryptophan metabolites, has received intensive attention due to its potential role in bone metabolism. The synthesis of peripheral serotonin is initiated by the tryptophan hydroxylase-1 (TPH-1) in the gut. LP533401 is a small-molecule inhibitor of TPH-1. Previously, we found that inhibition of TPH-1 by LP533401 may improve bone mineralization in rats with experimentally induced CKD (Pawlak et al, Bone, 2018). The aim of this study was to establish whether the inhibition of serotonin synthesis by LP533401 may affect kynurenine pathway activity in bone tissue of nephrectomized rats, and to determine the potential consequence of this process in relation to osteoblastogenesis.

Method: Nephrectomized rats were randomized into: untreated (CKD), treated with vehicle (VEH), treated with LP533401 at a dose of 30 (LP 30) and 100 mg/kg (LP 100) daily for 8 weeks. The shame-operated animals served as controls (CON). Tryptophan (TRP) and kynurenine (KYN) concentrations in trabecular and cortical homogenates of femoral bone were determined using high-performance liquid chromatography (HPLC). The expression of tryptophan 2,3-dioxygenase (TDO) as well as genes associated with osteoblastogenesis: activating transcription factor 4 (ATF4), forkhead box protein O1 (FOXO1), Cyclin D1, osteocalcin (Bglap) and sclerostin (Sost) were assessed using the QRT-PCR method.

Results: We demonstrated a presence of TDO-dependent, paracrine kynurenic system in bone homogenates of rats with CKD. The significant decrease in TDO mRNA level was observed in the bone of all nephrectomized groups in comparison with CON (all $p<0.0001$).

In LP 100 group, the TDO expression was still lower than in CON, but was significantly higher than in VEH and LP 30-treated groups (both $p<0.0001$). TDO expression was positively associated with KYN concentration and KYN/TRP ratio ($R = 0.426$, $p = 0.016$ and $R = 0.559$, $p = 0.001$; respectively) in trabecular bone region. ATF4 gene expression in bone was similar in LP 30 and CON, whereas it was significantly higher in other studied groups compared to healthy animals, and the positive relationship existed between ATF4 and TDO expression ($R = 0.372$, $p = 0.042$) as well as between ATF4 gene expression and KYN/TRP ratio both in trabecular and cortical bone tissue ($R = 0.485$, $p = 0.006$ and $R = 0.421$, $p = 0.023$; respectively) of LP-treated rats. In contrast, cyclin D1 mRNA level was the lowest in LP 100 group compared to other studied groups, and the inverse relationship was between this gene and TDO expression ($R = -0.622$, $p = 0.0002$). Bglap mRNA level was higher in CKD and VEH group compared to CON ($p<0.05$ and $p<0.0001$; respectively). CKD rats treated with LP 30 had the lowest Bglap mRNA levels among all analyzed uremic groups (all $p<0.0001$), and the positive relationship was between this gene expression and both TDO expression and KYN/TRP ratio ($R = 0.468$, $p = 0.011$ and $R = 0.474$, $p = 0.008$; respectively) in trabecular bone of uremic rats treated with LP. Similarly, Sost gene expression was significantly reduced in LP 30 group in comparison with other studied groups (all $p<0.0001$), and it was positively correlated with TDO expression and KYN/TRP ratio ($R = 0.540$, $p = 0.002$ and $R = 0.409$, $p = 0.022$; respectively) in trabecular bone tissue.

Conclusion: This study for the first time demonstrated the presence of a TDO-dependent, paracrine kynurenic system in the bone of rats with CKD. The modulation of this system during LP533401 treatment was closely associated with the expression of genes participating in osteoblastogenesis, particularly with osteoblast maturation markers. These results represent the next step in studying the role of tryptophan metabolites in renal osteodystrophy.

P0871

THE IMPACT OF ENDOGENOUS PTH/PTH1R/ATF4 AXIS ON TRABECULAR AND CORTICAL BONE REMODELING AND BONE GROWTH OF YOUNG RATS WITH EXPERIMENTAL CHRONIC KIDNEY DISEASES.

Krystyna Pawlak[1], Tomasz Domaniewski[1], Beata Sieklucka[2], Anna Pawlak[3], Marta Zieminska[1], Dariusz Pawlak[2]

[1]Medical University of Bialystok, Monitored Pharmacotherapy, Bialystok, Poland, [2]Medical University of Bialystok, Pharmacodynamics, Bialystok, Poland and [3]Medical University, Internal Medicine and Metabolic Diseases, Bialystok, Poland

Background and Aims: Chronic kidney disease - mineral bone disorder (CKD–MBD) is one of the major clinical complications in patients with chronic kidney disease (CKD). Bone remodeling has been suggested to play a fundamental role in the maintenance of skeletal integrity via a balance between the bone formation/resorption process. The parathyroid hormone (PTH) is a key hormone controlling bone metabolism. PTH is known to affect bone with a net catabolic and anabolic effect but the mechanisms responsible for these differing effects are poorly understood. Previously, we demonstrated the distinct effect of mild degree of CKD on trabecular and cortical bone strength in rapidly growing rats (Pawlak et al. PlosOne, 2016). The aim of the present study was to evaluate the effect of endogenous PTH, its receptor PTH1R and activating transcription factor 4 (ATF4) – the major regulators of the anabolic PTH response in osteoblasts on bone remodeling and growth of young rats with experimental CKD.

Method: Four-week old Wistar male rats were divided into 2 groups: with CKD induced by surgical 5/6 subtotal nephrectomy, and sham-operated (CON). After one (CON-1; CKD-1) and three months (CON-3; CKD-3) of the surgery the femurs were collected and their lengths were measured. The activity of alkaline phosphatase (ALP), a bone formation marker, and tartrate-resistant acid phosphatase (TRACP5b) reflecting bone resorption were determined in homogenates from trabecular and cortical left femurs. The expression of PTH1R and ATF4 gene was determined by QRT-PCR in right femurs. Serum PTH was analyzed using ELISA kit. Computations were performed using Statistica ver.10 computer software.

Results: Serum PTH was increased in CKD-3 compared to CKD-1, moreover the slight increase in PTH levels was noted in CKD-3 compared to appropriate controls (both $p<0.05$). The activity of ALP and TRACP5b in trabecular bone tissue were significantly lower in CKD-3 compared to CKD-1 rats ($p<0.01$ and $p<0.05$; respectively). There was a strong positive correlation between ALP and TRACP5b in this bone region ($R=0.624$, $p=0.002$), whereas both ALP and TRACP5b were inversely related to serum PTH ($R=-0.534$, $p=0.012$ and $R=-0.636$, $p=0.002$; respectively). The activity of TRACP5b in cortical bone tissue was significantly higher in CKD-3 compared to CKD-1 group ($p<0.05$), and it was positively associated with PTH levels ($R=0.597$, $p=0.004$). There was no difference in ALP activity between the studied groups, and ALP was not associated with TRACP5b in this bone region. The expression of ATF4 and PTH1R genes was significantly increased in the CKD-3 group compared with the appropriate control ($p<0.01$ and $p<0.05$; respectively) and with the CKD-1 group ($p<0.05$ and $p<0.01$; respectively). The expression of ATF4 was inversely correlated with ALP and TRACP5b in trabecular bone ($R=-0.534$, and $R=-0.528$, both $p<0.05$), whereas it was positively related to TRACP5b in cortical bone region ($R=0.418$, $p<0.05$). The femoral length was significantly increased during 3-month of CKD development ($p<0.000$), and it was positively associated with PTH levels ($R=0.571$, $p=0.007$), cortical TRACP5b activity ($R=0.609$, $p=0.002$) and tended to be related with ATF4 gene expression ($R=0.409$, $p=0.065$). In contrast, the femoral length was inversely related to ALP activity in trabecular bone tissue ($R=-0.656$, $p=0.0007$).

Conclusion: The endogenous PTH, through PTH1R/ATF4 axis, inhibited trabecular bone remodeling. In contrary, PTH/PTH1R/ATF4 system intensified bone resorption in cortical bone region. This opposite effect of PTH on bone remodeling was associated with the intensification of growth process in the long bones of young rats with CKD.

P0872

EFFECT OF PARATHYROID HORMONE OSCILLATIONS ON BONE HEALTH: FROM OSTEO-ANABOLISM TO CATABOLISM

Alhaji Cherif[1], Peter Kotanko[1,2]

[1]*Renal Research Institute, Research Division, New York, United States of America and* [2]*Icahn School of Medicine at Mount Sinai, New York, United States of America*

Background and Aims: In patients with chronic kidney disease or primary hyperparathyroidism, chronically elevated parathyroid hormones (PTH) levels exert catabolic effects on the bone. In contrast, PTH oscillations (as seen in healthy subjects) or daily application of teriparatide (a form of PTH consisting of the N-terminal 34 amino acids; it is used to treat osteoporosis) promote bone formation. These differential responses have important clinical and therapeutic implications. Although the anabolic effects of PTH (and teriparatide) cycling are widely accepted, the underlying osteo-anabolic dynamics are not well understood.

Method: A recently developed mechanistic physiology-based model quantitating the interrelations of osteoclasts, osteoblasts and osteocytes on bone remodeling is used (Cherif et al., NΔT 2018, 33 (συππλ. 1): 165–166). The model incorporates cell-to-cell signaling pathways (i.e., RANK-RANKL-OPG), intracellular pathways, cytokines (i.e. TGFβ), PTH, sclerostin, and endocrine and paracrine feedbacks. Using the validated model, we explore the effect of altered PTH (teriparatide) administration regimen (e.g., dosing frequency and amplitude) on bone catabolism and anabolism, respectively.

Results: As in previous studies, the model accurately predicts differential responses of osteo-anabolic and catabolic effects of continuously and intermittently elevated PTH (teriparatide) levels, respectively. In addition, we observe that intermittent administration of PTH with a high frequency and amplitude induces bone catabolism similar to that seen in pathologies with continuously elevated PTH (i.e. primary or secondary hyperparathyroidism). We see a more than 3-fold change from baseline in osteoclastic over osteoblastic activities, resulting in a bone efflux of calcium and phosphate. Low PTH frequency with high dosing amplitude induces both osteoclastic and osteoblastic activities, but the net result is bone anabolism. Further, Fig. 1 shows a nonlinear region where high osteoblastic activities exceed osteoclastic resorption. These findings suggest the existence of optimal PTH (teriparatide) frequency-amplitude combinations that enhance anabolic gains, beyond which there can be a detrimental effect on bone.

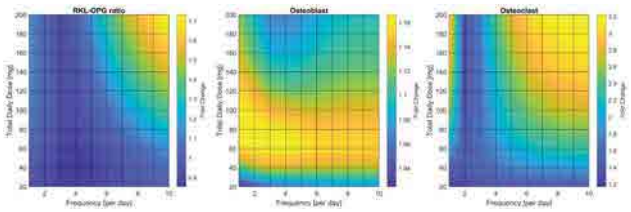


Figure 1: Illustrates regions with high osteoblastic and osteoclastic activities corresponding to anabolic gains and/or catabolic loss in bone health as a function of dosing frequency and amplitude.

Conclusion: Our results suggest that both frequency and amplitude of PTH (teriparatide) cycling affect the balance of osteo-catabolic and -anabolic effects. Understanding the underlying mechanism of differential osteo-anabolic and -catabolic responses induced by intermittent and continuous levels of PTH, respectively, may provide new therapeutic options for patients and minimize unintended consequences of intervention protocols.

P0873

GLA-RICH PROTEIN (GRP) AS AN EARLY AND NOVEL MARKER ASSOCIATED WITH VASCULAR CALCIFICATION AND CKD-MINERAL AND BONE DISORDER (MBD) IN DIABETIC PATIENTS WITH CKD: A PILOT COHORT STUDY

Carla Viegas[1,2], Ana Silva[3,4], Ana Macedo[4,5], Filipa Mendes[3], Patrícia Guilherme[6], Nelson Tavares[6], Carolina Dias[1,4], Fátima Rato[7], Nélio Santos[7], Marília Faísca[7], Edgar A.F. De Almeida[8], Pedro Neves[3,4], Dina Simes[1,2]

[1]Centre of Marine Sciences (CCMAR), Faro, Portugal, [2]GenoGla Diagnostics, Faro, Portugal, [3]Centro Hospitalar Universitário do Algarve, Department of Nephrology, Faro, Portugal, [4]Universidade do Algarve, Department of Biomedical Sciences and Medicine, Faro, Portugal, [5]Keypoint - Consultoria Científica, Lda, Oieiras, Portugal, [6]Centro Hospitalar Universitário do Algarve, Department of Cardiology, Faro, Portugal, [7]Centro Hospitalar Universitário do Algarve, Pathology Clinic, Faro, Portugal and [8]Universidade de Lisboa, Faculdade de Medicina, Lisboa, Portugal

Background and Aims: Cardiovascular disease (CVD) is the most life-threatening complication in chronic kidney disease (CKD) patients. In addition to traditional risk factors, most patients with CKD display abnormal mineral metabolism with underlying hormonal dysregulation, defined as chronic kidney disease-mineral and bone disorder (CKD-MBD). CKD-MBD involves changes in mineral ion homeostasis, bone quality and turnover, cardiovascular and soft tissue calcifications, which highly contribute for cardiovascular complications. Vascular calcification (VC) is associated with significant morbidity and mortality and a strong predictor of cardiovascular risk in CKD patients. Early preventive measures, including new diagnostic/prognostic tools, are required to reduce the development and progression of VC, left ventricular hypertrophy and arterial stiffness, which are crucial for the prevention of CVD outcomes in CKD patients. Gla-rich protein (GRP) is a vitamin K-dependent protein with a dual capacity to function as an inhibitor of pathological calcification and anti-inflammatory agent in the cardiovascular system, whose clinical utility is unknown. Our aim with this study was to evaluate the potential of GRP as a new marker for CKD-MBD and vascular calcification, in type 2 diabetic patients with chronic kidney disease (CKD) stages 2-4.

Method: In an observational prospective study including all eligible type 2 diabetic patients with CKD stages 2-4 (n=80) followed in outpatient nephrology consultation from 2010 to 2017, we explored correlations between levels of GRP in serum with mineral metabolism and inflammation markers, CKD developmental stage, vascular calcification and pulse pressure (PP). Vascular calcification score (VCS) was evaluated using the plain x-ray of the hands and pelvis (Adragão score), and increased cardiovascular risk was considered for VCS$\geq$3. Measurements of GRP in serum were performed using a recently developed sandwich ELISA assay. Descriptive statistics, ANOVA and post hoc analysis with Scheffe test were used for analysis. Forward stepwise logistic regression (likelihood ratio) analysis was applied to identify predictive factors for VCS and PP, and ROC curves were used to assess the sensitivity and specificity of GRP in relation to these exposure factors.

Results: Spearman's correlation analysis revealed the strong positive correlation between levels of serum GRP and eGFR (r=0.863, p<0.0001) and α klotho (r=0.647, p<0.0001), while a negative correlation with phosphate (P) (r=-0.715, <0.0001), FGF23 (r=-0.676, <0.0001), VCS (r=-0.822, p<0.0001), PP (r=-0.533, p<0.0001), calcium x phosphate (CaxP) (r=-0.302, p=0.006) and IL-6 (r=-0.349, p=0.002). Serum GRP levels were found to progressively decreased from stage 2 to stage 4 CKD. Multivariate analysis identified low levels of eGFR and GRP, and high levels of FGF-23 as independent risk factors for both the VCS and PP. The area under the ROC curves for GRP was 0.865$\pm$0.046, 95% CI (0.776-0.955), p<0.0001 for VCS and 0.782$\pm$0.054, 95% CI (0.677-0.887), p<0.0001 for PP.

Conclusion: Reduced levels of GRP were associated with higher levels of vascular calcification promoters such as P, FGF-23 and CaxP, and with lower levels of the VC inhibitor α-Klotho, indicating a correlation between GRP and the dysregulation of phosphate metabolism characteristic of CKD-MBD. In addition, this pilot cohort study indicates that GRP levels might be a significant clinical predictor of vascular calcifications in diabetic patients with CKD.

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P0874

THE IMPACT OF CHRONIC EXPOSURE TO INDOXYL SULFATE ON BONE TURNOVER MARKERS, PTH, VITAMIN D3, AND BIOMECHANICAL AND DENSITOMETRIC PROPERTIES OF BONES IN RAT MODEL

Malgorzata Karbowska[1], Beata Sieklucka[1], Alicja Roszczenko[2], Joanna Rogalska[2], Krystyna Pawlak[3], Dariusz Pawlak[1]

[1]Medical University of Bialystok, Department of Pharmacodynamics, Bialystok, Poland, [2]Medical University of Bialystok, Department of Toxicology, Bialystok, Poland and [3]Medical University of Bialystok, Department of Monitored Pharmacotherapy, Bialystok, Poland

Background and Aims: Chronic kidney disease (CKD) is a crucial risk factor for biochemical and bone disturbances, as well as non-skeletal calcifications known as Chronic Kidney Disease – Mineral and Bone Disorders (CKD-MBD). Etiopathogenesis of CKD-MBD still remains unknown and arouses much controversy. Indoxyl sulfate (IS) is one of the most potent protein-bound uremic toxin that accumulates during CKD, and exerts aggressive and multidirectional effect on the body. In vitro studies indicate that IS modulates the differentiation and activation of osteoblasts and osteoclasts, however IS impact on bone and mineral disorders still remains unclear.

The purpose of the study was to assess IS effect on bone turnover markers, parathyroid hormone (PTH), vitamin D_3, and densitometric and biomechanical properties of bones in rat model.

Method: Male Wistar rats weighting 180 – 210 g (n=48) were divided into three groups – control group that received pure water and two experimental groups. Experimental groups were exposed to IS in the doses of 100 or 200 mg/kg of b.w. (200 IS) in the drinking water during 4 weeks. At the end of experiment, rats were anesthetized and samples of blood, as well as tibiae, femurs and lumbar spines were collected. Next, the IS bone (cortical and trabecular), plasma and urine levels were determined by high-performance liquid chromatography (HPLC). We also assessed IS influence on bone turnover markers (alkaline phosphatase – ALP, and tartrate-resistant acid phosphatase - TRAP), and level of vitamin D_3, and PTH. Furthermore, we evaluated densitometric parameters of tibiae, femurs and lumbar spines using Horizon QDR Series X-ray Bone Densitometer, and performed biomechanical parameters analysis of the cortical bone of the femoral diaphysis using three-point bending test, and the mixed cortico-trabecular structure of the proximal femur by the bending test of the femoral neck.

Results: Chronic exposure to IS led to statistically significant increase in plasma, urine, cortical and trabecular bone IS concentrations. We observed reduction in bone turnover markers – bone formation marker ALP in trabecular and cortical bone, and bone resorption marker TRAP in cortical bone. Moreover, the highest dose of IS increased PTH. None of tested IS doses affected vitamin D_3. From data obtained due to biomechanical tests, the highest dose of IS decreased the main indicators of bone strength: yield load (Fy) and displacement at yield [dl(Fy)] of femoral diaphysis and femoral neck, and ultimate load (Fu) and displacement at ultimate [dl(Fu)] of femoral diaphysis. Furthermore, we observed the decrease in elasticity of femoral diaphysis (increased Young's modulus of elasticity E). Additionally, densitometric measurements revealed reduction only in the bone mineral density (BMD) and BMD of diaphyseal area (BMD R2) of tibiae, BMD R2 of femurs in 200 IS group, as well as BMD and BMD R2 of tibiae in 100 IS group.

Conclusion: Obtained data confirm that IS affects bones. We observed reduced bone metabolism and strength after exposure to IS. On the basis of the results, we concluded that IS can be one of crucial uremic factors responsible for increased risk of fracture during CKD.

P0875

INFLUENCE OF CHRONIC KIDNEY DISEASE AND LEFT VENTRICULAR HYPERTROPHY ON CHANGE IN FGF23 AND RENIN-ANGIOTENSIN-ALDOSTERONE-SYSTEM

Kohei Okamoto[1], Hideki Fujii[1], Shunsuke Goto[1], Keiji Kono[1], Kentaro Watanabe[1], YUMA NOSE[1], Shinichi Nishi[1]

[1]*Kobe University Graduate School of Medicine, Division of Nephrology and Kidney Center,, Kobe, Hyogo, Japan*

Background and Aims: Left ventricular hypertrophy (LVH) is a clinically important risk factor for mortality and often observed in patients with chronic kidney disease (CKD). Serum FGF23 levels are elevated in CKD patients, and the relationship between elevated FGF23 and LVH has been reported in the previous studies. However, whether elevated FGF23 is a cause or result of LVH and whether FGF23 directly or indirectly affects LVH remain unclear. Therefore, we investigated changes in heart weight, CKD-mineral and bone disorder (MBD) parameters, including FGF23, and renin-angiotensin-aldosterone system (RAAS) related-factors in the setting of LVH and CKD using a mouse model.

Method: In the present study, twenty-four C57BL/6J mice were used and divided into 4 groups; control group (N=6), CKD group (N=6), LVH group (N=6), and LVH+CKD group (N=6). The mice in the CKD group underwent left 2/3 nephrectomy at 11 weeks of age and right nephrectomy at 12 weeks of age. Those in the LVH group underwent transverse aortic constriction (TAC) at 10 weeks of age. Those in the LVH+CKD group, TAC at 10 weeks of age, and left 2/3 nephrectomy at 11 weeks of age, and right nephrectomy at 12 weeks of age were performed. At 16 weeks of age, echocardiography was performed for all the mice, and they were sacrificed for blood and urine analysis, histopathological analysis and evaluating mRNA expressions of CKD-MBD- and RAAS-related factors in the heart.

Results: The systolic blood pressure was significantly higher in the LVH+CKD group and the CKD group than in the control group. The heart weight/body weight ratio in the LVH+CKD group was the highest, and that in the LVH was higher than that in the CKD group. Although serum creatinine and phosphate levels increased in CKD condition, those were comparable between the CKD and LVH+CKD groups. The urinary albumin excretion also increased in the CKD and LVH+CKD groups compared to the LVH and control groups. Serum FGF23 levels increased in the LVH and CKD group compared to the control group, and those in the LVH+CKD group were the highest among all the study groups. The cardiac mRNA expressions of FGF23, angiotensinogen (ANG), angiotensin type 1 receptor (AT1R), and angiotensin-converting enzyme (ACE) were also increased by induction of LVH and CKD, and those in the LVH+CKD group significantly increased compared to other groups. Heart weight/body weight ratio was significantly correlated with serum FGF23 levels and mRNA expression of FGF23, ANG, AT1R, ACE. In addition, significant correlations of serum FGF23 levels and cardiac mRNA expression of FGF23 with cardiac mRNA expressions of RAAS-related factors were observed.

Conclusion: Our results suggest that serum FGF23 levels and cardiac mRNA expression of FGF23 increase with the development of LVH and CKD and the changes is possibly enhanced through the colocalized activation of RAAS.

P0876 THE ROLE OF TRPM7 IN VASCULAR CALCIFICATION: COMPARISION BETWEEN PHOSPHATE AND UREMIC TOXIN

Chien-Te Lee[1], Hwee-Yeong Ng[2]

[1]Kaohsiung Chang-Gung Memorial Hospital, Medicine, Nephrology, Kaohsiung, Taiwan, R.O.C. and [2]Kaohsiung Chang Gung Memorial Hospital, Medicine, Nephrology, Kaohsiung, Taiwan, R.O.C.

Background and Aims: Vascular calcification is a common complication in patients with chronic kidney disease (CKD) and associated with increased morbidity and mortality. Pathogenesis of vascular calcification in CKD is multiple and phenotypic transformation of vascular smooth muscle cell (VSMC) is of critical importance. TRPM7 is a magnesium channel that regulate magnesium transport. The role of TRPM7 in VSMC transformation during vascular calcification is not clear. We aim to investigate the effects of phosphate and indoxyl sulphate on the expression of TRPM7 in VSMC and 2-APB, the TRPM7 blocker was used to evaluate the alteration of calcification-related molecules.

Method: Human aortic smooth muscle cells (HASMC) were used and treated either with phosphate (3.3mM) or indoxyl sulphate (500uM) for 7 days. 2-APB, a channel blocker of TRPM7 was added simultaneously in blocking experiment. Cells were then examined grossly and alizarin red solution was employed for calcification staining assessment. For calcification process study, cells were harvested for gene expression and protein abundance analysis.

Results: Gross examination did not find evidence of cell death during experiment on both treatments. Alizarin staining revealed apparent calcification in phosphate-treated HASMC but it was unremarkable in indoxyl sulphate. Phosphate treatment induced significant increase in RUNX2(151±35.8% of control), BMP2(124±10.1%), BMP7(155±9.3%), vitamin D receptor (VDR, 138±21%), calcium sensing receptor (CaSR, 185± 39%) and TRPM7(172±33.7%, all $p< 0.05$), but DKK1 and sclerostin were not changed. The addition of 2-APB prevented the increase of RUNX2(107±31.2%), BMP2(80±4.9%), BMP7(72±32.9%), VDR (94±43.2%), CaSR (83±17%) and TRPM7(118±23.9%). Indoxyl sulphate treatment was associated with decrease in TRPM7 (45±22%, $p<0.05$), but increase in BMP2(136±10.4%), VDR (154±53.5%) were noted. There were no significant alterations in CaSR (108±43.7%) and sclerostin (110±27.1%). Co-administration with 2-APB partially reduced the increase in RUNX2(158±55.1%), VDR (149±35.9%). The abundance of BMP2/7were not changed. TRPM7 was decreased significantly (33±23.1%).

Conclusion: We concluded that both phosphate and indoxyl sulphate induced calcification in VSMC but it was less in indoxyl sulphate. TRPM7 was upregulated by phosphate but decreased in indoxyl sulphate treatment. Blocking TRPM7 with 2-APB can prevent phosphate-induced calcification but partially attenuated calcification during indoxyl sulphate administration.

P0877

ASSOCIATIONS OF DISORDERS IN BONE MINERAL PARAMETERS WITH MORTALITY IN STAGE 4 AND 5 CKD: INSIGHTS FROM THE PECERA STUDY

Pablo Molina[1,2], Mariola D. Molina[3], Luis M. Pallardó[1,2,4], Ramón López-Menchero[5], Francisco Javier Torralba[6], Veronica Escudero Quesada[1], Cristina Castro Alonso[1,2], Carlos Del Pozo[5], Josefa Martín-Rivas[7], Pilar Sánchez-Pérez[8], Amparo Soldevila[8], Miguel González-Rico[9], Ana Peris[8], Asunción Sancho Calabuig[1,2], Jose Luis Gorriz[2,4,9]

[1]Hospital Universitari Dr Peset, Department of Nephrology. FISABIO, Valencia, Spain, [2]Universitat de València, Department of Medicine, Valencia, Spain, [3]Universidad de Alicante, Department of Mathematics, Alacant, Spain, [4]Fundación Renal Tomás de Osma, Valencia, Spain, [5]Hospital Virgen de los Lirios, Department of Nephrology, Alcoi, Spain, [6]Hospital General Universitario de Alicante, Department of Nephrology, Alicante, Spain, [7]Hospital General de Elda, Department of Nephrology, Elda, Spain, [8]Hospital Universitari i Politècnic La Fe, Department of Nephrology, Valencia, Spain and [9]Hospital Clínic Universitari, Department of Nephrology. INCLIVA, Valencia, Spain

Background and Aims: Abnormalities of bone mineral parameters are associated with increased mortality in patients on dialysis, but their effects and the optimal range of these biomarkers are less well characterized in non-dialysis chronic kidney disease (CKD).

Method: PECERA (Collaborative Study Project in Patients with Advanced Chronic Kidney Disease) is a 3-year, multicentre, open-cohort, prospective study carried out in 995 adult patients with CKD stages 4-5 not on dialysis enrolled in 2007-09 from 12 centres in Spain. Associations between levels of serum calcium (corrected for serum albumin), phosphate, and intact parathyroid hormone (iPTH) and all-cause mortality were examined using time-dependent Cox proportional hazards models and penalized splines analysis adjusted by demographics and comorbidities, treatments and biochemical collected at baseline and every 6 months for 3 years.

Results: After a median follow-up of 30 months (IQR:14-37 months) there were 180 deaths (18%). The association of calcium and phosphate with all-cause mortality was U-shaped (Figure). The serum values associated with the minimum risk of mortality were 9.35 mg/dL for calcium and 3.56 mg/dL for phosphate, being the lowest risk ranges between 7.4 to 10.7 mg/dL and between 2.3 to 4.6 mg/dL for calcium and phosphate, respectively. For iPTH levels, the association was J-shaped, with an increased risk for all-cause mortality at levels $>$ 110 pg/mL.

Conclusion: As previously reported in dialysis patients, PECERA provided evidence on the association of serum calcium, phosphate and iPTH levels with all-cause mortality in stage 4 and 5 CKD patients, suggesting potential survival benefits of controlling bone mineral parameters in this population. Whereas the ranges of calcium and phosphate associated with the lowest mortality in the study were consistent with the current K-DIGO guidelines, our results suggested that the threshold for considering anti-parathyroid treatment might be lower than is currently recommended.

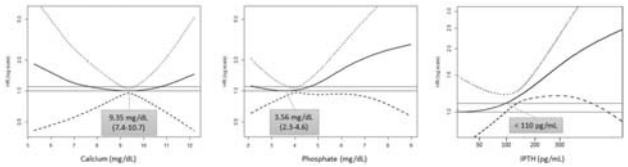


Figure:

P0878

INDEPENDENT EFFECTS OF SECONDARY HYPERPARATHYROIDISM ON CHRONIC KIDNEY DISEASE PROGRESSION AND CARDIOVASCULAR EVENTS IN THE NEFRONA COHORT

Marcelino Bermudez-Lopez[1], Carles Forne Izquierdo[1], Serafí Cambray[1], Milica Bozic[1], Jose Manuel Valdivielso[1]

[1]*IRBLleida, Experimental Medicine, Lleida, Spain*

Background and Aims: Secondary hyperparathyroidism (sHPT) is a common complication in patients with chronic kidney disease, and is associated with mortality in non-dialysis and CKD patients. However, it is not clear whether negative outcomes linked to sHPT are confounded by other factors associated to the disease. Furthermore, potential effects of sHPT on CKD progression are not entirely clear. Therefore, the present study was designed to identify the effect of sHPT (defined as patients treated with cinacalcet or phosphate binders, active vitamin D, or with PTH blood levels over the KDOQI recommended values (>70 in CKD3; >110 in CKD4; >300 in CKD5 or 5D)) on risk of CKD progression and cardiovascular incidence in a cohort of CKD patients (NEFRONA cohort) and whether hypercalcemia and/or hyperphosphatemia act as effect modifiers.

Method: We used the 2445 patients with CKD of the NEFRONA cohort (950 stage 3, 807 stage 4-5 and 688 on dialysis) followed for 2 years for the CKD progression outcome (defined as a 30% decrease of GFR or entering in renal replacement therapy) and for 4 years for cardiovascular events. Follow up periods were defined in the original NEFRONA protocol.

Results: After excluding 244 patients with missing values in PTH levels, 1693 (76.9%) patients presented with sHPT, 433 (57.4%) on stage 3, 625 (82.1%) on stage 4-5 and 635 (92.7%) on dialysis. From the 1283 patients with data on CKD progression, 301 (23.5%) fulfilled the criterion of CKD progression after 2 years. During the 4 years follow-up, 203 CVE were recorded in the whole cohort. Bivariate analysis showed that factors associated with the disease progression were male gender, higher age, lower BMI, present with hypertension, albuminuria, hyperphosphatemia or sHPT, being in a more advanced CKD stage, lower levels of glucose, LDL cholesterol or 25(OH)D. Multivariate logistic regression analysis adjusted by possible confounding factors showed that sHPT was still associated with higher odds of CKD progression (OR: 2.75; 95%CI: 1.55-4.88). Hyperphosphatemia also showed an effect on CKD progression (OR: 6.13; 95%CI: 1.48-25.3) and no statistically significant interaction with sHPT was detected. Factors showing statistical significance with the CVE outcome in the crude analysis were male gender, higher age, being diabetic or smoker, hyperphosphatemia, a more advanced CKD stage, presence of sHPT, higher levels of glucose or hsCRP and lower levels of HDL cholesterol or 25(OH)D. Multivariate Fine and Gray regression model showed that patients with sHPT showed higher hazards of presenting cardiovascular events (HR: 1.61; 95%CI: 1.07-2.43). Hyperphosphatemia maintained its independent effect on mortality (HR: 1.64; 95%CI: 1.20-2.23) and again no significant interaction was found with sHPT. A sensitivity analysis was performed eliminating treatment with phosphate binders from the definition of sHPT, yielding similar results.

Conclusion: We conclude that sHPT and hyperphosphatemia independently influence CKD progression and the incidence of cardiovascular events.

MODERATED POSTER SESSION 4

P0559 **AKI SEASONALITY IN ENGLAND**

Esther Wong[1], Dorothea Nitsch[1]
[1]*UK Renal Registry, Bristol, United Kingdom*

Background and Aims: Incidence of Acute Kidney Injury (AKI) is known to be seasonal, peaking in winter months among hospitalised patients. Previous studies have suggested that the seasonality of AKI is likely to be influenced by the seasonality of the underlying acute illnesses that are associated with AKI. Mortality of patients with AKI has also been reported as being higher in winter, reflecting well-described excess winter mortality associations.

Here we describe the seasonal variations of AKI alerts in England and the associated mortality rate using linked national databases.

Method: Serum creatinine changes compatible with KDIGO AKI stage 1, 2 and 3 are sent by laboratories in England as AKI alerts to the treating clinicians and the UK Renal Registry (UKRR). We linked the electronic AKI alerts to the Hospital Episode Statistics (HES) data, to identify patients who were hospitalised. We carried out descriptive statistics, and investigate the seasonal effect to the 30-day patient mortality from date of getting AKI alert, using multivariable Cox regression and sequentially adjusting for age, sex, Index of multiple deprivation (IMD) and peak AKI stage

Results: Winter has the highest number of AKI episodes (N=81,276), which is 6% higher than that in summer (N=76,329) (Table 1). For patients who had an AKI episode and admitted to hospitals, the crude 30-day mortality is higher in the winter season when compared to the summer [HR 1.28 (1.25-1.31), p<0.01] (Figure 1). After adjusting season by age, peak AKI stage, IMD and sex, winter season still has significantly higher 30-day mortality than summer [HR 1.24 (1.21-1.27), p<0.01]. Winter mortality peak is confounded by age and AKI severity, which explained the drop of hazard ratio at winter peaks; whereas season is not confounded by deprivation and sex. The pattern of seasonality varies with age, in age group 18-39, there were 26.1% of AKI episodes in summer and 23.3% in winter, whereas in age group >75, there were 23.7% in summer and 27.1% in winter.

Conclusion: Analysis of England data confirms seasonal peak in AKI during winter months. Additionally it shows increased risk of mortality for patients with AKI in winter months. Future work will investigate the impact of comorbidities and case-mix on outcomes. By understanding the seasonal variation of AKI, we can potentially plan preventive care and improve clinical practice.

Table 1 The number of hospitalised AKI episodes in 2017 by season and by patient characteristics

			Spring	Summer	Autumn	Winter	Chi-square test P-value
Total		N	76,177	76,329	80,150	81,276	
		Row %	24.3	24.3	25.5	25.9	
Age group	**<18**	Row %	23.2	21.1	29.5	26.3	p<0.01
	18-39	Row %	23.4	26.1	27.2	23.3	
	40-64	Row %	24.0	25.4	26.4	24.1	
	65-75	Row %	24.4	24.7	25.8	25.2	
	>75	Row %	24.4	23.7	24.8	27.1	
Peak AKI	**1**	Row %	24.3	24.3	25.8	25.6	p<0.01
	2	Row %	24.2	24.4	25.1	26.3	
	3	Row %	24.2	24.1	25.0	26.7	
Deprivation (IMD)	**Least deprived 1**	Row %	24.2	24.6	25.6	25.5	p=0.04
	2	Row %	24.2	24.3	25.2	26.3	
	3	Row %	24.5	24.0	25.4	26.1	
	4	Row %	24.2	24.5	25.8	25.5	
	Most deprived 2	Row %	24.2	24.2	25.6	26.0	
	Missing	Row %	25.8	25.8	19.8	28.6	
Sex	**F**	Row %	24.3	24.3	25.4	26.1	p=0.07
	M	Row %	24.3	24.3	25.7	25.7	

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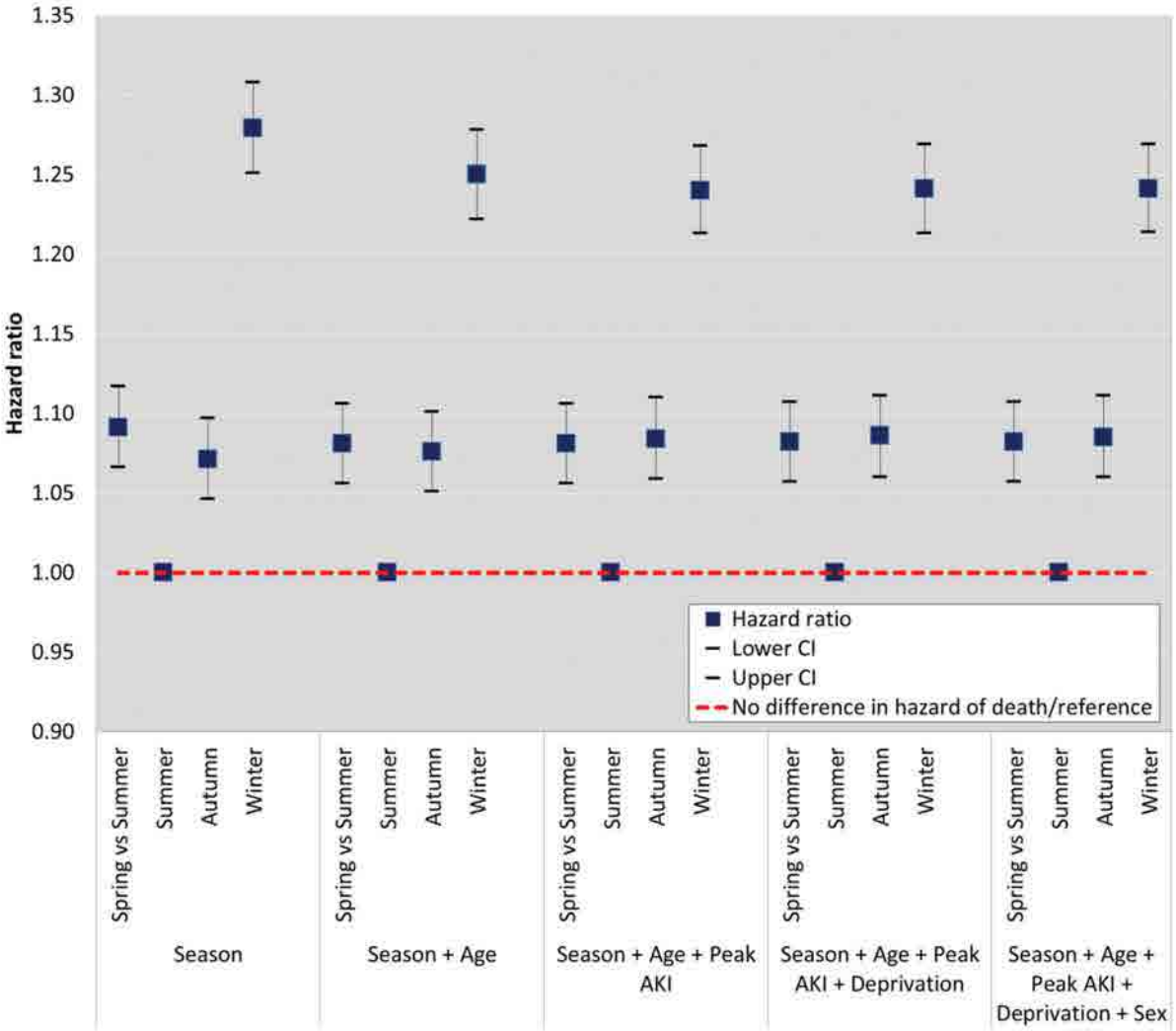


Figure 1. Hazard ratio (HR) in different seasons to show the impact of seasonal effect to 30-day mortality in hospitalised patients who had at an AKI episode in 2017, sequentially adjusting for age, peak AKI stage, deprivation and sex, with season summer as the reference group.

P0616 **REAL-TIME CLINICAL DECISION SUPPORT TO PREDICT AND MANAGE IN-HOSPITAL ACUTE KIDNEY INJURY UTILIZING RECURRENT NEURAL NETWORK**

Hea Eun Kim[1], Hyeonsik Yang[2], Sejoong Kim[1], Kipyo Kim[3]

[1]Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam-si, Korea, Rep. of South, [2]Seoul National University, Department of computer science and engineering, Seoul, Korea, Rep. of South and [3]Inha University Hospital, Department of Internal Medicine, Incheon, Korea, Rep. of South

Background and Aims: Rapidly Increasing electronic health record (EHR) data and recent development of machine learning methods offers the possibilities of improvement in quality of care in clinical practice. Machine learning can incorporate huge amount of features into the model, and enable non-linear algorithms with great performance. Previously published AKI prediction models have simple design without real-time assessment. Major risk factors in in-hospital AKI include use of various nephrotoxins, repeatedly measured laboratory findings, and vital signs, which are dynamic variables rather than static. Given that recurrent neural network (RNN) is a powerful tool to handle the sequential data, using RNN method in the prediction model is a promising approach. Therefore, in the present study, we proposed a RNN-based prediction model with external validation for in-hospital AKI and aimed to provide a framework to link the developed model with clinical decision supports.

Method: Study populations were all patients aged $\geq$ 18 years and hospitalized more than a week at Seoul National University Bundang Hospital (SNUBH) from 2013 to 2017 (training cohort) and at Seoul National University Hospital (SNUH) in 2017 (validation cohort). All demographics, laboratory values, vital signs, and clinical conditions were obtained from the EHR of each hospital. A total of 102 variables included in the model. Each variable falls into two categories: static and dynamic variable; static variable was time-invariant values during hospitalization, and dynamic variables were daily-updated values. Baseline creatinine was determined by searching the minimum serum Cr level within 2 weeks before admission. We developed two different models (model 1 and model 2) using RNN algorithms. The outcome for model 1 was the occurrence of AKI within 7 days from the present. In model 2, we constructed the prediction model of the trajectory of Cr values after 24 hours, 48 hours, and 72 hours, using available Cr values from 7 days ago to the present. Internal validation was performed by 5-fold cross validation using the training set (SNUBH), and then external validation was done using test set (SNUH).

Results: A total of 40,552 patients in training cohort and 4,000 patients in external validation cohort (test cohort) were included in the study. The mean age of participants was 62.2 years in training cohort and 58.7 years in test cohort. Baseline eGFR was 93.8 $\pm$ 40.4 ml/min/1.73m2 in training cohort and 88.4 $\pm$ 23.2 ml/min/1.73m2 in test cohort. In model 1 for the prediction of AKI occurrence within 7 days, the area under the curve was 0.93 (sensitivity 0.90, specificity 0.96) in internal validation, and 0.83 (sensitivity 0.83, specificity 0.82) in external validation. The model 2 predicted the creatinine trajectory within 3 days accurately; root mean square error was 0.1 in training cohort and 0.3 in test cohort. To support the clinical decision for AKI manage, we estimated the predicted trajectories of future creatinine levels after renal insult removal, such as nephrotoxic drugs, based on the established model 2.

Conclusion: We developed and validated a real-time AKI prediction model using RNN algorithms. This model showed high performance and can accurately visualize future creatinine trajectories. In addition, the model can provide the information about modifiable factors in patients with high risk of AKI.

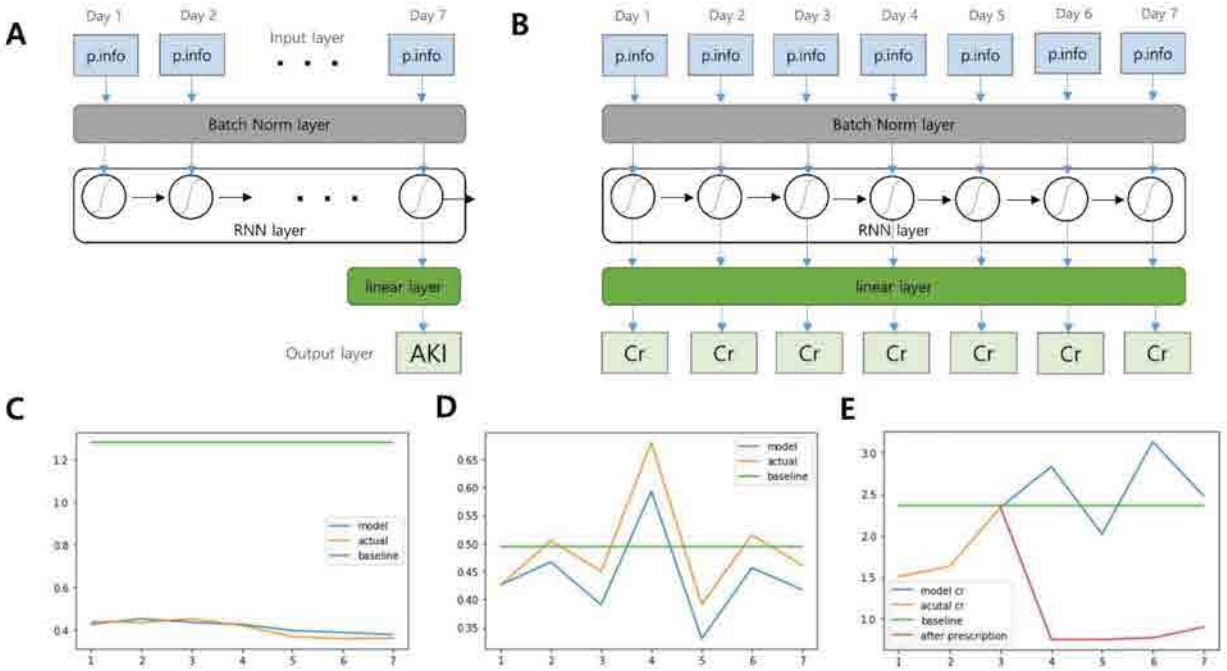


Figure: (A) Model 1 for the prediction of AKI occurrence within 7 days. (B) Model 2 for the prediction of the future creatinine trajectory within 3 days. (C) A case of patients without AKI in model 2 (blue, prediction; orange, actual results). (D) A case of patients with AKI in model 2. (E) Predicted Cr trajectories with and without renal insult (red, when renal insult is modified).

P0617 **LEISURE-TIME PHYSICAL ACTIVITY AND MORTALITY IN CHRONIC KIDNEY DISEASE: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) 1999-2012**

Nanhui Zhang[1], Ran Luo[1], Yichun Cheng[1], Dan Chang[1], Tingting Liu[1], Shuwang Ge[1], Gang Xu[1]

[1]*Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Department of Nephrology, Division of Internal Medicine, Wuhan, P.R. China*

Background and Aims: For patients with chronic kidney disease (CKD), evidence on the optimal dose of physical activity and possible harm with excessive exercise is limited. We aimed to analyze the dose-response association between leisure-time physical activity (LTPA) and mortality among participants with CKD and explore the optimal dose or possible harm associated with increased levels of physical activity.

Method: Leisure-time physical activity was self-reported. Data from 4604 adults with chronic kidney disease and without missing data for LTPA and mortality in the National Health and Nutrition Examination Surveys 1999-2012 were analyzed in 2019. Mortality was from baseline until 31 December 2015

Results: During the median follow-up of 114 months, 1449 (31%) all-cause deaths were recorded. Comparing with inactive groups, the multi-variable adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of 10-59, 60-149, 150-299, and 300-599 minutes/week of leisure-time physical activity for all-cause mortality were 0.71 (0.55-0.92), 0.78 (0.62-0.98), 0.79 (0.63-0.98), and 0.75 (0.57-0.99), respectively. The benefit appeared to reach a threshold of a 41% (HR,0.59; 95% CI, 0.41-0.84) lower risk of all-cause mortality among individuals reporting 600-1499 min/week for LTPA. And at $\geq$ 1500 min/week LTPA level, the HR and 95%CI were 0.66 (0.40-1.10).

Conclusion: LTPA was associated with reduced all-cause mortality in participants with CKD. We observed the optimal dose at the moderate-intensity LTPA level of approximately 600-1499 min/week and no longevity benefit at $\geq$1500 min/week.

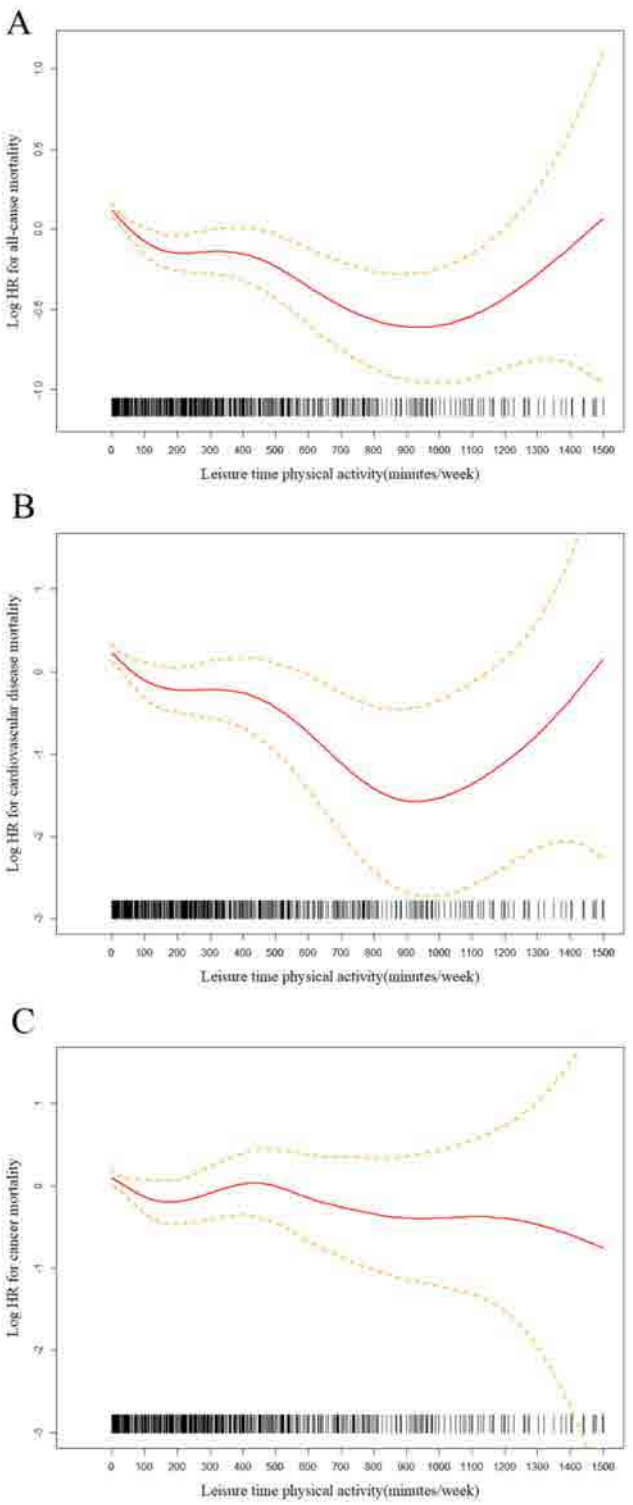


Figure 1. Does-response association between total leisure-time physical activity (as a continuous variable, min/week) and risk of all-cause, cardiovascular disease (CVD), and cancer mortality in patients with chronic kidney disease by Cox models with penalized spline (number of participants=4604, number of all-cause deaths=1449, number of CVD-specific deaths=354, number of cancer-specific deaths=258) . HR, hazards ratio.

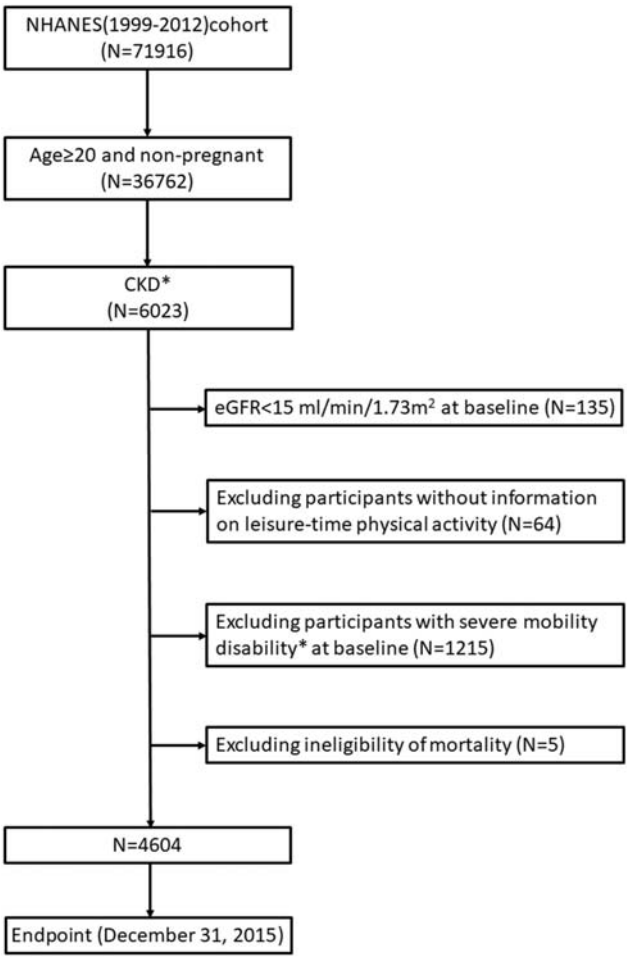


FIGURE S1. Flow chart of the selection of eligible subjects. *CKD is defined as an estimated glomerular filtration rate (eGFR) <60mL/min/1.73m2 (using the Chronic Kidney Disease Epidemiology Collaboration equation) and/or a urinary albumin-creatinine ratio >30mg/g. Participants with severe mobility disability were those who had much difficulty walking for a quarter of a mile or need special equipment to walk.

P0767 INTRAUTERINE GROWTH RESTRICTION AND RISK OF KIDNEY DISEASE DURING THE FIRST 50 YEARS OF LIFE

Anna Gjerde[1], Anna Varberg Reisater[2], Rannveig Skrunes[3], Hans-Peter Marti[4], Bjørn Egil Vikse[1]

[1]Haugesund Hospital, Department of Medicine, Haugesund, Norway, [2]Rikshospitalet, Department of Transplantation Medicine, Oslo, Norway, [3]Haukeland University Hospital, Department of Medicine, Bergen, Norway and [4]Haukeland University Hospital, Department of Medicine, Bergen, Norway

Background and Aims: Previous studies have shown that Low Birth Weight (LBW) and small for gestational age (SGA) are associated with increased risk of end-stage renal disease. Few population-based studies have however investigated risk of less severe kidney disease and in the present study, we investigate risk of chronic kidney disease and other kidney disease diagnoses.

Method: The Norwegian Patient Registry (NPR) has registered ICD diagnostic codes for all admissions and outpatient visits to Norwegian hospitals since 2008 (available for 2008-2016 in this study). The Norwegian Medical Birth Registry (MBR) has registered birth weight, gestational age and several other data on maternal and offspring health for all birth in Norway since 1967. Data from these registries were linked and risk of chronic kidney disease (CKD) and other groups of kidney disease were analyzed with logistic regression statistics. LBW (less than the 10th percentile), SGA (less than the 10th percentile) and preterm birth (less than 37 weeks) were analyzed as risk markers. Adjusted analyses were performed for the main analyses by including birth year, gender, maternal disease, maternal preeclampsia, maternal marital status and malformations in the newborn.

Results: Of the 2,663,010 included individuals, 4,495 had been diagnosed with CKD and 12,818 with acute kidney disease, glomerulonephritis, hereditary kidney disease or kidney disease due to kidney or urinary tract malformations. LBW was associated with an adjusted odds ratio (aOR) for CKD of 1.61 (1.48-1.74), SGA with an aOR of 1.51 (1.39-1.63) and preterm birth with an aOR of 1.47 (1.31-1.66). As compared to subjects with none of these risk factors (LBW, SGA or preterm birth), subjects with only one risk factor had an aOR of 1.49 (1.35-1.66), subjects with 2 risk factors had adjusted aOR of 1.72 (1.57-1.88) and subjects with 3 risk factors had aOR of 2.56(1.99-3.29). Analyses of chronic kidney disease stage 3, 4 and 5 showed similar results. There were no significant gender differences. We further analysed aOR for other groups of kidney disease and found that LBW was associated with aOR of 1.52 (1.40-1.65) for acute kidney disease, 1.26 (1.16-1.38) for glomerulonephritis, 1.55 (1.34-1.80) for hereditary kidney disease and 1.38 (1.27-1.49) for kidney disease due to kidney or urinary tract malformations; analyses for the other risk factors showed similar results.

Conclusion: LBW and SGA are strong risk factors for diagnosis of all stages of CKD during the first 50 years of life and the risks seem to be increased also for other groups of kidney disease. Our results underline the public health importance of LBW and SGA.

P1618 **DEVELOPMENT AND EXTERNAL VALIDATION OF A PREDICTION MODEL FOR ADVERSE OUTCOME FOLLOWING KIDNEY TRANSPLANTATION FROM OLDER DECEASED DONORS**

Chava Ramspek[1], Mostafa El Moumni[2], Martin Heemskerk[3], Eelaha Wali[1], Nichon Jansen[3], Andries Hoitsma[3], Friedo W. Dekker[1], Merel Van Diepen[1], Cyril Moers[4]

[1]Leiden University Medical Center, Clinical Epidemiology, Leiden, Netherlands, [2]University Medical Center Groningen, University of Groningen, Department of Trauma Surgery, Groningen, Netherlands, [3]Dutch Transplant Foundation, Leiden, Netherlands and [4]University Medical Center Groningen, University of Groningen, Department of Surgery - Organ Donation and Transplantation, Groningen, Netherlands

Background and Aims: With rising demand for kidney transplantation and the kidney donor pool lagging behind, the acceptance criteria for donor kidneys are expanding. Hence, reliable pre-transplant assessment of organ quality has become a top priority. Estimating the risk of adverse outcomes at the time of kidney allocation is challenging and particularly relevant for recipients of kidneys from older donors. The existing kidney donor risk index (KDRI) has been criticized for heavily depending on donor age. Therefore, the aim of the current study was to develop and validate a prediction model for adverse outcome after kidney transplantation from deceased donors aged 50 years or older and compare this model's performance to the KDRI.

Method: We utilized the Dutch kidney transplant registry (NOTR) and identified patients who received a kidney from a deceased donor aged 50 years or older between 2006 and 2019. These recipients were included for model development and temporal validation. The prediction model was externally validated on the United States organ transplantation registry (OPTN), in which we selected patients that were transplanted between 2006 and 2017. Potential pre-transplant predictors were selected by an expert panel of nephrologists and surgeons. The predicted adverse outcome was defined as a composite of graft failure, recipient mortality or CKD stage 4/5 within 1 year of transplantation. A logistic regression model was developed, internally validated and shrunk for optimism through bootstrapping. Missing data were multiply imputed in 10-fold, non-linear continuous predictors were modelled with restricted cubic splines and clinically relevant interaction terms were included. The KDRI was validated on the same NOTR and OPTN cohorts for graft survival within 1 year. The developed model and the KDRI were recalibrated to the baseline risk of outcome in external validation. Model performance was assessed by discrimination and calibration.

Results: The model was developed on 2510 patients of whom 823 experienced an adverse outcome within the first year. The temporal validation cohort contained 837 patients of whom 230 had an adverse outcome and the US external validation cohort consisted of 31987 patients with 6758 adverse outcomes. Selected donor predictors were: age, gender, BMI, cause of death, CPR, inotropes use, serum creatinine, hypertension, hypotension, diabetes, smoking, left/right kidney, warm ischemic time, cold ischemic time and proteinuria. Recipient predictors were: age, gender, BMI, diabetes, cardiovascular comorbidity, primary kidney disease, dialysis duration, number of previous kidney transplantations, HLA mismatches and PRA. Discrimination of the adverse outcome model was moderate, yet considerably better than discrimination of the KDRI (see table). The adverse outcome model's calibration and distribution of predicted risks were good in both the NOTR and OPTN (see figure).

Conclusion: A prediction model was developed and extensively validated for adverse outcome after kidney transplantation from older deceased donors. Despite the use of advanced and robust methodology, its discriminatory capacity was limited. However, the adverse outcome model showed good calibration and performed considerably better than the KDRI in this population of suboptimal donors. This model could potentially assist nephrologists in deciding whether to accept or decline a specific kidney from an older deceased donor.

Table: discrimination and calibration-in-the-large

		NOTR 2006-2016	Internal validation	NOTR 2016-2019	OPTN 2006-2017
Adverse Outcomes model	C-statistic (95% CI)	0.68 (0.65-0.70)	0.65	0.63 (0.58-0.67)	0.62 (0.62-0.63)
	Predicted vs observed	33% vs 33%	33% vs 33%	32% vs 27%	23% vs 21%
KDRI (1 year graft survival)	C-statistic (95% CI)	0.57 (0.54-0.60)	-	0.56 (0.50-0.63)	0.59 (0.58-0.60)
	Predicted vs observed	24% vs 15%	-	25% vs. 10%	10% vs 16%

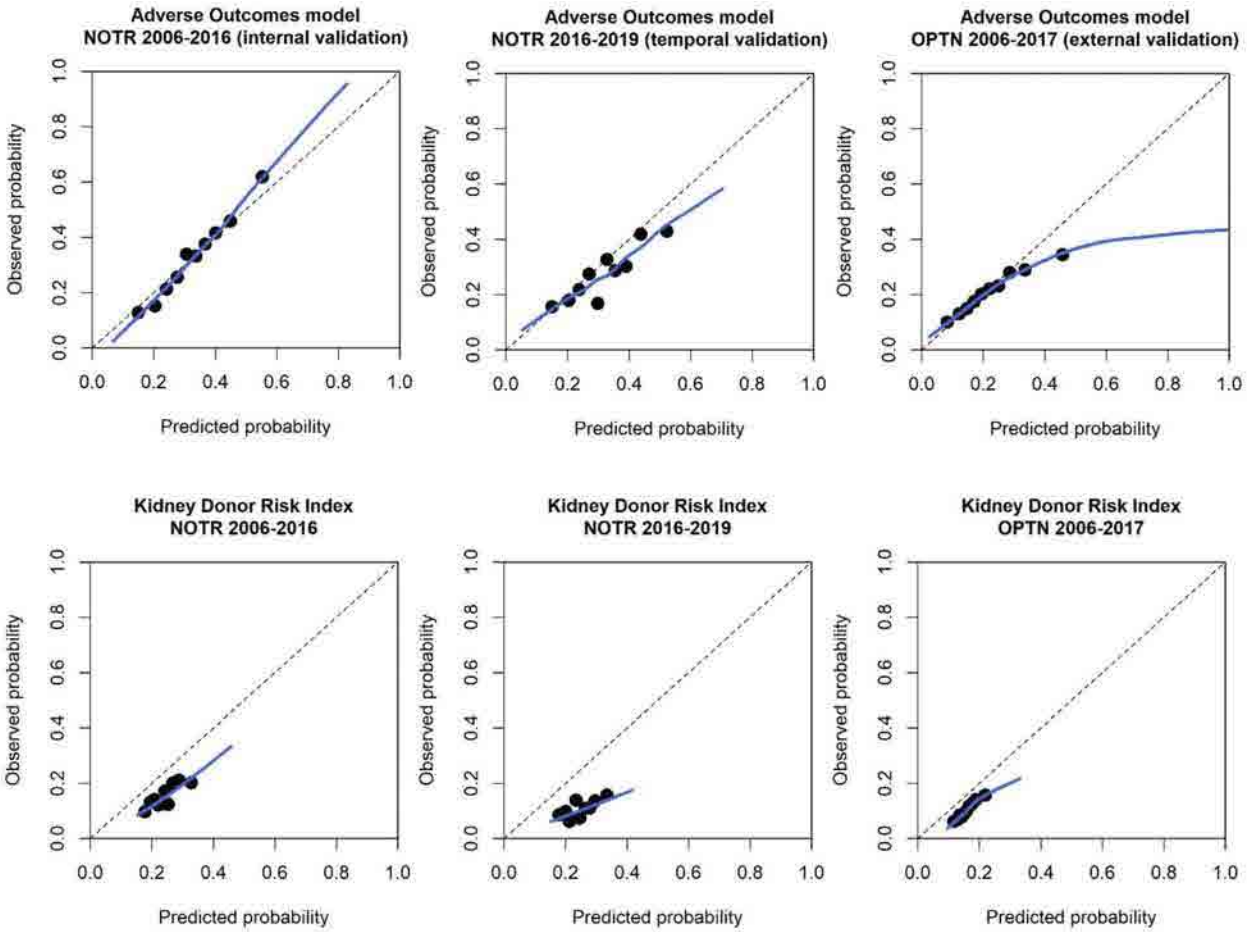


Figure: calibration plots

P1619 OUTCOME OF HIGH DONOR-RECIPIENT AGE GAP IN LIVE-DONOR RENAL TRANSPLANTS IN TACROLIMUS ERA

Hatem Kaies Ibrahim Elsayed Ali[1], Ahmed Daoud[2], Karim Soliman[3], Mahmoud Mohamed[4], Asam Murtaza[5]

[1]University Hospitals of Birmingham, Birmingham, United Kingdom, [2]Medical Institute, Houston, United States of America, [3]university of south carolina, United States of America, [4]University of Tennessee, Tennessee, United States of America and [5]Walsall Manor Hospital, United Kingdom

Background and Aims: High donor-recipient age gap among deceased-donor renal transplant patients leads to worse outcomes. However, the impact of this gap among live-donor renal transplants is unclear. The aim of this study is to assess the effect of this age gap on graft survival and acute rejection rates among renal transplants in tacrolimus era.

Method: 14390 live-donor renal transplant patients who received a single organ transplant, had no previous renal transplants, discharged on tacrolimus-based immunotherapy and were registered in the Organ Procurement Transplantation Network from January 2000 till June 2017 were included in the study. Donor–recipient age difference was divided into 5 groups; group A (difference <-10,n=4375), group B (difference from -10 to 10,n=7229), group C (difference between 10-20, n=861), group D (difference between 20–29, n=1406) and group E (difference $\geq$30 years, n=519). Poisson regression analysis was used to assess effect of age gap on acute rejection rates. Kaplan-Meier survival curves and Cox hazard regression analysis were used to assess this effect on graft survival.

Results: Regarding graft survival, groups with age difference $\geq$30 years and between 20-29 years showed a significantly higher risk of graft loss when compared to group with age difference <-10 (HR equals 4.6 and 3.8 respectively). Groups with age difference between 10 to 20 years and between -10 to 10 years showed no significant difference in graft survival when compared to same group (HR equals 1.03 and 0.95 respectively). Groups B,C,D,E were not associated with increased risk of acute rejection episodes when compared to group A (IRR=1.001, 1.001, 1.022, 1.027 respectively).

Conclusion: Donor-recipient age difference up to 20 years has similar renal transplant outcomes to those receiving kidneys from younger donors and therefore, should not be precluded from paired kidney donation programs. The donor-recipient age difference above 20 years is associated with worse outcomes in terms of graft survival.

P1620

PROGNOSTIC VALUE OF RENAL BIOPSY QUANTITATIVE HISTOLOGY IN LIVING KIDNEY DONORS AND RECIPIENTS OF KIDNEYS FROM LIVING DONORS

Niels Henrik Buus[1], Cecilie Molgaard Nielsen[2], Soren Krag[3], Lotte Ibsen[4], Karin Skov[1], Jens Randel Nyengaard[2]

[1]Aarhus University Hospital, Department of Renal Medicine, Denmark, [2]Aarhus University, Center for Molecular Morphology, Denmark, [3]Aarhus University Hospital, Department of Pathology, Denmark and [4]Aarhus University Hospital, Department of Radiology, Denmark

Background and Aims: Living kidney donors (LKD) have an increased risk of chronic kidney disease. Likewise, renal transplant recipients may experience early or unexplained loss of graft function. We examined the predictive value of stereology based on a CT-scan and a biopsy from the transplanted kidney in relation to renal function outcome in both LKD and recipients of kidneys from living donors.

Method: A pre-transplantation contrast-enhanced CT-scan was used to obtain cortical volume of both kidneys using the Cavalieri estimator. Glomerular number density in a baseline biopsy from the transplanted kidney (taken at the time of transplantation) was estimated by a model-based method and multiplied with cortex volume to estimate the total number of glomeruli in the donated kidney. Glomerular volume was estimated by the 2D nucleator (1). In addition, kidney fibrosis (point-counting), glomerular sclerosis, and arteriole dimensions (2D nucleator) were also calculated. Pre-donation single kidney glomerular filtration rate (GFR) was determined using ^{51}chrome EDTA clearance together with a renography and the GFR measurement was repeated one year after transplantation in both donors and recipients. We examined the association between GFR at one-year follow-up and cortex volume and various histology parameters from the baseline biopsy after adjustment of age, sex, body mass index, smoking status, 24-hour mean blood pressure and single-kidney GFR before transplantation.

Results: CT-scans, GFR measurements and kidney histology from 49 LKD and 38 recipients of kidneys from living donors were available for analysis. Mean age of donors was 50±12 years (55% women) and of recipients 46±13 years (26% women). In donors, GFR decreased from 113±24 to 71±16 ml/min while in recipients GFR was 61±18 ml/min at one-year follow-up (all with a functioning graft).

In *donors,* GFR at follow-up of the remaining kidney had increased by 28% as compared to baseline. Follow-up GFR correlated to cortex volume ($P<0.001$), but not to any of the histological parameters (total glomerular number, glomerular volume, % sclerosed glomeruli, % kidney fibrosis or arteriolar dimensions).

In *recipients*, GFR at follow-up had increased by 8% as compared to single-kidney GFR before donation. Follow-up GFR correlated to % kidney fibrosis ($P=0.02$) and % sclerosed glomeruli ($P=0.05$), but not any of the other histological parameters or cortex volume.

Conclusion: When adjusted for relevant clinical confounders the estimation of cortex volume had predictive value for renal function outcome in LKD while % kidney fibrosis and % sclerosed glomeruli had predictive value in recipients of kidneys from living donors.

P1621 **VITAMIN D SUPPLEMENTATION: CHANGES IN BONE MINERAL DENSITY IN KIDNEY TRANSPLANT PATIENTS WITH LONG TERM DURATION OF THE GRAFT.**

Yuri Battaglia[1], Michele Provenzano[2], Francesco Tondolo[3], Antonio Bellasi[4], Pasquale Esposito[5], Gaetano La Manna[3], Domenico Russo[6], Michele Andreucci[2], Alda Storari[7]

[1]St. Anna University-Hospital, Nephrology and Dialysis, Ferrara, Italy, [2]University of Catanzaro, Nephrology and Dialysis, [3]University of Bologna, Nephrology and Dialysis , [4]Papa Giovanni XXIII Hospital, Nephrology and Dialysis , [5]University of Genova, Nephrology and Dialysis , [6]University of Napoli, Nephrology and Dialysis and [7]St. Anna University-Hospital, Nephrology and Dialysis

Background and Aims: In the medical literature, several studies have linked bone mineral density (BMD) with vitamin D deficiency in kidney transplant patients (KTRs). However, in spite of the fact that ergocalciferol, cholecalciferol and calcifediol reduce parathyroid hormone (PTH) and improves calcium levels, their effects on the bone mineral density (BMD) in KTRs remain undefined. In consideration of the lack of data available, we aim at investigating the effect of inactive form of vitamin D supplementation on the BMD over a follow-up period up to 2 year, in a real-life cohort of long-term kidney transplant(KT).

Method: This study was carried out in KTRs who were followed up in a Nephrology Unit. Exclusion criteria were parathyroidectomy, therapy with bisphosphonate, previous history of bone fractures. Demographic, clinical and immunosuppressive agents were collected. Based on 25-OH-D levels, KTRs were classified as suffering from deficiency (< 30 ng/mL). BMD was evaluated at lumbar vertebral bodies (LV) and right femoral hip (FH) by a single operator, using a standard dual energy X-ray absorptiometry. According to WHO criteria, results were expressed as T-score (standard deviation [SD] relative to young healthy adults), and Z-score (SD relative to age-matched controls). Osteoporosis and osteopenia were defined as T score ≤ -2.5 SD and T score < -1 and > -2.5 SD, respectively. Laboratory data, 25-OH-D, and BMD were measured at baseline and after 24 months of supplementation therapy. Vitamin D deficiency was corrected using standard treatment strategy recommended for general population. Continuous variables were expressed as mean $\pm$ SD whereas categorical variables as percentage. The Student's t test and chi-square test were used to compare to compare continuous and categorical variables, respectively. For before and after comparisons of continuous variables, the paired t-test or one-sample Wilcoxon signed rank test were used based on variable's distribution.

Results: Data pertaining to 111 out of 133 consecutive outpatients were collected, of whom most were males (69.4%), no-smokers (89.1%) and treated with glucocorticoids (84%). The mean age was 53.9 ± 11.6 years and months after transplant was 161.6 ± 128.3. No statistical differences were found among patients with normal BMD, osteopenia or osteoporosis at LV and FH in terms of age at transplant, gender distribution, time on dialysis, BMI and eGFR, serum calcium, serum phosphate, 25-OH-D and iPTH. At baseline, 25-OH-D was 13.9 ± 7.2 ng/ml and the prevalence of osteopenia/osteoporosis was 40.9% (T-Score -1.69 ± 0.37; Z-score -1.16 ± 1.09) and 21.8 % (T-Score -3.15 ± 0.50; Z-score -2.27 ± 0.58) at LV; 55.3 % (T-Score -1.8 ± 0.46; Z-score -0.84 ± 0.633) and 14 % (T-Score -2.83 ± 0.39; Z-score -1.65 ± 0.49) at FH. After 27.6 ± 3.7 months of therapy with cholecalciferol at mean dose of 13.396 ± 7.537 UI at week, 25-OH-D values increased to 29.4 ± 9.4 ng/ml ($p<0.0001$) while no statistically significant changes were found in Z-score and T-score at both sites, except for a mild improvement in lumbar vertebral Z-score, reaching -0.82 ± 0.7 ($p = 0.06$) in KTRs with osteopenia

Conclusion: Our study showed BMD remained stable after up to 2 years of inactive vitamin D therapy in long-term kidney transplant with vitamin D deficiency. A mild increase in Z-score was observed in the L-spine. Further designated studies should be conducted to demonstrate the effect of vitamin D on BMD.

P1622

GROWTH DIFFERENTIATION FACTOR 15: A BIOMARKER WITH HIGH CLINICAL POTENTIAL IN THE EVALUATION OF KIDNEY TRANSPLANT CANDIDATES

Marina De Cos Gomez[1], Adalberto Benito Hernandez[1], M Angeles Ramos Barron[1], Covadonga Lopez del Moral Cuesta[1], Jaime Mazon Ruiz[1], David San Segundo Arribas[2], Gema Fernandez Fresnedo[1], Rosalía Valero San Cecilio[1], Juan Carlos Ruiz San Millán[1], Emilio Rodrigo[1]

[1]University Hospital Marques de Valdecilla-IDIVAL, Nephrology, Santander, Spain and [2]University Hospital Marques de Valdecilla-IDIVAL, Immunology, Santander, Spain

Background and Aims: Kidney transplantation results a significant improvement in patient survival. Nevertheless, mortality the first years after transplant remains relatively high, being mostly related to cardiovascular (CV) events. The selection of patients for kidney transplantation includes a general assessment focused on CV status. In spite of that, due to the complexity and heterogeneity of mechanisms leading to vascular disease in this population (not exclusively related to traditional CV risk factors and pathogenesis), this evaluation remains insufficient and not particularly effective. During the last years different strategies have been studied to stratify potential receptors better and optimize organ allocation, including the development of clinical prognostic scores and novel biomarkers.

Growth differentiation factor 15 (GDF-15) is a stress-responsive member of the TGF-β family. Although its mechanism of action is not completely understood, it acts as a cytokine with effects in regulation of inflammation, metabolism and senescence. In the recent years, interest has arisen regarding its use as a biomarker for diagnosis, prognosis and risk stratification in multiple scenarios. Encouraging results have shown its utility as a biomarker of mortality (all cause and CV), heart failure and acute coronary syndrome in different populations. The aim of this work is to assess the utility of GDF-15 to predict survival in kidney transplant candidates.

Method: 395 kidney transplant recipients between 2005 and 2015 were included. GDF-15 measurements were performed from stored serum samples obtained pretransplant. The concentration of GDF-15 was analyzed using an enzyme-linked immunosorbent assay (Quantikine, R&D Systems).

Results: Patient characteristics are shown in Table 1. The median GDF-15 was 5331.3 (50.49-16242.3) pg/ml. After a mean of 90.6 ± 41.5 months of follow up 82 (20.8%) patients died. Patients were stratified in tertiles according to GDF-15 levels: low (GDF-15 ≤ 4612.1 pg/ml), medium (GDF-15 4612.1-6296.5 pg/ml) and high risk tertile (GDF-15 > 6296.5 pg/ml). Higher GDF-15 concentrations were significantly associated with mortality: HR 2.16 95%CI (1.14-1.44), p = 0.018 for medium tertile and HR 3.28 95%CI (1.79-6.1), p <0.001 for high risk tertile (Figure 1). After adjusting for age, diabetes, coronary artery disease, peripheral vascular disease, non-renal solid organ transplant and dialysis at the time of transplant, the relation between survival and GDF-15 was significant (HR 2.24 95%CI (1.2-4.16), p = 0.011 for high risk tertile). After adjusting by EPTS (Estimated Post Transplant Survival score) the association with GDF-15 remained significant: HR 3.24 95%CI (1.2-8.8), p = 0.021 for medium risk tertile and HR 4.3 95%CI (1.65-11.54), p = 0.003 for high risk tertile (calculated only in first renal transplants). Mortality at 3 years was 6.9% (27 patients) and it was only related to coronary artery disease and GDF-15 (OR 7.1 95%CI (1.6-32.1), p = 0.01 for high risk tertile) after adjustment.

Conclusion: In our cohort, higher GDF-15 levels were independently associated with mortality in kidney transplant candidates. This study suggests that GDF-15 may be useful in stratifying recipient risk, adding value to the prognostic tools already available in clinical practice. Further work is needed to confirm these findings and elucidate the mechanisms linking this protein with mortality and CV disease in patients with CKD.

Patient characteristics	
Number of patients	395
Age (years)	52 ± 12,41
Sex (%)	68,1% males / 31,9% females
Race (% caucasian)	96,5%
Diabetes (%)	23%
Coronary artery disease (%)	10,4%
Peripheral vascular disease (%)	8,6%
Non renal solid organ transplant (%)	7,8%
Primary renal diagnosis	
Glomerular (%)	27,4%
Diabetes (%)	14,7%
Hypertension/vascular (%)	24,2%
Polycystic kidney disease (%)	12,4%
Other (%)	15,7%
Unknown (%)	5,6%
Dialysis at the time of transplant (%)	84,1%
Retransplant (%)	33,2%

Figure 1

P1623

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE) AFTER KIDNEY TRANSPLANTATION: A POPULATION-COHORT ANALYSIS OF ENGLISH TRANSPLANT CENTRES

Benjamin Anderson[1,2], Felicity Evison[3], Suzy Gallier[3], Charles Ferro[1,4], Adnan Sharif[1,5]

[1]Queen Elizabeth Hospital Birmingham, Department of Nephrology and Transplantation, United Kingdom, [2]University of Birmingham, Institute of Inflammation and Ageing, United Kingdom, [3]Queen Elizabeth Hospital Birmingham, Department of Informatics, United Kingdom, [4]University of Birmingham, Institute of Cardiovascular Sciences, United Kingdom and [5]University of Birmingham, Institute of Immunology and Immunotherapy, United Kingdom

Background and Aims: Due to a high burden of cardiovascular disease in end-stage kidney failure, candidates for kidney transplantation must undergo cardiac screening to determine their 'cardiac fitness' to proceed with surgery even when asymptomatic and in the absence of robust evidence. MACE rates within the first year after kidney transplantation in North American centres are reported at between 7.0% and 8.7% but data from an European cohort is lacking. Therefore, the aim of this population-cohort analysis was to determine the MACE rate within the first year after kidney transplantation for all kidney transplant recipients in England.

Method: We obtained data from every kidney transplant procedure performed in England between 1st April 2002 and 31st March 2018. Data was extracted from Hospital Episode Statistics using administrative ICD-10 and OPCS-4 codes, with linkage to the national death registry for mortality data (including causality). We excluded age $\leq$18, repeat transplant in same period, multi-organ transplant and residence outside England. MACE was defined as any hospital admissions with myocardial infarction, stroke, unstable angina, heart failure, any coronary revascularisation procedure and/or any cardiovascular-related death. Univariable and multivariable logistical regression analyses were conducted to investigate the odds for MACE after kidney transplantation.

Results: After exclusions, we had a cohort of 30,325 kidney transplant recipients for analysis. MACE events occurred in 781 kidney transplant recipients within the first-year post-transplantation (2.6% of all kidney transplant procedures). Of these 781 MACE events, 201 occurred during the index admission for kidney transplantation surgery (representing 25.7% of all first-year MACE events and 0.7% of all kidney transplant procedures). Predictors of long-term mortality on Cox regression include; age, non-White ethnicity, socio-economic deprivation, deceased donor, pre-existing diabetes, increased Charlson score, previous cardiac history and MACE within the first year (HR 2.59; 95% CI 2.34-2.88, $p<0.001$). Kidney transplant recipients who suffered a non-fatal MACE within the first year had 1-, 3-, 5- and 10-year patient survival of 80.5%, 70.2%, 54.5% and 38.6%, compared to 97.4%, 94.4%, 90.7% and 78.4% for kidney transplant recipients not developing MACE within the first year post-transplant ($p<0.001$). Kidney transplant recipients having MACE events during the index admission compared to subsequent admissions were differentiated by age, sex and previous cardiac history but had similar patient survival ($p=0.283$).

Conclusion: MACE events within the first year after kidney transplantation are associated with increased mortality risk in England but MACE rates are significantly lower at 2.6% than those reported in North America. This is despite similar cardiac screening strategies, which may reflect different patient demographics and kidney failure care. In the context of the increased debate concerning the utility of cardiac screening asymptomatic kidney transplant candidates, understanding baseline MACE rates can shape the design of clinical trials exploring non-inferiority of cardiac screening versus non-screening *before* joining the waiting list (which differs methodologically from the CARSK study). However, renal physicians and surgeons will need to determine the upper boundary of the 95% confidence interval for the hazard ratio of MACE risk in any future clinical trial.

P1734

INFORMATION AND COMMUNICATION TECHNOLOGY-BASED CENTRALIZED MONITORING SYSTEM TO INCREASE ADHERENCE TO IMMUNOSUPPRESSIVE MEDICATION IN KIDNEY TRANSPLANT RECIPIENTS: A RANDOMIZED CONTROLLED TRIAL

Hee-Yeon Jung[1], Yena Jeon[2], Sook Jin Seong[3], Jung Ju Seo[1], Ji-Young Choi[1], Jang-Hee Cho[1], Sun-Hee Park[1], Chan Duck Kim[1], Young-Ran Yoon[3], Se-Hee Yoon[4], Jong Soo Lee[5], Yong-Lim Kim[1]

[1]Kyungpook National University Hospital, Internal Medicine, Korea, Rep. of South, [2]Kyungpook National University, Statistics, Korea, Rep. of South, [3]Kyungpook National University Hospital, Biomedical Science and Clinical Trial Center, Korea, Rep. of South, [4]Konyang University College of Medicine, Internal Medicine, Korea, Rep. of South and [5]University of Ulsan College of Medicine, Internal Medicine, Korea, Rep. of South

Background and Aims: Innovative strategies to promote adherence to immunosuppressants in kidney transplant recipients (KTRs) is imperative. This study aimed to evaluate the efficacy and stability of the information and communication technology (ICT)-based centralized monitoring system in increasing medication adherence in Korean KTRs.

Method: A prospective, multicenter, randomized controlled study was conducted (ClinicalTrials.gov Identifier: NCT03136588). All KTRs were randomized into the ICT-based centralized monitoring or the control group and had follow-up visits every 4 weeks during 6 months. The ICT-based centralized monitoring system alerted both patients and medical staff with texts and pill box alarms if there was a dosage/dosing time error or a missed dose. Medication adherence and transplant outcomes were compared between the two groups, and patient satisfaction on the ICT-based monitoring system was evaluated.

Results: Among enrolled 114 KTRs, 57 patients were assigned to the ICT-based centralized monitoring group and 57 patients to the control group. Mean adherence at each follow-up visit was not significantly different between groups. No differences in intra-patient variability of tacrolimus and mycophenolic acid levels, renal function, and adverse transplant outcomes were observed between the intervention and control groups, as well as between the intervention group with feedback generation and the intervention group without feedback generation. Overall patient satisfaction with the ICT-based centralized monitoring system was high and significantly improved during the study period ($P = 0.012$).

Conclusion: Although the ICT-based centralized monitoring system did not maximize mediation adherence or enhance transplant outcomes in Korean KTRs due to high baseline adherence, patient satisfaction with the system was high. We identified the future possibility that the ICT-based centralized monitoring system could be successfully applied in clinical trials targeting other disease groups with impaired adherence.

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MODERATED POSTER SESSION 5

P0044

THE BIOLOGICAL AND FUNCTIONAL CHARACTERISATION OF GENES RESPONSIBLE FOR MONOGENIC DISORDERS OF THE KIDNEY

Mahan Salehi[1], Xiao Jiang[1], Xiaoguang Xu[1], James Eales[1], Maciej Tomaszewski[1]
[1]*The University of Manchester, Cardiovascular Health and Disease, Manchester, United Kingdom*

Background and Aims: Single mutations in over 620 genes are known as drivers of approximately 330 monogenic disorders of the kidney. These disorders are estimated to account for up to 10% of chronic kidney disease cases. Due to their disease-causing nature, these genes are particularly clinically relevant targets for molecular analysis, but, so far, there has been no systematic analysis of their expression profile and biological functions in the human kidney. We aimed to characterise and compare the genes responsible for monogenic disorders of the kidney with other non-monogenic protein-coding genes.

Method: We used RNA-sequencing profile of 430 kidneys to explore the characteristics of 530 monogenic genes whose expression was available for analysis in the dataset. The property of genes was characterised using in silico databases such as Genome Reference Consortium Human Build 37 (GRCh37), Drug Gene Interaction database (DGIdb) and the Human Protein Atlas (HPA). The PANTHER (protein analysis through evolutionary relationships) database was used to determine the biological network of interactions between the monogenic genes. A Fast Gene Set Enrichment Analysis (FGSEA) was carried out using single-cell RNA-sequencing data for eight cell types of the kidney from Young et al. Finally, we carried out a two-stage mendelian randomisation to discover a causal link between gene expression and estimated glomerular filtration rate (eGFR) and blood pressure (BP). We used the summary statistics from UK Biobank and the CKDGen consortium for BP and eGFR respectively.

Results: The expression of monogenic genes was both higher and more specific to the kidney, than other protein-coding kidney genes. The pathway analysis found both fetal and organ development to be overrepresented in this set of genes, when compared to non-monogenic kidney genes. We also found that monogenic genes are significantly overrepresented for cell-type specific expression in the proximal tubule and underrepresented in podocytes. Our Mendelian randomisation analysis identified a causal effect between the expression of 50 monogenic genes and either eGFR, systolic or diastolic blood pressure.

Conclusion: Our studies revealed differences in the renal expression profile of monogenic genes and protein-coding genes. The proximal tubule segment of the nephron is a particularly enriched segment of the nephron for monogenic disorders. Kidney expression of 50 of the monogenic genes is causally related to changes in eGFR and blood pressure in the general population.

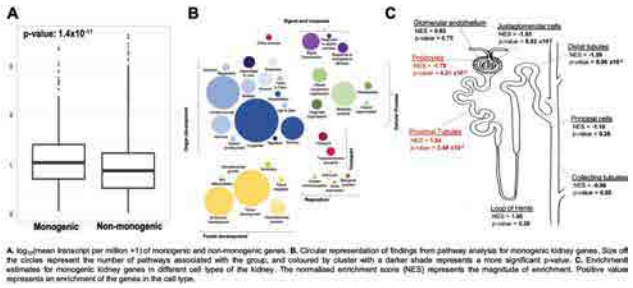


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P0045

GENETIC ABLATION OF NFAT5 IN THE PRINCIPAL CELLS OF THE COLLECTING DUCT LEADS TO A WATER HANDLING DEFECT

Federica Petrillo[1], Annika Fischer[2], Dmitry Chernyakov[2], Cristina Esteva Font[3], Søren B Poulsen[3], Toke P Krogager[3], Bayram Edemir[2], Robert A Fenton[3]

[1]Aarhus University, Department of Biomedicine, Aarhus, Denmark, [2]Martin-Luther-University Halle-Wittenberg, Department of Medicine, Hematology and Oncology, Halle (Saale), Germany and [3] Aarhus University, Department of Biomedicine, Aarhus, Denmark

Background and Aims: Nuclear Factor of Activated T-Cells 5 (NFAT5), also called TonEBP/OREBP, helps protecting kidney cells from the stress of extracellular hypertonic challenge. In response to hypertonicity, NFAT5 rapidly translocates into the nucleus and enhances the transcription of osmoprotective genes. Mice lacking NFAT5 have embryonic lethality, with those surviving having severe renal atrophy and hydronephrosis. Overexpression of a dominant-negative NFAT5 in all epithelial cells of the thick ascending limb, distal tubule and collecting duct (CD) leads to an impairment in the urine concentration, with reduced expression of AQP2 and urea transporters UT-A1 and UT-A2. Here, we generated a novel mouse model to assess the role of NFAT5 in the water transporting principal cells of the CD.

Method: The mouse model was generated by breeding floxed NFAT5 mice with mice specifically expressing Cre recombinase in AQP2 expressing cells (NFAT5f/f-AQP2cre+/-). AQP2cre+/- mice served as controls. For renal function analysis, mice were kept in metabolic cages for 5 days and water intake, urinary volume, osmolality, and serum and urine electrolytes were evaluated. Mice were euthanized and the kidneys were used for western blot analysis.

Results: NFAT5$^{f/f}$-AQP2$^{cre+/-}$ mice show a significant increase of 24 hour urine output compared to the control (KO: 6.267 ± 0.9367 µl/h/g BW vs WT: 0.9593 ± 0.0796 µl/h/g BW), a decrease in the urine osmolality (KO: 505.6 ± 107.6 mOsm/Kg H2O vs WT: 6205 ± 752.7 mOsm/Kg H2O) and urea concentration. After 3h and half intraperitoneal injection of dDAVP (1ug/kg) the osmolality was still significantly low in NFAT5$^{f/f}$-AQP2$^{cre+/-}$ mice (KO: 743.7 ± 81.77 vs WT: 3342 ± 80.14 mOsm/Kg H2O), as well as after 8h water restriction (KO: 732.8 ± 24.90 vs WT: 3784 ± 450.9 mOsm/Kg H2O). Immunoblotting demonstrated a significant decrease in AQP2, AQP3 and AQP4 abundance in cortical kidney fractions and inner medulla. There were no differences in vasopressin V2 receptor (V2R) and AVP-regulated transporters NKCC2, ROMK and alpha-ENaC.

Conclusion: We demonstrate that NFAT5 ablation from AQP2-expressing cells results in a urinary concentration defect. NFAT5f/f-AQP2cre+/- mice have a hypoosmotic polyuria, without major effects on the AVP-V2R axis, suggesting Nephrogenic Diabetes Insipidus.

P0046 ZHX2 DOWNREGULATION DUE INSERTIONS AND DELETIONS IN THE HAS2-ZHX2 INTERGENIC REGION PREDISPOSE TO PODOCYTE DISEASE RELAPSE

Maria Del Nogal Avila[1,2], Ranjan Das[1], Joubert Kharlyngdoh[1], Eduardo Molina Jijon[1], Hector Donoro Blazquez[1], Stephanie Gambut[1], Michael Crowley[3], David Crossman[3], Rasheed A. Gbadagesin[4], Stefan Nagel[5], Carmen Avila Casado[6], Lionel Clement[1], Camille Mace[1], Sumant S Chugh[1]

[1]Rush University Medical Center, Internal Medicine, Chicago, United States of America, [2]Facultad de Medicina, Universidad San Pablo-CEU, CEU Universities, Departamento de Ciencias Medicas Basicas, Boadilla del Monte, Spain, [3] University of Alabama at Birmingham, Heflin Center for Genomic Sciences, Birmingham, United States of America, [4]Duke University Medical Center, Division of Nephrology, Department of Pediatrics, Durham, United States of America, [5]Leibniz-Institute DSMZ, Department of Human and Animal Cell Lines, Braunschweig, Germany and [6]Toronto General Hospital, University of Toronto, Department of Pathology, Toronto, Canada

Background and Aims: ZHX2 transcriptional factor is normally found in podocyte membrane forming complexes with ZHX1 and APA or ZHX3 and Ephrin B1. Altered ZHX2 expression disrupts these interactions and is related with the worsening of different primary glomerular diseases such as focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD).

A small percentage of Hodgkin lymphoma (HL) patients develop nephrotic syndrome (NS). Studies of Reed-Sternberg cell line L-1236 reveals a chromosomal rearrangement that leads to ZHX2 downregulation suggesting a possible role of ZHX2 in the development of NS in these patients.

Human podocyte disease relapse is common after a common cold probably mediated by cytokines released by immune cells and the rhinovirus.

Our aim is to study how the presence of insertions and deletions (InDels) between HAS2 and ZHX2 in patients with MCD, FSGS and HL could alter ZHX2 expression and the implication in podocyte disease relapse after a common cold and in HL.

Method: Genomic DNA between *HAS2* and *ZHX2* (Chr8:122624000-124001000 from UCSC hg19 GRCh37) was sequenced from 28 NS patients and 27 controls using Agilent Custom capture and high throughput Illumina sequencing. The CLC Genomics software was used to identify InDels (3-20 bp) present exclusively in patients. One of the identified InDels was replicated in human podocytes using CRISPR Cas9 and homology directed repair technology to study changes in ZHX2.

A common cold cytokine cocktail containing IL-2, IL-4R, IL-6, IL-10, INF-γ, TNF-α and ICAM-1 was injected into control (BALB/c, n=5) and ZHX2 deficient mice (BALB/cJ, n=5) (Dose X); podocyte specific ZHX2 deficient (ZHX2 flox/flox cre$^{+/+}$, n=3) and floxed control mice (ZHX2 flox/flox, n=3) (dose X/15). Buffalo Mna (B. Mna) rats were also injected with the cytokine cocktail (X/50) to study relapse in FSGS (n=7).

Cell supernatant from HL Reed Sternberg cells (L-1236) (200μg of total protein) was injected into BALB/c (n=5) and BALB/cJ mice (n=5) and kidney function was assessed.

Results: Multiple InDels were found exclusively in the patient population, two of them, shared by two or more patients.

The insertion at 122,533,694 was presented in patients with MCD, FSGS and HL with NS and also in L-1236 cells. This insertion was replicated in human podocytes using CRISPR/Cas9 (CRISPR B). Another insertion noted both in patients and controls was generated for comparison (CRISPR A). A reduced ZHX2 expression was detected in CRISPR B but not in CRISPR A single cell clones.

The shared insertion at 122,787,088 was presented within the ZHX2 gene intron 1. BALB/cJ mice has lower ZHX2 expression in liver and podocytes due to an insertion in intron 1.

To study whether this insertion could be related with relapse of MCD and FSGS following a common cold, a cytokine cocktail was injected into BALB/cJ and BALB/c mice. BALB/cJ mice developed acute albuminuria after cytokine treatment (65.3±24.3 μg per 18h), but not control BALB/c mice (10.8±1.5 μg per 18h), when compared with baseline values (BALB/cJ 5.1±1.1 μg per 18h; BALB/c 6.5±1.1 μg per 18h) ($p<0.05$). BALB/cJ mice had also higher nuclear expression of ZHX1.

The cytokine cocktail also induced albuminuria in ZHX2 flox/flox/cre$^{+/+}$ mice but not in control ZHX2 flox/flox, suggesting that ZHX2 deficiency in podocytes is responsible of kidney injury after cytokine injection.

To study common cold related relapse in FSGS, B. Mna rats were injected with a rat cytokine cocktail, showing a significant increase in proteinuria (61.5±4.2 mg per 18h) compared with baseline (47±4.1 mg per 18h).

Cell culture supernatant from L-1236 was injected into BALB/cJ and BALB/c mice to study the effect of secreted soluble mediators in NS. L-1236 supernatant (200 μg) had a nephrogenic effect in ZHX2 deficient mice but not in controls.

Conclusion: InDels between HAS2 and ZHX2 genes presented in patients with MCD, FSGS and HL, alter ZHX2 expression and are related to relapse following a common cold and in HL.

P0168 **FRUCTOSE IS A CAUSE OF CALCIUM PHOSPHATE UROLITHIASIS IN RATS**

Mariusz Flisiński[1], Andrzej Brymora[2], Natalia Skoczylas-Makowska[3], Anna Stefańska[4], Jacek Manitius[1]

[1]Collegium Medicum of Nicolaus Copernicus University, Nephrology, Hypertension and Internal Medicine, Bydgoszcz, Poland, [2]Nowy Szpital, Hemodialysis Unit, Świecie, , [3]Collegium Medicum of Nicolaus Copernicus University, Clinical Pathology, Bydgoszcz, Poland and [4]Collegium Medicum of Nicolaus Copernicus University, Clinical Chemistry, Bydgoszcz, Poland

Background and Aims: Excessive consumption of fructose (Fr) leads to obesity, metabolic syndrome and insulin resistance, which are known risk factors for kidney stones. Along with the epidemic of obesity and diabetes there is also a growing incidence of kidney stones in both adults and children. The epidemiological studies have shown that the relative risk of nephrolithiasis significantly increases with fructose intake in diet.

The aim of the study was to assess the effect of high-fructose diet on kidney tubules disorders and predisposition to the development of kidney stones.

Method: Male Wistar rats were assigned for 8 weeks to 3 groups differing in the content of Fr in the diet: RD - regular diet with a fructose content <3%; F10 - regular diet with an addition of 10% Fr in drinking water; F60 - 60% Fr as a solid feed. Serum concentration of Fr, creatinine (Cr), insulin (Ins), triglycerides (Tg), homocysteine (Hcs), uric acid (UA), calcium (Ca), phosphorus (P), magnesium (Mg) were measured. Based on a 24-hour urine collection the following tests were performed: urine pH, proteinuria (PCR), excretion of N-Acetyl-(D)-Glucosaminidase (NAG), monocyte chemoattractant protein (MCP-1), uric acid (UAE), phosphorus (PE), calcium (CaE), magnesium (MgE) and sodium (NaE). The creatinine clearance (CrCl) was calculated. Calcium deposits in kidney sections were examined using H+E and von Kossa staining. Statistical analysis was performed using one-way analysis of variance ANOVA. Statistical significance was considered as $p<0,05$.

Results: The results are presented in table as mean ± SD.

The rats did not differ in total calories intake in their diet.

	RD	F10	F60	Anova
Fr [mg/dl]	0,6±0,1	1,3±0,7	1,0±0,5	0,08
Ins [ng/ml]	3,8±2,0	5,5±2,4	5,3±1,2	NS
Cr [mg/dl]	0,54±0,04	0,59±0,09	0,47±0,04	<0,05
CrCl [ml/min/100 g]	0,47±0,08	0,40±0,08	0,44±0,09	NS
UA [mg/dl]	1,76±0,4	1,45±0,3	1,56±0,1	NS
Hcs [µmol/l]	4,5±0,2	5,8±1,4	6,4±1,5	<0,05
Tg [mg/dl]	158±34	180±27	221±83	NS
CaxP [$mmol^2/l^2$]	5,85±0,36	6,04±0,49	6,34±0,59	NS
PCR [mg/mg Cr]	1,0±0,4	1,1±0,5	0,8±0,5	NS
MCP-1/Cr [ng/mg Cr]	3,5±0,6	4,4±4,0	11,2±2,5	<0,01
NAG/Cr [U/g Cr]	8,6±5	15,1±7,6	20,8±5	<0,05
Urine pH	8,5±0,57	8,2±0,83	5,6±0,51	<0,001
UAE [mg/day]	3,28±0,51	2,58±0,57	2,18±0,66	<0,05
PE [umol/day]	60±52	143±166	2090±1050	<0,001
CaE [umol/day]	51±22	143±76	69±17	<0,05
MgE [mg/day]	5,2±1,9	5,9±2,1	3,9±1,4	NS
NaE [mg/day]	33,3±8,5	40,9±10,8	144,2±60,5	<0,001

Histopathological examination revealed the presence of calcium phosphate stones in the renal tubules and interstitium in both F10 (Figure 1) and F60 groups (Figure 2).

Conclusion: The high-fructose diet, in a dose-dependent manner, exacerbated inflammation and induced damage to the proximal tubules. Both F10 and F60 led to hypouricosuria, hypercalciuria and hyperphosphaturia. Those disturbances, in turn, caused precipitation of calcium phosphate deposits in kidney tubules and parenchyma.

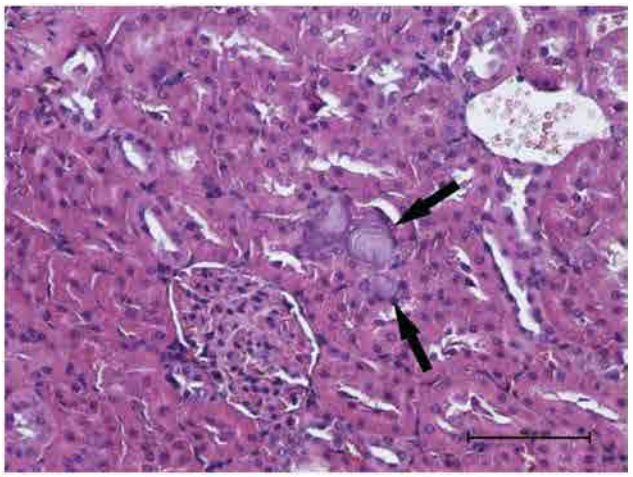


Figure 1: Interstitial and tubule associated bluish-purple calcium concretions with a ring-like substructure (arrows) in group F10. (HE, objective magnification 20x)

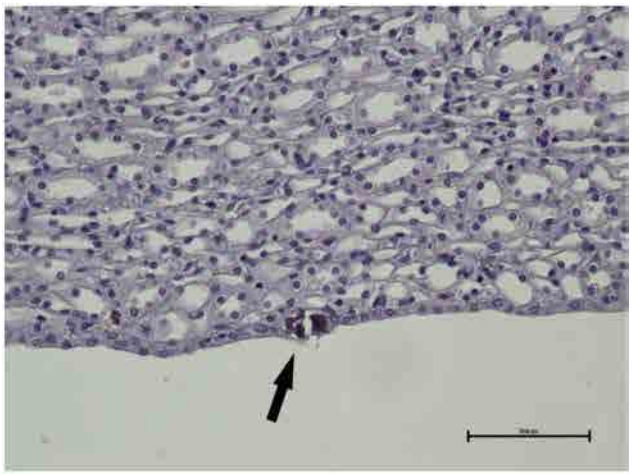


Figure 2: Basophilic calcium concretions involving renal papilla (arrow) in group F60. (HE, objective magnification 20x).

P1799 GENOTYPE-PHENOTYPE CORRELATION IN A PEDIATRIC ADPKD COHORT

Dorien Van Giel[1,2], Stéphanie De Rechter[2,3], Luc Breysem[4], An Hindryckx[5], Peter Janssens[2], Jean-Paul Decuypere[2], Bert Bammens[6,7], Anniek Corveleyn[8], Claude Férec[9], Rudi Vennekens[1], Marie-Pierre Audrezet[9], Peter Harris[10], Djalila Mekahli[2,3]

[1]VIB Center for Brain and Disease Research, Laboratory of Ion Channel Research, Leuven, Belgium, [2]KU Leuven, Department of Development and Regeneration - PKD Research Group, Leuven, Belgium, [3]University Hospitals Leuven, Department of Pediatric Nephrology, Leuven, Belgium, [4]University Hospitals Leuven, Department of Radiology, Leuven, Belgium, [5]University Hospitals Leuven, Department of Gynaecology and Obstetrics, Leuven, Belgium, [6]KU Leuven, Department of Microbiology and Immunology, Leuven, Belgium, [7]University Hospitals Leuven, Department of Nephrology, Dialysis and Renal Transplantation, Leuven, Belgium, [8]University Hospitals Leuven, Centre for Human Genetics, Leuven, Belgium, [9]University Hospital of Brest, Institut National de la Santé et de la Recherche Médicale, Laboratory of Molecular Genetics and Histocompatibility, Brest, France and [10]Mayo Clinic College of Medicine, Division of Nephrology and Hypertension, Rochester, United States of America

Background and Aims: The correlation between genotype and phenotype is well described in ADPKD adults. *PKD2* is milder than *PKD1* disease, with end stage kidney disease (ESKD) occurring on average 20 years later, and patients with *PKD1* truncating mutations having a more severe outcome than *PKD1* non-truncating mutations. Still, large differences in outcome occur even within families carrying the same gene variation. Only a few cases series reported the genetic profile of severely affected ADPKD children and suggest an additional effect of hypomorphic genes. We therefore aim to analyse the geno-phenotype profile in a well characterized pediatric ADPKD cohort.

Method: Clinical, familial, biological and imaging data were collected longitudinally in children diagnosed with ADPKD. Genotypic analysis was done using a custom Agilent SureSelect gene panel containing 136 ciliopathy-associated genes, including *PKD1* and *PKD2*. Mutations and/or variants identified were individually evaluated for pathogenicity.

Results: 57 ADPKD children from 44 families were diagnosed at a mean (± SD) age of 4.1 (±4.8) years. ADPKD diagnosis was made in 32 children (56%) because of asymptomatic screening as requested by the family; 7 (12%) due to presenting symptoms (6 due to urinary tract infection and 1 due to post-traumatic macroscopic hematuria); 9 (16%) due to a coincidental finding of renal cysts on US performed for another reason and in 9 cases (16%) a prenatal diagnosis was performed. Twenty-nine children (51%) met the definition of very-early onset (VEO) disease.

We identified pathogenic mutations in 100% of our patients, in which the prevalence of PKD1 truncating, PKD1 non-truncating, PKD2 and GANAB mutations was 75%, 19%, 4%, and 2%, respectively. Four cases (7%) were due to a de novo mutation. Interestingly, in 29 patients (51%) the germline mutation was the only identified mutation. However, in the rest of the subjects additional variants were identified in other ciliopathy-associated genes. In 12 cases (21%) the additional identified variants found in either the *PKD*, *PMM2*, *HNF1B*, *DNAJC1*, *CEP290*, *NEK1*, *MKKS*, *NPHP4* or *PKHD1* genes were scored to have a potential phenotypic effect, which will be evaluated by continued follow-up of this cohort.

Conclusion: We report the first large cohort of genotyped ADPKD children, including an extensive panel of ciliopathy genes next to the *PKD* genes. Interestingly, we found a high prevalence of additional and potentially modifying variants in this young population.

P1800 **RITUXIMAB ENHANCES THE EXPRESSION OF INTERLEUKIN-6 VIA TOLL-LIKE RECEPTOR 3 SIGNALING IN HUMAN PODOCYTE**

Shojiro Watanabe[1], Koji Hirono[1], Tomomi Aizawa[1], Koji Tsugawa[1], Hiroshi Tanaka[1]

[1]*Hirosaki University Hospital, Department of Pediatrics, Hirosaki, Japan*

Background and Aims: The etiology of idiopathic nephrotic syndrome (INS) in children remains unclear, but it is well known that viral infections often cause relapses of INS. Since toll-like receptor 3 (TLR3), a ligand of viral dsRNA exists in podocytes, dysregulation of TLR3 signaling in podocytes may be involved in the pathogenesis of INS. Recently, rituximab (RTX) a specific antibody to human CD20, has been successfully used to treat children with intractable nephrotic syndrome (frequent relapse nephrotic syndrome, FRNS, and steroid dependent nephrotic syndrome, SDNS). It has been reported that depletion of B cell is main mechanism of RTX treatment. However, some patients experienced recurrence before peripheral blood B cell recovery, whereas selected patients have sustained remission even after peripheral blood B cell recovery. Considering that dramatic effects of RTX in the treatment of INS, it is speculated that some B cell-independent mechanisms of RTX exist. In this context, some recent studies have reported a direct effect of RTX on podocyte, targeting sphingomyelinase phosphodiesterase acid-like 3b (SMPDL3b), but detailed mechanisms remain to be determined. In this study, we examined whether RTX influences TLR3 signaling in cultured human podocyte.

Method: Immortalized human podocytes in culture were treated with polyinosinic-polycytidylic acid (poly IC), a synthetic analogue of viral dsRNA. RTX were added before or after the treatment of poly IC. Then, expression of interleukin (IL)-6 were measured using real time RT-PCR and ELISA. Direct binding of RTX to podocyte were confirmed by immunofluorescence.

Results: Poly IC induced the expression of IL-6 in cultured human podocyte in a concentration and time-dependent manner. IL-6 expression induced by poly IC were enhanced in both mRNA and protein level by pretreatment of RTX. RTX itself were apparently stained on podocyte by immunofluorescence.

Conclusion: RTX binds directly to cultured human podocyte and enhances the IL-6 expression induced by poly IC. Since IL-6 from podocyte was reported to be engaged in regulating glomerular inflammation by cross-talk with endothelial cells, exploring the role of enhanced IL-6 from podocyte by RTX, at least in a part, suggests a direct mechanism of RTX in treating intractable nephrotic syndrome in children.

P1836 GOUT A PAPAL DISEASE: A STUDY ON 20 PONTIFFS (540-1830 AD)

Carmela Bisacccia[1], Luca Salvatore De Santo[2], Natale Gaspare De Santo[3]

[1]"Mazzini" Institute, Naples, Italy, [2]Univ. of Campania "L. Vanvitelli", Heart Surgery, Naples, Italy and [3]University of Campania "L. Vanvitelli", Nephrology, Naples, Italy

Background and Aims: Pope Gregory I (*Magnus*)-born c.540 AD, Pope 580-604 AD-in a letter to Bishop Venanzio ofLuni (later venerated as a saint) wrote **"**I have been confined to bed for the last eleven months, because of pain and malaise and suffer because of goutand my life has been turned into a penitence for my sins thus I am waiting death as a physician who will give me health". He was the first Pope to suffer of gout and opens a list including in the years 20 pontiffs that includes Sisinnius, (b.650, pope 21 day in 708); Boniface VI (b. 806, Pope 15 days in 886), Honorius IV (b.1210, Pope 1285-1287); Boniface VIII (b. 1230, Pope 1294-1303); Clement VI (b.1281,Pope 1342-1352), Nicholas V (b.1387, Pope 1447-1455); Pius II(b. 1405, Pope 1458-1464); Sixtus IV (b. 1414, Pope 1471-1474); Pius III (b.1440, Pope 26 days in 1503); Pius IV (b. 1499, Pope 1559-1565); Julius II (b. 1443, Pope 1503-1516); Julius III (b.1481, Pope 1550-1555); Clement VIII (b. 1536, Pope 1592- 1605); Clement X (b.1581, Pope 1670-1676); Innocent XI (b.1681, Pope 1676-1689); Innocent XII (b.1649, Pope 1676-2692); Innocent XIII (b.1655, Pope 1721-1724); Benedict XIV (b. 1765, Pope 1740-1758), and Pius VIII (b.1761, Pope 1829-1830). Their mean age at death was 69.4 years, the youngest being Sisinnius (59 years), the oldest being Clement X (96 years).

Results: Some popes were strong eaters like Boniface VIII. He was chronically affected by gout and renal stone disease and by the fear for death, and the search for therapies capable to prolong life. Cosmacini says "podagroso e gottoso"*. . .* the Pope is affected by arthritis and renal disease due to overalimentation very rich (*strarica*) in meat". He enrolled various archiaters among them Taddeo Alderotti (1223-1295), Pietro da Abano (1257-1315), Anselmo da Bergamo *(artisphysicae professor)*, Simone of Genova (author of *Clavissanationis*), Accursino from Pistoia, Manzia from Fabriano, Gugliemo da Brescia, Angelo da Camerino and Campano da Novara *(Magister Campanus)*, the naturalist he too affected by renal stone disease. Julius III too was a strong eater (he loved fatty foods seasoned with garlic) as was Pius IV, the hard worker who everyday used to take a nap after lunch and a long walk later in the day. By contrast Nicholas V (his Pontiff saw in 1453 the Fall of Costantinople and the end of the Hundred Years War) was a sober eater and drinker as were Pius II who made use of simple common foods, little wine and slept up to 5-6 hours. Probably Nicholas V died uremic since his pale natural color switched into yellowish-brown (*itaque ex naturali et subcandido in croceumsubcinericiumque color suusconversusest*). Pius III "was a sober eater and drinker and used to dine every two days. Some of the above popes were patrons of universities (Boniface VIII, Nicholas V, Pius II), some were patrons of arts and science (Nicholas V, Sixtus IV). Boniface VIII is remembered for the *Bulla detestandeferitatis* (against dismemberment and evisceration of cadavers), issued on September 27, 1299). For that*Bulla,* during the subsequent centuries he was wrongly accused even by Herman Boerhaave and Albrecht von Haller to have retarded the advancement of medicine by impeding anatomical dissections. By contrast Sixtus IV is remembered not only for modernizing Rome and embelling it, but for the 1482 *Breve* to the University of Tubingen allowing-for teaching purposes -dissection of dead bodies of people sentenced to death.

P1837 THE HISTORY OF THE URINES SPECIFIC GRAVITY TEST FROM THE 15TH CENTURY UNITL TODAY

Athanasios Diamandopoulos[1]

[1]*Louros Foundation for the History of Medicine,Athens, Greece, Board, Athens, Greece*

Background and Aims: To present the history of the specific gravity test in the study of urines from the 15th cent. AD until today.

Method: The first description of a hydrometer, the progenitor of the urinometer, appears in the fifteenth letter from Synesius of Cyrene to the Greek scholar Hypatia of Alexandria, from the 5th century AD. However, its evolution to the urinometer took 15 centuries until 1849, when Johann Florian Heller (1813-1871) introduced it. During the next two centuries, we note a rapid improvement of the appropriate laboratory instruments and a wide acceptance of the importance of specific gravity for the evaluation of urine. We present passages from relevant texts from the discussed period.

Results: The first call for attention to measuring urine weight comes from Nicolas of Cusa's work The Layman: Experiments with Weights, *where we read* "*Accordingly, since the weight of blood or the weight of urine is different for a healthy man and for a sick man or for a youthful man and an elderly man or for a German and an African, wouldn't it be especially useful to a physician to have all these differences recorded? Orator: Most certainly*". The theoretical proposal was solidified in Francis Bacon's Novurn Organum (1620): "Neither the naked hand nor the understanding left to itself can effect much. It is by instruments and helps that the work is done". Herman Boerhaave, in 1753, weighed the distilled urine residue in order to calculate its density, a complicated and time-consuming procedure. Later, Groenevelt J. in *The Rudiments of Physick* writes "The particles in it sink or float according to their own gravity [specific!], but their position is also dependent on the thickness of the urine [albumin in it plus formed particles]." Osborne, in 1820, made a genius comparison "*When a mucous cloud is present [in the urine] it ascends and descends in the fluid according to specific gravity, thus serving the purpose of a hydrometer*". Becquerel, in 1842, laid out tables calculating the solid articles in urines of given specific gravity. Graves, in 1866, reported intermittent albuminuria with a parallel variation of the specific gravity of urine in infectious disease. The same year, an article in the London Medical Gazette: Or, Journal of Practical Medicine, and another one in *The New York Lancet* stress the variation of specific gravity in the course of a renal disease. Clover R.M. in the Case of sialorrhoea (1846) states that specific gravity may vary greatly even with the same amount of solids and fluid due to fluid heterogeneity. In 1848, Garrod describes a bottle for measuring urine specific gravity. Johann Florian Heller introduced the mercury-based floating urinometer in 1849 thus greatly facilitating the test of urine specific gravity.

The increasing demand for the test's application resulted in the discovery of refined laboratory instruments, such as the refractometer. Very recently, urine specific gravity is considered an accurate renal function marker, equal to creatinine clearance or proteinuria levels (Constantiner M. et al, Am J Kidney Dis., 2005 May;45(5):833-41. and Anestis SF et al, Am J Primatol., 2009 Feb;71(2):130-5).

Conclusion: It seems that the understanding of urine specific gravity underwent "mechanisation", from its inception as the use of the sediment's location in the vial to access it, during the Middle Ages to complex apparatuses like refractometers. Originating in the Classical and Middle Ages mainly from the East, it obtained its sound scientific background in the West from the Renaissance onwards. After debate on its usefulness, it is again a vital tool for assessing renal damage.

P1838

THE CONTRIBUTION OF MICROSCOPE IN THE KNOWLEDGE OF KIDNEY DISEASES AS DESCRIBED BY GIULIO BIZZOZERO

Guido Bellinghieri[1], Guido Gembillo[2], Vincenzo Savica[3], Ersilia Satta[4], Antonino Salvo[2], Domenico Santoro[2]

[1]Member of the Accademia Peloritana dei Pericolanti at University of Messina, Italy., [2]Policlinic G. Martino, Department of Clinical and Experimental Medicine, Unit of Nephrology and Dialyis, ME, Italy, [3]A. Monroy Institute of Biomedicine and Molecular Immunology, National Research Council, Palermo. and [4]Nefrocenter Research Network, Napoli, Italy

Background and Aims: Giulio Bizzozero (20 March 1846 - 8 April 1901) was an eminent Italian scientist, the father of the modern microscopy. In 1879 he published his masterpiece "Manuale di Microscopia Clinica "(Handbook of Clinical Microscopy). Here he underlined how the microscopic examination of the urine gave to the physicians of the time indicative criteria of alteration of the kidney, often essential for diagnosis.

Method: Bizzozero operates in his book a detailed analysis of the methods of time, laying the foundations of microscopy and diagnosis of renal diseases. He proposed a classification of pathological urine and gave large space to the role of the presence of red blood as a great diagnostic sign in urinary sediment (Figure 1 and Figure 2).

The author emphasized the use of microscopy against the obsoleted vision of old academics and promulgated the experimental methods in opposition to the vitalistic philosophy of the time. Bizzozero underlined the idea of "teamwork" and the strong connection with his close collaborators, he says that on a laboratory "*a mind should give the idea and the direction of work while other minds join together dealing with particular executions*".

Results: Bizzozero's revolutionary vision of medicine had the purpose to allow every scientist to reach new discoveries in their field, previously being the privilege of an elite, making him a model both as a doctor as a humanist. In one of his memorable speeches he declared: "*We need to undress the science of the cloak of mystery and authority: the professor in the school must not offer a series of dogmas supported by the prestige of his name, he must instead expose science in the real state in which it is found, with its doubts and its unresolved mysteries*".

Conclusion: This Bizzozero's masterpiece definitely represents a milestone of scientific literature, a witness of the radical evolution of modern medicine and experimental research.

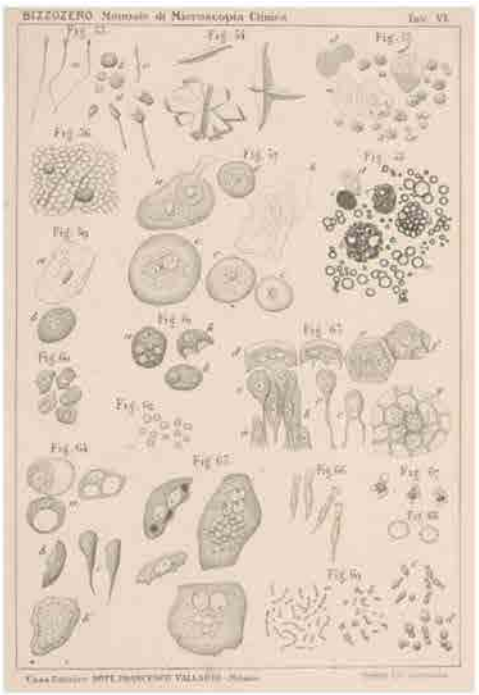


Figure 1

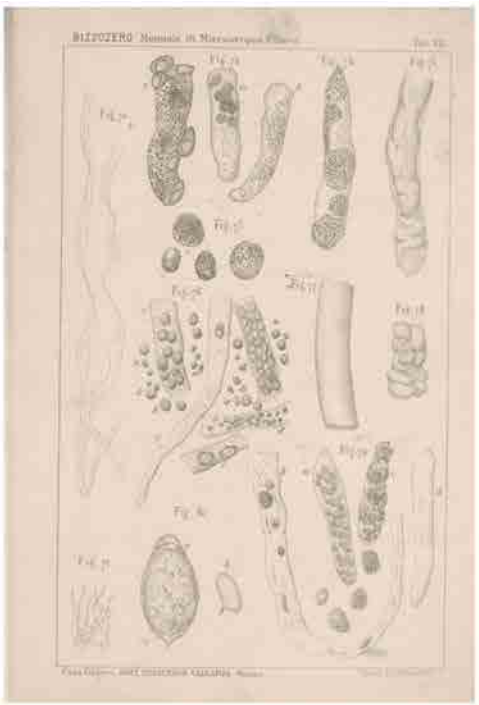


Figure 2

P1839 GLOMERULAR HYPERFILTRATION: THEORY AND APPLICATIONS

Ali Moustafa Shendi Mohamed[1]

[1]*Faculty of Medicine, Zagazig University, Nephrology Unit, Egypt*

Background and Aims: The role of glomerular hyperfiltration in the development and progression of diabetic and non-diabetic chronic kidney disease (CKD) was established during the 80's of the last century and represented a paradigm shift in current nephrology practice.

Method: A web-based review of relevant bibliography: articles and textbooks, reporting the development of hyperfiltration theory and its clinical applications was conducted.

Results: In 1982, after a series of animal studies, Brenner and colleagues proposed that glomerular hyperfiltration, in diabetic and other glomerulopathies, contributes to intrarenal hypertension and predispose to progressive glomerular sclerosis and deterioration of renal function. Clinical trials during late 80's and early 90's then focused on inhibition of Renin Angiotensin Aldosteron system (RAAS) to reverse glomerular hyperfiltration, and suggested that ACE inhibitors can be anti-proteinuric independent of their blood pressure-lowering effect in non-diabetic and diabetic nephropathies. In 1993, a randomized controlled trial (RCT) by Lewis and colleagues proved a beneficial effect of captopril in patients with nephropathy caused by type 1 diabetes. Few years later, the results of Ramipril Efficacy in Nephropathy (REIN) study proved the renoprotective role of ACE inhibition in patients with non-diabetic nephropathies with nephrotic and non-nephrotic proteinuria in 2 Lancet articles in 1997 and 1999 respectively. The renoprotective role of RAAS inhibition with ARBs in patients with type 2 diabetes was proven in 3 RCTs published in the New England Journal of Medicine in 2001: Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria (IRMA) Study, Irbesartan Diabetic Nephropathy Trial (IDNT), and Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study. Dual blockade with an ACE inhibitor and an ARB was then attempted to further ameliorate glomerular hyperfiltration. Yet this approach was faced by an increased risk of hyperkalemia and acute kidney injury in 2 RCTs: the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) in 2008 and The Veterans Affairs Nephropathy in Diabetes (VA NEPHRON-D) study in 2013.

It was until 2014 when evidence appeared for a potential role of SGLT2 inhibition in attenuating glomerular hyperfiltration. The 1st clinical evidence of renoprotective effect of SGLT2i appeared in 2016 when the results of the EMPA-REG OUTCOME study found that empagliflozin was associated with lower rates of renal events. Subsequently, the Canagliflozin Cardiovascular Assessment Study (CANVAS) Program trials and the Dapagliflozin Effect on Cardiovascular Events–Thrombolysis in Myocardial Infarction 58 (DECLARE-TIMI 58) trial found similar reductions in composite renal endpoints. The Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial published in 2019 was the first study designed to assess the effects of a SGLT2i, canagliflozin, on renal outcomes in patients with type 2 diabetes and albuminuric CKD, and proved significant reduction in the composite renal outcome with canagliflozin.

The potentiality for renoprotective role of SGLT2i in patients with non-diabetic CKD has stimulated a number of ongoing clinical trials: DIAMOND and Dapa-CKD using Dapagliflozin and EMPATHY and EMPA-KIDNEY using Empagliflozin.

Conclusion: The hyperfiltration theory represents the basis for current therapeutic interventions in diabetic and non-diabetic CKD. Current guidelines recommend using RAAS blockers in diabetic and non-diabetic proteinuric CKD and SGLT2i in patients with type 2 diabetes and CKD. Whether SGLT2i could be considered in patients with CKD independent of the diabetic state awaits the results of ongoing studies which might change the management practice of CKD.

MODERATED POSTER SESSION 6

P0768 **NOVEL URINARY PROTEIN BIOMARKERS FOR UROTHELIAL CANCER IN PATIENTS WITH CHRONIC KIDNEY DISEASE**

Chiu-Ching Huang[1], Che-Yi Chou[2], Kuo-Hsiung Shu[3], Hung-Chun Chen[4], Ming-Chang Wang[5], Chia-Chu Chang[6], Bang-Gee Hsu[7], Mai-Szu Wu[8], Yuan-Lung Yang[9], Chao-Jung Chen[10]

[1]China Medical University Hospital, Division of Nephrology and the Kidney Institute, Taichung, Taiwan, R.O.C., [2]Asia University Hospital, Internal Medicine, Taiwan, Taiwan, R.O.C., [3]Lin Shin Hospital, Medicine, Taichung, Taiwan, R.O.C., [4]Kaohsiung Medical University Chung-Ho Memorial Hospital, Nephrology, Kaohsiung, Taiwan, R.O.C., [5]National Cheng Kung University Hospital, Nephrology, Tainan, Taiwan, R.O.C., [6]Kuang Tien General Hospital, Internal Medicine, Taichung, Taiwan, R.O.C., [7]Buddhist Tzu Chi General Hospital, Nephrology, Hualien, Taiwan, R.O.C., [8]Taipei Medical University Hospital, Nephrology, Taipei, Taiwan, R.O.C., [9]Camillian Saint Mary's Hospital Luodong, Nephrology, Yi Lan, Taiwan, R.O.C. and [10]China Medical University, Graduate Institute of Integrated Medicine, Taichung, Taiwan, R.O.C.

Background and Aims: Introduction: Chronic kidney disease (CKD) patients are known to have greater risk of urothelial cancer (UC) than general population. Urine is the most non-invasive examination and is directly linked to UC. Urinalysis and urine cytology are the major screening tools; however, these tests have low sensitivity or specificity in early disease. In this study, we used both normal and Non-UC CKD patients as controls to discover novel and more specific protein biomarkers in urine for early UC diagnosis.

Aims: To discover novel and more specific urinary protein biomarkers for screening of urothelial cancer (UC) in CKD patients.

Method: This is a multicenter prospective cohort study, carried out at 10 nationwide hospitals covering different regions of Taiwan from 2013-2018. Subjects were Taiwanese healthy adults (healthy controls, n=210), patients with CKD but without UC (disease controls, n=273) and patients with ongoing UC (n=211). For non-UC patients, urine and blood specimens were collected at the time of the structured interview. For UC patients, urine and blood samples were collected before operation. iTRAQ-LC-MS/MS approach was applied to compare protein expression among normal, CKD and UC cohorts.

Results: A total of 3838 proteins in urine were identified and 2497 proteins of them can be quantified. By filtering with fold changes, published papers and Human ATLAS, 27 candidates were selected as potential biomarkers and were validated with ELISA assay in a large sample size of urine specimens. Among the 27 candidates, we found BRDT, CYBP, GARS and HDGF were highly-expressed in the UC cohort when compared to normal and CKD cohorts (Figure 1). To increase the diagnostic value of UC, we combined ROC of our newly discovered 4 protein biomarkers. The AUC values of our newly discovered 4-biomarker panel were higher than the AUC values of the published biomarker panel, including the FDA-approved protein biomarkers (Figure 2).

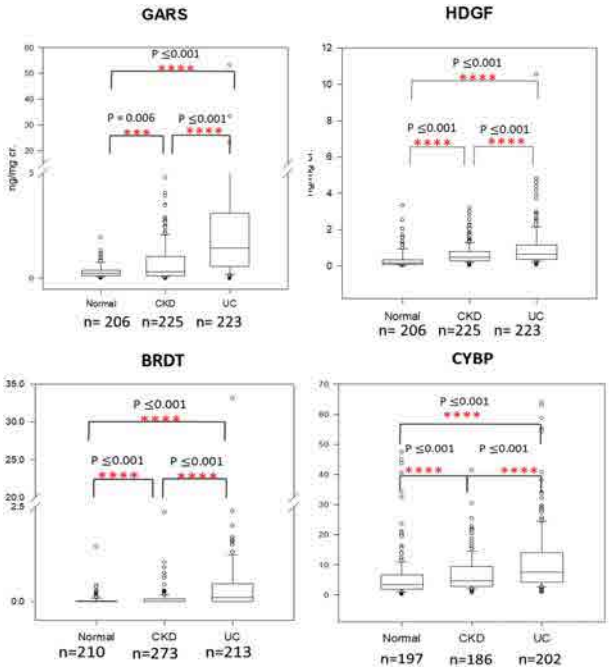


Figure 1. Box-plot of GARS, HDGF, BRDT and CYBP protein level in urine samples of normal, CKD and UC subjects.

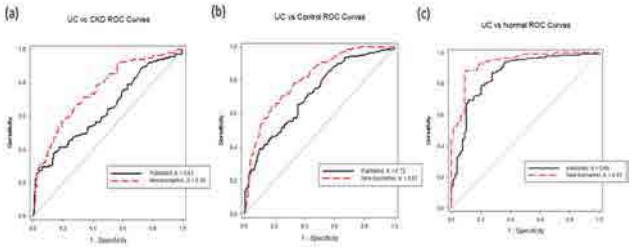


Figure 2. The ROC comparison of a published marker panel (Midkine, CYFRA 21.1 and NUMA1) and our novel four marker panel (GARS, BRDT, CYBP and HDGF) in the discrimination of (a) UC and CKD controls (b) UC and controls (normal+CKD controls) (c) UC and normal controls. UC, n=211; CKD, n=273; normal, n=210.

Conclusion: We discover and validate a highly specific urinary protein biomarker panel (BRDT, GARS, HDGF and CYBP) to distinguish UC from CKD and healthy controls. It may be used for high throughput screening of subjects, such as CKD patients, who are at high risk to develop UC.

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P1233 M2 MACROPHAGES PROMOTE MOUSE AORTIC SMOOTH MUSCLE CELLS CALCIFICATION BY SGK1-TGFB1 AXIS

Beibei Wu[1], Xiaodong Zhang[1], Yuqiu Liu[1], Xiao liang Zhang[1]

[1]*Institute of Nephrology, Zhong Da Hospital, Southeast University School of Medicine, Nanjing, P.R. China*

Background and Aims: Vascular calcification is an independent risk factor for all-cause mortality in patients with CKD. Macrophages play an important role in vascular calcification, which involve in the osteo-/chondrogenic transdifferentiation of vascular smooth muscle cells (VSMCs). Recent research shows SGK1 is a highly attractive candidate for developing VSMCs calcification. Previous studies indicated that TGFβ1 induces vascular calcification by regulating osteo-/chondrogenic transdifferentiation of VSMCs. This study focus on the effects of macrophages-derived SGK1 on VSMCs transdifferentiation via regulating TGFβ1 expression.

Method: Before induced into M2 phenotype with IL-4, RAW 264.7 cells were treated with SGK1 inhibitor EMD638683 for 24 hours to reduce SGK1 expression. The above cells were grouped as: M0, M2, M2+EMD to explore the expression of SGK1 and TGFβ1 by using western blot, qRT-PCR and immunofluorescence staining, respectively. The culture medium (CM) of the above group macrophages was collected. Then mouse aortic smooth muscle cells (MAoSMCs) were cultured in these supernatants with normal medium or osteogenic medium (OM) with or without TGFβ1 receptor inhibitor SB-431542 for 3 weeks to explore the transdifferentiation and calcification of MOVAS by using western blot, RT-qPCR, immunofluorescence staining, calcium quantification, Alizarin Red and Von Kossa Staining.

Results: As Alizarin Red and Von Kossa Staining shown, MAoSMCs contained more calcium deposits in the M2-CM group compared with either in the group of NC nor M0-CM. Consistent with the above results, We also found that M2-CM promoted MAoSMCs transdifferentiation, which was characterized by markedly increase of expression of osteo-/chondrogenic markers (Runx2, ALPL, FGF23) and decrease of the MAoSMCs marker (SM22α). Exploring the mechanism of the above phenomenon we found the expression of SGK1 and TGFβ1 were significantly increased in M2 group compared with M0 group. Interestingly, both SGK1 inhibitor EMD638683 which reduced TGFβ1 expression in M2 and TGFβ1 receptor inhibitor SB-431542 could partially blocked MAoSMCs osteo-/chondrogenic transdifferentiation and calcification. Furthermore, recombinant mouse TGFβ1 Protein increased calcium content in MAoSMCs by using calcium quantification, Alizarin Red and Von Kossa Staining and promoted MAoSMCs osteo-/chondrogenic transdifferentiation, which was characterized by markedly increase of expression of osteo-/chondrogenic markers (Runx2, ALPL, FGF23) and decrease of the MAoSMCs marker (SM22α).

Conclusion: Our findings shed light M2 macrophages promotes MAoSMCs osteo-/chondrogenic transdifferentiation and calcification by up-regulating TGFβ1 expression.

P1234

SNF472 IMPROVES LIMB BLOOD PERFUSION AND WALKING ABILITY IN A PERIPHERAL ARTERY DISEASE VASCULAR CALCIFICATION RAT MODEL

Firas Bassissi[1], Miguel David Ferrer Reynes[1,2], M. Mar Pérez[1], Joan Perelló[1,2], Carolina Salcedo[1]

[1]Sanifit Therapeutics, Palma, Spain and [2]University of the Balearic Islands, Palma, Spain

Background and Aims: Peripheral Artery disease (PAD) is a common vascular disease associated with functional impairment and increased risk of cardiovascular events in End Stage Kidney Disease (ESKD) patients undergoing dialysis. Poor limb salvage outcomes and high post-amputation mortality in hemodialysis (HD) patients highlight the need for earlier medical therapies. Cilostazol and pentoxifylline are approved for PAD. Their use in HD patients stays limited and cilostazol use requires caution in this population. Clinical studies demonstrate associations between arterial calcification and adverse outcomes in PAD patients. SNF472, a selective calcification inhibitor that interferes in the formation and growth of hydroxyapatite, is in Phase 3 for calciphylaxis treatment. This study aims to evaluate the effects of SNF472 on limb functional recovery and blood perfusion in a Vitamin D3 (VitD)-induced arterial calcification rat model.

Method: Arterial calcification was induced in 32 Sprague Dawley rats by 3 consecutive daily s.c. doses of 120 kIU/kg VitD. Rats were divided into four groups and treated during 12 days by: placebo s.c, placebo p.o, SNF472 (20 mg/kg/day, s.c.) or cilostazol (20 mg/kg/day, p.o.). An additional group of 8 rats without VitD received vehicle only (sham). Efficacy was evaluated at day 12 and 17 (5 days after treatment stop). Posterior limb blood perfusion was measured using Laser Doppler Imaging and limb walking ability was evaluated by measuring Maximum Walking Distance (MWD) and Maximum Walking Time (MWT) using a treadmill. Rats were sacrificed at day 26 (14 days after treatment stop), and aortas were collected for calcium analysis.

Results: VitD-induced arterial calcification was associated with decreased blood perfusion and impairment of limb walking ability (MWT and MWD) compared to sham. SNF472 reduced aorta calcification by 41% compared to placebo. No effects of cilostazol on vascular calcification were observed. The inhibition of calcification in SNF472-treated animals was associated with significant higher limb blood perfusion compared to placebo or Cilostazol (1.28 and 1.37-fold higher, respectively at day 12: $p < 0.001$) and it was translated into a significant improvement in walking ability compared to placebo (515 ± 114 meters vs 334 ± 187 meters, respectively: $p < 0.05$).

Conclusion: SNF472 shows improvements in vascular calcification, blood perfusion and a functional parameter like walking distance in a PAD vascular calcification rat model. These results suggest that SNF472 may represent a new therapeutic approach for the treatment of PAD associated with high vascular calcification such as in renal disease.

P1235 **THE IMPACT OF SPIRONOLACTONE ON DIASTOLIC FUNCTION IN HEMODIALYSIS PATIENTS - THE MIRENDA RCT**

Tobias Gregor Hauser[1], Vivien Dornberger[2], Uwe Malzahn[3], Dan Liu[1], Stefan Störk[1,4], Matthias Nauck[5], Nele Friedrich[5], Christoph Wanner[1,4], Vera Krane[1,4], Fabian Hammer[2]

[1]University Hospital Würzburg, Department of Medicine I, Division of Nephrology, Würzburg, Germany, [2]University Medicine Greifswald, Department of Internal Medicine B, Division of Cardiology, Greifswald, Germany, [3]University Hospital Würzburg, Clinical Trial Centre, Würzburg, Germany, [4]University and University Hospital Würzburg, Comprehensive Heart Failure Centre, Würzburg, Germany and [5]University Medicine Greifswald, Institute for Clinical Chemistry and Laboratory Medicine, Greifswald, Germany

Background and Aims: Patients on maintenance hemodialysis (HD) treatment are particularly prone to develop cardiovascular disease. Heart failure with preserved ejection fraction (HFpEF) characterized by diastolic dysfunction (DD) is highly prevalent and lacks an effective treatment to date. We investigated the effect of the mineralocorticoid receptor antagonist spironolactone compared to placebo on diastolic function in maintenance HD patients.

Method: The MiREnDa trial was a multicenter randomized-controlled trial that recruited 97 HD patients without previous spironolactone treatment. Participants were randomized 1:1 to spironolactone 50 mg once daily (n=50) or placebo (n=47). Changes in parameters of diastolic function were secondary endpoints of the trial whereas the primary endpoint was change in left ventricular mass index (LVMi). At baseline and after 40 weeks, subjects underwent echocardiography and biomarker testing. DD was defined according to the American Society of Echocardiography 2016 guidelines.

Results: At baseline, mean age was 58.3 ± 13.0 years, 13 subjects were female and 28 presented with NYHA grade II or higher. Median serum level of NT-proBNP was 2,803 (quartiles: 1,060; 10,676) pg/ml, median previous time on dialysis was 45.0 (quartiles: 21.0; 79.0) months. 28 patients (45.9%) had normal diastolic function, 16 (26.2%) were diagnosed with grade 1 DD, 15 (24.6%) with grade 2 DD and 2 (3.3%) with grade 3 DD. In the remaining cases, the grade of DD was rated indeterminate. There were no significant disparities between the placebo and spironolactone group regarding baseline characteristics.

At follow-up, diastolic function improved in two and deteriorated in three subjects on spironolactone treatment, whereas in the placebo group, diastolic function improved in three and deteriorated in two patients. No change in diastolic function was observed in 14 individuals on spironolactone treatment and in 10 receiving placebo (Pearson's $\tilde{X}$: p=0.87). According to the diagnostic algorithm proposed by the American society of Echocardiography 2016 guideline, 18 patients (11 on spironolactone; 7 on placebo) could no longer be allocated to a distinct group of DD. These patients needed to be classified as indeterminate, even though they only showed mild alterations in diastolic function parameters.

Conclusion: In this randomized, placebo-controlled trial, 40 weeks of spironolactone treatment did not change diastolic function in HD patients.

P1386 EFFICACY AND SAFETY OF MODIFIED RELEASE NICOTINAMIDE IN THE TREATMENT OF HYPERPHOSPHATEMIA IN HEMODIALYSIS PATIENTS

Markus Ketteler[1,2], Walter Zidek[3], Michael Karus[4], Burkhard Hellmann[4], Richard Ammer[4]

[1]Robert-Bosch-Krankenhaus, Department of General Internal Medicine and Nephrology, Stuttgart, Germany, [2]University of Split, School of Medicine, Split, Croatia, [3]MEOCLINIC GmbH, Department of Endocrinology and Nephrology, Berlin, Germany and [4]MEDICE Arzneimittel Pütter GmbH & Co KG, Iserlohn, Germany

Background and Aims: Despite the introduction of several new phosphate binders over the last decades, adequate control of hyperphosphatemia in haemodialysis (HD) patients still remains a crucial challenge as more than half of the population still remains hyperphosphataemic in daily practice. A growing amount of clinical data suggests that nicotinamide (NA) represents a complementary and effective treatment option for hyperphosphataemia. Efficacy and safety of once daily intake of modified release (MR) NA were investigated for fixed doses between 250 and 1,000 mg in hyperphosphatemic HD patients. Additionally, the MR formulation was compared to trice daily intake of an immediate release (IR) formulation of NA.

Method: This multicenter, controlled trial included HD patients with serum phosphate concentrations between 4.7 and 7.5 mg/dL after initial discontinuation of phosphate binder treatment. Patients were randomized to either once daily intake of 250 mg (N=48), 500 mg (N=50), 750 mg (N=50) or 1,000 mg of MR NA (N=53) in a double-blind setting, or intake of 1,000 mg of IR NA (N=51), divided over three daily doses in an open-label setting over a treatment period of 8 weeks.

Results: Based on the ITT population the study revealed a highly significant ($p<0.001$) dose-response relationship between dose of MR NA and serum phosphate concentrations in week 4 (primary endpoint). At this time point, significant reductions of serum phosphate concentrations were observed only for the 750 and 1,000 mg dose groups. Between week 5 and 8, all dose groups revealed significant reductions of serum phosphate. The different formulations exhibited a comparable phosphate lowering capacity (mean change from baseline until week 4: MR -1.07 mg/dL, IR -1.12 mg/dL; p=0.8163).

The most frequently reported adverse events were gastrointestinal symptoms in 31.4% of patients and skin reactions in 19.8% of patients. The study also revealed a nonsignificant decrease in mean platelet count. Overall, the number of adverse events increased in the 750 and both 1,000 mg dosage groups. For individual adverse events, dose dependency was observed for diarrhea, headache, vomiting and nausea.

NA treatment resulted in a dose dependent increase of plasma concentrations of NA and its terminal metabolites (N-methyl-2-pyridone-5-carboxamide, N-methyl-4-pyridone-5-carboxamide, Nicotinamide-N-oxide).

The tolerability profile as well as the plasma concentrations of NA metabolites were similar for both formulations although the proportion of patients that terminated treatment due to adverse events was higher in the IR arm compared to the MR formulation (33.5% versus 26.4% of patients). However, this study was not powered to reliably assess clinical superiority with regard to AE.

Conclusion: Our study characterised the NA modified release preparation NoPhos as an effective novel therapeutic option for the treatment of hyperphosphatemia in HD patients. In the monotherapy setting a clear dose-response relationship was revealed for daily doses between 250 and 1,000 mg, while best tolerability was observed at a dose of 500 mg/d.

P1431

MULTI-CENTER REGISTRY ANALYSIS COMPARING SURVIVAL ON HOME HEMODIALYSIS AND KIDNEY TRANSPLANT RECIPIENTS IN AUSTRALIA AND NEW ZEALAND

Isabelle Ethier[1,2], Yeoungjee Cho[2,3,4], Carmel Hawley[2,3,4,5], Elaine M Pascoe[4,6], Matthew A Roberts[7], David Semple[8,9], Annie-Claire Nadeau-Fredette[10], Germaine Wong[11,12,13], Wai Lim[14,15], Matthew P Sypek[3], Andrea Viecelli[2,4], Scott Campbell[2], Carolyn Van Eps[2], Nicole M Isbel[2,4], David W Johnson[2,3,4,5]

[1]Centre Hospitalier de l'Université de Montréal, Nephrology, Montréal, Canada, [2]Princess Alexandra Hospital, Nephrology, Brisbane, Australia, [3]Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, Adelaide, Australia, [4]Australasian Kidney Trials Network, Brisbane, Australia, [5]Translational Research Institute, Brisbane, Australia, [6]University of Queensland, School of Medicine, Brisbane, Australia, [7]Monash University, Eastern Health Clinical School, Melbourne, Australia, [8]Auckland District Health Board, Renal Medicine, Auckland, New Zealand, [9]University of Auckland, School of Medicine, Auckland, New Zealand, [10]Hôpital Maisonneuve-Rosemont and Research Center, Nephrology, Montréal, Canada, [11]Westmead Hospital, Centre for Transplant and Renal Research, Sydney, Australia, [12]The Children's Hospital at Westmead, Centre for Kidney Research, Sydney, Australia, [13]University of Sydney, School of Public Health, Sydney, Australia, [14]Sir Charles Gairdner Hospital, Renal Medicine, Perth, Australia and [15]University of Western Australia, School of Medicine, Perth, Australia

Background and Aims: In the era of organ shortage, home hemodialysis (HHD) has been identified as the possible preferential bridge to kidney transplantation. Data are conflicting regarding the comparability of HHD and transplantation outcomes. This study aimed to compare patient and treatment survival between HHD patients and kidney transplant recipients.

Method: The Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry was used to include incident HHD patients on day 90 after initiation of kidney replacement therapy and first kidney-only transplant recipients in Australia and New Zealand from 1997 to 2017. Survival times were analyzed using the Kaplan-Meier product limit method comparing HHD patients to subtypes of kidney transplant recipients using the log-rank test. Adjusted analyses were performed with multivariable Cox proportional hazards regression models for time to all-cause mortality. Time-to-treatment failure or death was assessed as a composite secondary outcome.

Results: The study compared 1411 HHD patients to 4960 living donor (LD) recipients, 6019 standard criteria donor (SCD) recipients and 2427 expanded criteria donor (ECD) recipients. While LD and SCD recipients had reduced risks of mortality compared to HHD patients (LD adjusted hazard ratio [HR] 0.57, 95%CI 0.46-0.71; SCD HR 0.65 95%CI 0.52-0.79), the risk of mortality was comparable between ECD recipients and HHD patients (HR 0.90, 95%CI 0.73-1.12). LD, SCD and ECD kidney recipients each experienced superior time-to-treatment failure or death compared to HHD patients.

Conclusion: This large registry study showed that kidney transplant offers a survival benefit compared to HHD but that this advantage is not significant for ECD recipients.

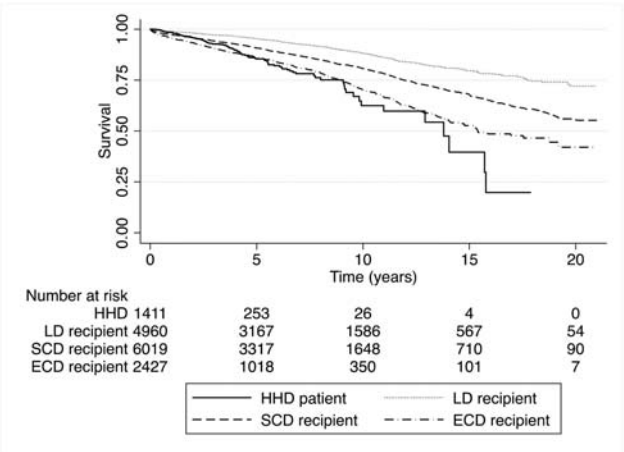


Figure: On-treatment survival comparing HHD patients and kidney transplant recipient subtypes (LD, SCD and ECD), unadjusted. Overall log-rank, HHD vs LD log-rank, and HHD vs SCD log-rank p-values<0.001; HHD vs ECD log-rank p-value=0.545. ECD = expanded criteria donor; HHD = home hemodialysis; LD = living donor; SCD = standard criteria donor

P1432

THE PRE-DIALYSIS CARE TRAJECTORIES OF ESRD PATIENTS: WHAT TYPES AND WHAT FACTORS OF EMERGENCY DIALYSIS START?

Maxime Raffray[1], Adélaïde Pladys[1], Fei Gao[1], Cécile Couchoud[2], Cécile Vigneau[3,4], Sahar Bayat[1]

[1]1Univ Rennes, French School of Public Health (EHESP), Pharmaco-epidemiology and health Services Research, (REPERES)-EA 7449, Rennes, France, [2]REIN Registry, Biomedecine Agency, Saint-Denis-La-Plaine, France, [3]Univ Rennes, Inserm, UMR 1085, Rennes, France and [4]Department of Nephrology, Centre Hospitalier Universitaire, Rennes, France

Background and Aims: According to the REIN registry, in France in 2017, 30% of incident end-stage renal disease (ESRD) patients started dialysis in emergency. Emergency dialysis start (ES) is associated with higher risks of morbidity and mortality as well as a decreased quality of life for patients. The objectives were to describe groups of patients with similar care trajectories (or "types") and identify the factors associated with ES.

Method: Data from the French REIN registry linked with the French national health insurance database (SNDS) were used. Patients aged 18 years old and older who started dialysis in 2015 in France were included. The 2 years pre-dialysis care trajectory was defined using 8 key components of ambulatory and hospital CKD care consumption. Multiple Correspondence Analysis (MCA) on these components was performed before a Hierarchical Clustering on Principal Components (HCPC) in order to identify types of care trajectories. Logistic regression models including both patients' characteristics and the key CKD healthcare consumption were used to identify factors associated with ES.

Results: Among the 8856 patients included, 2681 (30.3%) started dialysis in emergency. The HCPC identified 6 types of pre-dialysis care trajectories. ES rate ranged from 11% to 62% depending on the type. Patient's profiles were also different between types of trajectories, including age and comorbidities (diabetes prevalence ranged from 22% to 56%). For example, the 5th and 6th types of pre-dialysis care trajectories with high ES rates were characterized by low and absent CKD healthcare consumption respectively. They were shared by younger and less comorbid patients (26.7% and 25.7% aged $<$ 45 years old, 66.5% and 59.4% without any cardiovascular diseases respectively). Conversely to the absence of nephrologist follow-up, the absence of general practitioner follow-up was not significantly associated with ES (OR=1.83, CI 95% [1.58-2.13] and OR=0.79, CI 95% [0.61-1.04] respectively).

Conclusion: Exploiting the strength of the combined use of clinical and healthcare consumption data, our study shows the diversity of pre-dialysis care trajectories of CKD patients. While some of these types of trajectories can be explained by patients' clinical and demographic characteristics, complementary qualitative approaches are required to fully understand ES. Some types, as well as ES associated factors, highlight the need for earlier CKD screening and nephrologist referral.

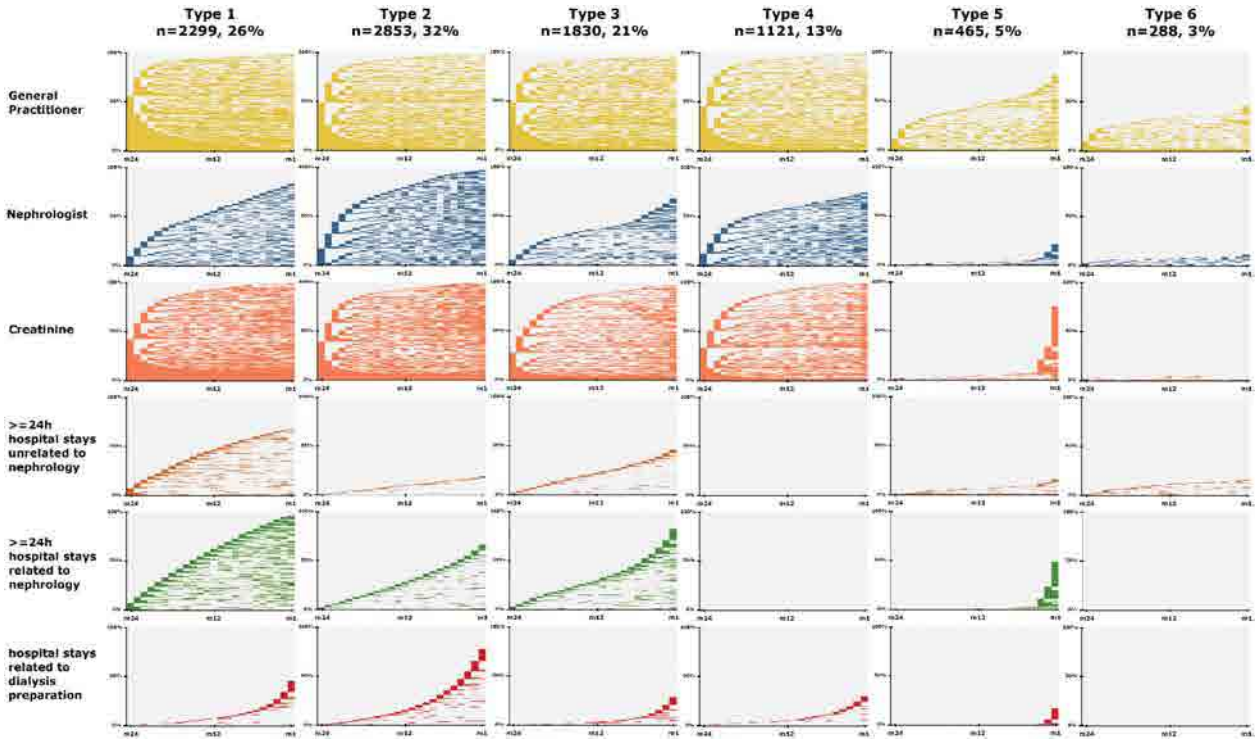


Figure:

P1433 **VALIDATION OF A SERUM CALCIFICATION PROPENSITY TEST FOR THE PREDICTION OF ALL-CAUSE MORTALITY AMONG DIALYSIS PATIENTS**

Rosa Ramos Sanchez[1], Adam Zawada[2], Melanie Wolf[2], Abraham Rincon Bello[1], Elisabet Masso Jimenez[3], Sara Hurtado Munoz[4], Laura Ribera Tello[5], Josep Mora-Macia[6], Stefano Stuard[7], Manuela Stauss-Grabo[2], Anke Winter[2], Bernard Canaud[8,9]

[1]Fresenius Medical Care España, S.A, Medical Department, Tres Cantos, Madrid, Spain, [2]Fresenius Medical Care Deutschland GmbH, EMEA Medical Office, Bad Homburg, Germany, [3]NephroCare, Centro de Diálisis Barcelona – Rosselló, Barcelona, Spain, [4]NephroCare, Centro de Diálisis Barcelona – Diagonal, Barcelona, Spain, [5]NephroCare, Centro de Diálisis Barcelona – Glories, Barcelona, Spain, [6]NephroCare, Centro de Diálisis Granollers, Granollers, Spain, [7]Fresenius Medical Care Deutschland GmbH, Global Medical Office - Clinical & Therapeutic Governance EMEA, Bad Homburg, Germany, [8]Fresenius Medical Care Deutschland GmbH, Global Medical Office, Bad Homburg, Germany and [9]University of Montpellier, School of Medicine, Montpellier, France

Background and Aims: Vascular calcification as cause of vascular stiffness is a major contributor to the high cardiac burden among stage 5 chronic kidney disease dialysis (CKD5HD) patients. Early identification of patients with high calcification propensity is crucial for proper risk stratification and management of these patients. Recently, a novel in vitro test (T50-test) was developed which determines calcification propensity of human serum and predicts mortality among ND-CKD (non-dialysis chronic kidney disease) patients, kidney transplant recipients and CKD5HD patients suffering from secondary hyperparathyroidism. We now evaluated whether these results can be confirmed in an unselected cohort of CKD5HD patients and can be used in the future for improving care of these patients.

Method: This prospective clinical study included 776 incident and prevalent hemodialysis patients from 8 Fresenius Medical Care NephroCare centers in Cataluña (Spain). T50 was determined at Calciscon AG, all other clinical data were retrieved from the European Clinical Database (EuCliD®). After their baseline T50 measurement, patients were followed for two years for the occurrence of the primary endpoint all-cause mortality. The association between T50 and all-cause mortality was examined by using proportional subdistribution hazards regression modelling accounting for kidney transplantation as competing event. In sensitivity analyses we adjusted for age, sex, vascular access (fistula/graft, catheter), treatment modality (HD, HDF), Charlson comorbidity index and dialysis vintage.

Results: Mean age of the study population was 72.2 years and 63.8% were male. 42.5% had diabetes and 55.0% past history of cardiovascular disease. Mean T50 was 283.4 min among the total cohort. During follow-up, 185 (23.8%) patients died. Patients who reached the endpoint had a significantly lower T50 at baseline as compared to those who survived during follow-up (269.6 vs 287.7 min, $p = 0.001$). A cross-validated model (mean c statistic: 0.5767) identified T50 as a linear predictor of all-cause-mortality (subdistribution hazard ratio (per min): 0.9957, 95% CI [0.9933;0.9981]). T50 remained a significant predictor of all-cause mortality after adjusting for relevant confounding in sensitivity analyses.

Conclusion: In this prospective study, we confirmed that T50 is an independent predictor of all-cause mortality among a large unselected cohort of hemodialysis patients. T50 may be used to identify patients with high vascular calcification propensity and mortality risks and may help physicians to implement a personalized and more precise renal replacement therapy option.

P1434 **ALDOSTERONE ANTAGONISTS FOR PATIENTS UNDERGOING DIALYSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

Takeshi Hasegawa[1,2], Hiroki Nihiwaki[2], Erika Ota[3], William Levack[4], Hisashi Noma[5]

[1]Showa University, Showa University Research Administration Center (SURAC), Tokyo, Japan, [2]Showa University Fujigaoka Hospital, Division of Nephrology, Department of Medicine, Yokohama, Japan, [3]St. Luke's International University, Global Health Nursing, Graduate School of Nursing Science, Tokyo, Japan, [4]University of Otago, Wellington, Rehabilitation Teaching & Research Unit, Wellington, New Zealand and [5]The Institute of Statistical Mathematics, Department of Data Science, Tachikawa, Japan

Background and Aims: Patients with chronic kidney disease (CKD) requiring dialysis are at a particularly high risk of cardiovascular mortality and morbidity. Several clinical trials suggested that aldosterone antagonists would be a promising treatment option for patients undergoing dialysis. However, the clinical efficacy and potential harm of aldosterone antagonists for patients with CKD on dialysis have yet to be determined. This review aimed to evaluate the benefits and harms of aldosterone antagonists, both non-selective (spironolactone) and selective (eplerenone), in comparison to control (placebo or standard care) in patients with CKD requiring haemodialysis or peritoneal dialysis.

Method: We searched the Cochrane Kidney and Transplant Register of Studies up to 29 July 2019 using search terms relevant to this review. Studies in the Register are identified through searches of CENTRAL, MEDLINE, and EMBASE, conference proceedings, the International Clinical Trials Register Search Portal and ClinicalTrials.gov. We included individual and cluster randomised controlled trials (RCTs), cross-over trials, and quasi-RCTs that compared aldosterone antagonists with placebo or standard care in patients with CKD requiring dialysis. Two review authors independently extracted data and assessed risk of bias for included studies. We used a random-effects model meta-analysis to perform a quantitative synthesis of the data. We used the I statistic to measure heterogeneity among the trials in each analysis. We indicated summary estimates as a risk ratio (RR) for dichotomous outcomes, mean difference (MD) for continuous outcomes, or standardised mean differences (SMD) if different scales were used, with their 95% confidence interval (CI). We assessed the certainty of the evidence for each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) approach.

Results: We included 14 trials (12 parallel RCTs and two cross-over trials) involving a total of 1,375 participants. Most included studies had an unclear or high risk of bias. Compared to control, aldosterone antagonists reduced the risk of all-cause death for patients with CKD requiring dialysis (9 trials, 1,119 participants: RR 0.45, 95% CI 0.30 to 0.67; I=0%; moderate certainty of evidence). Aldosterone antagonist also decreased the risk of death due to cardiovascular disease (6 trials, 908 participants: RR 0.37, 95% CI 0.22 to 0.64; I=0%; moderate certainty of evidence) and cardiovascular and cerebrovascular morbidity (3 trials, 328 participants: RR 0.38, 95% CI 0.18 to 0.76; I=0%; moderate certainty of evidence). While aldosterone antagonists had an apparent increased risk of gynaecomastia compared with control (4 trials, 768 participants: RR 5.95, 95% CI 1.93 to 18.3; I=0%; moderate certainty of evidence), the elevated risk of hyperkalaemia (9 trials, 981 participants: RR 1.41, 95% CI 0.72 to 2.78; I=47%; low certainty of evidence) and increase in serum potassium (7 trials, 519 participants: MD 0.21, 95% CI -0.06 to 0.47; I^2=84%) due to aldosterone antagonists was uncertain. Aldosterone antagonists had a marginal effect on left ventricular mass among participants undergoing dialysis (7 trials, 562 participants: SMD -0.33, 95% CI -0.72 to 0.05; I^2=76%).

Conclusion: Based on moderate certainty of the evidence, aldosterone antagonists could reduce the risk of all-cause and cardiovascular death and morbidity due to cardiovascular and cerebrovascular disease but increase the risk of gynaecomastia in patients with CKD requiring dialysis. Two ongoing studies will provide better certainty of evidence in the future.

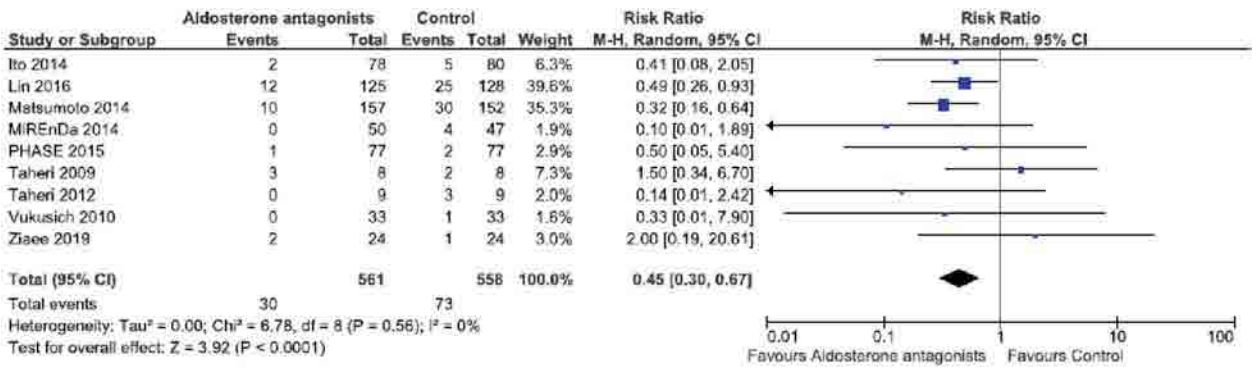


Figure:

P1435 RELATIONSHIP BETWEEN INTRA-DIALYTIC OXYGEN EXTRACTION RATIO (OER) CHANGE AND IDH

Silverio Rotondi[1,2], Lida Tartaglione[1], Maria Luisa Muci[3], Sara Caissuti[1], Marzia Pasquali[4], Sandro Mazzaferro[1]

[1]Sapienza University of Rome, Roma, Italy, [2]Alma Mater Studiorum - Università di Bologna, Bologna, Italy, [3]ICOT, Latina, Italy and [4]Policlinico Umberto I, Roma, Italy

Background and Aims: Intradialytic hypotension (IDH) involves a reduced tolerance to hemodialysis (HD), a poor quality of life and is associated with mortality. Intradialytic monitoring systems (blood pressure, heart rate, volemia) are not able to identify patients at greater risk of IDH. IDH is a hemodynamic phenomenon and attention has recently been given to the evaluation of oxygen saturation to evaluate its role in IDH. Oxygen Extraction Ratio (OER), the ratio between SaO2 and ScvO2, is a parameter used to monitor parenchyma oxygen consumption and stress. Recent evidence showed that HD patients with a greater delta OER (ΔOER) during HD (threshold 40%)had higher mortality risk. OER could be a new monitoring instrument to measure hemodialysis induced sub-clinical parenchyma hypoxia and stress, two elements included in the pathogenesis of IDH. The aim of the study was to evaluate the relationship between OER and IDH incidence.

Method: Inclusion criteria: age ≥18 years, chronic HD treatment by means of permanent jugular CVC, no evidence of acute underlying illness. We evaluated OER ([(SaO2 − ScvO2)/SaO2] × 100) before HD and at 15', 30', 60' and post HD in three HD sessions (*HD OER sessions*). For the statistic analysis we considered for each patient the median OER value obtained from the three HD OER sessions. Then we started the follow-up study with a minimum follow-up of three months and end follow-up of two years, to record IDH (defined according to K/DOQI guidelines) for each patient. We divided the population in two groups using as a threshold the median percentage number of IDH in our population and evaluate the differences between the obtained two groups in pre HD OER, Delta OER and intradialytic OER trends.

Results: During the follow-up period (mean 12 ± 1.2 months), we enrolled 28 patients with permanent jugular CVC: 13 males and 15 females, aged 74±2.6 years, HD vintage 46 ± 6.5 months. The *HD OER sessions* for each patient were asymptomatic. Pre HD OER was 34 ± 1.4, post HD OER 46 ± 1.8, with a Delta OER of 39 ± 5 %. OER change during HD was evident since after 15 minutes (OER% 15': 40 ± 1.2 p<.001) and continued to increase progressively (OER% end HD 46 ± 1.8; p<.0001). During the follow up period we monitored 4342 HD sessions of which 186 with IDH, the median incidence of IDH was 3.6% of all HD sessions. We divided patients into two groups based on the median value of IDH incidence: (*IDH % ≤ 3.6* and *IDH % > 3.6)*. The two groups were not different for age (76 ± 2.4 vs 73 ± 3.0 years; p <ns), HD vintage (52 ± 8.6 vs 40 ± 4.0 months; p <ns), systolic (125 ± 3.2 vs 129 ± 4.0 mmHg; p <ns) and diastolic blood pressure (67 ± 2.2 vs 70 ± 2.2 mmHg; p <ns) and heart rate (70 ± 2.2 vs. 76 ± 2.3 bpm; p <ns) (Tab. 2). The *IDH % >3.6* group had 159 IDH out of a total of 1911 sessions (9%), while *IDH % ≤ 3.6* group had 27 IDH out of 2431 sessions (0.9%). Pre HD OER values were not different between the groups while the *IDH % >3.6* group had greater delta OER% than the *IDH % ≤ 3.6* group (43 ± 4.8 vs. 35 ± 3.0 %; p <.05) (Figure). Evaluating the OER trend during HD session a higher ΔOER% was found at 15 minutes of HD treatment in the *IDH % > 3.6* group (ΔOER 20± 3.0 % vs. 8.0 ± 3.0 %; *IDH % > 3.6* group vs. *IDH % ≤ 3.6* group, p <.05), data confirmed at 30' (24 ± 3.0 % vs. 13 ± 5.0 %; p <.05), and post HD (43 ± 5.0 % vs 35 ± 3.0 %; p <.05), but not at 60 minutes of HD treatment (19 ± 4.0 % vs. 17 ± 4.6 %; p <ns).

Conclusion: Our data show that intradialytic ΔOER, representative of the extent of tissue hypoxic stress, identifies patients at greater risk of IDH. In particular, a ΔOER of 20% after the first 15 minutes of HD and of 43% at the end of the HD session characterizes the more hemodynamically fragile patients. The measurement of the OER can be a new and easy monitoring instrument to identify the most hemodynamically fragile patients already after the first 15 minutes of HD treatment.

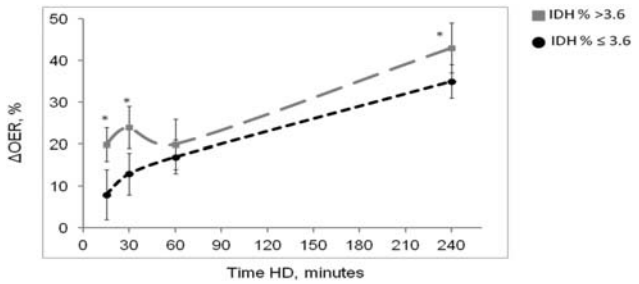


Figure: Figure ΔOER increment in *IDH % > 3.6* was greater than *IDH % ≤ 3.6* and was different after 15′ and 30′ e post HD but not after 60′. Bonferroni post-hoc test, *IDH % > 3.6 vs. IDH % ≤ 3.6*: *p < 0.05;

P1436

FRAILTY INDEX AND CLINICAL FRAILTY SCALE ARE SUPERIOR TO FRAILTY PHENOTYPE AND EDMONTON FRAIL SCALE IN MORTALITY PREDICTION: RESULTS FROM A LARGE EUROPEAN HAEMODIALYSIS COHORT

Benjamin Anderson[1,2], Gonzalo Correa[1], Muhammad Qasim[1,3], Thomas Jackson[2,4], Adnan Sharif[1,3]

[1]Queen Elizabeth Hospital Birmingham, Department of Nephrology and Transplantation, United Kingdom, [2]University of Birmingham, Institute of Inflammation and Ageing, United Kingdom, [3]University of Birmingham, Institute of Immunology and Immunotherapy, United Kingdom and [4]Queen Elizabeth Hospital Birmingham, Department of Healthcare for Older People, United Kingdom

Background and Aims: Frailty, a clinical syndrome of accelerated ageing with increased vulnerability to stressors, is prevalent among dialysis populations and associated with poor outcomes. However, no gold standard definition for frailty screening exists and this translates into heterogeneously reported epidemiology. Most published studies are from US cohorts, which may not translate to European cohorts. The aim of the FITNESS study was to compare commonly cited frailty scores in their predictive capacity for adverse events.

Method: Prevalent (>3-months) adult haemodialysis patients were recruited into this prospective cohort component of the FITNESS study after informed consent between January 2018 and April 2019. Exclusion criteria included any inpatient admission within the previous 4-weeks. Prospective data collection at recruitment included calculation of the Frailty Index (FI), Fried Frailty Phenotype (FP), Clinical Frailty Scale (CFS) and Edmonton Frailty Scale (EFS), alongside comprehensive medical and social history. FI, FP and EFS were obtained through a combination of physical performance testing and patient questionnaires; the CFS was obtained by MDT discussion led by patients' lead nephrologist. Follow-up data on hospitalisation and mortality were collected from national datasets including hospital episodes statistics and civil registration data respectively (up to 31st August 2019). Univariate and Multivariate Hazard ratios were obtained using Cox regression analyses.

Results: In total, 486 participants gave informed consent for the prospective study and were followed-up over a median of 55 weeks. During this study period we observed 726 emergency and 219 elective hospital admissions, with 46 (9.47%) participant deaths. Frailty prevalence was heterogenous based upon definition criteria; highest using FI (63.2%), lowest with CFS (26.5%) and FP (41.8%) and EFS (50.2%) in between. On univariate analysis, hazard ratios (HRs) for mortality were 4.25 for frailty defined by FI (p=0.001), 2.96 defined by CFS (p=0.001), 2.50 defined by FP (p=0.003) and 1.88 defined by EFS (p=0.040). After adjustment for age, gender, previous admission and Charlson Comorbidity Score, HRs for mortality were 4.45 for frailty defined by FI (p=0.001), 3.05 defined by CFS (p=0.002), 2.48 defined by FP (p=0.004), and 2.07 defined by EFS (p=0.019). Univariate HRs for death/emergency admission were 1.53 for frailty defined by FI (p=0.001), 1.46 defined by CFS (p=0.05), 1.60 defined by FP (p<0.001) and 1.77 defined by EFS (p<0.001). After adjustment for age, gender, Charlson score and previous admissions, adjusted HRs for death/emergency admission were 1.62 for frailty defined by FI (p<0.001), 1.54 defined by CFS (p=0.001), 1.55 defined by FP (p<0.001) and 1.62 defined by EFS (p<0.001).

Conclusion: Frailty was prevalent in this cohort regardless of the measure used, however there was wide variation in the prevalence of frailty by different scores. All frailty scores demonstrated predictive ability for mortality and hospitalisation on adjusted analyses. The FI demonstrated superior prediction of mortality to other scores, but identified the greatest proportion of participants as frail, and is the most time-consuming of the scores to implement. These limitations may impact routine clinical use. The subjective CFS is more selective at identifying frailty (with lowest reported prevalence) and demonstrates comparable predictive power to more detailed and time-consuming objective frailty tools. Considering the simplicity and predictive ability of CFS, it may prove an attractive option for frailty screening for healthcare professionals. Further work must focus on whether frailty can be intervened to improve observed adverse outcomes.

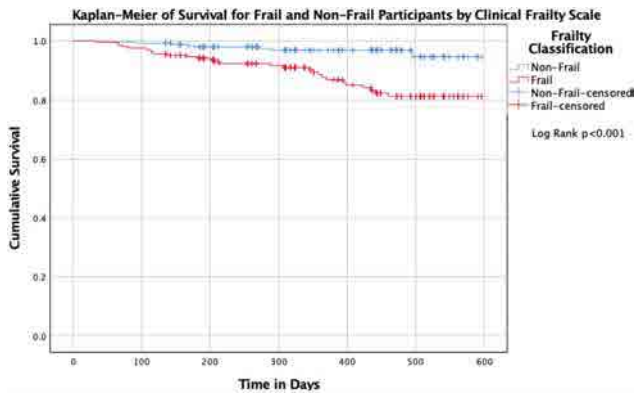


Figure:

Nephrology Dialysis Transplantation 35 (Supplement 3): iii274–iii286, 2020

MODERATED POSTER SESSION 7

P0336

INHIBITION C-C CHEMOKINE RECEPTOR TYPE 2 (CCR2) ON ACTIVATED KIDNEY PARIETAL EPITHELIAL CELLS REVEALS A NEW THERAPEUTIC APPROACH FOR CHRONIC KIDNEY DISEASES

Bin Zhao[1], Zhenhua Miao[2], James Campbell[2], Linda S. Ertl[2], Yu Wang[2], Chris Li[2], Rajinder Singh[2], Israel F. Charo[2], Thomas J. Schall[2]

[1]*ChemoCentryx Inc., Biology, Mountain View, United States of America and* [2]*ChemoCentryx Inc.*

Background and Aims: We have recently demonstrated that small molecule inhibitors of CCR2 rapidly reduced proteinuria and preserved renal structure in animal models of diabetic nephropathy (DN) and focal segmental glomerular sclerosis (FSGS). Similar beneficial effects of CCR2 inhibition were also observed in DN patients in a large diabetic nephropathy Phase 2 clinical trial. Despite its rapid and robust effects in these kidney diseases, the mechanism by which CCR2 inhibition affords such renal protection remains unclear. CCR2 is well-known to be expressed on cells of the immune system, where it mediates inflammation and immunological functions by controlling the trafficking of monocytes and T cells. However, immune cell expression of CCR2 may not adequately explain the rapid pharmacologic benefits of CCR2 inhibitors in DN and FSGS because these diseases do not exhibit appreciable kidney inflammation. To better understand the protective mechanism(s) of CCR2 inhibition in renal diseases, we have used a variety of *in vivo* nephropathy models to determine if CCR2 is expressed on kidney parenchymal cells. Our results suggest that a subset of CD45 negative, renal parietal epithelial cells express CCR2.

Method: To characterize CCR2 expression in the kidney we used CCR2 RFP heterozygous mice ($CCR2^{RFP/+}$) in which one copy of CCR2 was replaced by red fluorescent protein (RFP), whose expression is under the control of the endogenous CCR2 promoter. This approach provided a highly sensitive method for CCR2 detection by both flow cytometry and immunofluorescence, and compensated for the lack of validated, commercially available anti-CCR2 antibodies. Enriched glomerular cells were obtained by a non-enzymatic disruption of kidneys, followed by centrifugation at low speed (80gs), and sieving through 300μm and 150μm meshes. The Adriamycin (ADR)-nephropathy model with CCR2 RFP heterozygous mice was used to determine CCR2 expression on renal cells. 5/6 nephrectomy models of FSGS, as well as the db/db diabetic nephropathy model were used to access the change of activated parietal epithelial cells and proteinuria, both in the presence and absence of a CCR2 inhibitor in the setting of kidney injury.

Results: We observed dramatic increases in the number of activated parietal epithelial cells (PECs, identified as $CD133^{+}CD24^{+}CD44^{hi}$ cells by flow cytometry) in all three renal disease models. In the ADR nephropathy model, we found that in 30-40% of activated PEC cells within an enriched population of glomerular cells expressed CCR2/RFP. $CD44^{hi}$ RFP^{+} increased much more dramatically than $CD44^{hi}$ RFP^{-} cells in response to ADR, and this was highly correlated with proteinuria, suggesting that CCR2 plays an important role in PEC cell activation and kidney pathology in ADR induced kidney injury. Furthermore, we found that blocking CCR2 with the CCR2-specific antagonist CCX872 significantly reduced both proteinuria and the number of activated PECs in the 5/6 nephropathy and db/db diabetic nephropathy models.

Conclusion: This is the first report that CCR2 is present on a subset of activated renal PECs. This population is markedly upregulated during kidney injury in a variety of murine models of nephropathy. Changes in the abundance CCR2+ activated PECs in the glomerular enriched preparations in response to CCR2 inhibition suggests that CCR2 antagonism may represent a novel approach for the treatment of chronic kidney disease.

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P0337 PROTEOME CHANGES IN TUBULOINTERSTITIAL TISSUE OF PROGRESSIVE VS NON-PROGRESSIVE IGAN

Flavia Teodora Paunas[1], Kenneth Finne[2], Sabine Leh[3], Hans-Peter Marti[4], Bjørn Egil Vikse[5]

[1]Haugesund Hospital, Internal Medicine, Bergen, Norway, [2] University of Bergen, Department of Clinical Medicine, Bergen, , [3]Haukeland University Hospital, Department of Pathology, Bergen, , [4]University of Bergen, Department of Clinical Medicine and [5]Haugesund Hospital, Department of Medicine

Background and Aims: IgA nephropathy (IgAN), a common glomerulonephritis worldwide, is associated with a significant risk of progression to end-stage renal failure. In the Oxford classification, tubular atrophy is an established important risk factor for the risk of progression but few studies have investigated possible tubulointerstitial markers and the mechanisms of progression in IgAN. The present study investigated changes in the tubulointerstitial proteome from patients with IgAN.

Method: Based on data from the Norwegian Kidney Biopsy Registry and the Norwegian Renal Registry, two groups were included: IgAN patients with (n=9) or without (n=16) progression to ESRD during 10 years. Tubulointerstitial tissue without discernible interstitial expansion or pronounced tubular alterations were microdissected, proteome was analysed using mass spectrometry and protein abundances were compared between groups.

Results: Proteomic analyses quantified 2562 proteins with 2 or more unique peptides . Of these, 201 proteins had significant different abundance between progressive and non-progressive IgAN patients, 96 were more abundant and 105 less abundant. Periostin was the protein with the highest fold change between progressive and non progressive IgAN (fc 9.59, $p<0.05$). Proteins related to inflammation were more abundant and proteins involved in the aerobic energy metabolism and energy demanding ion channels were significantly less abundant in progressive vs non-progressive patients.

Conclusion: Our study describes extensive proteome changes of tubulo-interstitial tissue in patients with progressive IgAN and indicates several proteins and pathways that are important in the progression of the disease.

P0338

CRUMBS HOMOLOG2-EZRIN SIGNALING INDUCED PODOCYTE INJURY, LEADING TO MINIMAL-CHANGE DISEASE(MCD) AND FOCAL SEGMENTAL GLOMERULOSCLEROSIS(FSGS).

Ichiro Hada[1]

[1]*Kyorin University School of Medicine, Department of Pediatrics, Tokyo, Japan*

Background and Aims: The etiology and cellular pathogenesis of podocyte injury leading to minimal-change disease (MCD) and focal segmental glomerulosclerosis (FSGS) remain largely obscure. Genetic mutation of crumbs homolog 2 (CRB2) is a cause of congenital nephrotic syndrome. Type-1 transmembrane proteins including CRB2 transduce outside-in signals that are involved in various cellular events including changes in the cytoskeletal network. The aim of the present study is to determine whether alteration of CRB2-mediated signaling in podocytes causes MCD and FSGS.

Method: Mice were immunized with a partial recombinant protein including the extracellular part of mouse CRB2. Urinalysis was obtained, and the kidney was subjected to histopathology. Kidney samples were also subjected to immunofluorescence microscopy and glomerular isolation to determine whether activation of the ezrin/radixin/moesin (ERM) family of cross-linkers between plasma membrane proteins and the actin cytoskeleton is involved in the pathogenesis of this nephrotic model. A CRB2-expressing mouse podocyte cell line was generated and incubated with anti-CRB2 antibody, and cell lysates were subjected to immunoblot analysis of ERM phosphorylation. The presence of anti-CRB2 antibody in the serum was determined by Western blot analysis.

Results: Apparent anti-CRB2 antibody was detected in the serum from 4 weeks onward. Immunized mice developed proteinuria at 4 weeks, which continued at least until 29 weeks. Mice developing extremely heavy proteinuria also developed hematuria from 18 weeks onward. Light microscopy revealed MCD in mice with proteinuria alone and FSGS in mice with heavy proteinuria and hematuria. Immunofluorescence microscopy revealed positive granular IgG staining in podocyte foot processes, but not complement C3. Electron microscopy and immuno-electron microscopy revealed alteration of actin organization associated with prominent foot process effacement. Strong phosphorylation of ezrin was observed in the glomerulus from the proteinuric stage and in the cellular lysates from the CRB2-expressing podocyte cell line incubated with anti-CRB2 antibody.

Conclusion: The current data revealed that binding of anti-CRB2 antibody to the extracellular domain of CRB2 on the podocyte foot process activated the ezrin-cytoskeleton network, leading to podocyte injury. Our data also indicated that signaling by this one molecular can induce two different phenotypes of glomerular injury: MCD and FSGS. In our model, the signaling was activated by anti-CRB2 antibody, but in patients with nephrotic syndrome the CRB2 ligands remain unknown. Therefore, it will be important to identify the soluble factors interacting with CRB2, which may be novel factors contributing to the pathogenesis of MCD and FSGS.

P0339 URINE METABOLOMIC ASSAY IN EARLY IGA NEPHROPATHY PATIENTS REVEALS URINE GLYCINE AS A PROGNOSTIC BIOMARKER

Sehoon Park[1], Seung Hee Yang[2], Kwon Wook Joo[2], Jung-Hyun Kim[3], Dong Ki Kim[2]

[1]Armed Forces Capital Hospital, Seongnam-si, Korea, Rep. of South, [2]Seoul National University Hospital, Seoul, Korea, Rep. of South and [3]PAICHAI University, Department of Home Economics Education, Korea, Rep. of South

Background and Aims: A urine metabolomic biomarker from early immunoglobulin A nephropathy (IgAN) can be a useful tool for early detection or prognostic prediction of the disease.

Method: We profiled the urine metabolomes, using nuclear magnetic resonance (NMR) spectrometry, from 197 IgAN patients with eGFR $\geq$ 60 mL/min/1.73 m^2, and the patients with same kidney function range but have diagnosis of membranous nephropathy (n=81) and minimal change disease (n=50) were included as the disease-control group. Additional 146 healthy controls who received routine health screenings and donated urine samples were included. We calculated the creatinine-adjusted urine concentrations of 27 urine metabolites. Urine metabolites specifically increased in urines from IgAN patients were identified, and their associations with the prognosis of the disease, determined with the outcome of eGFR 30% reduction from baseline, were investigated. Additional kidney biopsy samples from independent patients and controls were stained for molecules included in related biological process for experimental validation.

Results: Among the 15 metabolites higher in the urines from IgAN patients than those from the healthy controls, only glycine was the metabolite that the median level was significantly higher also than that of the disease-control group. We found that the higher levels of glycine, alanine, citrate, threonine, and valine were significantly associated with higher risks of 30% eGFR reduction in IgAN patients. Among the molecules related to metabolism of glycine, expressions of T and H proteins from glycine cleavage system were significantly reduced in the kidney biopsy slides from independent IgAN patients when compared to the controls.

Conclusion: Urine glycine may be a prognostic and pathophysiology-related biomarker of IgAN. A further study confirming the clinical usefulness and pathophysiologic significance of urine metabolites in IgAN patients is warranted.

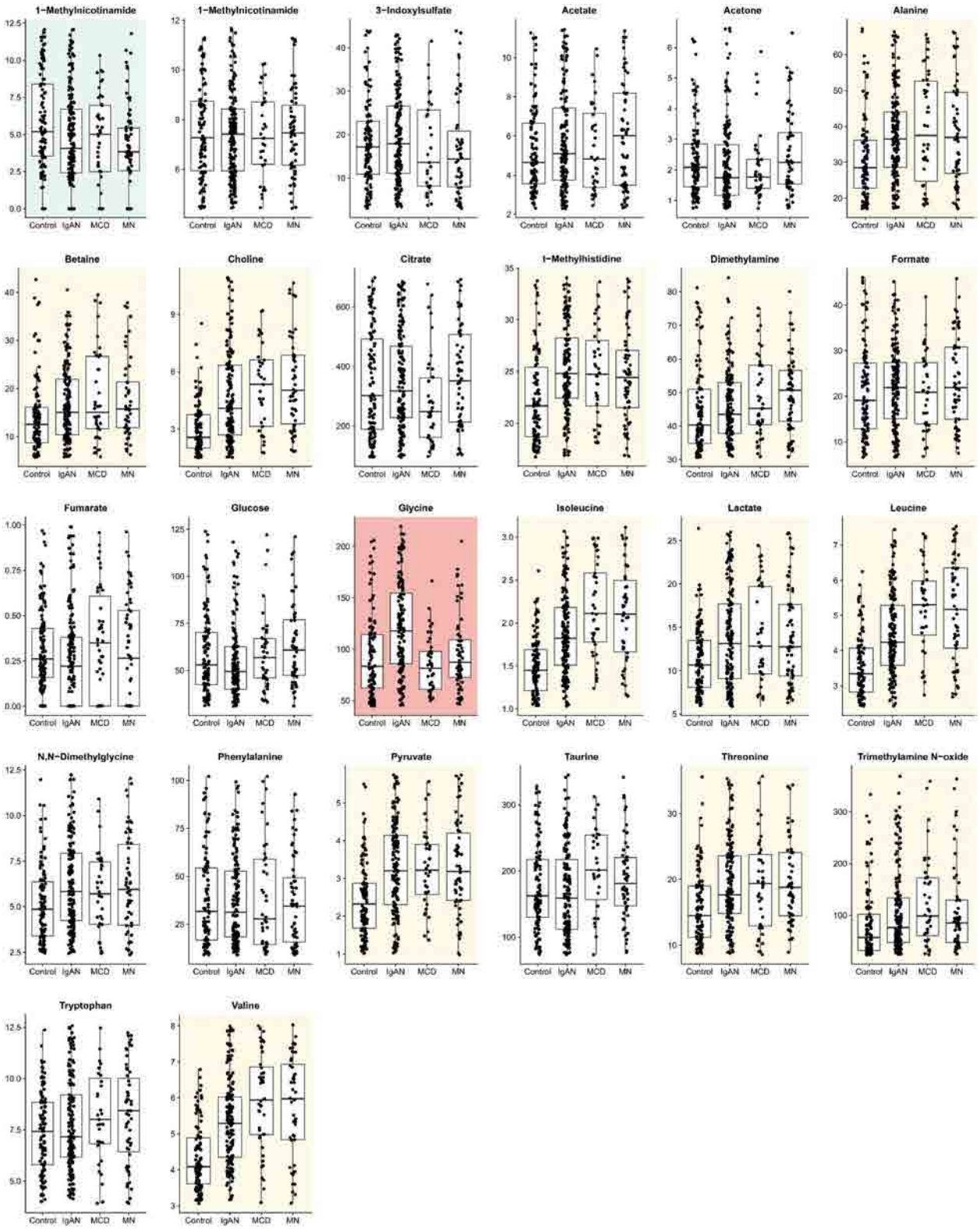

1-Methylnicotinamide
1-Methylnicotinamide
3-Indoxylsulfate
Acetate
Acetone
Alanine
Betaine
Choline
Citrate
1-Methylhistidine
Dimethylamine
Formate
Fumarate
Glucose
Glycine
Isoleucine
Lactate
Leucine
N,N-Dimethylglycine
Phenylalanine
Pyruvate
Taurine
Threonine
Trimethylamine N-oxide
Tryptophan
Valine
Control
IgAN
MCD
MN

Figure:

P0340 CYPD DEFICIENCY AMELIORATES AUTOIMMUNE VASCULITIS IN MOUSE MODEL VIA THE INHIBITION OF PROGRAMMED NECROSIS

Takashi Kudo[1], Daigo Nakazawa[1], Kanako Watanabe[1], Satoka Shiratori[1], Nishio Saori[2], Utano Tomaru[2], Akihiro Ishizu[3], Tatsuya Atsumi[3]

[1]Hokkaido University, Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Sapporo, Japan, [2]Hokkaido University, Department of Pathology, Faculty of Medicine and Graduate School of Medicine, Sapporo, Japan and [3]Hokkaido University, Department of Medical Laboratory Science Faculty of Health Sciences, Sapporo, Japan

Background and Aims: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a necrotizing vasculitis that affects systemic organs. Although the standard immunosuppressive therapy in AAV could control disease activity, these existing treatments have no effect to regulate the necrosis, which could cause the persistent organ damage. ANCA binds to neutrophils, leading to neutrophil extracellular (NETs) formation. The formed NETs induce vascular injury and become auto-antigens against ANCA, resulting in an auto-amplification loop of necrosis and inflammation. NETs work as innate immunity and simultaneously undergo programmed cell necrosis. However, the signaling pathway of ANCA-mediated NETs remains elusive. Cyclophilin D (CypD) regulates program necrosis via the opening of mitochondrial permeability transition pores (mPTP) with the consequence of mitochondrial ROS release. The Inhibition or genetic deletion of CypD has been reportedly to protect organ damage in brain and kidney ischemia-reperfusion injury mice. Herein, we hypothesized that CypD would be involved in ANCA-mediated NETs pathway and the pathogenesis of AAV.

Method: Animal experiment;

Autoimmune vasculitis was induced in 10 week-old CypD(+/+) or CypD deficient (-/-) mice by the intravenous injection with anti-mouse MPO serum. At 24 hours after injection, we evaluated the renal and lung involvements. The severity of glomerulonephritis was assessed by the levels of BUN, haematuria, histological findings and TUNEL positivity. The lung injury was evaluated by histopathological alveolar haemorrhage scores and TUNEL positivity. The mPTP related necrosis in tissues was identified by immunostaining against cytchrome C. The NETs-forming neutrophils in peripheral bloods were detected as Sytox Green (SG)-positive neutrophils by flow cytometry (FCM).

In vitro experiment;

We investigated whether CypD inhibitor and genetic ablation suppresses ANCA-mediated NETs. Healthy human neutrophils were incubated with ANCA-IgG derived from AAV patients with pre-treatment of CypD inhibitor (cyclosporine A) or PBS for 4 hours. Next, WT or CypD (-/-) mice neutrophils were cultured with anti mouse MPO antibody for 4 hours. The NETs induction was assessed as Sytox green positive neutrophil using FCM and live imaging.

Results: The amount of haematuria, histological severity including glomerulonephritis and pulmonary haemorrhage in CypD(-/-) mice significantly decreased compared to those in CypD(+/+) mice. Furthermore, TUNEL and cytochrome C positivity of tissues in CypD(-/-) mice was lower than that of CypD(+/+) mice, respectively. The level of BUN in AAV-induced CypD (-/-) mice was significantly lower than that of AAV-induced CypD(+/+) mice (92.4 $\pm$ 41.8 vs 36.8 $\pm$ 21.5 mg/ dL, $p < 0.05$). FCM analysis showed that circulating NETs and mitochondrial ROS in CypD(-/-) mice were lower than those in CypD(+/+) mice (NETs; 4.7 $\pm$ 2.4 vs 7.5 $\pm$ 2.6 %, $p < 0.05$, ROS; 1.9 $\pm$ 0.38 vs 4.7 $\pm$ 0.78%, $p < 0.05$).

In vitro experiments, CypD inhibitor suppressed ANCA-induced NETs formation (Control; 0.45 $\pm$ 0.14 vs CypD inhibitor; 0.16 $\pm$ 0.04%, $p < 0.05$). In addition, CypD(-/-) mice neutrophils-treated with ANCA showed lower NETs induction rate compared to CypD(+/+) neutrophils (CypD+/+: 4.27 $\pm$ 2.09 vs CypD-/-: 0.63 $\pm$ 0.35%, $p < 0.05$).

Conclusion: Our data indicate that the inhibition of CypD might ameliorate autoimmune vasculitis via the suppression of programmed NETs formation.

P0341

RITUXIMAB IN THE TREATMENT OF PRIMARY MEMBRANOUS NEPHROPATHY - A COMPARATIVE STUDY OF THREE REGIMEN

Harbir Singh Kohli[1,2], Raja Ramachandran[2], Manish Rathi[2], Ranjana Minz[3], Ritambhra Nada Duseja[4]

[1]PGIMER Chandigarh, Chandigarh, India, [2]PGIMER Chandigarh, Nephrology, Chandigarh, India, [3]PGIMER Chandigarh, Immunopathology, Chandigarh, India and [4]PGIMER Chandigarh, Pathology, Chandigarh, India

Background and Aims: Different rituximab dosing schedules have been used to manage primary membranous nephropathy (PMN). Better response rate and toxicity needs to be balanced to arrive at correct dose. The dosing schedules in PMN as of now are an on the lines of the management of lymphoma or rheumatoid arthritis. In the current study, we report the 1-year outcome of patients treated with three dosing schedules of rituximab in PMN.

Method: The current report is a study of patient of PMN treated with three different dosing schedules of rituximab treatment. The study included PMN patients with nephrotic syndrome (proteinuria>3.5 g/day and serum albumin of < 3.5 g/dL). Patients with secondary membranous nephropathy and a history of prior exposure of immunosuppressive therapy in the last three months were excluded from the study. The three dosing schedules of rituximab were 1 g (on day 0,15) (regimen 1), 375 mg/m^2 (weekly for four weeks) (regimen 2) or CD19 targeted rituximab therapy (375 mg/m^2 as the initial dose and additional dose 100 mg, when the CD19 cell count was> 5/ul or >1%, done every month for 12 months) (regimen 3). Serum PLA2R autoantibodies were done before rituximab therapy and at six months of therapy initiation. Primary outcomes: Remission at the end of 12 months of therapy initiation. Secondary outcome: Complete remission (CR) and partial remission (PR), remission with different treatment schedules and adverse events. Definition: CR: reduction of proteinuria to <0.5 g/d and with creatinine clearance of >60 ml/min/1.73m^2 and serum albumin > 3.5 g/dl. PR: reduction of proteinuria to 0.5–3.5 g/day and stable serum creatinine. A p-value of <0.05 was considered significant.

Results: The study included 87 patients of PMN. The mean age of the patients was 33.36±15.38 (range 15-61) years. Thirty-two (36.4%) and 56 (63.6%) patients received rituximab as the first-line therapy and for relapsing/resistant disease, respectively. Forty, 15 and 33 patients received regimen 1, 2 and 3, respectively. The median proteinuria, serum albumin and creatinine at the baseline before rituximab therapy was 5.90 (IQR 4.20,9.75) gm, 2.50 (IQR 2.15,3.25) g/dl and 0.88 (IQR 0.77,1.09) mg/dl, respectively. At the end of 12 months of follow-up, 55 (56.8%) patients received remission. Nineteen (21.6%) and 32 (36.3%) patients achieved CR and PR, respectively. In regimen 1, 12 (30%) and 13 (32.5%) patients achieved CR and PR, respectively. In regimen 2, 2 (13.3%) and 5 (33.3%) patients achieved CR and PR, respectively. In regimen 3, 5 (15.6%) and 14 (43.7%) patients achieved CR and PR, respectively. One patient in the CD19 targeted therapy (regimen 3) was lost to follow-up after the 1st dose; all but one patient in the received regimen three as a second-line treatment. There was a significant association of anti-PLA2R to clinical response (p<0.05). There was no difference in the response rate among the three groups (p>0.05). A total of 7 (7.9%) patients had severe adverse events, there was no difference in the 3 regimens. (p>0.05) The cumulative dose in regimen 3 was significantly less as compared to regimen 1 & 2 (p<0.01)

Conclusion: Rituximab induces remission in two-thirds of the patients with PMN. There is no significant difference in the remission rates between different rituximab regimens. CD19 targeted therapy is equally effective with lower cumulative dose.

P0769

ESTABLISHING AN AFRICAN NETWORK FOR CHRONIC KIDNEY DISEASE EPIDEMIOLOGY: THE CKD-AFRICA COLLABORATION

Cindy George[1], Mark Woodward[2], Ikechi Okpechi[3], Andre Kengne[1]

[1]South African Medical Research Council, Non-Communicable Diseases Research Unit, Cape Town, South Africa, [2]University of Oxford, The George Institute for Global Health, Oxford, United Kingdom and [3]University of Cape Town, Division of Nephrology and Hypertension, Cape Town, South Africa

Background and Aims: Chronic kidney disease (CKD) is a global public health problem, disproportionately affecting individuals of African ancestry. Unfortunately, due to the lack of data in various African countries or the limitations of available data, the true magnitude of CKD on the continent is still unknown. Although there has been an increase in the number of reports on CKD prevalence in recent years, up to now there has been no coordinated effort to provide reliable estimates to adequately support the health service and policy solutions to address the adverse consequences of CKD in Africa. The Chronic Kidney Disease in Africa Collaboration (CKD-AFRICA Collaboration), which is an initiative of the South African Medical Research Council, seeks to address this issue by collating data, at individual participant data (IPD) level, from existing African studies. Thus, the main aims for establishing this platform are, (1) to utilize the available data from all relevant prevalence studies of CKD, to provide an updated and comprehensive synthesis on the burden of CKD in Africa, and (2) to bring together active investigators in the field of CKD epidemiology and prevention, by providing a platform to plan, in a more coordinated way, future observational and interventional studies on CKD across the continent.

Method: To establish the CKD-AFRICA Collaboration as a continental resource, a stepwise approach was utilized, which included, 1) the identification of data sources through various systematic literature searches and contacting health agencies to access publicly available population-based measurement surveys; 2) establishing a database platform, by inviting active CKD research groups to contribute data on CKD at IPD level; 3) data processing and quality control and 4) piloting the consortium, by using the data from existing studies to determine the prevalence of CKD in the African adult population, by two-stage IPD meta-analysis.

Results: Through extensive systematic literature searches, 134 potential collaborators were identified. These included studies conducted in general adult populations and high-risk sub-populations, such as those with HIV/AIDS, hypertension and diabetes. Of those identified, 101 principal investigators (PIs) were contacted, via email, to gauge their interest in collaborating in the consortium, as 33 PIs lacked contact information. Of the 101 PIs, 42 responded positively to the call and have agreed to participate in the consortium, spanning 12 African countries, namely Ghana, Kenya, Nigeria, Burundi, Cameroon, Maputo, Sudan, South Africa, Egypt, Uganda, Senegal and Tanzania (Figure 1). To date, the consortium has potential access to 27,346 IPD, with 11,810 IPD already received.

Conclusion: The strength of this Consortium has far-reaching potential for Africa. Indeed, by harnessing IPD from numerous African studies, important research questions can be explored, and by connecting active CKD researchers, this platform could aid a more coordinated way of developing future observational and interventional studies on CKD in Africa. The research obtained from this collaboration will therefore permit the exploration in understanding the diversity of clinical manifestations of CKD in Africa.

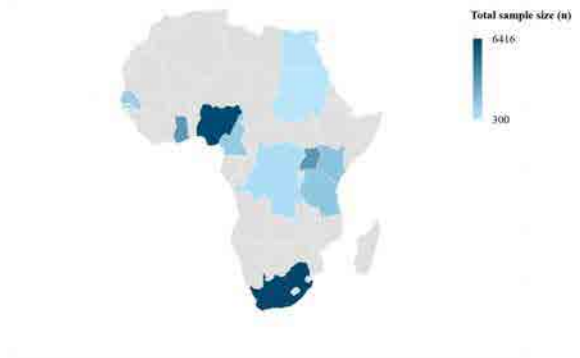


Figure 1: Distribution of African countries agreeing to participate in the consortium. The IPD ranges from 300 participants to 6,416 participants. The 12 shaded countries represent those for which IPD is available. The shading from light blue to dark blue represents the increasing number of IPD available per country, thus the darkest blue shading represents the countries with the most available IPD.

P1129 **PERITONEAL DIALYSIS TECHNIQUE FAILURE IN A LARGE POPULATION IN COLOMBIA**

Jasmin Vesga[1], Nelcy Rodriguez[2], Angela Rivera[3], Mauricio Sanabria[4]

[1]Renal Therapy Services (RTS) Colombia, Clinical Research, Bogota, Colombia, [2]Pontifical Xavierian University, Clinical Epidemiology, Bogotá, Colombia, [3]Baxter Healthcare Corporation, RCS Medical & Quality, Deerfield, IL, United States of America and [4]Baxter Renal Care Services (BRCS) Latin America, Clinical Research, Bogota, Colombia

Background and Aims: Peritoneal dialysis (PD) is a renal replacement therapy widely used in the world; about 197,000 patients use it. The main limitation of the use is related to technique failure. Extending time free of technique failure remains a long-term challenge in PD.

To estimate the incidence of technique failure in PD and, describe the main reasons for failure.

Method: A historical, multicenter, observational cohort study of all adult patients starting PD between January 1, 2010, and December 31, 2015, with follow-up until December 31, 2018, at Renal Therapy Services (RTS) network. The definition of technique failure applied when a patient was switched to Hemodialysis (HD) for at least 30 days. Socio-demographic and clinical characteristics of all patients were summarized descriptively by PD modality. We estimate the failure rate with an analysis of Kaplan Meier and analysis that incorporate competing risks as death and transplant.

Results: 6452 patients met the inclusion criteria for data analysis, 67% were in CAPD modality. The mean age was 59 years, 54% were male, and 53.7% had a history of diabetes, see Table 1. There were 1462 technique failures events with a rate of 10.67 events per 100 patients-year [95% CI, 10.14 – 11.24]. The median technique survival time was 5.8 years [95% CI: 5.11 to 5.45]. Technique failure rates did not differ by PD modality (Wilcoxon test = 0.4986), Figure 1.

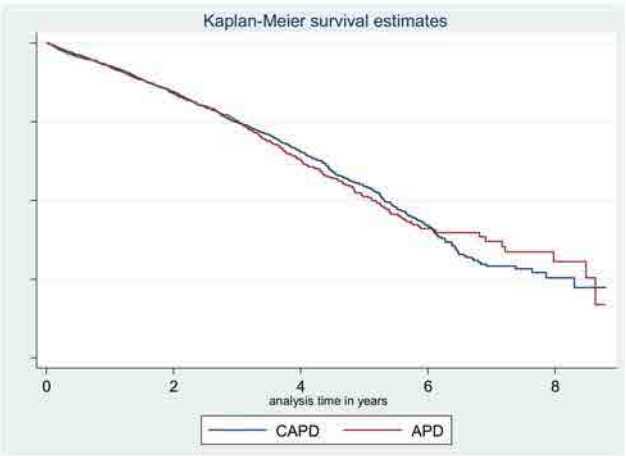


Figure: Technique Failure survival

Table 1. Baseline demographic and clinical characteristics.

Characteristics	CAPD n= 4342		APD n= 2110		Total n= 6452	
	n	%	n	%	n	%
Sex: Male	2276	52.4	1229	58.3	3505	54.3
Age, [median,IQR] years	61	21.0	61	20.0	61	21.0
Socioeconomic level						
Low	2076	48.6	832	40.0	2908	45.8
Medium	1851	43.3	1145	55.1	2996	47.2
High	345	8.1	103	5.0	448	7.1
Education level						
Elementary school or none	2842	65.5	1248	59.2	4090	63.4
High school	1312	30.2	688	32.6	2000	31.0
University degree	188	4.3	174	8.3	362	5.6
Caregiver: Yes	2912	67.1	1446	68.5	4358	67.5
Size center: > 25 new patients per year	2540	58.5	1409	66.8	3949	61.2
Diabetes History	2329	53.6	1136	53.8	3465	53.7
Hypertension history	3696	85.1	1804	85.5	5500	85.2
Cerebrovascular history	136	3.1	75	3.6	211	3.3
Major abdominal surgery history	227	5.2	122	5.8	349	5.4
Obesity history	549	12.7	289	13.7	838	13.0
Uncontrolled blood pressure	1838	42.3	946	44.8	2784	43.2
Catheter used in first 7 days	2290	59.3	1276	62.5	3566	60.4
Urine output, ml/day						
< 100	596	13.7	255	12.1	851	13.2
100 a 400	681	15.7	412	19.5	1093	16.9
> 400	3065	70.6	1443	68.4	4508	69.9

In the presence of competing events, the cumulative incidence of technique failure for the first year was 6.9 events per 100 persons-risk [95% CI: 6.27 to 7.56], Table 2. The most common causes of technique failure were catheter complications, followed by psychological and medical indications, Table 3.

Table 2. Cumulative incidence adjusted by competing events: Death and transplant

Time (Year)	Cumulative Incidence*	CI 95%	
1	0.07	0.06	0.08
2	0.13	0.13	0.14
3	0.20	0.19	0.21
4	0.25	0.24	0.26
5	0.30	0.28	0.31
6	0.34	0.33	0.36
7	0.37	0.35	0.39
8	0.38	0.36	0.40

***** Events of technique failure per patient - year

Table 3. Main reasons of PD technique failure.

Main reasons by technique failure	90 days		1 year		3 years	
	n	%	n	%	n	%
Peritonitis/ Infection	5	3.8	36	8.8	168	16.5
Clearance/Ultrafiltration	6	4.6	33	8.1	120	11.8
Catheter Problems	56	42.4	152	37.1	323	31.8
Hernias/Leaks	2	1.5	6	1.5	15	1.5
Psychological/Medical	51	38.6	120	29.3	227	22.3
Others	12	9.1	63	15.4	163	16.0
Total	132	100.0	410	100.0	1016	100.0

Conclusion: The incidence of PD technique failure is around ten events per 100 patient-year, and this is lower than the previous cohort reports in the literature. Catheter problems remain the leading cause of technique failure

P1130

A CELLULAR MODEL OF HUMAN MESOTHELIUM TO STUDY OF WATER TRANSPORT DURING PERITONEAL DIALYSIS AND THE BIOCOMPATIBILITY OF INNOVATIVE GLUCOSE-SPARING SOLUTIONS.

Francesca Piccapane[1], Rosa Caroppo[1], Arduino Arduini[2], Roberto Corciulo[3], Roberto Russo[3], Jose Carolino Divino[4], Mario Bonomini[5], Andrea Gerbino[1], Monica Carmosino[1], Maria Svelto[1], Giuseppe Procino[1]

[1]University of Bari Aldo Moro, Department of Biosciences, Biotechnologies and Biopharmaceutics, Bari, Italy, [2]Department of R&D SAGL Corequest, Manno, Switzerland, [3]University of Bari, Department of Emergency and Organ Transplantation, Italy, [4]Karolinska Institute, Division of Renal Medicine, Sweden and [5]University of Chieti G. D'Annunzio, Department of Nephrology

Background and Aims: The three pore model postulates that the endothelium of peritoneal capillaries is the major limiting barrier regulating water transport across peritoneal membrane during peritoneal dialysis (PD).

We hypothesize that the mesothelium may represent an additional selective barrier to water diffusion in PD. We previously demonstrated that the water channel AQP1 is expressed in vivo by mesothelial cells.

Here, we characterized an immortalized cell line of human mesothelium (HMC) to study the functional role of the water channel AQP1 in mediating water transport during PD and also to test the biocompatibility of glucose-sparing PD solutions (Xylocore), containing xylitol and L-carnitine as the main osmotic agents.

Method: Cells were grown onto porous cell culture inserts to achieve polarization. Polarization was demonstrated by expression of the tight junction markers Zo-1 and occludin. Transepithelial water transport was measured by TEA^+-sensitive microelectrodes.

HMC cell monolayers were exposed to PD solutions at the apical side for 8 hours.

The biocompatibility of conventional *versus* innovative PD solutions was evaluated by MTT-test, measurement of transepithelial electrical resistance (TEER) and production of pro-inflammatory cytokines by by Luminex xMAP technology.

Results: HMC cells showed polarized expression of Na^+/K^+-ATPase and tight junctions markers but no endogenous expression of AQP1.

HMC showed a low TEER ($40\Omega/cm^2$) compared to renal cells not expressing AQP1($1000\Omega/cm^2$). However, the transepithelial water transport was comparable between the two cell types.

Experiments in HMCs transfected with AQP1 cDNA, suggested that the water permeability of HMC was increased by two-fold in the presence of AQP1.

Biocompatibility assays indicated that in conventional dialysis solutions glucose concentration decreased cell viability in a dose-dependent manner. Glucose concentration also strongly decreased the TEER, suggesting reduction of the barrier integrity, and increased pro-inflammatory cytokines production.

Interestingly, substitution of part of the glucose with xylitol and L-carnitine minimized these effects.

Conclusion: These results suggest that the mesothelium may represent an additional selective barrier regulating water transport through the water channel AQP1 in PD. Importantly, we also demonstrate that the formulation of glucose-sparing PD solutions containing xylitol and L-carnitine better preserve mesothelial cells viability and may represent a useful means to prolong the dialysis life of patients undergoing peritoneal dialysis.

P1131

STEADY CONCENTRATION PERITONEAL DIALYSIS INCREASES ULTRAFILTRATION AND SODIUM REMOVAL COMPARED TO CAPD

Ola Carlsson[1], Ann-Cathrine Johansson[2], Olof Heimbürger[3], Giedre Martus[4], Martin Wilkie[5], Jörgen Hegbrant[6], Ann Johansson[1], Charlotte De Leon[1]

[1]Triomed AB, Lund, Sweden, [2]Skåne University Hospital, Department of Nephrology, Malmö, Sweden, [3]Karolinska Institute, CLINTEC, Solna, Sweden, [4]Skåne University Hospital, Department of Nephrology, Lund, Sweden, [5]Sheffield Teaching Hospital National Health Service Foundation Trust, Department of Nephrology, Sheffield, United Kingdom and [6]Lund University, Department of Nephrology, Lund, Sweden

Background and Aims: Fluid and sodium removal may be a challenge during glucose-based PD, leading to increased use of high glucose solutions to maintain sufficient fluid removal. This may in turn lead to increased sodium sieving, resulting in a decreased sodium removal.

Carry Life® UF uses Steady Concentration PD (SCPD), where the infusion of glucose compensates for glucose uptake and maintains the intraperitoneal glucose concentration at a sufficient level providing a continuous ultrafiltration throughout the dwell. The present study investigated the effect of Carry Life UF compared to a standard CAPD dwell regarding ultrafiltration, sodium removal and glucose absorption.

Method: Eight stable PD patients were included in the study. Subjects were treated with 5-hour Carry Life UF treatments using three different glucose doses (11, 14, 20 g/h). An initial fill with 1500 ml, 13.6 g/l glucose PD solution was used. A small volume of dialysate was drained hourly to avoid overfill. A standard 4-hour Peritoneal Equilibration Test (PET) (2000 ml, 22.7 g/l glucose) was used as control. Data expressed as mean ± SD, statistical analysis using one-way ANOVA.

Results: Ultrafiltration was significantly increased during the Carry Life UF treatments compared to PET (646±256, 739±312, 863±380 ml for 11 g/h, 14 g/h and 20 g/h, respectively, vs. 162±242 ml for PET, $p<0.01$). Sodium removal increased significantly during Carry Life UF treatments (86±27, 92±33, 110±37 mmol/dwell for 11, 14, and 20 g glucose/h) compared to PET (22±33 mmol/dwell, $p<0.001$). Figure a shows that the intraperitoneal glucose concentration increased during the first hours of the Carry Life UF treatments and remained stable during the remainder of the treatments. During PET the glucose concentration decreased gradually during the treatment. The maximum intraperitoneal glucose concentration did not exceed 26 g/l (144 mmol/l) during the Carry Life UF treatments. The UF volume per gram of glucose uptake was significantly higher for the two lower Carry Life UF glucose doses compared to PET (Figure b).

Conclusion: SCPD performed with Carry Life® UF maintained a stable intraperitoneal glucose concentration during the 5-hour treatment which generated significantly higher UF volumes compared to 4-hour PET. During the Carry Life UF treatments glucose was used more efficiently, particularly for the two lowest doses, in comparison to PET. The increased sodium removal with Carry Life® UF enables a better balance between UF volume and sodium removal than for example during APD. In summary, SCPD using Carry Life® UF increases the efficiency of PD compared to standard, glucose-based CAPD with respect to ultrafiltration and sodium removal.

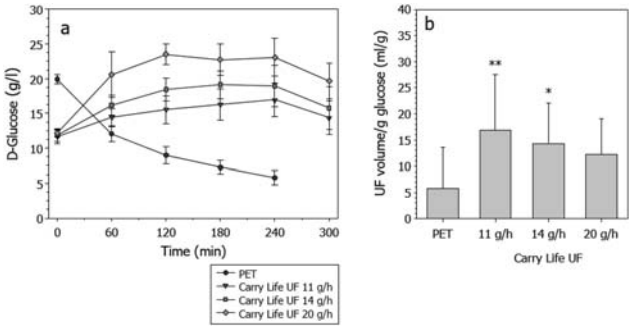


Figure: Intraperitoneal glucose concentration in g/l during treatments. Initial concentration calculated from residual volume and instilled fluid. Last measurement measured in total drained volume (a).

Ultrafiltration efficiency expressed as ultrafiltration volume in ml per gram of glucose absorbed during treatments, *$p<0.05$, **$p<0.01$ (b).

P1132

EXIT-SITE CARE PROTOCOLS IN PORTUGAL AND ITS ASSOCIATION WITH CATHETER-RELATED INFECTIONS RATE

Ana Carina Ferreira[1,2], Cristina Pinto Abreu[3], Marta Sofia Henriques Pereira[3], Anabela Rodrigues[4], Anabela Malho Guedes[5], Ana Marta Gomes[6], António Cabrita[4], Carlos Soares[7], Catia Pêgo[8], Francisco Ferrer[9], Idalécio Bernardo[5], João Carlos Fernandes[6], José Assunção[10], Luís Oliveira[11], Manuel Amoedo[12], Maria João Carvalho[4], Patricia Branco[13], Pedro Maia[14], Raquel Chorão[15], Rui Castro[11], Tânia Sousa[8], Teresa Mendes[14], Vasco Fernandes[1]

[1]Centro Hospitalar de Lisboa Central | Hospital Curry Cabral, Nephrology, Lisboa, Portugal, [2]Nova Medical School, ., Lisboa, Portugal, [3]Hospital Santa Maria, Nephrology, Lisbon, Portugal, [4]Hospital Geral de Santo António, Nephrology, Porto, Portugal, [5]University Hospital Center of Algarve, Faro, Nephrology, Faro, Portugal, [6]Centro Hospitalar Vila Nova de Gaia / Espinho, Nephrology, Vila Nova de Gaia, Portugal, [7]Braga Public Hospital, Nephrology, Braga, Portugal, [8]Hospital São Teotónio, Nephrology, Viseu, Portugal, [9]Centro Hospitalar Médio Tejo - Hospital Rainha Santa Isabel - Torres Novas, Nephrology, Torres Novas, Portugal, [10]Centro Hospitalar De Setúbal E.P.E., Nephrology, Setúbal, Portugal, [11]Centro Hospitalar De Trás-Os-Montes E Alto Douro, E.P.E., Nephrology, Vila Real, Portugal, [12]Hospital do Espírito Santo de Évora, EPE, Nephrology, Évora, Portugal, [13]Hospital Santa Cruz, Nephrology, Carnaxide, Portugal, [14]Centro Hospitalar e Universitário de Coimbra, Nephrology, Coimbra, Portugal and [15]Unidade Local De Saúde De Castelo Branco - Uls De Castelo Branco, E.P.E., Nephrology, Castelo Branco, Portugal

Background and Aims: Exit-site infections (ESi) are frequent complications in peritoneal dialysis (PD) patients and their prevention and treatment are key aspects to lower peritonitis' risk.

The aim of this study was to evaluate the annual incidence rate of ESi and peritonitis in Portugal and to study possible associations between exit-site (ES) care protocols in each Portuguese unit and the number / rate of ESi and peritonitis.

Method: We performed a national study using two questionnaires at each Portuguese PD Unit: one about the incidence of catheter-related infections, the other characterizing patients' education and ES care protocols. ESi and peritonitis were defined according to ISPD guidelines. Associations between variables were performed using T-student test or pairwise correlation test. STATA software was used.

Results: Of the 23 Portuguese PD Units, 14 units answered both questionnaires. In the last two years (2017 & 2018), those units followed 1453 patients. Portuguese ESi incidence rate was 0.41 episodes per year [1 episode per 29.2 months (MSSA incidence rate 0.13; MRSA incidence rate 0.03; Pseudomonas incidence rate 0.07)] and the peritonites incidence rate was 0.37 (1 episode per 32.5 months). We found a trend between the absolute number of ESi episodes and the number of peritonites in each unit (r=0.5, p=0.05).

Although ESi prevention guidelines were known by 100% of the Portuguese units, only three out of 5 of the selected guidelines for this study were followed by 100% of the units: monitoring catheter-related infections on a yearly basis; using antibiotic prophylaxis at time of catheter placement and treating nasal carriage of S. *aureus*. The other 2 guidelines have variable implementation: 12 out of 14 units (86%) perform screening of nasal carriage of S. *aureus* and only 6 out of 14 (43%) of the units recommend daily topic antibiotic cream at the ES. We didn't find associations between those differences and ESi incidence.

Whenever S. *aureus* carriage is detected, 100% of the units proceed treating with mupirocine using different posology (twice or three times a day, 5 or 7 or 21 days, with/out chlorexidine). Also, the screening of nasal carriage of S. *aureus* is different: only pre catheter implantation (n=4); annually (n=4); semi annually (n=3); bimonthly (n=2). Oral antibiotics are prescribed after catheter placement in 4 units. We didn't find statistical differences in ESi / peritonitis, comparing those practices.

Regarding to ES care protocols, ESi rate was lower with non-occlusive dressing (0.38 vs. 0.57) immediately after catheter insertion. ESi and peritonitis rate were lower in units where bathing without ES dressing is advocated (n=9, 0.58 & 0.37 vs. 0.32 & 0.34). The use of bath sponge is associated with higher ESi rate (0.57 vs. 0.34). The use of colostomy bags in beach baths was associated with lower incidence rate of ESi compared to regular dressing or waterproof dressing (o.32 vs. 0.54).

100% of units use two different empirical antibiotics for initial ESi treatment. In the presence of chronic ESi, 3 units don't perform shaving of external cuff and peritonitis rate is higher in those who do not apply this procedure (0.38 vs. 0.31).

Conclusion: in Portuguese PD units there is a wide variability in ISPD guidelines implementation and ES care protocols. We found that using non-occlusive dressing immediately after catheter insertion, removing ES dressing before shower, bathing not using a sponge and using colostomy bags at beach baths were associated with lower incidence rate of ESi. Shaving of the external cuff was associated with lower incidence rate of peritonitis. A regular national audit of PD Units is an important tool of quality improvement to clarify the best procedures for reduction of catheter-related infections in PD.

MODERATED POSTER SESSION 8

P0149 PREVALENCE OF MASKED HYPERTENSION IN HEMODIALYSIS PATIENTS

Ekaterina Borodulina[1], Alexander M. Shutov[2]

[1]*Kirov Branch of Medical Private Institution of additional professional education "Nefrosovet", Department of Nephrology and hemodialysis, Kirov, Russia and*
[2]*Ulyanovsk State University, Department of Internal Medicine, Ulyanovsk, Russia*

Background and Aims: Arterial hypertension is main cause of left ventricular hypertrophy (LVH) in hemodialysis patients. Masked hypertension is associated with asymptomatic organ damage, including the development of LVH. The aim of this study was to investigate the prevalence of white-coat hypertension and masked hypertension in hemodialysis patients.

Method: Hemodialysis patients (n=88; 42 males, 46 females, mean age was 51.7±13.3 years) were studied. Office blood pressure measurements were performed before and after hemodialysis within 30 days. Home Blood Pressure Measurements (HBPM) was collected in the morning and in the evening during 4 weeks including hemodialysis session days. 24 hours blood pressure monitoring (ABPM) was performed in the next day after hemodialysis. Systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) were analyzed. White-coat hypertension was diagnosed when blood pressure elevated in the office, but was normal when was measured by ABPM, HBPM, or both. Masked hypertension was determined when blood pressure was normal in the office, but increased when was measured by HBPM or ABPM. The definitions of the European Society of Cardiology (2018 ESC/ESH Guidelines for the management of arterial hypertension) were used for the diagnosis of hypertension according to office, ambulatory, and home blood pressure levels. Echocardiographic evaluation was performed on the day after dialysis and left ventricular mass index (LVMI) was calculated.

Results: Arterial hypertension was diagnosed by office blood pressure measurements in 39 (44.3%) patients. Arterial hypertension was defined by ABPM (mean 24h BP > or = 130 and 80 mmHg) in 48 (54.5%) patients. The number of non-dipper patients was 59 (67.0%). According to HBPM arterial hypertension was observed in 61 (69.3%) patients. Left ventricular hypertrophy was detected in 71 (80.7%) patients. Mean LVMI was 140.5±43.0 g/m^2. According to the results of three methods of blood pressure measuring arterial hypertension was diagnosed in 53 (60.2%) patients, white-coat hypertension was observed in 5 (5.7%) patients, masked hypertension – in 19 (21.6%) patients.

Conclusion: According to office blood pressure measurements arterial hypertension was diagnosed in 44.3% hemodialysis patients. Masked hypertension was often observed in hemodialysis patients and when using not only ABPM, but also HBPM was detected in 21.6% of patients. The results indicate the importance of using not only ABPM, but also HBPM in hemodialysis patients.

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P0178

COMPARATIVE EFFECTIVENESS OF RENIN-ANGIOTENSIN SYSTEM INHIBITORS AND CALCIUM CHANNEL BLOCKERS IN INDIVIDUALS WITH ADVANCED CHRONIC KIDNEY DISEASE: A NATIONWIDE COHORT STUDY

Edouard L. Fu[1], Catherine M. Clase[2], Marie Evans[3], Bengt Lindholm[3], Joris Rotmans[4], Merel Van Diepen[1], Friedo W. Dekker[1], Juan Jesus Carrero[5]

[1]Leiden University Medical Center (LUMC), Clinical Epidemiology, Leiden, Netherlands, [2]McMaster University, Medicine and Health Research Methods, Evidence and Impact, Hamilton, Canada, [3]Karolinska Institute, Clinical Science, Intervention and Technology, Stockholm, Sweden, [4]Leiden University Medical Center (LUMC), Internal Medicine, Leiden, Netherlands and [5]Karolinska Institute, Medical Epidemiology and Biostatistics, Stockholm, Sweden

Background and Aims: There is a lack of data that could help to guide the choice of antihypertensive agents in patients with advanced chronic kidney disease (CKD). We evaluated whether initiating treatment with a renin-angiotensin system inhibitor (RASi) is superior to calcium channel blockers (CCB) in preventing mortality, major adverse cardiovascular events (MACE) or kidney replacement therapy (KRT) in patients with advanced CKD.

Method: Observational study from the Swedish Renal Register, 2007-2017. We identified all nephrologist-referred patients in Sweden who initiated RASi or CCB treatment and had non-dialysis dependent advanced CKD (eGFR <30 ml/min/1.73m^2). The associations between RASi vs CCB initiation, mortality, MACE and KRT were assessed by Cox regression. Analyses were adjusted with propensity score weighting for a wide range of confounders, including demographics, blood pressure, laboratory measures, comorbidities and medications. As a positive control we evaluated new use of the same drugs in patients with CKD G3 (N = 2608; eGFR between 30-60 ml/min/1.73m^2). Furthermore subgroup, as-treated and competing risk analyses were performed.

Results: The propensity-score weighted cohort included 2479 RASi and 2327 CCB initiators who were well-matched for baseline confounders (all standardized differences <0.1). Median follow-up was 4.1 years, with a maximum follow-up of over 10 years. Compared to CCB, initiation of RASi was associated with a similar risk of mortality (adjusted HR 0.94; 95% CI 0.85-1.03) and MACE (0.99; 0.87-1.13), but with a lower risk of KRT (0.87; 0.78-0.98). Results were consistent across subgroups, in as-treated analyses and after accounting for the competing risk of death. In the control cohort of patients with CKD G3, initiation of RASi (versus CCB) was associated with lower KRT risk (adjusted HR 0.67; 0.47-0.96), and similar risk of mortality (0.91; 0.76-1.08) and MACE (1.06; 0.82-1.35).

Conclusion: Compared with CCB, initiation of RASi in patients with advanced CKD was associated with a lower risk of KRT, but no different risk of mortality or MACE.

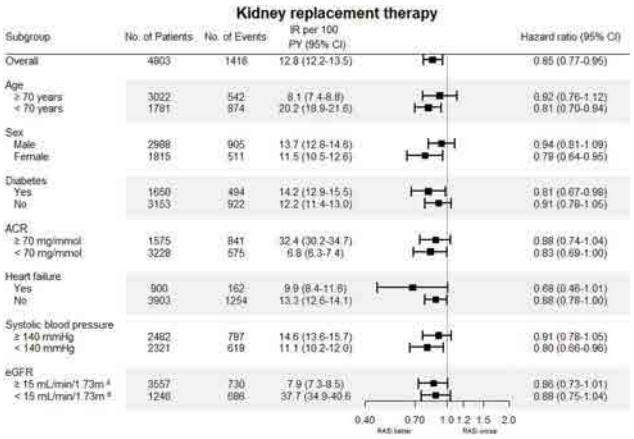


Figure: Number of events, incidence rates and adjusted hazard ratios for KRT according to subgroups of age, sex, diabetes, albumin-to-creatinine ratio (ACR), heart failure, systolic blood pressure and eGFR.

P0179 **ECULIZUMAB USE IN A TERTIARY CARE NEPHROLOGY CENTER**

Christof Aigner[1], Gunar Stemer[2], Martina Gaggl[1], Natalja Haninger-Vacariu[1], Zoltán Prohaszka[3], Raute Sunder-Plassmann[4], Renate Kain[5], Schmidt Alice[1], Gere Sunder-Plassmann[1]

[1]Medical University of Vienna, Department of Medicine III, Division of Nephrology and Dialysis, Wien, Austria, [2]Vienna General Hospital, Pharmacy Department, Vienna, Austria, [3]Semmelweis University, IIIrd Department of Medicine, Research Laboratory, Budapest, Hungary, [4]Medical University of Vienna, Department of Laboratory Medicine, Vienna, Austria and [5]Medical University of Vienna, Department of Pathology, Vienna, Austria

Background and Aims: Practice patterns of Eculizumab use in patients with thrombotic microangiopathies (TMA) and C3-glomerulopathy (C3G) are not well described.

Method: We used the "Vienna TMA cohort" and the hospital pharmacy database at the Medical University of Vienna to identify adult patients with a history of eculizumab use between 2012 and 2019. We describe clinical characteristics, details of eculizumab use, and outcomes of patients with complement gene variant mediated TMA (cTMA), secondary TMA (sTMA) and C3G.

Results: As of December 2019, 212 individuals were enrolled in the Vienna TMA cohort comprising 51 cTMA, 144 sTMA, and 17 TTP patients. We included also our cohort of 14 patients with C3G for this analysis. 47 patients (22 TMA and 2 C3G, 23 other indications, *i.e.* paroxysmal nocturnal haemoglobinuria) received at least one dose of eculizumab at the Medical University of Vienna (**Figure 1**). **Table 1** indicates demographic and clinical details of 15 cTMA (29.4% of all cTMA), 7 sTMA (4.9% of all sTMA) and 2 C3G (14.3% of all C3G) patients treated with eculizumab. 60% of cTMA patients showed a rare complement gene variant, while sTMA was ruled out in the remaining 40%. Causes of sTMA were bone marrow transplantation (BMT) (n=2), malignant hypertension, malignoma, systemic lupus erythematodes, antiphospholipid syndrome and lung transplantation (each n=1). One sTMA patient, a BMT recipient, had a donor with a thrombomodulin gene variant. Patients with cTMA had a greater delay from first diagnosis to treatment with eculizumab than the other groups and received maintenance therapy for a longer period of time. More female patients received eculizumab as compared to male patients. Chronic kidney disease stage improved in 60% and 43% of cTMA and sTMA patients, respectively. TMA relapses did not occur during administration of eculizumab. The 2 patients with C3G didn't respond to eculizumab in our center. Eculizumab therapy was stopped in 66% of patients with cTMA and in all patients presenting with sTMA or C3G. In general, eculizumab was well tolerated and we did not observe life threatening infections of our patients. Three adverse drug reactions included exanthema, liver injury, and hypertensive emergency. Two patients died during therapy with eculizumab (1 cTMA, 1 C3G,) and two after cessation of eculizumab therapy (1 cTMA, 1 sTMA) resulting in a mortality of 16.7%.

Conclusion: Improvement of CKD stage was achieved in 60% of patients with cTMA and in 43% of patients with sTMA. In our patients with C3G, eculizumab did not improve kidney function. In general, therapy with eculizumab was well tolerated.

Table 1. Characteristics of TMA patients treated with eculizumab

Characteristic	cTMA	sTMA	C3G
N	15	7	2
Age at diagnosis of TMA/C3G, years	27 (19-46)	30 (22-41)	51/26
Sex, female	12 (80%)	5 (71.4%)	2
Biopsy proven disease/ number of biopsies	13/13 (100%)	5/6 (83.3%)	2
Rare complement gene variant	9 (60%)	1 (14.3%)	0
PE/PI before 1st ECU use	12 (80%)	5 (71.4%)	0
Age at 1st ECU use	31 (24-46)	30 (27-40)	51/29
Dialysis at 1st ECU use	6 (40%)	4 (57.1%)	0
KTX at 1st ECU use	4 (27%)	0	0
Improvement of CKD stage during ECU	9 (60%)	3 (42.9%)	0
Number of ECU doses per patient	17 (8-70)	14 (4-24)	2/16
Duration of ECU therapy, months	6 (1-49)	4 (1-10)	1/8
CKD G stage at last follow up			
1	0	1 (14.3%)	0
2	1 (6.7%)	0	0
3	4 (26.7%)	2 (28.6%)	0
4	1 (6.7%)	2 (28.6%)	0
5	1 (6.7%)	0	1
5D	1 (6.7%)	1 (14.3%)	0
KTX	5 (33.3%)	0	0
Deceased	2 (13.4%)	1 (14.3%)	1 (50%)
TMA relapse during ECU use	0	0	-
AE related to ECU use	3 (20%)	0	0
Pregnancies during ECU use	2 (13.4%)	0	0
ECU discontinued	10 (66.6%)	7 (100%)	2
Weaning after response	5 (33.3%)	3 (42.9%)	0
Non-response	2 (13.3%)	4 (57.1%)	1
Other (*i.e.* patient preference, death)	3 (20%)	0	1
Lost to follow-up	0	1 (14.3%)	0

Data are given as median and inter quartile range or count and frequency

PE/PI, plasma exchange/plasma infusion; ECU, eculizumab; KTX, kidney transplantation; CKD, chronic kidney disease; G, GFR; D, dialysis; AE, adverse event.

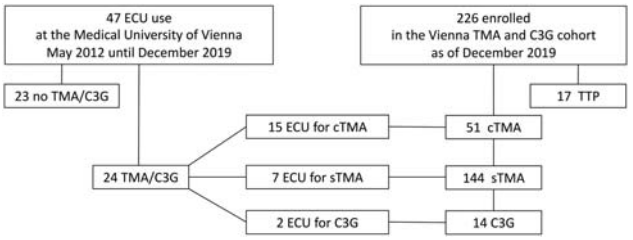


Figure: Patient disposition (ECU, eculizumab)

P0964 EFFECTS OF XANTHINE OXIDASE INHIBITORS AND DAPAGLIFLOZIN ON RENAL GLUCOSE AND URATE TRANSPORTERS IN METABOLIC SYNDROME

Hwee-Yeong Ng[1], Chien-Te Lee[1], Foong-Fah Leung[1], Yuai-Ting Lee[1]

[1]*Kaohsiung Chang Gung Memorial Hospital, Division of Nephrology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C.*

Background and Aims: Metabolic syndrome consists of several medical conditions that collectively predict the risk for cardiovascular disease. Hyperglycemia and hyperuricemia are the major disorders of metabolic syndrome. Kidney reabsorbs almost all filtrated glucose by active transport at normal concentrations of plasma glucose via members of the sodium glucose transport (SGLT) family. Besides, the kidney plays a pivotal role in handling uric acid homeostasis. Uric acid is mainly controlled by urate transporter (UAT), urate anion exchanger 1 (URAT1) and glucose transporter 9 (GLUT9). The aims of the study were to determine the alteration of renal glucose and uric acid transporters in animals with metabolic syndrome after treatment of xanthine oxidase inhibitors and SGLT2 inhibitor.

Method: Sprague-Dawley rats were fed with normal chow (Control) or high fructose diet (60%) for totally 6 months. For those animals fed with high fructose diet for 3 months, they were divided into 4 groups including high fructose diet without treatment (FR), treatment with allopurinol (150 mg/L in drinking water), with febuxostat (30 mg/L in drinking water) or with dapagliflozin (1mg/kg/day intraperitoneal injection). Blood, urine and blood pressure were collected and measured at the end of study. Gene and protein expression of renal glucose and uric acid transporters were determined by reverse transcriptase polymerase chain reaction. The changes of transporters were then confirmed by immunohistochemical staining.

Results: High-fructose diet induced higher levels of fasting glucose, insulin resistance index, uric acid, triglyceride and blood pressure in FR group (all $p < 0.05$ vs. control). Treatment of allopurinol, febuxostat and dapagliflozin reduced body weight significantly. Fasting glucose, insulin resistance index and hyperuricemia were improved in all drug treatment groups (all $p < 0.05$). In the kidney, high fructose diet significantly upregulated SGLT1, SGLT2 and GLUT2 but downregulated GLUT1 expression. Urate transporters, including GLUT9, UAT and URAT1 were also increased ($p < 0.05$). The improvement of insulin resistance by xanthine oxidase inhibitors was associated with suppression of renal SGLT1, SGLT2 and GLUT2 expression. Dapagliflozin alleviated hyperuricemia and induced uricosuria without affecting serum xanthine oxidase activity. Compared to FR, dapagliflozin significantly inhibited fructose-induced overexpression of GLUT9, UAT and URAT1 in the kidney.

Conclusion: Long term high fructose diet induced metabolic syndrome in rats. Treatment of xanthine oxidase inhibitors and dapagliflozin ameliorated components of metabolic syndrome. Both allopurinol and febuxostat improved insulin resistance in association with suppression of renal SGLT1, SGLT2 and GLUT2 expression. Although dapagliflozin and xanthine oxidase inhibitors reduced uric acid in different mechanisms, they shared a similar molecular changes in the kidney by downregulating GLUT9, UAT and URAT1 expression.

P0965 CAN EMPAGLIFLOZIN BE A CANDIDATE FOR THE ROLE OF A UNIVERSAL CARDIO- AND NEPHROPROTECTIVE DRUG IN CHRONIC HEART FAILURE WITHOUT DIABETES MELLITUS?

Sergey Okovityy[1], Dmitry Ivkin[1], Marina Krasnova[1], Andrey Karpov[4], Galina Ivanova[5], Olga Beresneva[6], Elena Kashina[7], Mikhail Zaraiski[8], Olga Galkina[9], Marina Parastaeva[9], Mokhamad Khasun[9], Ivan Kayukov,[9], Alexei Smirnov[10], Aleksander Kulikov[10]

[1]St. Petersburg state chemical-pharmaceutical university, Center of experimental pharmacology, St. Petersburg, Russia, [4]VA Almazov Federal medical research center, St. Petersburg, Russia, [5]Pavlov Institute of Physiology Russian Academy of Sciences, Laboratory of Physiology of Cardiovascular and Lymphatic Systems, St. Petersburg, Russia, [6]Pavlov First St. Petersburg State Medical University, Institute of Nephrology, St. Petersburg, Russia, [7]Charité-Universitätsmedizin Berlin, Institute of Pharmacology, Center for Cardiovascular Research, Berlin, Germany, [8]Pavlov First St. Petersburg State Medical University, Department of Clinical Laboratory Diagnostics, St.-Petersburg, Russia and [9]Pavlov First St. Petersburg State Medical University, Institute of Nephrology, St. Petersburg, Russia

Background and Aims: The multi-system nature of chronic heart failure (CHF) requires therapeutic approaches and medications that can have pleiotropic effects. For example, it is desirable that drugs for the treatment of CHF have direct cardio- and nephroprotective effects. These conditions are largely met by angiotensin converting enzyme (ACE) inhibitors and, possibly, inhibitors of the membrane sodium/glucose cotransporter (SGLT-2) inhibitors. The study aimed to investigate the effects of the SGLT2 inhibitor empagliflozin on CHF in normoglycemic rats. The effects of empagliflozin were compared with the standard medications for CHF - ACE inhibitor fosinopril, which has cardio - and nephroprotective effects in CHF.

Method: Myocardial infarction (MI) was induced in male Wistar rats via permanent ligation of the left descending coronary artery. One-month post MI 30 animals were randomized into 3 groups (n=10): vehicle-treated, empagliflozin (1.0 mg/kg) and fosinopril (10 mg/kg). One month after surgery all medications administered *per os* daily for 3 months. Echocardiography, 24-hour urine volume test, albuminuria, proteinuria or miRNA-21 expression in urine and treadmill exercise tests (0.7 m/sec and the slope angle 15°) were performed at the beginning and at the end of the study.

Results: At the finish of the study (4 months after MI - 3 months on treatment) all empagliflozin treated animals survived, one animal died in vehicle group and 3 animals in the fosinopril group. In vehicle group sizes of the left ventricle (LV) increased and the ejection fraction (EF) decreased in comparison with the initial values. Rats of fosinopril group confirm well known beneficial effect ACE inhibitors on cardiac remodeling and function; LV sizes and EF didn't change except 2 atrial dimensions enlargement. Treatment with empagliflozin slowed the progression of left ventricular dysfunction: LV sizes and EF didn't change and the minute volume significantly increased (from 52,0±15,5 ml/min to 61,2±21,2 ml/min) as compared to baseline.

Moreover, empagliflozin exhibited maximal physical exercise tolerance in comparison with all groups (289 ± 27 sec versus 183 ± 61 sec in fosinopril group, p=0,0035 for multiple comparisons). Recently, using this model of CHF in the normoglycemic rats we have found that SGLT2 inhibition for 3 months increased the tolerance to physical exercise. This effect was associated with an improvement of cardiac function as demonstrated by increased stroke volume, minute volume and LV ejection fraction as well as with the improvement of renal function.

In rats of empagliflozin group 24-hour urine volume (9.8±0.92 ml) was slightly but not significantly higher than in the vehicle (6.9±1.25 ml) and in the fosinopril group (7.39±0.53 ml); p=0,09 for multiple comparisons. So, it could be suggested that other mechanisms apart from SGLT2 inhibition in kidneys and decrease of the volume overload are involved in protective action of empagliflozin. In any case, due to increased water and sodium excretion empagliflozin treatment can lead to *decreased* cardiac *preload*. There were no significant differences in levels of albuminuria and proteinuria or miRNA-21 expression in urine in groups with and without empagliflozin.

Conclusion: Sodium-glucose co-transporter 2 inhibitor empagliflozin reduced progression of left ventricular dysfunction and improved tolerance of physical exercise in normoglycemic rats with HF. Empagliflozin treatment compared with fosinopril was superior in respect of physical tolerance and not inferior in terms of nephroprotective action. Taking into account the obtained results one can be considered empagliflozin as a potential universal cardionephroprotector.

P0966 **PLACENTAL GROWTH FACTOR DEFICIENCY AGGRAVATES DIABETIC NEPHROPATHY**

Ji Hee Lim[1], Yaeni Kim[1], Eun Nim Kim[1], YONGJIE JIN[1], Hyung Duk Kim[1], Tae Hyun Ban[1], Bum Soon Choi[1], Cheol Whee Park[1]

[1]Division of Nephrology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South

Background and Aims: Placental growth factor (PlGF) is a member of the vascular endothelial growth factor (VEGF) family. PlGF exerts favorable angiogenetic and lymphangiogenic activity by binding to VEGF-R1 and -R3, respectively. Due to its functional synergy with VEGF-A, it is required for a correct neovascularization during pathological conditions while inactivation of PlGF contributes to decrease of pathological angiogenesis. Because reduced angiogenesis and lymphagiogenesis that contribute to defective lipid drainage are implicated in the progression diabetic kidney disease, we investigated the role of PlGF in the development of diabetic nephropathy by using PlGF-knockout mice.

Method: Diabetes was induced by a low-dose streptozotocin injection in 9-week-old male C57BL/6J PlGF-KO and wild-type mice and biochemical and morphological parameters were examined at 12 weeks later.

Results: In diabetic PlGF-KO mice, fasting blood glucose and HbA1c levels increased significantly and the development of glomerular sclerosis and mesangial area expansion were accompanied by albuminuria. Diabetic PlGF-KO mice exhibited increased expression of type IV collagen, transforming growth factor-β1 and glomerular IHC staining for nephrin, PECAM-1 and WT-1-positive cells and VEGF-R1,-R2,-R3 expression decreased, suggesting decreased endothelial cell and podocyte structure. Intrarenal expression of pLKB1, and pAMPK decreased and that of PPARα, PGC1α, ERRα, p-eNOS, and urinary Nox concentration decreased while iNOS increased, indicating disturbed lipid metabolism and endothelial dysfunction in the same group. Increased intrarenal FFA, TG, and cholesterol concentration represents presence of lipid accumulation. F4/80- and TUNEL-positive cells increased, suggesting increased inflammatory cell infiltration and apoptosis. CD68 and arginase-II increased indicating that macrophage subtype M1 polarization is involved in the inflammatory process. Expression of Bcl2/bax decreased and that of SOD1 and 2 decreased, indicating increased apoptosis and oxidative stress, respectively. Increased expression of intrarenal 8-OHdG and urinary isoprostane level indicates increased oxidative stress.

Conclusion: Impaired angiogenesis and lymphangiogenesis are implicated in PlGF deficiency and this promotes lipotoxicity-induced inflammation, oxidative stress and deteriorates renal functional and phenotypic parameters in the diabetic kidney.

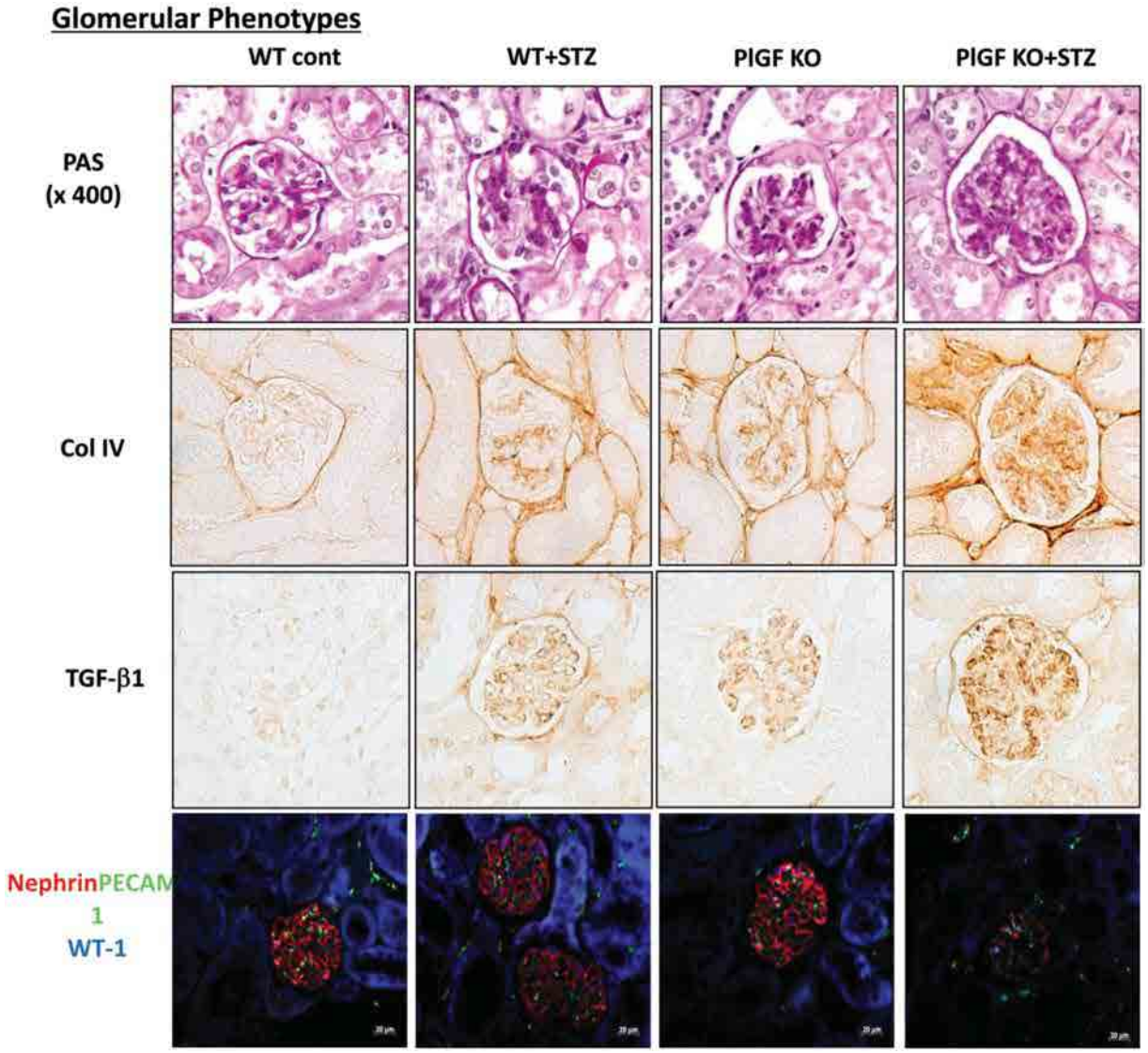


Figure:

P0967

ENHANCING PODOCYTE REGENERATION WITH BROMOINDIRUBIN-3′-OXIME (BIO) AS A POTENTIAL TERAPEUTIC TARGET IN DIABETIC KIDNEY DISEASE.

Irene Mesas[1], Monika Swiederska[1], Hans-Joachim Anders[1], Lidia Anguiano[1]

[1]*Medizinische Klinik und Poliklinik IV, Klinikum der Universität München, Nephrologisches Zentrum, Munich, Germany*

Background and Aims: Diabetic nephropathy (DN) is a leading cause of end-stage kidney disease. RAS and SGLT2 inhibitors are well established in reducing the progression of DN in early stages but true tissue regeneration is not achieved. BIO, a glucose synthase kinase 3 inhibitor (GSK3β), improves outcomes in non-diabetic kidney injury by enhancing podocyte regeneration from local podocyte progenitors. We hypothesized that treating podocytes in hyperglycemic conditions with BIO could revert the oxidative stress damage typically seen in DN.

Method: To study the effect of BIO on podocytes, we isolated glomeruli from wildtype mice by perfusing them with magnetic beads and stimulated the purified glomeruli for 24 hours with or without 10μM BIO in presence or absence of 30mM glucose. The response to the stimuli was assessed by characterizing the overall gene expression via RT-qPCR. Additionally, differentiated murine podocytes (K5P5) and murine glomerular endothelial cells (GEnCs) were stimulated under the same conditions with the same subsequent readouts to differentiate the response of podocytes from that of the endothelial compartment.

To understand, if BIO could represent a potential new therapeutic option under the aspect of pharmacological safety, we uninephrectomized male BKS-Lepr$^{-/-}$ mice, fed them with a salt-free chow to induce DN. To mimic the human condition more closely we treated the mice with and without BIO, but in presence of the human standard of care therapy (SOC; metformin, ramipril, empagliflozin), which could potentially identify adverse pharmacological interactions. After 16 weeks kidney, heart, pancreas, sciatic nerve, liver, blood, skeletal muscle and adipose tissue were collected for histopathological and gene expression analysis.

Results: While glucose exposure induced a strong reduction of nephrin gene expression in whole glomeruli, BIO reverted the effect, indicating a protective effect on podocytes (30 mM glucose: 0.447, ci 0.224 – 0.724; 30 mM glucose+BIO: 1.837, ci 1.205 – 2.505, p-value=0.029, Fig.A). Similar results were found in differentiated murine podocytes, in which BIO treatment significantly increased podocin gene expression after 7 days of culture (0.920, ci 0.820 – 1.34, 3.561 ci 1.756 – 7.909, p-value=0.029), also here suggesting a protective effect of BIO on glucose-induced podocyte (Fig.B). In contrast, BIO showed no effect on endothelial cell-specific markers in murine GEnCs, indicating a podocyte-specific effect of BIO.

A comparable effect of BIO on podocytes was observed in vivo, as well. Diabetic mice treated with SOC and BIO showed borderline increased renal podocin gene expression levels (2.177 ci 0.830 – 2.739) compared to SOC alone (1.188 ci 0.378 – 2.194 ,p-value = 0.064), but did not modify markers of inflammation, such as IL-6, or fibrosis, such as fibronectin (Fig.C). The extended safety analysis of non-renal organs did not reveal any safety concern of the SOC/BIO combination in comparison to SOC alone in any of the analyzed tissues.

Conclusion: The current study revealed that BIO has protective effects on podocytes in vitro and might as well have renoprotective effects in DN in vivo by enhancing podocyte regeneration without showing any safety-related issues.

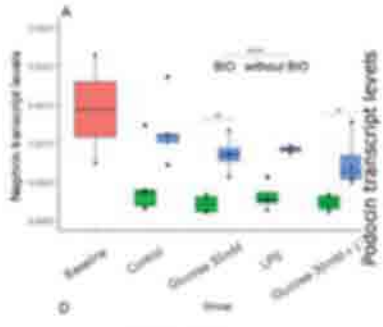


Fig. A

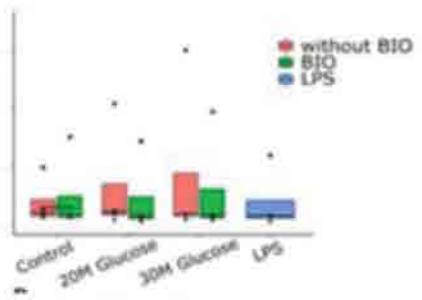


Fig. B

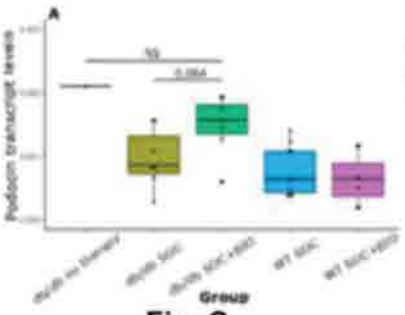


Fig. C



Fig. D

Fig. A Isolated glomeuli Nephrin mRNA/ 18S mRNA
Fig B. Podocytes -Podocin mRNA/ 18S mRNA
Fig. C Kidney tissue-Podocin mRNA/ 18S mRNA
Fig. D Isolated Glomeruli

Figure:

P0968 **THE INFLUENCE OF ALPHA KLOTHO ON NPP1 ACTIVITY IN CULTURED RAT PODOCYTES.**

Agnieszka Piwkowska[1,2], Irena Audzeyenka[1,2], Dorota Rogacka[1,2]

[1]Mossakowski Medical Research Centre Polish Academy of Sciences, Laboratory of Molecular and Cellular Nephrology, Warsaw, Poland and [2]University of Gdańsk, Department of Molecular Biotechnology, Gdańsk, Poland

Background and Aims: Kidney is the principal contributor to circulating αKlotho (αKL), and simultaneously, constitutes the major organ where circulating αKlotho is taken up from the circulation. Klotho is mainly expressed in proximal renal tubule and in distal tubular epithelium. In the kidney soluble αKlotho acts from the urinary luminal side as an autocrine or paracrine enzyme to regulate transporters and ion channels. Recently, it has been demonstrated that the glomerulus is another source of αKlotho production.

NPP1 is the best characterized nucleotide pyrophosphatases/phosphodiesterases (NPP) family member, encoded by the ENPP1 gene, and is a type II transmembrane glycoprotein that forms disulfide-bonded homodimers in the plasma membrane and in the mineral-depositing matrix vesicles. The major function of NPP1 is generation of PPi from adenosine triphosphate (ATP). Recently, we demonstrated that extracellular nucleotides stimulate an increase in glomerular albumin permeability, in part due to glomerular NO production and actin reorganization in podocytes . Furthermore, both αKlotho and NPP1 regulate insulin-dependent signaling. Thus, a key aim of this study is to fully examine the role of αKlotho on NPP1 function and its role in the protection of glomerular filtration barrier and podocyte function in diabetes.

Method: We measured glomerular permeability to albumin (P_{alb}) in a single isolated rat glomerulus based on the video-microscopy method and permeability to albumin across the podocyte monolayer. Expression of αKlotho and NPP1 was confirmed in podocytes using Western blotting and immunofluorescence. Ecto-nucleotide pyrophosphatase/phosphodiesterase activity in podocytes was assessed using p-nitrophenyl-5′-thymidine monophosphate (p-Nph-5′-TMP) as a substrate. The ATP concentration was measured using luciferin-luciferase reaction.

Results: Since NPP1 and Klotho regulate insulin-dependent signaling we investigated the role of Klotho on NPP1 dimerization and NPPs activity. Podocyte treatment withαKlotho (0.5 nM, 30 min) in non-reducing conditions (maleimide, 100 mM) increased the disulfide bond formation of NPP1 (Fig. 1A). The percentage of dimerized (260 kDa) NPP1 increased approximately by 45%. This effect was abolished in the presence of ATP (100 μM, 30 min). As a positive control, we used hydrogen peroxide (100 μM, 5 min) which induces oxidative disulfide bond formation (Fig. 1A). We also demonstrated time-dependent decrease of NPPs activity in the presence of αKL (Fig. 1B). Klotho also induces an increase of extracellular ATP concentration by 76% (from 3.19±0.01 to 5.62±0.43, n=6, P<0.05). Moreover, we confirmed the role of soluble αKlotho in ATP-evoked increases of glomerular and podocyte albumin permeability.

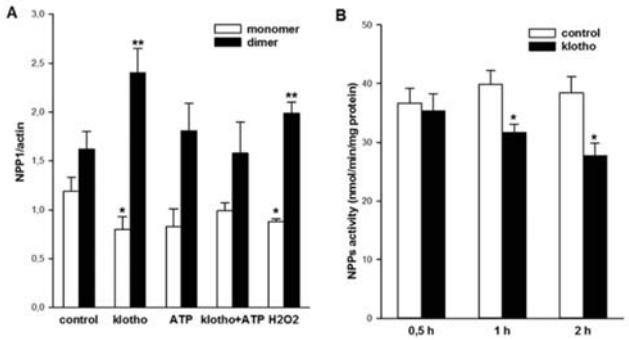


Fig.1. The role of αKlotho on NPP1 dimerization (A) and NNP1 activity (B) in cultured rat podocytes. Results from five experiments are shown as mean ± SEM. *P<0.05 *vs.* appropriate control; **P<0.05 *vs.* control of dimerized form.

Conclusion: Summarizing, we have clearly demonstrated an interaction between αKL and NPP1 in podocytes. Moreover, we observed the protective role of αKlotho in podocyte permeability to albumin.

P0969

PARKIN INHIBITS THE PROGRESSION OF DIABETIC NEPHROPATHY BY PROMOTING GATA4 DEGRADATION TO REDUCE THE SENESCENCE OF RENAL TUBULAR CELLS

Kehong Chen[1], Jia Chen[1], Yani He[2]

[1]*Daping Hospital, Army Medical University, Nephrology, Chongqing, P.R. China and*
[2]*Daping Hospital, Army Medical University, Nephrology, P.R. China*

Background and Aims: Diabetic nephropathy (DN) can cause end-stage renal disease. During the progression of DN, hyperglycemia accelerates the senescence of renal tubular epithelial cells (RTECs), leading to the tubulointerstitial inflammation and fibrosis. E3-ubiquitin ligase Parkin can regulate several pathophysiological processes. This study explored the role and mechanisms of Parkin in the progression of diabetic nephropathy (DN).

Method: 149 cases of patients with DN diagnosed by renal biopsy were recruited in our study. 32 normal kidney samples were obtained from renal carcinoma as control. Renal Parkin expression was detected by immunohistochemistry. The correlation between Parkin expression and renal pathological injury scores, renal function injury parameters were analyzed. In vivo, we generated Parkin overexpressed streptozotocin-induced DN mice using ultrasound- mediated adenovirus transfection. In vitro, knockdown and overexpression experiments were performed by parkin siRNA or Parkin overexpressed adenovirus in high glucose (HG) stimulated mouse primary RTEC. Moreover, we used co-immunoprecipitation and pull down experiments to evaluate the interaction of GATA4 with parkin.

Results: We found that Parkin expression gradually decreased and was inversely associated with IL-6, TGF-β1 and GATA4 expression in the kidney during the progression of DN. Parkin over-expression (OE) reduced inflammation, fibrosis, premature senescence of RTECs and improved renal function while Parkin knockout (KO) had opposite effects in DN mice. Parkin-OE decreased GATA4 protein, but not its mRNA transcripts in the kidney of DN mice and high glucose (HG)-treated RTECs. Immunoprecipitation indicated that Parkin directly interacted with GATA4 in DN kidney. Parkin-OE enhanced GATA4 ubiquitination. Furthermore, Parkin-KO up-regulated growth arrest specific gene 1 (GAS1) expression in renal tubular tissues of DN mice and GATA4-OE enhanced the HG-up-regulated GAS1 expression in RTECs. Conversely, GAS1-OE mitigated the effect of Parkin-OE on HG-induced P21, IL-6 and TGF-β1 expression in RTECs. These results indicate that Parkin inhibits the progression of DN by promoting GATA4 ubiquitination and downregulating the GATA4/GAS1 signaling to inhibit premature senescence, inflammation and fibrosis in DN mice. Thus, these findings uncover new mechanisms underlying the action of Parkin during the process of DN.

Conclusion: Parkin inhibited the progression of DN by promoting GATA4 ubiquitination and downregulating the GATA4/GAS1 signaling to inhibit premature senescence, inflammation and fibrosis. Our findings uncover a novel endogenous protective mechanism by which Parkin regulates the senescence of RTECs, inflammation and fibrosis during the pathogenesis of DN.

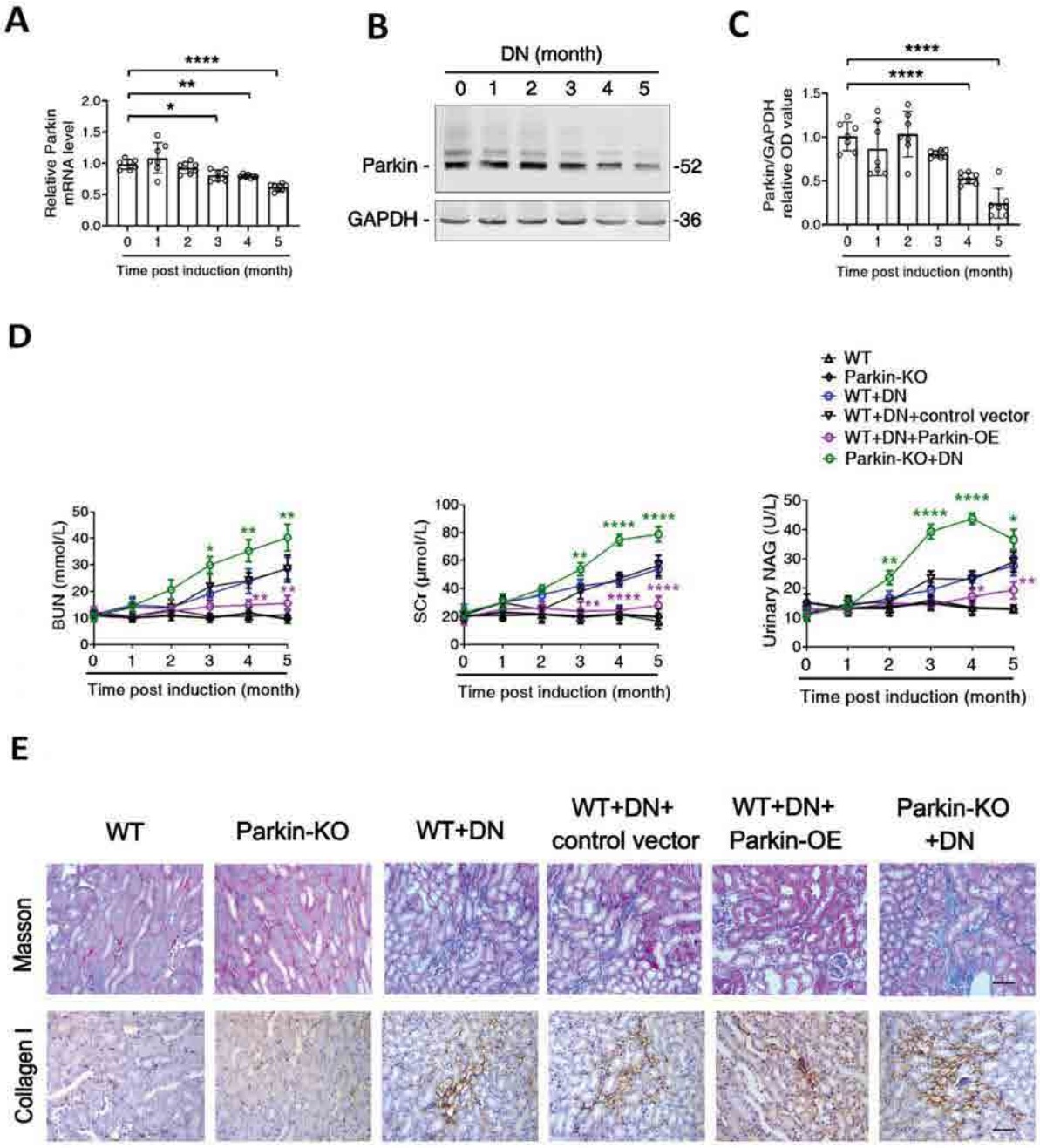

A
Relative Parkin mRNA level
Time post induction (month)
B
DN (month)
0 1 2 3 4 5
Parkin -
-52
GAPDH -
-36
C
Parkin/GAPDH relative OD value
Time post induction (month)
D
WT
Parkin-KO
WT+DN
WT+DN+control vector
WT+DN+Parkin-OE
Parkin-KO+DN
BUN (mmol/L)
SCr (μmol/L)
Urinary NAG (U/L)
Time post induction (month)
E
WT
Parkin-KO
WT+DN
WT+DN+ control vector
WT+DN+ Parkin-OE
Parkin-KO +DN
Masson
Collagen I

Figure:

P1000 URINE MYO-INOSITOL AS A NOVEL PROGNOSTIC BIOMARKER FOR DIABETIC KIDNEY DISEASE

Chun Soo Lim[1,2], Soie Kwon[2], Jung Pyo Lee[1,2]

[1]Seoul National University Boramae Medical Center, Department of Internal Medicine, Seoul, Korea, Rep. of South and [2]Seoul National University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Diabetic kidney disease (DKD) is a leading cause of chronic kidney disease (CKD) and end-stage kidney disease (ESRD). Metabolomics has been increasingly applied to identify the cause of CKD, as it can present epigenetics and suggest corresponding treatment options. Only a few metabolomics studies were conducted in DKD patients, and the results are inconclusive. We investigated the association between urine metabolites and renal disease progression and mortality in DKD, using 800 MHz NMR spectroscopy based targeted metabolomics profiling.

Method: Prospectively stored urine samples from consecutive patients with DKD stage 1 to 5 (n=208) and their healthy controls (n=26) were analyzed. Cross-sectional associations were evaluated between eGFR or urine protein creatinine ratio (UPCR) and 26 urinary metabolites. Multivariable adjusted Cox models were conducted for the risk prediction of ESRD and mortality. The receiver-operating characteristic (ROC) analyses were used to assess the additive effect of each metabolite to predict the progression to ESRD.

Results: ESRD occurred in 103 (44.0%) patients and 65 (27.8%) deaths occurred during median 4.5 years (IQR, 2.06–6.58) follow-up period. The median fold change in 9 metabolites (glucose, mannose, myo-inositol, glycerol, lactate, fumarate, creatine, taurine and choline) in patient group revealed a trend corresponding to DKD stages. Linear regression showed that myo-inositol had a strongest association with eGFR. The relationship between the competitive metabolites and outcomes (ESRD and mortality) was investigated by multivariate Cox models after adjusting for the baseline covariates. Of these, 4 metabolites (myo-inositol, glycerol, fumarate, oxoisocaproate) had predictive values for ESRD, and among them, only myo-inositol retained predictive significance in mortality (adjusted HR 1.004, 95% confidence interval 1.002-1.006, $P < 0.001$). At ROC analysis, urinary myo-inositol had additive effect to serum creatinine concentration and UPCR in the prediction for ESRD progression (NRI = 2.9%, P = 0.03; IDI = 35.1%, P = 0.02).

Conclusion: These results suggest that myo-inositol can be a predictive biomarker for the risk of ESRD progression and mortality in DKD. Further studies are needed to elucidate the pathophysiological roles of myo-inositol in DKD.

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10.1093/ndt/gfaa142

ACID-BASE AND URIC ACID

P0001

EFFECTS OF VEVERIMER ON SERUM BICARBONATE AND PHYSICAL FUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND METABOLIC ACIDOSIS ARE INDEPENDENT OF ALBUMINURIA: SUBGROUP ANALYSES FROM A RANDOMIZED TRIAL

Donald E. Wesson[1], Vandana Mathur[2], Navdeep Tangri[3], Yuri Stasiv[4], Dawn Parsell[4], Elizabeth Li[5], Gerrit Klaerner[4], David Bushinsky[7]

[1]Baylor Scott & White All Saints Medical Center - Temple, Temple, United States of America, [2]MathurConsulting, Nephrology/Clinical Research, Woodside, United States of America, [3]University of Manitoba, Winnipeg, Canada, [4]Tricida, Inc., South San Francisco, United States of America, [5]PharmaStat, LLC, Newark, United States of America and [7]University of Rochester, Rochester, United States of America

Background and Aims: Veverimer, an investigational, novel, orally-administered, non-absorbed polymer that binds gastrointestinal hydrochloric acid and results in an increase in serum bicarbonate, is being developed as a treatment for metabolic acidosis in patients with chronic kidney disease (CKD). Metabolic acidosis is a complication of CKD that has deleterious effects on kidney function, bone (demineralization), and muscle (protein catabolism).[1] Albuminuria and metabolic acidosis are independently associated with CKD progression and treatment of each may reduce the risk of kidney failure.[2,3] We sought to assess (post-hoc) if albuminuria impacts the ability of veverimer to increase serum bicarbonate level and improve physical functioning.

Method: TRCA-301E is a multicenter, Phase 3, randomized, blinded, placebo-controlled trial in 196 patients with CKD (eGFR 20 - 40 ml/min/1.73 m^2) and metabolic acidosis (serum bicarbonate 12 - 20 mEq/L) who were treated for up to 1 year with veverimer (previously TRC101) or placebo, with dose titration targeted to achieve a normal serum bicarbonate. [4] The randomization was performed in a ratio of 4:3 (veverimer:placebo).

Results: We previously reported[4] that, compared with placebo, veverimer significantly increased serum bicarbonate and significantly improved physical function as reported on the Kidney Disease and Quality of Life-Physical Function Domain (KDQOL-PFD) (e.g., walking several blocks, climbing stairs) and as measured objectively using the 5-times repeated chair stand test with a safety profile that was similar to placebo. Baseline characteristics of the subgroups of patients by baseline urine albumin to creatinine ratio (UACR) $\leq$ 300 vs. >300 mg/g are shown in the Table.

Neither albuminuria (log UACR) as a continuous covariate nor the presence of UACR > 300 mg/g had an effect on the efficacy of veverimer treatment in correction of acidosis or improvement of physical function (interaction p-values >0.4).

In patients with UACR > 300 mg/g, at Week 52, serum bicarbonate increased by 4.1 (0.5) mEq/L on veverimer (p = 0.047 vs. placebo) and a significantly higher percentage (vs. placebo) had a $\geq$ 4 mEq/L increase or normalization of serum bicarbonate (59% vs. 30%, p = 0.014). Patient-reported limitations of physical function (KDQOL-PFD) improved in the veverimer vs. placebo group (+10.4 vs. +1.2 seconds, respectively, p = 0.034). Objective physical performance on the chair stand test at Week 52 also improved in the veverimer group vs. placebo (p < 0.001).

In patients with UACR $\leq$ 300 mg/g, at Week 52, serum bicarbonate increased by 5.2 (0.5) mEq/L on veverimer (p = 0.003 vs. placebo) and a numerically higher percentage (vs. placebo) had a $\geq$ 4 mEq/L increase or normalization of serum bicarbonate (65% vs. 45%, p = 0.063). KDQOL-PFD improved in the veverimer vs. placebo group (+12.5 vs. -2.8 seconds, respectively, p = 0.001). The chair stand test at Week 52 also improved in the veverimer group vs. placebo (p = 0.002).

Conclusion: The drug candidate veverimer effectively treated metabolic acidosis and improved the ability to repeatedly stand from a seated position and physical function related to daily activities independent of albuminuria, and therefore independent of the kidney injury reflected by albuminuria.

	UACR $\leq$ 300 mg/g	UACR > 300 mg/g
N	100 (veverimer: 59; placebo: 41)	92 (veverimer: 53; placebo: 39)
Age (years) [a]	65.1 (11.2)	59.3 (12.1)
Male (%)	51	71
Baseline eGFR (mL/min/1.73 m^2) [a]	30.0 (6.0)	27.5 (6.0)
Baseline UACR (mg/g) [b]	59.2 (46.2, 75.9)	1142.0 (957.4, 1362.2)
Baseline serum bicarbonate (mEq/L) [a]	17.2 (1.5)	17.2 (1.4)
Background oral alkali (%)	8.0	9.8
Baseline ACE inhibitors or ARBs (%)	72	74
Diabetes (%)	57	75
Congestive heart failure (%)	36	24

[a]Mean (SD)

[b]Geometric mean (95% CI)

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P0002

A NEW INSIGHT INTO THE MECHANISM OF HYPERCHLOREMIC METABOLIC ACIDOSIS IN KIDNEY TRANSPLANT RECIPIENTS: INCREASED POSTGLOMERULAR PERITUBULAR BLOOD FLOW IS A KEY CONDITION FOR THE DEVELOPEMENT OF CALCINEURIN INHIBITOR-INDUCED RENAL TUBULAR ACIDOSIS

Shuzo Kaneko[1], Joichi Usui[1], Kazuhiro Takahashi[2], Tomokazu Kimura[3], Akio Hoshi[3], Hiroyuki Nishiyama[3], Tatsuya Oda[2], Kunihiro Yamagata[1]

[1] University of Tsukuba, Nephrology, Tsukuba, Japan, [2] University of Tsukuba, Gastroenterological and Hepatobiliary Surgery and Organ Transplantation, Tsukuba, Japan and [3] University of Tsukuba, Urology, Tsukuba, Japan

Background and Aims: Hyperchloremic metabolic acidosis (HCMA) due to renal tubular acidosis is a common complication in kidney transplant recipients(KTR). Potential renal dysfunction, rejection, ischemia, persistent hyperparathyroidism, calcineurin inhibitors (CNIs), etc. have been identified as causes but have not been fully proven, and whether HCMA is a determinant of poor graft prognosis in KTR is still controversial. The purpose of this study is to elucidate the actual mechanism of HCMA in KTR.

Method: HCMA was defined as follows: i) simple strong ion difference (SID) Na-CL, which is the most dominant metabolic factor in physicochemical approach for acid-base balance, is 34 or less, or â. . .±) the alkalizing drugs have been started after the KT to correct HCMA. And all the cases of having diarrhea from mycophenolate mofetil(MMF), and gastroenterocolitis from cytomegalovirus infection were excluded. The study group consisted of 47 KTRs who underwent living-kidney transplantation(KT) at our hospital as well as a control group of 43 of the matched donors. Among them, a total of 26 KTRs received the renal hemodynamic studies which were based on urinary clearance of inulin and para-aminohippuric acid 1year after KT. 1) The incidence of HCMA in KTR at 3 months(3m) and 1 year(1y) after KT were examined. 2) To elucidate factors related to HCMA in KTR at 1y, we comprehensively examined factors and compared HCMA groups with non-HCMA groups; donor and recipient background (gender, age, body size), immunological factors, information on transplant surgery, salt and protein intake, effective buffering factors for extracellular body fluids such as albumin and hemoglobin, serum calcium and phosphate concentrations and their ratios, administration of renin-angiotensin system inhibitors and diuretics,Tac trough level and Banff score of each histopathological lesion in 1y biopsy. As for the 26 KTRs who received the renal hemodynamic studies, glomerular filtration rate (GFR), renal plasma flow (RPF), filtration fraction(FF) (GFR/RPF) and pre-/post-glomerular vascular resistance (pre-/postVR) calculated from the Gomez' equations were also analyzed.

Results: 1) The incidence of HCMA in the KTR at 3m was 51% (24/47), which was much higher than the 6.9% (3/43) in those donors ($p<0.001$), and the range of odds ratios (vs donor) adjusted by the background factors (age,gender, estimated GFR, albumin and hemoglobin) was 6.7-15.7 (p=0.0001-0.001). The incidence of HCMA in KTR at 1y decreased to 34%. 2)The univariate analysis of HCMA in KTR at 1y compared with non-HCMA showed an increase in RPF (p= 0.016), a decrease in post-VR (p= 0.003), and a decrease in FF (p= 0.0001), suggesting an increase in post-glomerular peritubular blood flow. In addition, the aah lesion score, an indicator of CNI vasculopathy, was also significantly higher in the HCMA (p = 0.015). There was no difference in Tac trough levels between HCMA and nonHCMA, and no independent factors were found by multivariate analysis. All cases with HCMA were classified into low post-VR (Fig.1). Furthermore, in low post-VR alone (n= 15), the Tac trough level at 1y was significantly higher in the HCMA (p= 0.002) (Fig.2).

Conclusion: In kidney transplant recipients, increased post-glomerular peritubular blood flow is a key condition for the development of CNI-induced renal tubular acidosis. The presence of HCMA suggests that it is probably not a serious condition, but rather a desirable hemodynamic state, however, more attention should be paid not to elevate CNI concentration levels in such conditions.

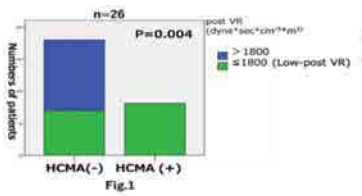


Fig.1

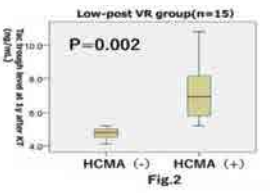


Fig.2

Figure:

P0003

ADHERENCE BENEFITS OF ADV7103, AN INNOVATIVE PROLONGED-RELEASE ORAL COMBINATION PRODUCT, IN PATIENTS WITH DISTAL RENAL TUBULAR ACIDOSIS

Aurélia Bertholet-Thomas[1], Catherine Guittet[2], Maria Asunción Manso-Silván[2], Victor Navas Serrano[3], Luc André Granier[2], Pierre Cochat[1]

[1]Centre de référence des Maladies rénales rares – Néphrogones – Hôpital Femme Mère Enfant, Hospices Civils de Lyon, Bron, France, [2]Advicenne, Nîmes, France and [3]Advicenne, Madrid, Spain

Background and Aims: Distal renal tubular acidosis (dRTA) is a rare disorder leading to impaired net acid excretion by the kidney inducing hyperchloremic metabolic acidosis and hypokalemia. The therapeutic effect of the standard of care is of short duration and requires multiple day and night administrations; it is also often accompanied by gastrointestinal discomfort and poor palatability impacting medication adherence. ADV7103, the first advanced therapy for dRTA, consists of a combination of prolonged-release potassium citrate and prolonged-release potassium bicarbonate granules providing round-the-clock alkali and potassium coverage with twice daily administration. Long-term adherence with ADV7103 is reported, along with acceptability of the product.

Method: B22CS is a multicentre, open-label long-term extension study, evaluating safety, tolerability, acceptability and efficacy of ADV7103 in adult and paediatric patients with dRTA. Adherence was assessed at each study visit up to 24 months, based on accountability of study drug retrieval, laboratory results, and interview of the patients in a diary and expressed as the proportion of patients that presented adherence lower than 50%, between 50% and 74%, between 75 and 90%, and higher than to 90%. Treatment acceptability as well as quality of life of the patients and their parents were assessed using a 100-mm visual analogue scales (VAS).

Results: Table 1 shows the evolution of compliance between Month 6 and Month 24. Overall, of the 29 patients remaining in the study after 24 months, 18 (62%) had adherence rates >90%, 5 (17%) had adherence rates of 75-90%, 6 (21%) had adherence rates of 50-74%, and there were no patients with adherence <50%. Adherence was good in all age groups, with rates of ≥75% in 100% of adults, 63% of adolescents 85% of children, and 67% of infants and toddlers.

Compared to the alkalising treatments they had before the study, more than 80% of the patients perceived both the improvement of the formulation and of the number of daily doses at scores ≥ 75 mm. The overall improvement of quality of life reported by the patients was of 89 ± 19 mm and that reported by their parents was of 90 ± 14 mm after 24 months of treatment.

Conclusion: Adherence to treatment was maintained at a high level throughout the 24 months of the study confirming the good acceptance of ADV7103 therapy.

Table 1. Adherence over time by age group and overall at month 6 and month 24

Adherence	Adults >18 Y N=6	Adolescents 12-17 Y N=8	Children 4-11 Y N=13	Infants/toddlers 6M-3Y N=3	Overall N=29
	6 months				
>90%	2 (40)	5 (62.5)	11 (84.6)	1 (33.3)	19 (65.5)
[75-90%]	2 (40)	1 (12.5)	2 (15.4)	2 (66.7)	7 (24.1)
[50-74%]	1 (20)	1 (12.5)	0	0	2 (6.9)
<50%	0	1 (12.5)	0	0	1 (3.4)
	24 months				
>90%	4 (80)	2 (25.0)	10 (76.9)	2 (66.7)	18 (62.1)
[75-90%]	1 (20)	3 (37.5)	1 (7.7)	0	5 (17.2)
[50-74%]	0	3 (37.5)	2 (15.4)	1 (33.3)	6 (20.7)
<50%	0	0	0	0	0

N = number of patients; M = months; Y = years

P0004

REDUCED EXPRESSION OF PROXIMAL ACID-BASE TRANSPORT PROTEINS IN KIDNEY TRANSPLANT PATIENTS WITH METABOLIC ACIDOSIS

Anna Wiegand[1], Arezoo Daryadel[2], Pedro Henrique Imenez da Silva[2], Ariana Gaspert[3], Rudolf Peter Wuthrich[1], Carsten Wagner[2], Nilufar Mohebbi[1]

[1]University Hospital of Zürich, Division of Nephrology, Zürich, Switzerland, [2]University of Zurich, Institute of Physiology, Zürich, Switzerland and [3]University Hospital of Zürich, Institute of Pathology and Molecular Pathology, Zürich, Switzerland

Background and Aims: Metabolic acidosis (MA) is a frequent complication of chronic kidney disease and an independent risk factor for kidney disease progression and mortality. MA is highly prevalent after kidney transplantation (12%-58%)(1). However, there are scarcely any data available on the underlying pathomechanisms and in particular molecular mechanisms involved in metabolic acidosis after kidney transplantation. Thus, we wanted to investigate the expression of key acid base transport proteins in kidney biopsies of kidney transplant recipients with and without metabolic acidosis.

Method: We evaluated 22 kidney transplant biopsies including 9 biopsies from kidney transplant recipients (KTR) with MA, nine biopsies from KTRs without MA (control) and four biopsies from KTRs with MA that were consequently subjected to alkali therapy (Alkali therapy). Immunofluorescence staining was used to identify key renal acid-base transport proteins. Additionally, six control kidneys were analyzed. Immunofluorescence staining was used to identify key renal acid-base transport proteins along the nephron. In addition, RNA extraction and full RNA sequencing analysis of all biopsies –where available- was performed.

Results: In the proximal tubule, we observed reduced immunostaining for the sodium bicarbonate cotransporter NBCe1 (SLC4A4) in the MA group compared to the control and alkali group, whereas the alkali group demonstrated the strongest staining of all three groups. In the distal nephron, expression of the chloride/bicarbonate exchanger Pendrin (SLC26A4) and the B1 subunit of the V-ATPase (ATP6V1B1) were markedly stronger in the alkali and control group compared to the MA group.

Expression of other acid base proteins such as Renal ammonia transporter RhCG (SLC42A3), Carbonic Anhydrase II, Glutamate dehydrogenase, anion exchanger AE1 (SLC4A1) and the B2 subunit of the V-ATPase (ATP6V1B2) showed no difference among all groups. Interestingly, the B2 subunit was absent in the proximal tubule in transplant biopsies of all groups.

In kidney biopsies of transplant recipients with metabolic acidosis RNA abundance of NBCe1, CAII and Pendrin was lower while RhCG and B1 RNA counts were not different when compared to recipients without metabolic acidosis.

Conclusion: Our data demonstrate altered protein and mRNA expression of several key acid base transporters in kidney biopsies of transplant recipients with metabolic acidosis. Treatment with alkali may have the potential to reverse or prevent these changes in renal allografts after transplantation.

P0005

TIME-VARYING DIALYSATE BICARBONATE CONCENTRATIONS CAN REDUCE PEAK INTRADIALTIC SERUM BICARBONATE CONCENTRATIONS

Anna Ebinger[1], Jacek Waniewski[1], Jolanta Malyszko[2], Monika Wieliczko[2], Pietribiasi Mauro[1], John (Ken) Leypoldt[2]

[1]Nalecz Institute of Biocybernetics and Biomedical Engineering Polish Academy of Sciences, Warsaw, Poland and [2]Department of Nephrology, Dialysis and Internal Diseases, Warsaw Medical University,

Background and Aims: Hemodialysis (HD) treatments using bicarbonate-containing dialysis solutions can result in large intradialytic increases in serum bicarbonate concentration, potentially inducing intradialytic alkalemia. It has been suggested that a time-varying, compared with a constant, dialysate bicarbonate concentration may limit the intradialytic increase in serum bicarbonate concentration (Tobvin & Sherman, Semin Dial 2016). We tested this hypothesis using a mathematical model of bicarbonate transport during HD.

Method: We used the H^+ mobilization model describing bicarbonate transport during HD (Sargent et al, Semin Dial 2018) to compare intradialytic serum bicarbonate concentrations when using constant or time-varying dialysate bicarbonate concentrations that deliver the same total amount of buffer base to the patient during the HD treatment. We employed this model to evaluate different time-varying dialysate bicarbonate concentration profiles that started at a high value and then decreased as a step function with a 10-minute timing resolution. Dialysis time was 210 minutes, dialysis solutions were assumed to contain acetate at 3 mEq/L, and all kinetic parameters were assumed to be identical to those reported by Sargent et al (Semin Dial 2018). All results with time-varying dialysate bicarbonate concentrations were compared to a constant dialysate concentration of 32 mEq/L.

Results: Example results comparing time-varying (36.0 mEq/L for the initial 40 min, 31.2 mEq/L thereafter) and constant (32 mEq/L) dialysate bicarbonate concentrations are shown in the figure. The time-varying dialysate bicarbonate concentration lowered the peak intradialytic serum bicarbonate by 0.4 mEq/L for approximately one-half of the treatment. Similar reductions in the peak intradialytic serum bicarbonate concentration could be achieved if the initial high dialysate bicarbonate concentration was 37.6 mEq/L for 30 min or 40.8 for 20 min. The optimal initial high dialysate bicarbonate concentrations and the reduction in the peak intradialytic serum bicarbonate concentrations were somewhat dependent on the assumed patient-dependent H^+ mobilization coefficient.

Conclusion: We conclude that a time-varying dialysate bicarbonate concentration can lower the peak intradialytic serum bicarbonate concentrations while delivering the same total amount of buffer base to the patient. Whether this approach will yield improved patient outcomes requires further evaluation.

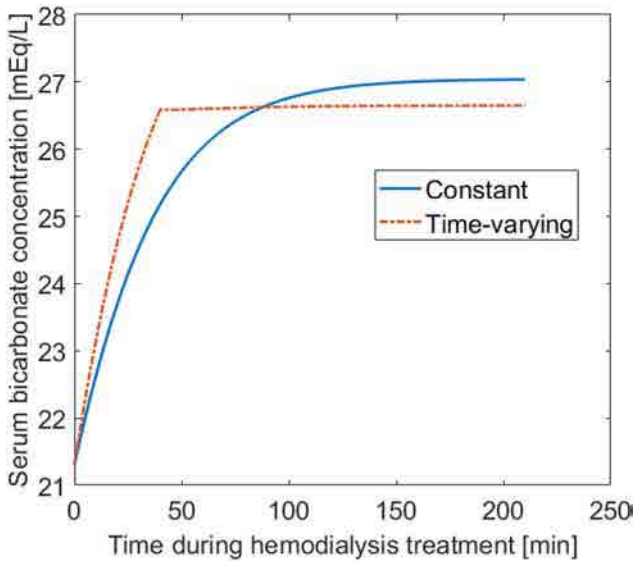


Figure 1

P0006 **THE DELTA GAP - AN UPDATED AND VALIDATED APPROACH TO MIXED ACID-BASE DISORDERS**

Chang Yin Chionh[1], Wenxiang Yeon[1], Chee Yong Ng[1], Cheng Boon Poh[1], Sreekanth Koduri[1], Alvin Kok Heong Ng[1], Roy Malakar Debajyoti[1]

[1]*Changi General Hospital, Department of Renal Medicine, Singapore, Singapore*

Background and Aims: The urea & electrolyte panel (U&E) is a basic test commonly performed in clinical medicine. A quick evaluation can often reveal the presence of acid-base disturbances which in turn flags up potentially serious physiologic disturbances and critical conditions.

While there are a few ways to screen for acid-base disorders, evaluation of the anion gap remains popular today. The AG is the difference between measured cations and anions and calculated from the main components of the U&E. For mixed acid-base disorders, the delta gap (ΔGap) provides further information (Table 1).

However, every test has a range within tolerance limits. The tolerance limit in turn depends on the precision of the laboratory methodology. Figure 1 illustrates how tolerance intervals are determined in a normal distribution.

To date, most clinical texts quote a tolerance interval of ±6 mEq/L for ΔGap, referencing the 1990 article by Dr Kieth Wrenn (Ann Emerg Med. 1990 Nov;19(11):1310). The range of ±6 mEq/L was calculated using the standard deviation (SD) of the tests for Na, Cl and bicarbonate in the 1980s, and an ΔGap > +6 or < –6 mEq/L suggests a mixed disorder.

Derivation of tolerance interval of ΔGap:

$\Delta Gap = \Delta AG - \Delta HCO_3^-$

$\Delta Gap = (AG - 12) - (24 - HCO_3^-)$

$\Delta Gap = (Na^+ - Cl^- - HCO_3^- - 12) - (24 - HCO_3^-)$

Variance (SD^2) of ΔGap = Sum of variances of component electrolytes

Variance (SD^2) of $\Delta Gap = SD^2_{Na} + SD^2_{Cl} + SD^2_{HCO} + SD^2_{HCO}$

Standard deviation (SD) of $\Delta Gap = \sqrt{(SD^2_{\Delta Gap})}$

Tolerance interval of $\Delta Gap = \pm 1.96 \times SD_{\Delta Gap}$

However, laboratory techniques have improved in precision since the 1980s. A ΔGap of ±6 mEq/L may be too wide, inadvertently missing mixed metabolic disorders.

The aim of this study was to update the reference range of the ΔGap based on current laboratory precision. Interpretation of the acid-base disorder will be applied using the updated ΔGap range in a validation cohort.

Method: The current SD for Na, Cl and bicarbonate was obtained from the laboratory system data sheet and the tolerance interval of ΔGap was calculated .

A validation cohort was generated retrospectively from electronic medical records according to a pre-determined criteria from 1 Jan – 31 Dec 2018. We identified a group of patients with a strong possibility of mixed HAGMA and MALK in the presence of:

1. High AG

2. Significant organic acidosis (lactic acidosis, ketosis or elevated salicylates) AND

3. A serum bicarbonate ≥19.0 mmol/L despite the presence of organic acids.

The ΔGap was computed and interpreted based on the original vs new tolerance range. The Chi Square test was used to compare the interpretations based on the 2 tolerance ranges.

Results: The current SD of Na, Cl, bicarbonate was 0.9, 0.7, 0.3 respectively and the new tolerance interval of AG was ±2.3 mEq/L (rounded to ±2 mEq/L)

The validation cohort comprised of 1,565 patients with HAGMA and MALK, aged 58.0±30.9 years with 873 (55.8%) males.

Using the original range of ±6 mEq/L, 165 (10.5%) cases were classified correctly. With the new range of ±2 mEq/L, the 813 (51.9%) cases were classified correctly (P<0.001).

Conclusion: In summary, based on the precision of current laboratory techiques, the tolerance interval of AG is proposed as ±2 mEq/L. This was validated to significantly increase correct classification of mixed acid-base disorders.

Table 1: Interpreting the ΔGap. ΔAG, change in AG, ΔHCO, change in bicarbonate levels, HAGMA, high AG metabolic acidosis; NAGMA, normal AG metabolic acidosis; MALK, metabolic alkalosis

ΔGap = ΔAG □ΔHCO	Intepretation
0	HAGMA
below 0	HAGMA & NAGMA
above 0	HAGMA & MALK

Table 2: Intepretation of acid-base disorder according to tolerance interval use

	Tolerance interval for ΔGap		P
	±6 mEq/L	±2 mEq/L	
Interpreted asHAGMA and M Alk	165 (10.5%)	813 (51.9%)	<0.001
Interpreted asHAGMA only	1386 (88.6%)	651 (41.6%)	<0.001

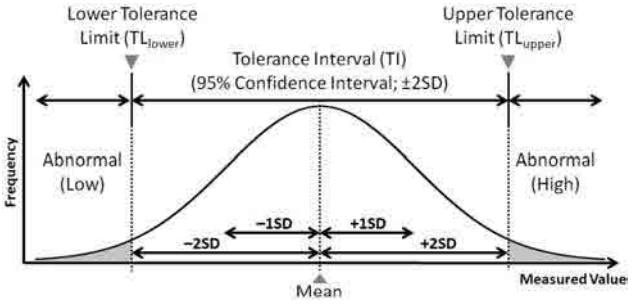


Figure 1: Illustration of the tolerance intervals and limits of a test.

P0007

EFFECT OF SODIUM BICARBONATE LOAD ON URIC ACID LEVELS IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND METABOLIC ACIDOSIS: PRELIMINARY RESULTS OF THE SOBIC-STUDY

Alexandra Repitz[1], Christof Aigner[1], Gere Sunder-Plassmann[1], Martina Gaggl[1]

[1]*Division of nephrology and dialysis, Department of medicine III, Vienna, Austria*

Introduction and Aims: Sodium bicarbonate is a commonly used drug that balances metabolic acidosis in patients with chronic kidney disease (CKD) and is said to delay disease progression. Elevated serum uric acid levels are frequently seen in CKD and the prevalence of gout disease in CKD patients is higher than in the normal population. Animal studies suggest that excessive sodium bicarbonate intake may increase uric acid levels, and in Korean Native Broilers led to visceral and articular gout. In turn, individuals with Gitelman/Bartter tubulopathy present alkemic and also show increased gout prevalence. The aim of the study was to evaluate the effect of oral sodium bicarbonate supplementation on uric acid levels after 20 weeks of treatment in patients with CKD and metabolic acidosis.

Methods: Patients with CKD stage 3 and 4 and HCO_3^- < 21mmol/l enrolled in the ongoing randomized controlled SoBic-study (since 2013) were randomized into the intervention group (target HCO_3^- 24±1mmol/l) or the rescue group (target HCO_3^- 20±1mmol/l). Baseline serum uric acid levels were determined prior to sodium bicarbonate supplementation and after 20 weeks. We used Spearman's correlation and regression analysis to detect a possible association between the amount of sodium bicarbonate intake (milligrams per day) and the alteration of uric acid in patients using a significance level of p=0.05.

Results: Forty-five patients were included in the study until January 2019 (23 intervention group, 22 rescue group) and demographic data is given in table 1. Of the total patient population 24.4% were already affected by hyperuricemia (serum uric acid ≥6.5mg/dl) before participating in the study (47.8% of the intervention group, 13.6% of the rescue-group). During the study period, none of the patients showed symptoms of gout. The mean uric acid level at baseline was 7.3(±1.3) and 7.4(±1.6) after 20 weeks. The median uric acid increased by 0.1 in the intervention group (p=0.651) and decreased by 0.1 in the rescue group (p=0.889) from baseline until 20 weeks. Serum bicarbonate levels and uric acid were not correlated (r_s=0.201, p=0.185). The regression analysis showed no association between the uric acid level and the total daily intake of sodium bicarbonate over 20 weeks.

Conclusions: In patients with CKD and metabolic acidosis the treatment with oral sodium bicarbonate for 20 weeks hat no adverse effect on the uric acid level.

Table SEQ Table * ARABIC 1: Demographic data, relevant blood values and daily dosage of sodium bicarbonate intake during the study

		Intervention	Rescue
N		23 (51.1%)	22 (48.9%)
Age [years]		60.0±14.0	61.0±23.0
Female [%]		9 (39.1%)	9 (40.9%)
BMI [kg/m̊]		27.7±8.3	26.6±7.2
Baseline eGFR [ml/min/1.73m̊]		23.5±12.0	23.9±16.6
HCO_3^- [mmol/l]	Baseline	19.3±2.2	19.4±3.12
	Week 20	23.3±2.2	20.2±1.7
Uric acid [mg/dl]	Baseline	7.2±1.8	7.1±1.9
	Week 20	7.3±2.8	7.0±2.7
Sodium bicarbonate [mg/d]	at week 20	6720.0±2520.0	420.0±1680.0

P0008

CASE REPORT: METABOLIC ALKALOSIS RESULTING IN RESPIRATORY COMPROMISE IN A PATIENT UNDERGOING HIGH DOSE METHOTREXATE THERAPY

Darragh O'Donoghue[1], Heather Truong[1], Heidi Finnes[1], Jennifer McDonald[1], Nelson Leung[1]

[1]*Mayo Clinic, Nephrology, Rochester, United States of America*

Background and Aims: High dose Methotrexate (HDMTX) is an important component of several modern oncological/haematological treatment protocols due to its central nervous system penetrance. Nephrotoxicity represents a significant adverse effect and can limit therapeutic options. Therefore, strategies to prevent this are paramount. Urinary alkalinisation and large volume resuscitation to maintain adequate hydration and urine output are the typical strategies. Urinary alkalinisation prevents tubular precipitation of methotrexate and therefore, a strict urinary pH target of 7 is maintained via a continuous bicarbonate infusion.

Method: We describe a case report, of Iatrogenic metabolic alkalosis leading to respiratory compromise in a patient receiving HDMTX from Mayo Clinic, Rochester.

Results: We present the case of a 76-year-old woman with a Diffuse Large B-Cell Lymphoma with CNS involvement who presented for elective admission for her 1st cycle of HDMTX. She received 7g of Methotrexate at dosing of 8 g/m^2. She received the standard urinary alkalinisation with pre- and post-hydration. Her baseline HCO3- was 28 mEq/L. Her 48 hour MTX level was elevated at 1.2 so the urinary alkalinisation protocol was continued until $<$0.1 mcmol/L. On day 4, she developed frequent episodes of apnoea. Her ABG demonstrated a metabolic alkalaemia pH 7.54, pCO 53, pO2 91, HCO3 45. She was transferred to the ICU for close monitoring. Her bicarbonate infusion was discontinued and she received acetazolamide. Her bicarbonate improved to 31 after 12 hours. She had a significant improvement in her respiratory status with no further episodes of apnoea. Her bicarbonate infusion was restarted due to elevated MTX levels. She was discharged home with no further complications.

Conclusion: Iatrogenic Metabolic alkalosis leading to respiratory compromise represents a rare but important complication of urinary alkalinsation protocols for High-dose Methotrexate therapy.

P0009 **EVALUATION OF THE POTENTIAL FOR DRUG INTERACTIONS WITH VEVERIMER**

Jun Shao[1], Dawn Parsell[1], Robert Guttendorf[2], Yick Sen Wu[1], Li Tsao[1], Scott Tabakman[1], Yuri Stasiv[1], Angela Lee[1], Kalpesh Biyani[1], Gerrit Klaerner[1]

[1]Tricida Inc., South San Francisco, United States of America and [2]Aclairo Pharmaceutical Development Group, Inc., Vienna, United States of America

Background and Aims: Veverimer is an investigational drug being developed as an orally administered hydrochloric acid binder for the treatment of metabolic acidosis associated with chronic kidney disease (CKD). In clinical studies, treatment with veverimer safely and effectively increased serum bicarbonate and improved objective and subjective measures of physical functioning[1-3]. Veverimer, a free-amine polymer, is not systemically absorbed; therefore, its potential for drug-drug interactions (DDIs) is limited to those that occur in the gastrointestinal (GI) tract (i.e., direct binding or indirect effects resulting from transient increases in gastric pH). We assessed the potential for DDIs with veverimer both in vitro and in vivo in healthy subjects.

Methods: In vitro binding to veverimer was evaluated with 16 drugs of varying molecular weight and charge. In a separate study, the effect of veverimer on gastric pH was measured continuously in vivo in healthy subjects using a microelectrode pH probe placed in the gastric compartment. Human DDI studies were conducted with 4 orally administered drugs, including those that demonstrated the most in vitro binding to veverimer and those with pH-dependent solubility (furosemide, aspirin, warfarin, dabigatran).

Results: Veverimer did not bind to any of the positively charged, neutral or zwitterionic drugs tested in vitro. It bound to 3 small (MW <332 Da), negatively charged drugs (aspirin, ethacrynic acid, furosemide); these interactions were reduced or eliminated in the presence of physiologically relevant concentrations of chloride. Neither furosemide nor aspirin showed clinically meaningful changes in pharmacokinetic parameters when coadministered with veverimer in human DDI studies (**Figure 1**).

Veverimer increased gastric pH by ~3.0 and 1.5 pH units in fasted and fed subjects, respectively. The increase in gastric pH was short-lived, with a peak within 1 hour after dosing and a return to baseline after ~1.5 hours and ~3 hours under fasting and fed conditions, respectively. The effect of veverimer on gastric pH was similar in the presence and absence of omeprazole. No clinically meaningful changes in systemic exposure, as indicated by C_{max} and AUC, were observed when 3 drugs with pH-dependent solubility were coadministered with veverimer in human DDI studies (**Figure 1**).

Conclusions: In human DDI studies, we observed: a) no effect of veverimer on the bioavailability of drugs with physicochemical characteristics most susceptible to direct binding to the polymer; b) small, short-lived effects of veverimer on gastric pH; and c) no effect of veverimer on the bioavailability of drugs with pH-sensitive solubility. Therefore, it is concluded that there is a negligible risk of veverimer involvement in clinically significant DDIs.

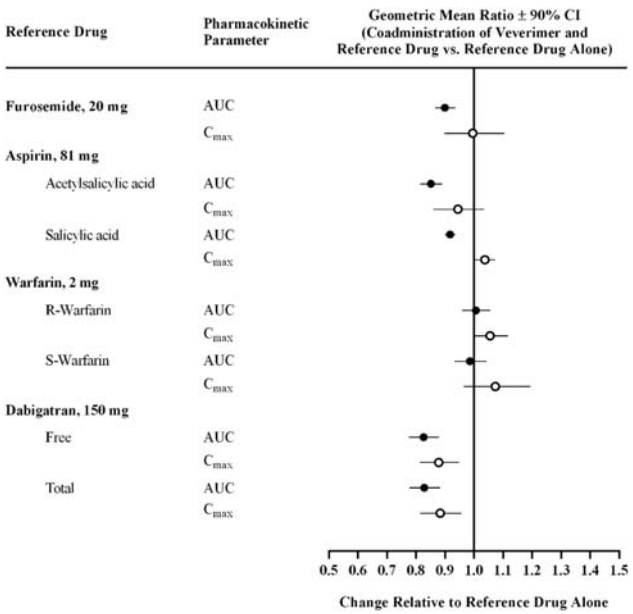


Figure 1. Effects of veverimer on the systemic exposures of other orally administered medications

P0010 **INCREASED SERUM URIC ACID LEVELS ARE ASSOCIATED TO RENAL ARTERIOLOPATHY AND PREDICT POOR OUTCOME IN IGA NEPHROPATHY**

Elisa Russo[1], Stefania Drovandi[1], Gennaro Salvidio[1], Michela Saio[1], Elisabetta Bussalino[1], Barbara Bonino[1], Pasquale Esposito[1], Daniela Verzola[1], Giacomo Garibotto[1], Francesca Viazzi[1]

[1]*Ospedale Policlinico San Martino, Internal Medicine, Genoa, Italy*

Background and Aims: IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide and a leading cause of End Stage Renal Disease (ESRD). In addition to the classical progression factors, including hypertension, proteinuria, and decreased renal function, other atherosclerosis-related factors, such as hypertriglyceridemia, have been reported to the renal progression of IgAN. Above all, many studies have indicated an association between hyperuricemia and progression of IgAN. Increased serum uric acid (SUA) levels are also well known to be associated with hypertension, endothelial dysfunction and development of cardiovascular and kidney diseases both in general population and high-risk patients. Previous studies suggested that uric acid induces proliferation of vascular smooth muscle cells, activates the renin–angiotensin–aldosterone system (RAAS) and also reduces the synthesis of nitric oxide. Furthermore, there is evidence that uric acid can promote the oxygenation of low-density lipoproteins (LDL) and increase the production of free oxygen radicals, increasing inflammation and oxidative stress.

In consequence of these processes, SUA might specifically promote atherosclerosis and arteriolar damage, possibly playing a major role in pathogenesis and progression of IgAN.

The aim of the present study was to explore the correlation between SUA levels, renal damage and its implication for renal outcome and all cause death in IgAN patients.

Method: The data for clinical features, laboratory and renal pathological examination were collected from 145 renal biopsy-proven IgAN patients and were retrospectively analyzed to determine the correlation between SUA levels, renal damage and overall outcome. Hyperuricemia (HU) was defined as the highest SUA gender-specific tertile. Biopsy-proven arteriolar damage was defined by the presence of arteriolar hyalinosis or intimal thickening. The primary outcome was death or ESRD.

Results: The mean baseline serum uric acid levels of the 42 female and 103 male patients at the time of kidney biopsy were 5.4 $\pm$1.7 and 7.2 $\pm$1.8 mg/dL, respectively. HU was >7.7 mg/dl for males and > 6.2 mg/dl for females.

Patients were stratified on the basis of baseline gender-specific SUA level tertiles. Clinical and histologic characteristics are described in table 1.

The higher the gender-specific SUA tertile, the greater the prevalence of arteriolar damage (p=0.02). No other histologic feature was significantly correlated with uric acid levels, therefore we analyzed laboratory and clinical characteristics on the basis of the presence/absence of biopsy-proven arteriolar damage (Table 2).

At logistic regression analyses SUA was associated with arteriolar damage at univariate (OR 1.45 CI [1.12-1.87], p=0.004) and multivariate analyses (OR 1.75 CI [1.10-2.93], p=0.03), recorded in Table 3.

Receiver Operating Curve (ROC) was performed and the sensitivity and specificity of SUA for predicting arteriolar damage were showed in Figure 1. The area under the ROC curve was 0.67 (IC95% 0.61 to 0.73) indicating that SUA is a fair test for detecting arteriolar damage.

TABLE 1 – Baseline characteristics based on Serum Uric Acid Tertiles

	SUA I Tertile (M <6.56 mg/dl; F <4.20 mg/dl) n 45	SUA II Tertile (M 6.56-7.74 mg/dl; F 4.20-6.20 mg/dl) n 45	SUA III Tertile (M >7.74 mg/dl; F >6.20 mg/dl) n 45	p value
Age, years	44 ± 19	47 ± 16	50 ± 15	0.1591
eGFR, ml/min/m2	67 ± 40	51 ± 27	34 ± 20	<0.0001
Proteinuria (g/die)	2.2 ± 2.8	3.0 ± 2.7	2.9 ± 2.4	0.2633
Mean BP, mmHg	101 ± 13	103 ± 12	105 ± 12	0.2086
Hypertension, %	44	64	80	0.0022
CKD, %	47	58	76	0.0187
Diabetes, %	11	9	9	0.9184
M1, %	31	36	34	0.9017
E1, %	11	9	7	0.7775
S1, %	69	71	57	0.3124
T1-T2, %	53	69	66	0.2700
C1-C2, %	16	9	16	0.5342
Arteriolar damage, %	38	58	71	0.0252
Cholesterol, mg/dl	201 ± 55	214 ± 55	218 ± 68	0.3702
LDL, mg/dl	115 ± 47	126 ± 52	130 ± 64	0.4802
TG, mg/dl	135 ± 104	134 ± 105	159 ± 66	0.0453
ESRD, %	11	27	29	0.0869
Death, %	2	2	13	0.0361
ESRD or death, %	13	29	38	0.0295

Data are presented as media ±standard deviation or percentage.
Abbreviations: SUA, serum uric acid; eGFR, estimated filtation rate; BP, blood pressure; CKD, cronic kidney disease; LDL low density lipoproteins; TG, triglycerides; ESRD, end stage renal disease.

Figures:

Patients with arteriolar damage had a worst outcome compared to patients without it (Kaplan Maier survival analysis, log rank test p=0.002, Figure 2a). HU and arteriolar damage had a synergic impact on progression of IgAN. Patients having both arteriolar damage and HU, showed a reduced survival free from the primary outcome as compared to those having only one risk factor or neither (log rank test p=0.003, Figure 2b).

Conclusion: SUA levels are directly associated with arteriolar damage and poor prognosis in patients with IgAN. Our study suggests the presence of higher SUA levels in IgAN patients identifies a sub-population at increased risk of progressing to ESRD or death, for whom a particular surveillance is warranted, possibly because of the pathogenetic role of SUA on arteriolar damage.

P0011 THE ROLE OF AQUAPORIN-11 (AQP11) IN THE THYMUS DEVELOPMENT

Kei Masaka[1], Yasuko Tanaka[1], Kenichi Ishibashi[1]

[1]*Meiji Pharmaceutical University, Pathophysiology, Kiyose, Tokyo, Japan*

Background and Aims: Some aquaporins transport not only water but also small non-ionic molecules such as glycerol. In fact, aquaporin-9 (AQP9) has been shown to transport glycerol which is critical to support memory T cell survival through metabolic fitness (Cui G et al. Cell. 161:750, 2015). As AQP11 is widely expressed and transport glycerol as well as water, AQP11 may also play a role in immunological system, which will expand the repertoire of the aquaporin research field.

Method: The AQP11 expression in the thymus was examined by RT-PCR, Western blot and immunohistochemistry in mice. Phenotypic analysis and microarray analysis of the thymus were conducted in wild and AQP11 null mice at 21 day old before the development of uremia due to polycystic kidneys.

Results: Both mRNA and protein expressions of AQP11 in the thymus were higher than those of the kidney by RT-PCR and Western blot. Interestingly, the size of the thymus from AQP11 null mice was smaller than that of the wild mice: 28mg vs. 56mg, even after the correction by the body weight: 0.59 % vs. 0.82 %, as the body size of AQP11 null mice was smaller. The vacuolated medullary epithelial cells were observed in the thymus of AQP11 null mice with narrowed cortex. The immunohistochemical analysis revealed the AQP11 expression at the stromal-epithelial cells in the thymus. The microarray analysis of the gene expression in the thymus was compared between the wild and AQP11 null thymus by the annotation analysis based on the David Bioinformatics Resources 6.8 (beta). The up-regulated 66 genes more than 1.5 folds in AQP11 null thymus are mainly related to the PI3K/Akt signaling pathway to promote metabolism, proliferation, cell survival, growth and angiogenesis. On the other hand, the down-regulated 55 genes less than half in AQP11 null thymus are related to energy production and the peroxisome proliferator-activated receptor (PPAR) signaling pathway. Further RT-qPCR analysis confirmed the enhanced expression of Egfr (Epidermal Growth Factor Receptor), Itgb4 (Integrin beta-4) and Il2ra (interleukin 2 receptor alpha) and the diminished expression of aquaglyceroporin AQP7, Pck1 (Phosphoenolpyruvate carboxy-kinase 1) and Ucp1 (Mitochondrial uncoupling protein 1). The up-regulated genes for growth signaling was unexpected with the smaller thymus but may support the survival of the hypoplastic thymus as a compensation. On the other hand, the down-regulated genes may compromise fat-glucose-energy metabolism in the thymus leading to the smaller thymus, which may be aggravated by the decreased expression of AQP7, another glycerol channel.

Conclusion: AQP11 may play an important role in the metabolic control of the developing thymus possibly through its glycerol transport. The smaller thymus with narrower cortex in AQP11 null mice may lead to immunological dysfunction, which is currently under study.

P0012 SHOULD WE DEFINE A NEW STANDARD PRESCRIPTION OF BICARBONATE (HCO3-) IN HEMODIALYSIS (HD)?

Ana Rita Valerio Alves[1], Cátia Figueiredo[1], HernÂNi Ricardo Martins GonÇAlves[1], Karina Lopes[1], Flora Sofia[1], Ana Vila Lobos[1]

[1]*Hospital Rainha Santa Isabel - Torres Novas (Centro Hospitalar Médio Tejo, EPE), Nephrology, Torres Novas, Portugal*

Background and Aims: One of the aims of the regular, intermittent HD therapy prescribed for patients with end-stage chronic kidney disease, is correction of metabolic acidosis by addition of HCO_{3-} to dialysate fluid. The KDOQI guidelines therapeutic goal is to maintain pre-dialysis $HCO_{3-} \geq 22$mmol/L.

The aim of the study was to evaluate an individualized HCO_{3-} hemodialysis prescription as a preventing factor of metabolic changes in a HD facility and define a new standard HCO_{3-} prescription.

Method: 36-month prospective study of patients on online high-flux hemodiafiltration. Every 3 months (13 time points) HCO_{3-}, Calcium (Ca^{2+}), Phosphorus (P^{+}), intact Parathyroid hormone (iPTH) and protein C reactive (PCR) blood levels were analyzed. HCO_{3-} prescription was changed using the following rules:

- $HCO_{3-} > 30$mmol/L: reduce 4mmol/L HCO_{3-};
- $HCO_{3-} \geq 25$mmol/L: reduce 2mmol/L HCO_{3-};
- $20\text{mmol/L} < HCO_{3-} < 25\text{mmol/L}$: no change;
- $HCO_{3-} \leq 20$mmol/L: increase 2mmol/L HCO_{3-};
- $HCO_{3-} < 18$mmol/L: increase 4mmol/L HCO_{3-}.

The data collected comprised demographic information, renal disease etiology, comorbidities, HD treatment information and lab results.

Categorical variables are presented as frequencies and percentages, continuous variables as means and standard deviations, or medians and interquartile ranges (IQR) for variables with skewed distributions. A p-value<0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 23 for Mac OS X.

Results: From the 50 patients that were evaluated at Time point 0, only 24 patients completed the follow-up period. Sixteen (66.7%) were males, 54.2% (n=13) diabetic and 58.3% (n=14) hypertensives and the median age was 76 years (IQR 13). At baseline (time point 0), median pH was 7.4 (IQR 0.09) and serum HCO_{3-} 26.5 mmol/L (IQR 2.32). At time point 12, pH was 7.35 (IQR 0.12) and serum HCO_{3-} 23.25mmol/L (IQR 1.93).

A repeated measures ANOVA determined that prescribed HCO_{3-} differed with statistical significance during time ($F(2.787,83.308)=39.055$, $p=0.001$), and the post Hoc tests confirmed those assumptions between time point 1 and all the others time points, as an example the mean difference between initial prescribed HCO_{3-} and time point 12 was 5.39mmol/L ($p=0.001$).

Wilcoxon Sign-Rank Tests determined that throughout the analyzed period the serum HCO_{3-} approached the reference serum HCO_{3-} (23mmol/L) that we have defined as ideal (at time point 0, median=26.5mmol/L, $Z=4.144$, p=0-001; at time point 12, median 23.25mmol/L, $Z=1.243$, $p=0.214$).

On the other hand, a one sample T-Test determined that the HCO_{3-} prescription differed more in each time point from the 32mmol/L defined as standard (at time point 12, $t=-2.798$, $p=0.01$) and approached a new suggested value of 26mmol/L. However, at time point 8, 62.5% (n=15) patients had a HCO_{3-} prescription of 28mmol/L, ($t(23)=0.001$,$p=1$) and at that time we had hypothesized that that a prescription of 28 mmol/L should be the new standard.

Gender, Diabetes Mellitus, Hypertension, and renal disease etiology did not influence the HCO_{3-} prescription neither serum HCO_{3-}.

Conclusion: HCO_{3-} prescription and serum HCO_{3-} were not influenced by comorbidities like DM and Hypertension.

Our findings suggest that the standard HCO_{3-} prescription of 32mmol/L should be rethought, as an individualized HCO_{3-} prescription could be beneficial for the patient. At this time, we suggest that a prescription of 26 mmol/L should be the new standard. However, the limitations of our findings include the small sample size, so further studies with larger samples should be attempted.

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CELL SIGNALLING. CELL BIOLOGY. HORMONES

P0014

MYELOID-SPECIFIC TARGETING OF NOTCH AMELIORATES RENAL FIBOSIS VIA REDUCED INFILTRATION AND ACTIVATION OF BONE MARROW-DERIVED MACROPHAGE

Yali Jiang[1]

[1]*xijing hospital, department of nephrology, Xi an, P.R. China*

Background and Aims: Macrophages play critical roles in renal fibrosis. However, macrophages exhibit ontogenic and functional heterogeneities, and which population of macrophages contributes to renal fibrosis and the underlying mechanisms remain unclear.

Method: In this study, we genetically targeted Notch signaling by disrupting the transcription factor recombination signal binding protein-Jκ (RBP-J), to reveal its role in regulation of macrophages during the unilateral ureteral obstruction (UUO)-induced murine renal fibrosis.

Results: Myeloid-specific disruption of RBP-J attenuated renal fibrosis with reduced extracellular matrix deposition and myofibroblast activation, as well as attenuated epithelial-mesenchymal transition, likely owing to the reduced expression of TGF-β. Meanwhile, RBP-J deletion significantly hampered macrophage infiltration and activation in fibrotic kidney, although their proliferation appeared unaltered. By using macrophage clearance experiment, we found that kidney resident macrophages made negligible contribution, but bone marrow (BM)-derived macrophages played a major role in renal fibrogenesis. Further mechanistic analyses showed that Notch blockade reduced monocyte emigration from BM by down-regulating CCR2 expression. Finally, we found that myeloid-specific Notch activation aggravated renal fibrosis, which was mediated by $CCR2^{+}$ macrophages infiltration.

Conclusion: In summary, our data have unveiled that myeloid-specific targeting of Notch could ameliorate renal fibrosis by regulating BM-derived macrophages recruitment and activation, providing a novel strategy for intervention of this disease.

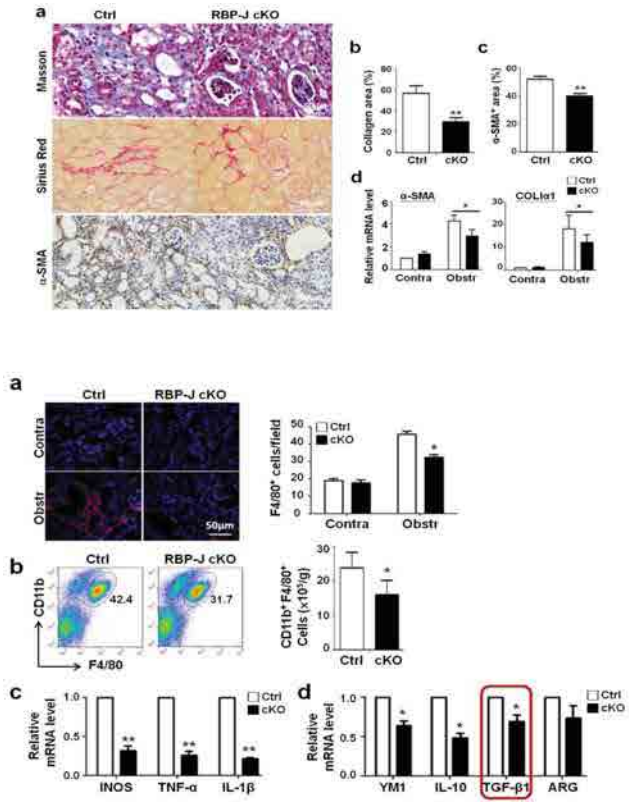


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P0015 **SIRT2 REGULATES CISPLATIN-INDUCED ENDOPLASMIC RETICULUM STRESS THROUGH HEAT SHOCK FACTOR 1 DEACETYLATION**

Woong Park[1], Hyeongwan Kim[1], Yujin Jung[1], Kyung Pyo Kang[1], Won Kim[1]

[1]*Chonbuk National University Medical School, Internal Medicine, Jeonju-si, Korea, Rep. of South*

Background and Aims: Nephrotoxicity is an important cisplatin-induced adverse reaction and restricts the use of cisplatin to treat malignant tumors. Endoplasmic reticulum (ER) stress is caused by the accumulation of misfolded proteins, and is induced by cisplatin in kidneys. SIRT2 nicotinamide adenine dinucleotide (NAD^+)-dependent deacetylase is a member of the sirtuin family, but its role in cisplatin-induced ER stress remains unclear.

Method: To investigate the effect of SIRT2 on cisplatin-induced ER stress using SIRT2 knockout mice and human proximal tubular epithelial cells (HK-2 cells). We treated cisplatin (20 μg/mL) or induced by intraperitoneal injection of cisplatin (20 mg/kg) and evaluated the changes of ER stress and its signal mechanism.

Results: Cisplatin administration was found to significantly increase the expressions of PRKR-like ER kinase (PERK), phosphorylation of eukaryotic translation initiation factor 2α (eIF2α), and the C/EBP homologous protein (CHOP) and caspase-12 in the kidneys of SIRT2-wild type mice. However, cisplatin-induced increases in the expressions of p-PERK, p-eIF2α, CHOP and, caspase-12 were diminished in kidneys of SIRT2 knockout mice. *In vitro*, cisplatin significantly increased the expressions of p-PERK, p-eIF2α, CHOP, and caspase-12 in HK-2 cells. When the effect of SIRT2 on cisplatin-induced ER stress was evaluated using SIRT2-siRNA (ON-TARGET plus human SIRT2 siRNA) or the SIRT2 inhibitors, AGK2 and AK1, knockdown or inhibition of SIRT2 significantly attenuated the cisplatin-induced protein expression of p-PERK, p-eIF2α, CHOP, and caspase-12. Immunoprecipitation studies showed SIRT2 bound physically to heat shock factor (HSF)1 and that HSF1 acetylation was significantly increased by cisplatin. In addition, knockdown of SIRT2 increased cisplatin-induced HSF1 acetylation and increased the expression of heat shock protein (HSP)70.

Conclusion: These observations suggest that suppression of SIRT2 ameliorates cisplatin-induced ER stress by increasing HSF1 acetylation and HSP expression.

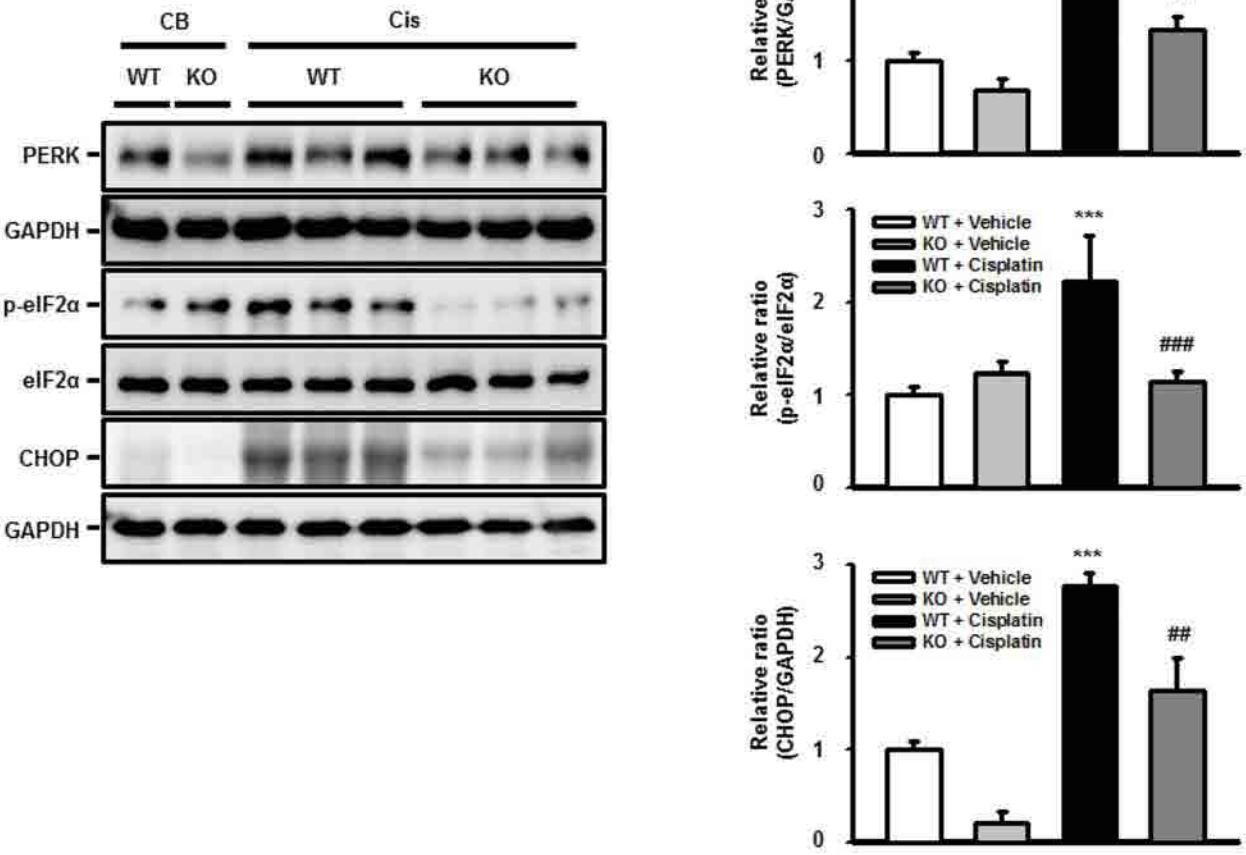


Figure:

P0016

EFFECT OF GEMFIBROZIL ON KYNURENINE AMINOTRANSFERASE ACTIVITY AND KYNURENIC ACID PRODUCTION IN RAT KIDNEY

Izabela Zakrocka[1], Katarzyna Targowska-Duda[2], Artur Wnorowski[2], Tomasz Kocki[3], Krzysztof Jóźwiak[2], Waldemar Turski[3], Wojciech Załuska[1]

[1]Medical University of Lublin, Department of Nephrology, Lublin, Poland, [2]Medical University of Lublin, Department of Biopharmacy, Lublin, and [3]Medical University of Lublin, Department of Experimental and Clinical Pharmacology, Lublin, Poland

Background and Aims: Hypertriglyceridemia is the most common lipid disorder in chronic kidney disease. Lifestyle changes and fibrates administration are main methods of lowering triglycerides' level. PPARα (peroxisome proliferator-activated receptor-α) activation is the primary mechanism of action of fibrates.

A tryptophan metabolite, kynurenic acid (KYNA), is produced from L-kynurenine (L-KYN) by kynurenine aminotransferases (KATs). KAT I and KAT II isoenzymes are the best analyzed KATs. KYNA acts predominantly as a nonselective antagonist of ionotropic glutamatergic receptors, particularly N-methyl-D-aspartate (NMDA) type, which are highly expressed in the kidney. Natriuretic and hypotensive effects of KYNA are well described. Diet rich in fatty acids was reported to elevate central and peripheral KYNA level.

The goal of presented study was to analyze the influence of gemfibrozil, one of the fibrates given to treat hypertriglyceridemia, on KYNA production and the activity of KAT isoenzymes: KAT I and KAT II, in rat kidney *in vitro*. Additionally, the molecular docking of gemfibrozil to KAT I and KAT II structures was performed to study drug-enzyme interaction. On the final step the microarray datamining was carried out to investigate whether gemfibrozil affects the expression of KAT-coding genes.

Method: The effect of gemfibrozil on KYNA synthesis together with KAT I and KAT II activity was tested in rat kidney homogenates *in vitro* after 2 hours incubation in the presence of L-KYN and gemfibrozil. The drug was examined at the concentration of 1 μM, 10 μM, 50 μM, 100 μM, 500 μM and 1 mM. Production of KYNA was analyzed using the high performance liquid chromatography (HPLC) with fluorometric detector.

Results: Gemfibrozil at 100 μM, 500 μM and 1 mM decreased KYNA production in kidney homogenates *in vitro* to 66% ($P < 0.05$), 58% ($P < 0.01$) and 41% ($P < 0.01$) of control value, respectively. At 100 μM, 500 μM and 1 mM concentration gemfibrozil lowered renal KAT I activity *in vitro* to 68% ($P < 0.05$), 56% ($P < 0.01$) and 52% ($P < 0.01$) of control value, respectively. Moreover, gemfibrozil at 500 μM and 1 mM concentration decreased kidney KAT II activity *in vitro* to 47% ($P < 0.001$) and 26% ($P < 0.001$) of control value, respectively. Results of the molecular docking suggested that gemfibrozil may affect the active site of both KAT I and KAT II. Publicly available microarray datasets suggested that the expression of KAT-coding genes does not change after gemfibrozil administration.

Conclusion: Gemfibrozil decreases KYNA production in rat kidney *in vitro* through inhibition of KAT I and KAT II isoenzymes. Presented results indicate a novel mechanism of gemfibrozil's action in the kidney. Its potential role in nephrotoxicity needs verification in upcoming studies.

P0017 **ESTIMATION OF KIDNEY MITOCHONDRIA TOLERANCE VIA FLUORESCENCE MICROSCOPY**

Egor Plotnikov[1,2], Vasily Popkov[1], Anna Tvorogova[3], Nadezda Andrianova[1,4], Marina Buyan[4], Dmitry Zorov[1]

[1]Lomonosov Moscow State University, A.N. Belozersky Institute of Physico-Chemical Biology, Moscow, Russia, [2]Sechenov First Moscow State Medical University, Institute of Molecular Medicine, Moscow, Russia, [3]Lomonosov Moscow State University,, Faculty of Biology, Moscow, Russia and [4]Lomonosov Moscow State University, Faculty of Bioengineering and Bioinformatics, Moscow, Russia

Background and Aims: The functioning of mitochondria is a key parameter that determines the normal activity of kidney cells and triggers life/death transition in pathological conditions. The main pathological event in the mitochondria is the opening of a permeability transition pore, observed in renal ischemia and other acute nephrological pathologies. The development of non-specific mitochondrial permeability leads to a burst of ROS generation and the release of proapoptotic factors.

Assessment of mitochondrial resistance to induction of permeability transition is an important characteristic for the analysis of kidney tolerance to damaging factors, such as ischemia. In this study, we developed a method for evaluating mitochondrial permeability transition in renal tubular cell culture using fluorescence microscopy.

Method: The primary renal tubular epithelial cells were loaded with a fluorescent probe, TMRE, which accumulates in the mitochondria depending on the transmembrane potential. Cells in the culture were analyzed on a fluorescent microscope for 180 seconds under constant exposure with exciting light and the video was recorded at a frequency of 1 frame/sec. To analyze the images, a Python algorithm was created that allocated the individual mitochondria in the image and analyzed the shape, size, and dynamics of the TMRE fluorescence of each mitochondrion. In total, more than 10^5 mitochondria were analyzed in each experiment.

Results: The initial state of mitochondrial transmembrane potential was evaluated by the intensity of TMRE fluorescence in the first frame in each series when phototoxicity of the dye was not manifested yet. Population analysis revealed that the total distribution of mitochondria by TMRE fluorescence intensity was a single-modal. In this case, the histogram of the distribution had a wide arm of mitochondria with greater TMRE fluorescence (that means high transmembrane potential). This distribution suggests that renal cells have mitochondria with high and low TMRE fluorescence values. This can be interpreted as the presence of mitochondria in cells with higher transmembrane potential values.

Analysis of the dynamics of TMRE fluorescence intensity revealed that some mitochondria after a certain time demonstrated a sharp drop in the fluorescence intensity, which we interpret as the opening of the mitochondrial pore (Fig.1). However, this drop did not occur in all kidney cells mitochondria, but only in about 15% of the cells. A small number of mitochondria had several repeated falls/rises in TMRE fluorescence. This can be interpreted as the closing and subsequent opening of the permeability transition pores.

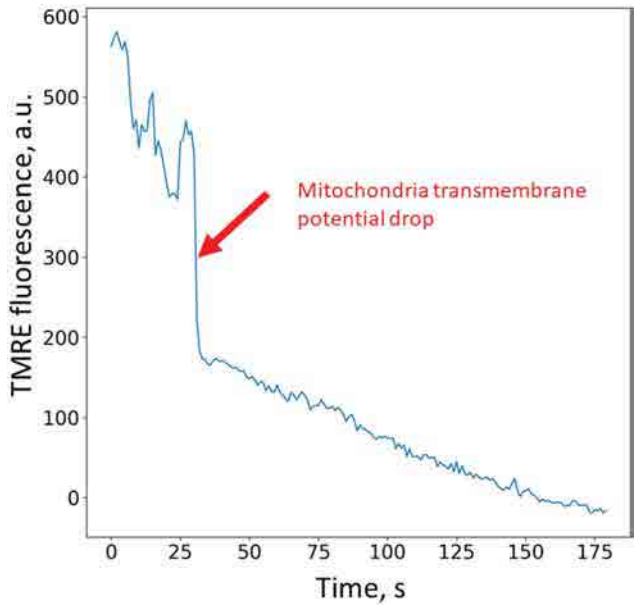


Figure:

Analysis of a subpopulation of mitochondria with low TMRE values revealed that low-energized mitochondria have a later pore opening time. It is important to note that mitochondria with higher TMRE fluorescence are more susceptible to photodynamic effects when the probe is excited by light.

Conclusion: Renal epithelial cells happen to be very heterogeneous in terms of mitochondrial potential and the time of the induction of mitochondrial permeability transition. Correlations were found between the value of the mitochondrial potential (TMRE accumulation) and the cell's resistance to induction of non-specific mitochondrial pore.

P0018 **GLOMERULAR ENDOTHELIAL CELL SENESCENCE DRIVES AGE-RELATED KIDNEY DISEASE THROUGH PAI-1**

Camille Cohen[1], Legoff Oceanc[1], Frederic Soysouvanh[2], Marine Tanou[1], Florence Vasseur[1], Clement Nguyen[1], Lucile Amrouche[3], Tanguy Meunier[4], Marion Rabant[5], Dominique Nochy[6], Christophe Legendre[3], Dany Anglicheau[3], Fabien Milliat[2], Fabiola Terzi[1]

[1]INSERM U1151, Paris, France, [2]Institute for Radiological Protection and Nuclear Safety - IRSN, Fontenay-aux-Roses, France, [3]Necker, Nephrology, Paris, France, [4]Hôpital Européen Georges-Pompidou, Geriatrics, Paris, France, [5]Necker, Pathology, Paris, France and [6]Hôpital Européen Georges-Pompidou, Pathology, Paris, France

Background and Aims: In age-related chronic kidney disease (CKD), the most frequent histological lesion observed is glomerulosclerosis. The molecular mechanisms involved in this deterioration process are unclear, but cellular senescence might play a role.

Method: By combining several murine models of physiological and accelerated aging with transgenic animals and *in vitro* models, we discovered the role of endothelial senescence in the development of glomerular lesions.

Results: These senescent glomerular endothelial cells secreted several molecules, grouped under the senescence associated secretory phenotype (SASP) including the plasminogen activator inhibitor 1 (PAI-1). Specific deletion of *PAI-1* in endothelial cells prevented the development of glomerulosclerosis during physiological and accelerated aging, by decreasing podocyte loss. In addition, we showed that PAI-1 mediates a detrimental endothelial-podocyte crosstalk, as incubation of podocytes by supernatant of senescent glomerular endothelial cells led to their detachment. Consistently, preincubation of the senescent supernatant with tiplaxtinin, a PAI-1 inhibitor, preserved podocytes. More importantly, we demonstrated that these data are relevant to humans. In fact, PAI-1 staining the day of the transplantation was predictive of kidney allograft dysfunction 12 months after transplantation from elderly donors.

Conclusion: In conclusion, our study uncovers the critical role played by endothelial senescence in the development of glomerulosclerosis during aging and identified PAI-1 as a novel promising biomarker for predicting kidney dysfunction in patients receiving a kidney from elderly donors.

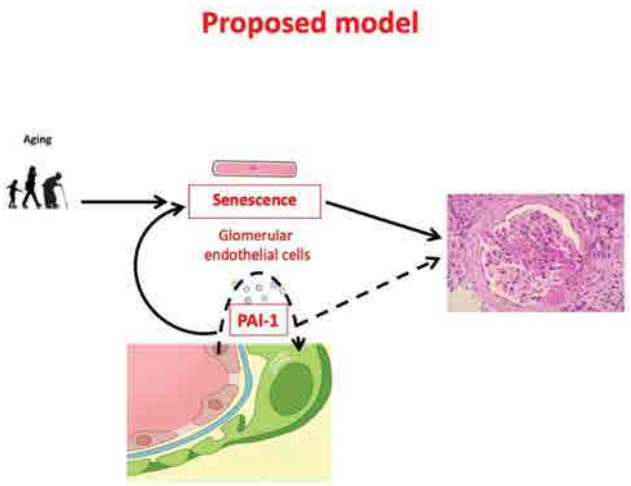


Figure:

P0019

MICROVESICLES FROM MESENCHYMAL STEM CELLS OVEREXPRESSING MIR-34A INHIBIT TGF-BETA-1-INDUCED EPITHELIAL-MESENVHYMAL TRANSITION IN RENAL TUBULAR EPITHELIAL CELLS IN VITRO

Juan He[1], Yali Jiang[1], Yan Wang[1], Xiujuan Tian[1], Shiren Sun[1]

[1]*Xijing Hospital, the Fourth Military Medical University., Nephrology, xian, P.R. China*

Background and Aims : The application of microRNAs (miRNAs) in the therapy of kidney diseases is hampered by difficulties in delivering miRNAs effectively. Nano-sized microvesicles (MVs) are known as natural carriers of small RNAs. Our prior work has demonstrated that MVs isolated from mesenchymal stem cells (MSCs) attenuated kidney injuries induced by unilateral ureteral obstruction and 5/6 subtotal nephrectomy in mice. The present work aimed at evaluating the effects of miR-34a-5p (miR-34a)-modified MSC-MVs on transforming growth factor (TGF)-β1 induced fibrosis and apoptosis in vitro.

Method : Bone marrow MSCs were further modified by lentiviruses overexpressing miR-34a, and MVs were collected from these MSCs to treat HK-2 renal tubular cells exposed to TGF-β1. Alterations in epithelial-mesenchymal transition (EMT) and cell survival were further determined.

Results : We first demonstrated that MVs generated by miR-34a-modified MSCs contained more miR-34a. By analyzing the expression levels of epithelial markers (E-cadherin and Tight Junction Protein 1 (TJP1)) and mesenchymal markers (α-SMA and fibronectin), we found that the pro-fibrotic TGF-β1 induced EMT was remarkably suppressed by miR-34a-enriched MSC-MVs. Notch-1 receptor and Jagged-1 ligand, two major molecules of Notch signaling pathway, are predicted targets of miR-34a. We further found that the elevation in Notch-1 and Jagged-1 induced by TGF-β1 was inhibited by miR-34a-enriched MSC-MVs. The inhibitory effects of miR-34a-enriched MSC-MVs on EMT and Notch signaling pathway were stronger than the control MSC-MVs. In addition, TGF-β1 exposure also induced apoptosis in HK-2 cells. Although miR-34amofidied MSC-MVs could inhibit TGF-β1-triggered apoptosis in HK-2 cells, the effects were less significant than the control MSC-MVs. This phenomenon may be resulted from the pro-apoptotic effects of miR-34a.

Conclusion : Our study demonstrates that miR-34a-overexpressing MSC-MVs inhibit EMT induced by pro-fibrotic TGF-β1 in renal tubular epithelial cells, possibly through inhibiting Jagged-1/Notch-1 pathway. Genetic modification of MSC-MVs with anti-fibrotic molecule may present a novel strategy for treatment of renal injuries.

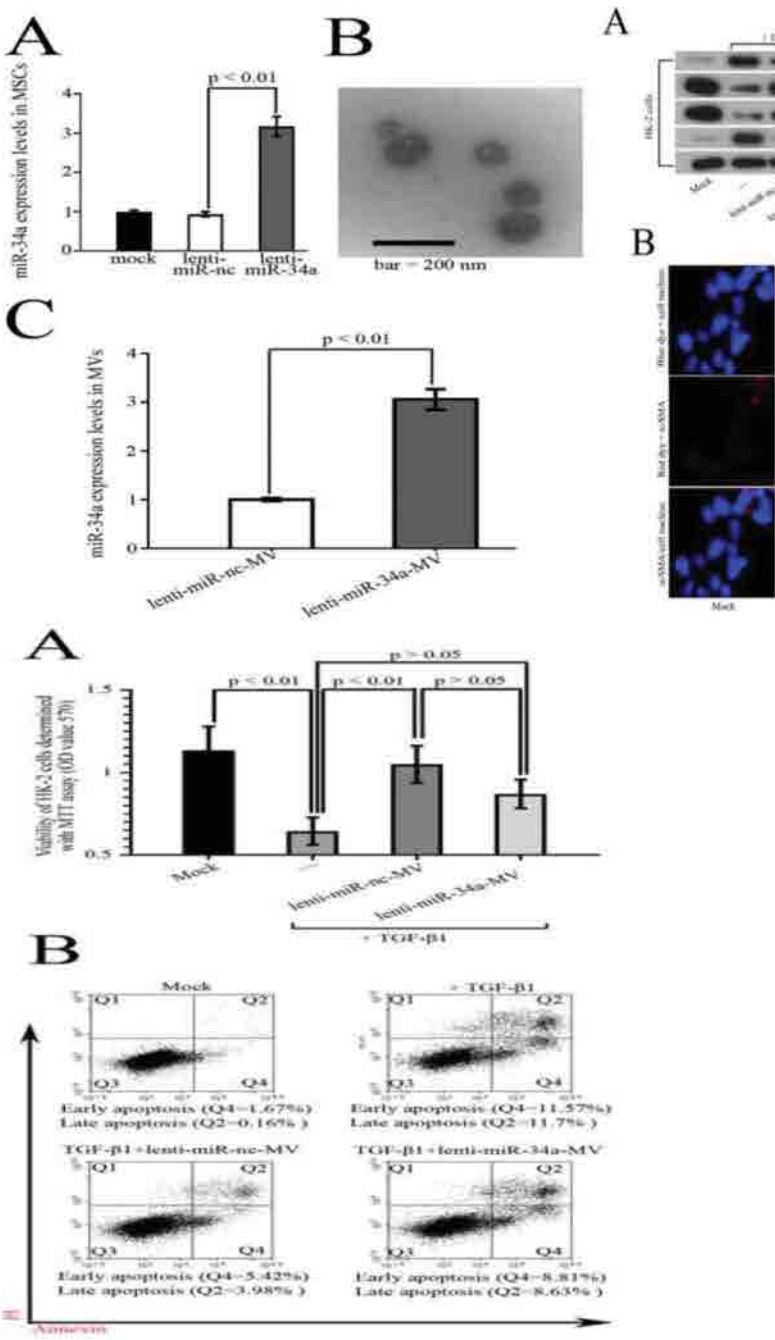


Figure:

P0020

THE NEPHRO-PROTECTIVE ROUTE OF CGMP DOES NOT COMPENSATE NPRHOGENIC DIABETES INSIPIDUS, BOTH CONDITIONS MEDIATED BY RENAL INTEGRIN LINKED KINASE (ILK)

Mercedes Griera-Merino[1,2], Diego García-Ayuso[1,2], Elena Gutiérrez-Calabrés[1,2,3], Lourdes Bohorquez Magro[1,2], Sofía Campillo de Blas[1,2], Marta Barrionuevo-González[3], Laura Calleros[1,2], Diego Rodríguez-Puyol[1,3,4], Manuel Rodríguez-Puyol[1,3], Sergio De Frutos García[1,2,3]

[1]Instituto Ramon y Cajal de Investigación Sanitária (IRYCIS), Fundación Renal Iñigo Álvarez de Toledo (FRIAT), REDinREN from Instituto de Salud Carlos III and NOVELREN from Comunidad de Madrid, Madrid, Systems Biology, Physiology Unit,, Alcalá de Henares, Spain, [2]Universidad de Alcalá, Systems Biology, Physiology Unit,, Alcalá de Henares, Spain, [3]Hospital Príncipe de Asturias, Biomedical research foundation, Alcalá de Henares, and [4]Hospital Príncipe de Asturias, Nephrology Unit and Department of Medicine from Universidad de Alcalá, Alcalá de Henares,

Background and Aims: Renal ILK transgenic deletion on mice (cKD-ILK) address basal polyuria compatible with nephrogenic diabetes insipidus (NDI), due to disrupted tubular water channel aquaporin 2 (AQP2) AQP2 expression and vesicular trafficking to the apical membrane [Cano-Peñalver JL et al. FASEB J. 2014; Mamuya FA et al. Am J Physiol Renal Physiol. 2016]. An early symptom of chronic renal diseases (CKD) is NDI. ILK depletion also have a nephron-protective effect in renal damage in mice due to the increase in cGMP [Cano-Peñalver JL et al. Mol Med. 2016; de Frutos S et al. Biochim Biophys Acta Mol Basis Dis. 2019], the latter an alternative anti-NDI mediator. Here we demonstrate that ILK-mediated regulation of AQP2, under basal or CKD contexts, does not depend on cGMP.

Method: cKD-ILK and controls (WT) were treated orally with a NO donor, as precursor of cGMP formation (IDN, 300mg / Kg / day) for 24 hours. Urine volume was determined as a measure of tubular functionality. Fresh kidneys from non-treated mice were cultured ex vivo with precursors of cGMP (NO donor SNP, 1 μM or cGMP analogue 8Br-cGMP, 0.2 mM) for 30 minutes. AQP2 in the apical membrane of the tubules was quantified by immunohistochemistry. More cKD-ILK and WT were subjected for 6 weeks to a diet supplemented with 0.2% adenine (A) as CKD inducer or baseline standard diet. Urine volume and total ranal AQP2 levels were determined.

Results: Compared to WT, cGMP axis activation in vivo did not compensate the basal NDI present in cKD-ILK and the activation ex vivo did not improve the apical presence of AQP2 in cKD-ILK. Both WT and cKD-ILK subjected to CKD showed exacerbated polyuria and decreased levels of renal AQP2, but no differences were observed between groups.

Conclusion: ILK regulates AQP2, both in a basal and pathological context (CKD) independent of cGMP which otherwise is nephron-protective. Our results probably explain the co-existence of cGMP increase together with AQP2 decrease observed in the cKD-ILK kidneys.

P0021 LONG NON-CODING RNAS HOTAIR AND LINC00511 CAN EXPLAIN HUMAN RENAL STEM/PROGENITOR CELLS CAPACITY TO REPAIR DAMAGE INDUCED BY CISPLATIN.

Claudia Curci[1,2], Fabio Sallustio[1,3], Angela Picerno[1], Alessandra Stasi[1], Maria Teresa Cimarrusti[1], Paola Pontrelli[1], Giuseppe Castellano[4], Simona Simone[1], Pertosa Giovanni[1], Loreto Gesualdo[1]

[1]University of Bari, DETO, Bari, Italy, [2]University of Bari, Department of basic medical sciences, neurosciences and sense organs, Bari, Italy, [3]University of Bari, Department of Interdisciplinary medicine, Bari, Italy and [4]University of Foggia, Department of Medical Science, Foggia, Italy

Background and Aims: The recent discovery of a complex system of human Adult renal stem/progenitor cells (ARPCs) dedicated to the renewal of epithelial renal cells has allowed scientists to better understand how the regenerative process can occur in the adult kidney. ARPCs have a great potential in view of developing future treatments for both acute and chronic renal injury. However, to completely take advantage of their capability it is essential to study the factors regulating the stem cell behavior. Recently, long noncoding RNAs (lncRNAs) have been recognized as a crucial class of gene expression regulators.

lncRNAs have several distinguishing characteristics that provide particular regulatory functions, including cell- and tissue-specific expression and the ability to transduce higher-order spatial information. Several lncRNAs modulate some somatic stem cell renewal or differentiation, while others promote a differentiation program. Their functions are often helped by proteic co-factor that convey the ability to activate or repress gene expression or to post-transcriptionally regulate other RNAs. Furthermore, numerous lncRNAs have been shown to act as competing endogenous RNAs, where the lncRNAs are proposed to bind to and compete miRNAs away from cognate mRNA targets. The aim of the study was to evaluate the basal expression profile of lncRNA expressed specifically in ARPCs.

Method: lncRNA expression profile was obtained from ARPCs and renal proximal tubular cells (RPTECs) alone or following cisplatin damage induction. We used Agilent SurePrint G3 Human Gene Expression Microarrays providing comprehensive coverage of genes and transcripts using the latest annotation databases. Genespring and R software were used for the analysis. lncRNA expression was validated by Real-time PCR. CrispR/Cas9 system has been used to knock-down specific lncRNA.

Results: We compared lncRNA expression between ARPCs and RPTECs: 45 lncRNA were differently modulated in ARPCs vs RPTECs (Fold change 1.5; FDR <0.05). In particular, we found 13 lncRNA upregulated and 32 lncRNA downregulated. Classification analysis showed that most of lncRNA modulated in ARPCs interfere with WNT signaling pathway, immune cell activation, and G-protein signaling pathway. Moreover, the overrepresentation test showed their involvement in calcium-mediated signaling, cell cycle and protein glycosylation processes ($p<0.005$). Among most significantly modulated lincRNAs we found HOTAIR and CCND2-AS1 that were upregulated in ARPCs compared to RPTECs. When we knocked-down the HOTAIR lncRNA ARPCs were not able to normally proliferate in cell culture. However, following cisplatin damage induced in RPTECs, ARPCs upregulated the LINC00511 and the miR210-HG. LINC00511 binds histone methyltransferase enhancer of zeste homolog 2 (EZH2, the catalytic subunit of the polycomb repressive complex 2 - PRC2), a highly conserved protein complex that regulates gene expression by methylating lysine 27 on histone H3. It acts as a modular scaffold of EZH2/PRC2 complexes, coordinates their localization, and specifies the histone modification pattern on the target genes, including p57. LINC00511 can affect cell proliferation, invasiveness, and apoptosis.

Conclusion: ARPCs express specific lncRNAs that could explain some of the ARPC stemness properties and their capacity to repair damage induced by cisplatin. Our findings suggest that lncRNA may represent a novel therapeutic target in acute and chronic renal injury.

P0022

INNATE IMMUNE RESPONSES ELICITED BY TOLL-LIKE RECEPTORS ARE POSSIBLY INVOLVED IN THE PATHOGENESIS OF NEPHROTIC SYNDROME.

Eriko Tanaka[1], Ichiro Hada[1], Naoaki Mikami[1], Kunimasa Yan[1]

[1]*Kyorin University School of Medicine, Department of Pediatrics, Tokyo, Japan*

Background and Aims: Pathogenesis of idiopathic nephrotic syndrome (INS) is yet to be fully elucidated. Immunological disorders are reported to be involved in the etiology of INS. Due to the efficacy of immunosuppressant agents such as calcineurin inhibitor and rituximab in treating nephrotic syndrome, aberrant activation of the acquired immune system through T and B cells are considered to be the underlying pathogenic mechanisms of INS. Nevertheless, there is a possibility that the innate immune system plays a key role in INS pathogenesis. This study aims to investigate the involvement of innate immunity in INS pathogenesis by examining the expressions of toll-like receptors (TLRs).

Method: Kidney tissue samples from two INS patients were collected at two points of time: the first biopsy was performed during nephrosis and the second during remission. Total RNA was extracted from the kidney tissue samples, and RNA-sequencing was performed to investigate RNA expression profiles. The differences between RNA expression profiles of TLRs and molecules related to TLR pathways in the tissue samples collected during nephrosis and remission were analyzed.

Results: There was a significant decrease in RNA expression of TLR9 and TLR10 during remission compared to nephrosis: fold change in each patient was -2.12 and -2.12 for TLR9, and -2.51 and -2.09 for TLR10. RNA expression of TLR8 also decreased: fold change in each patient was -1.19 and -1.75. There were no significant changes in the RNA expression profiles of TLR1, 2, 3, 4, 5, 6, and 7. In addition, there were no differences in the RNA expression profiles of MYD88, IRAK family, and TRAF family molecules that are associated with TLR pathways. However, RNA expressions of IL6, IL1B, IL12B, and TNF, as well as the cytokines controlled by TLR8 and TLR9 pathways, which were activated during nephrosis, disappeared or decreased during remission.

Conclusion: The involvement of the innate immune system in the pathogenesis of nephrotic syndrome has been suggested in some reports. Based on the fact that the onset or recurrence of nephrosis is triggered by non-specific viral infection, it is highly possible that innate immunity is involved in the pathogenesis of nephrotic syndrome. TLRs play a key role in innate immunity as they elicit the innate immune system after detecting pathogens, induce inflammatory cytokine production, and trigger signaling pathways that activate lymphocytes via maturation of dendritic cells. Specifically, TLR8, 9, and 10 mediate pathways of the first immune response to viral infections. Our study reveals that TLRs play a pivotal role in innate immunity associated with renal tissue during the onset of nephrosis.

P0023 **RNA-BINDING PROTEIN HUR REGULATES HYPOXIA-INDUCED PARKIN/BNIP3L EXPRESSIONS AND MITOPHAGY IN RENAL TUBULAR CELLS**

Chi-Yuan Li[1,2], Xin Li[1]

[1]Graduate Institute of Biomedical Science, China Medical University, Taichung City, Taiwan, R.O.C. and [2], Department of Anesthesiology, China Medical University Hospital,, Taichung City,

Background and Aims: Mitochondrial dysfunction contributes to the pathophysiology of acute kidney injury (AKI). Mitophagy selectively degrades damaged mitochondria and thereby regulates cellular function and homeostasis. RNA-binding proteins (RBPs) regulate RNA processing at multiple levels and thereby control cellular function. In this study, we report that RBP, human antigen R (HuR) regulates mitophagy in renal tubular cells (HK-2) under hypoxia condition.

Method: Human kidney proximal tubular 2 (HK-2) were cultured in Rosewell Park Memorial Institute (RPMI) 1640 medium (Gibco, Invitrogen, GmbH, Germany) supplemented with 10% fetal bovine serum (FBS) (Gibco, Invitrogen, GmbH, Germany), 1% penicillin/streptomycin (Gibco, Invitrogen, GmbH, Germany) at 37°C and 5% CO2. The cells were exposed to normoxia (37°C; 5% CO2) or hypoxia (serum and glucose deprived RPMI medium, 37°C, 1% O2) conditions. Mitophagy marker expressions (Parkin, p-Parkin, PINK1, BNIP3L, BNIP3, LC3) were determined by western blot analysis. ROS and mitochondrial membrane potential were determined using DCF-DA and JC-1 dye. Parkin and LC3 localization to mitochondria were performed by confocal laser scanning microscopy. HuR bound Parkin/BNIP3L mRNA expressions were determined by RNA-immunoprecipitation analysis.

Results: In this study, up-regulated mitophagy markers such as Parkin, PINK1, BNIP3 and BNIP3L protein expressions and mitophagosome formation were found in HK-2 cells under hypoxia condition. Stable HuR knockdown studies revealed that, HuR regulates mitophagy by mitophagosome (LC3 co-localization with mitochondria) and mitolysosome (mitochondria co-localization with lysosome) formation under hypoxia. Further, we show that HuR significantly regulated hypoxia-induced mitophagy by regulating Parkin/BNIP3L protein expressions and their mitochondrial localization. Bioinformatics studies showed that, HuR specifically binds to the AU-rich region in 3'UTR and CDS of Parkin and BNIP3L mRNA sequence. HuR was significantly bound to Parkin and BNIP3L mRNA and thereby regulated their mRNA stability under hypoxic conditions.

Conclusion: Altogether our data highlight on the functional importance of HuR in regulating mitophagy under hypoxic conditions in renal tubular cells through Parkin/BNIP3L expressions.

P0024

TRIPARTITE MOTIF-CONTAINING 55 (TRIM55) PARTICIPATES IN THE IMMUNE RESPONSE IN THE EXPERIMENTAL ANTI-THY1 GLOMERULONEPHRITIS

Lei Chen[1], Hongli Jiang[1]

[1]*The First Affiliated Hospital of Xi'an Jiaotong University, Dialysis Department of Nephrology Hospital, Xi'an, P.R. China*

Background and Aims: Mesangial proliferative glomerulonephritis (MsPGN) is considered as an immune- related disease. In the previous study, tripartite motif family was reported to be closely related to immune regulation. Therefore, we performed a series of experiments in vivo and vitro to investigate the role of tripartite motif-containing 55 (TRIM55), a member of tripartite motif family, in the progression of MsPGN.

Method: 36 male SD rats were randomly divided into 6 groups to induce anti-Thy1 nephritis. Specimens of the negative control group were collected at 0d after the injection, while those of other groups were collected at 1d, 2d, 3d, 4d, 5d after the injection, respectively. Renal cortex slices were obtained for histological and immunohistochemistry assessmen of CD68. qPCR analysis of glomerulus was performed to examine the expression of TRIM55 . Primary RMCs with overexpression of TRIM55 were obtained through plasmid transfection. In addition, si-RNA tranfection was used to knock down the expression of TRIM55 in primary RMCs. qPCR analysis was conducted to detect the level of cytokines, such as TNF-α, CCL2, CXCL6, CXCL10, and IL-6.

Results: PAS staining results indicated mesangial dissolution occurred since 1d, followed by inflammatory cell infiltration. CD68 immunohistochemical staining results showed that macrophages infiltration peaked at 1d and then decreased gradually. The expression of TRIM55 mRNA also peaked at 1d and decreased gradually, which was consistent with the trend of macrophages infiltration. In primary RMCs, knockdown of TRIM55 led to down-regulation of the expression of cytokines (TNF-α, CCL2, CXCL6, CXCL10 and IL-6). On the other hand, the expression of those cytokines(TNF-α, CCL2, CXCL6, CXCL10 and IL-6) significantly increased in TRIM55-overexpressed primary RMCs.

Conclusion: The above results indicate that TRIM55 participates in the immune response in experimental anti-Thy1 glomerulonephritis by regulating the production of cytokines. We duce TRIM55 may be a promising therapeutic intervention to ameliorate leukocyte infiltration in MsPGN.

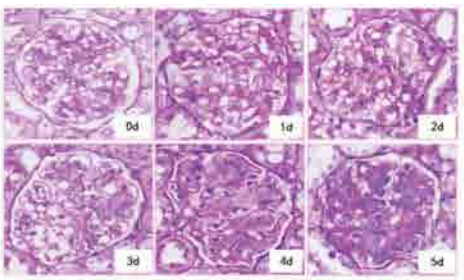


Figure 1. PAS staining of glomeruli during the development of anti-Thy1 nephritis

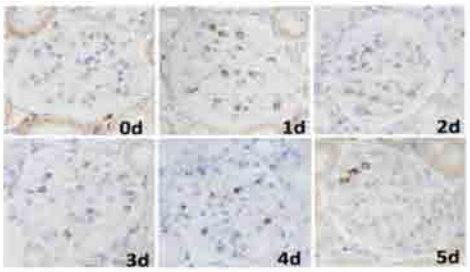


Figure 2. CD68 immunohistochemical staining of glomeruli during the development of anti-Thy1 nephritis

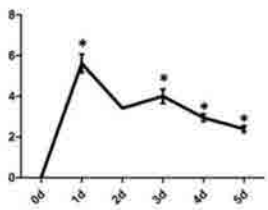


Figure 3. Trends in TRIM55 expression during development of anti-Thy1 nephritis



Figure 4. The rat mesangial cells that transfected by si-TRIM55

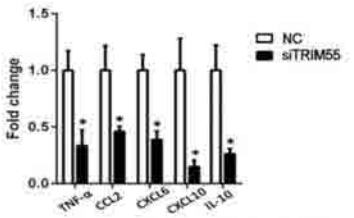


Figure 5. Trends in expression of genes involved in the immune response in the transfected rat mesangial cells

Figure:

P0025

BARIATRIC SURGERY MAY REDUCE UPREGULATED EXPRESSION OF FIBROBLAST GROWTH FACTOR 21 AND ANGIOTENSIN-CONVERTING ENZYME 2 IN OBESE PATIENTS.

Byung Chul Yu[1], Hyoungnae Kim[2], Mooyong Park[1], Soon hyo Kwon[2]

[1]Soonchunhyang University Bucheon Hospital, Division of Nephrology, Department of Internal Medicine, Bucheon, Korea, Rep. of South and [2]Soonchunhyang University Seoul Hospital, Division of Nephrology, Department of Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Recent studies showed that the fibroblast growth factor 21 (FGF21) and angiotensin-converting enzyme 2 (ACE2)/Angiotensin 1-7 (Ang (1-7))/MAS axis of the renin-angiotensin system counteract to the negative role of Ang II in various disease. In this study, we examed FGF21 and ACE2/Ang (1-7) in obesity and its change after bariatric surgery.

Method: We prospectively enrolled obese patient who performed bariatric surgery and age-sex matched healthy volunteers (HV) (n=12 each). We obtained their clinical information and serum samples. Serum FGF-21, Ang II, ACE2, and Ang (1-7) levels were measured by enzyme-linked immunosorbent assay kits. We measured also FGF-21, Ang II, ACE2, and Ang (1-7) 6 months after bariatric surgery in obese patients (n=12).

Results: FGF21, Ang II, and ACE2 levels were significantly higher in obese patients compared with HV (p= 0.045, < 0.001, and 0.020, respectively). FGF21, Ang II, and ACE2 levels were significantly decreased after bariatric surgery (p = 0.002, 0.005, and 0.023, respectively). There was no significant difference in Ang (1-7) levels between obese patients and HV (p = 0.887) (Figure 1). Although Ang (1-7) levels did not change after bariatric surgery (p = 0.480), changes in Ang (1-7) levels were positively correlated with changes in body mass index (BMI) (R^2 = 0.580, p = 0.048) (Figure 2).

Conclusion: FGF21 and ACE2 were upregulated in obese patients and they are reduced after bariatric surgery. A decrease in BMI after bariatric surgery could lead to decrease in Ang (1-7).

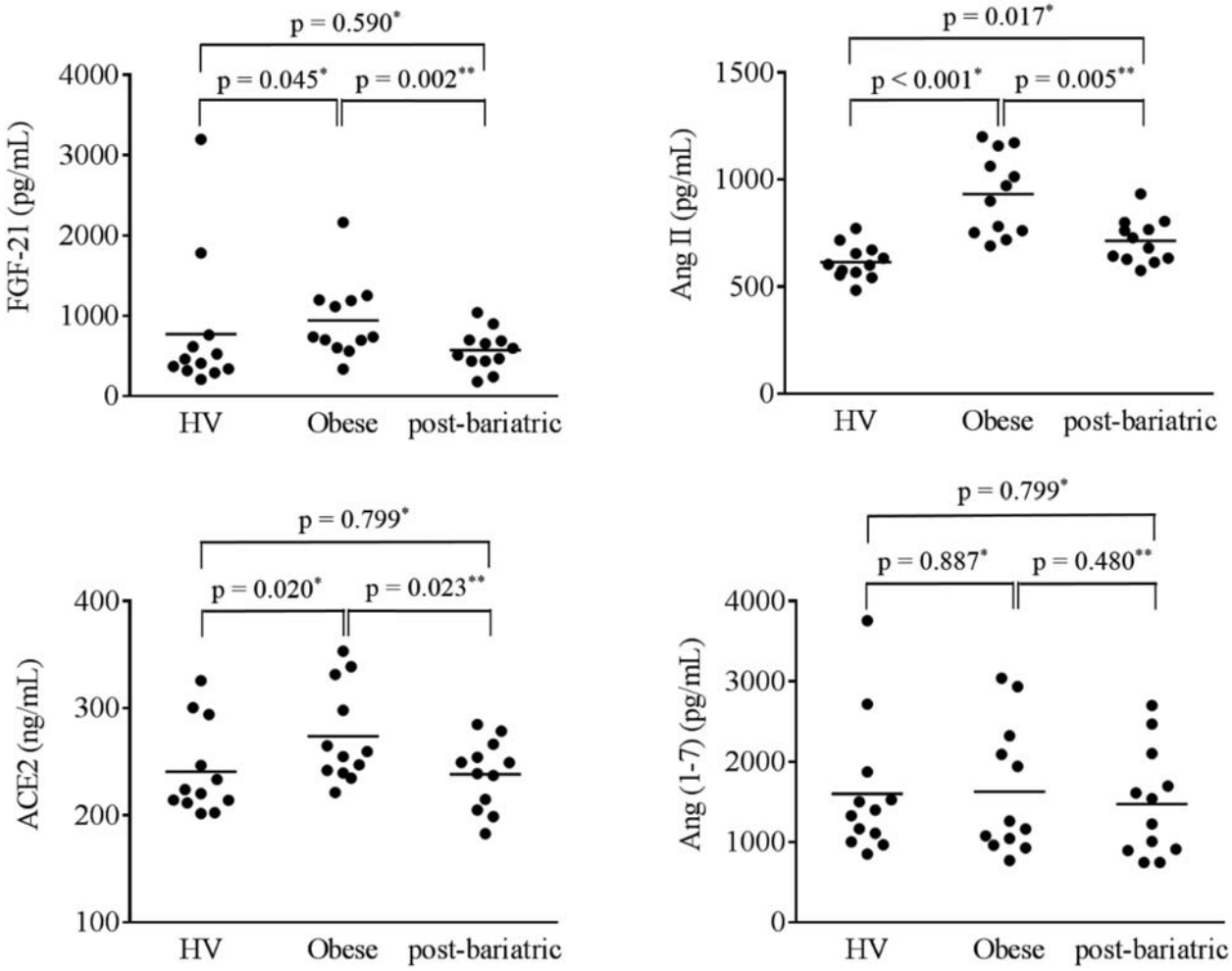


Figure 1. Changes in FGF21, Ang II, ACE2, and Ang (1-7) levels after bariatric surgery. Data were analyzed by *Mann-Whitney and **Wilcoxon matched-pairs signed rank tests. *ACE2*, angiotensin-converting enzyme 2; *Ang (1-7)*, Angiotensin 1-7; *Ang II*, angiotensin II; *FGF21*, fibroblast growth factor 21; *HV*, healthy volunteers.

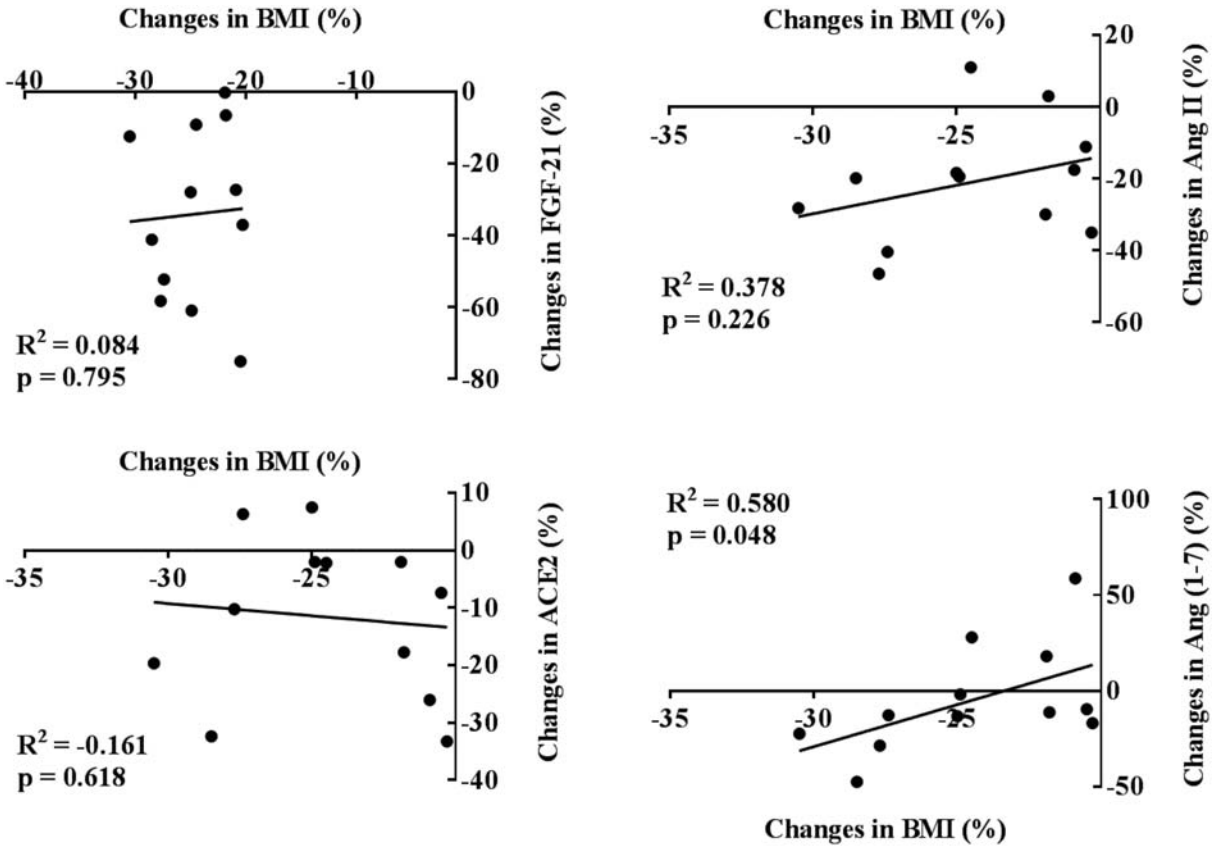


Figure 2. Relationships among changes in FGF21, Ang II, ACE2, Ang (1-7) levels and BMI after bariatric surgery. Data were analyzed by Spearman's rank correlation coefficient. *ACE2*, angiotensin-converting enzyme 2; *Ang (1-7)*, Angiotensin 1-7; *Ang II*, angiotensin II; *BMI*, body mass index; *FGF21*, fibroblast growth factor 21.

P0026

METFORMIIN IMPROVES DYSFUNCTION OF MESENCHYMAL STEM CELLS ASSOCIATED WITH CHRONIC KIDNEY DISEASE VIA SENESCENCE INHIBITION

Hyunjin Noh[1], Mi Ra Yu[2], Kyoungin Choi[3], Dohui Hwang[3]

[1]Soon Chun Hyang University, Dept of Internal Medicine, Hyonam Kidney Laboratory, Seoul, Korea, Rep. of South, [2]Soon Chun Hyang University, Hyonam Kidney Laboratory, Seoul, Korea, Rep. of South and [3]Soon Chun Hyang University, Dept of Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Mesenchymal stem cells (MSC) are promising source of cell-based regenerative therapy; however, adequate cell functionality is a critical factor for the success of autotransplantation.

Method: We investigated the effects of metformin on chronic kidney disease (CKD)-associated cellular senescence using MSC isolated from sham operated and subtotal nephrectomized mice and further explored the protective role of metformin-treated CKD MSC in renal progression.

Results: When compared to normal MSC, MSC isolated from CKD mice displayed reduced proliferation and early senescence as determined by enlarged cell morphology, increased oxidative stress, accumulation of DNA damage response marker p53 binding protein 1 (53BP1), phospho p53, $p16^{INK4a}$, and β-gal expression, and decreased cyclin-dependent kinase 4 (CDK4) and cyclin D. CKD MSC exhibited activation of NFκB resulting in expression of senescence-associated secretory phenotype (SASP) factors compared to normal MSC. All of these changes were significantly prevented by metformin treatment. In vivo, metformin-treated CKD MSC attenuated inflammation and fibrosis in UUO kidney as compared to CKD MSC. Co-culture of LPS or TGF-β1-treated HK2 cells with metformin-treated CKD MSC markedly decreased LPS or TGF-β-induced tubular expression of proinflammatory markers and fibrogenesis when compared to CKD MSC suggesting paracrine action of CKD MSC enhanced by metformin treatment.

Conclusion: Our data suggest that metformin inhibits cellular senescence of CKD MSC and improves their renoprotective effects.

P0027

METFORMIN INHIBITS TGF-BETA1-INDUCED FIBROTIC RESPONSE IN MOUSE INNER MEDULLARY COLLECTING DUCT CELLS IN ASSOCIATION WITH ACTIVATION OF PPARA SIGNALLING

Shanying Liu[1], Yan Li[1], Dan Liu[1], Diefei Liang[1]

[1]*Sun Yat-sen University, Sun Yat-sen Memorial Hospital, Guangzhou, P.R. China*

Background and Aims: Metformin has been recognized to inhibit renal fibrosis through protection of proximal tubular epithelial cells from inflammation and fibrotic response. However, the role of other segments of renal tubular epithelial cells in the development of renal fibrosis remains unclear. This study aimed to investigate the pro-fibrotic effects of TGF-beta1 and the anti-fibrotic effects of metformin in mouse inner medullary collecting duct cells using mIMCD-3 cell line.

Method: Cultured mIMCD-3 cells were treated with TGF-beta 1 and metformin either alone or in combination. The morphological change of cells was inspected under an inverted microscope. The mRNA of genes associated with renal fibrosis was evaluated by real-time quantitative PCR. The protein expression of E-cadherin, Vimentin, alpha-SMA were evaluated by Western blot.

Results: The shape of mIMCD-3 cells changed from cobblestone to spindle-like after exposure to TGF-beta 1 at 10ng/mL for 72 hours, which can be inhibited by co-treatment with metformin. TGF-beta 1 remarkably increased the expression of alpha-SMA and PAI-1, while decreased E-cadherin mRNA in mIMCD-3 cells. Metformin inhibited TGF-beta 1-induced reduction of E-cadherin and upregulation of PAI-1. The protein level of E-cadherin was also decreased and alpha-SMA increased by TGF-beta 1. Metformin inhibited TGF-beta 1-induced protein expression of alpha-SMA and vimentin, and downregulation of E-cadherin. It has been reported that impaired renal PPARα signaling promoted renal fibrosis. In this study, we found that metformin upregulated basal level of PPARα mRNA. PPARα target genes including Acadvl and Cpt1a were downregulated by TGF-beta 1 in mIMCD-3 cells, which could be prevented by metformin.

Conclusion: Metformin inhibits the profibrotic effects of TGF-beta 1 probably through suppression of EMT and maintaining PPARα signaling in mouse inner medullary collecting duct cells.

P0028 **THE ACTIVATION OF P75NTR RECEPTOR SIGNALING PROMOTES EMT IN ADPKD CELL LINE WT9-12**

Giuseppina Toteda[1], Simona Lupinacci[1], Anna Perri[1], Donatella Vizza[1], Antonella La Russa[1], Danilo Lofaro[1], Paolo Gigliotti[1], Francesca Leone[1], Renzo Bonofiglio[1]

[1]*Centro di Ricerca Rene e Trapianto., UOC Nefrologia, Dialisi e Trapianto, Ospedale Annunziata, Cosenza, Italy*

Background and Aims: ADPKD cystic epithelial cells have been shown to display an undifferentiated phenotype and to undergo epithelial to mesenchymal transition (EMT) changes as part of their phenotype. Thus, in ADPKD kidneys there is upregulation of EMT-related genes and increased fibrosis that support the proliferation of the cyst-lining cells and the progression of ADPKD. In our previous study, we provided that TGFβ1-induced $p75^{NTR}$ receptor activation promotes EMT in renal tubular cells, HK2. $p75^{NTR}$ is the common receptor for all the neurotrophins and their precursors. Since its identification and cloning in the 1980s, $p75^{NTR}$ has been reported to be involved in different and often contradictory functions such as survival, apoptosis, differentiation, proliferation and migration, depending on the cell type and cellular context. Furthermore, $p75^{NTR}$ is known to be overexpressed in some human cancer, where it participates in the stimulation of tumor growth and dissemination. $p75^{NTR}$, through

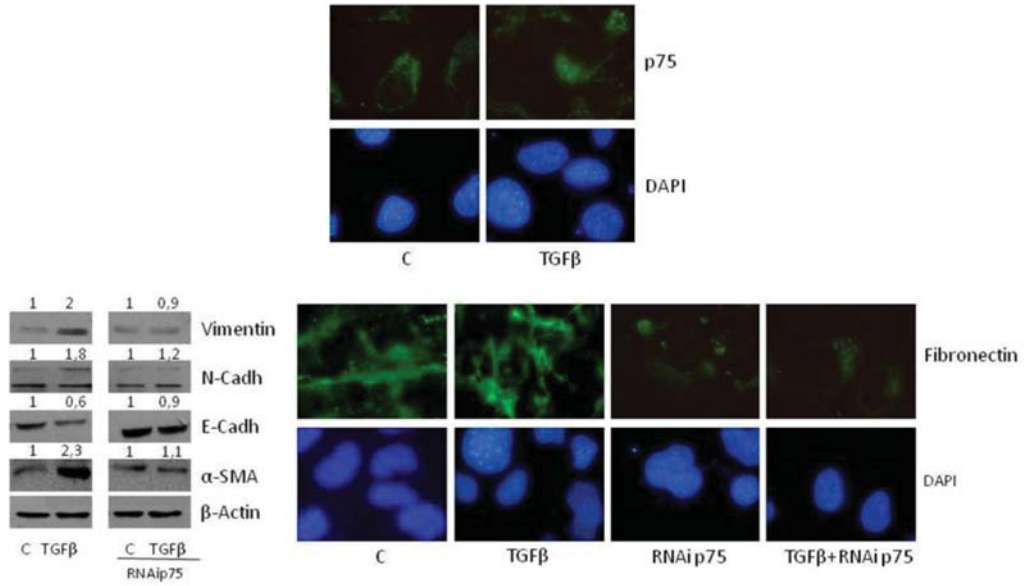


Figure 1. In the WT9-12 cell line, TGFβ1 upregulates proteic expression of p75, Fibronectin, N-Cadherin, α-SMA, Vimentin and downregulates E-Cadherin. These effects are significantly reversed in cells transfected with RNAi-p75NTR after TGFβ1 treatment.

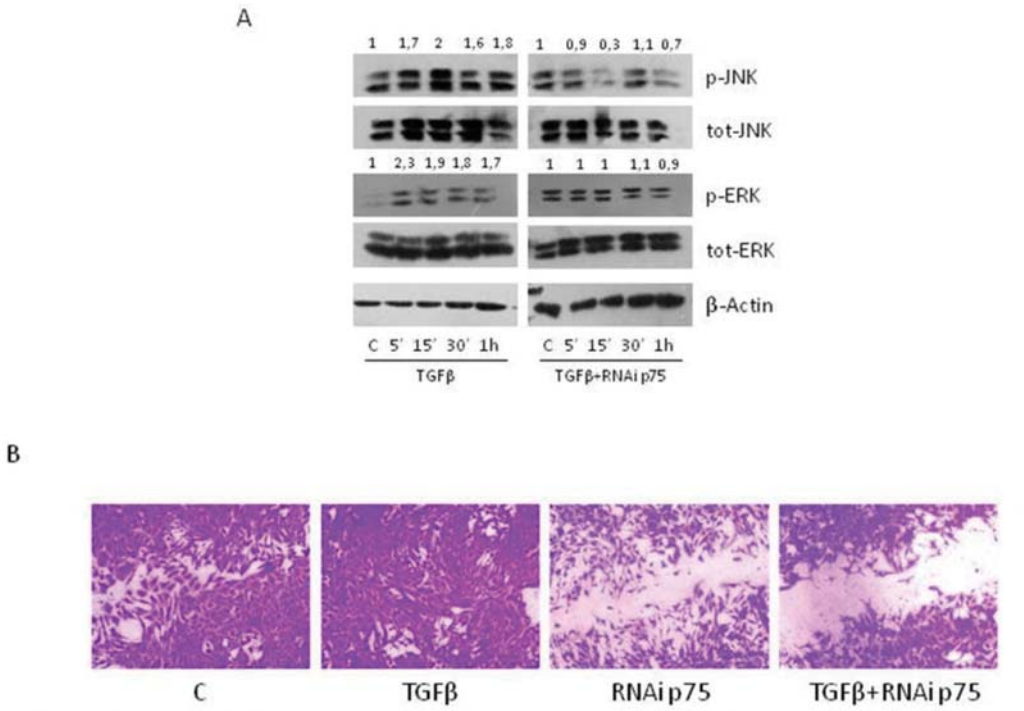


Figure 2. (A) Time course assays, performed in cells transfected with RNAi-p75NTR and TGFβ1-treated, demonstrated downregulation of pERK1/2 and pJNK. (B) Scratch and Trans-well migration assays showed a reduced cell motility in p75NTR-knocked-down cells.

Figure:

a neurotrophin-dependent mechanism, dramatically enhances migration and invasion of melanoma and glioma cells.

Therefore, starting from these pieces of evidence and since WT9-12 cells exhibit higher constitutive expression of $p75^{NTR}$ and TGFβ1 than that of HK-2, the aim of this study is to carry out in vitro studies to investigate whether $p75^{NTR}$ is involved in EMT of cyst-lining cells and in renal fibrosis in ADPKD.

Method: Immortalized tubular renal cells homozygous for a truncating PKD1 mutation (WT9-12); Western Blot (WB); Real-Time PCR; Scratch and Trans-well migration assays; Immunofluorescence (IF); RNA interference (RNAi); Transfection assay.

Results: WB and IF assays showed that in WT9-12 cells TGFβ1 (5ng/ml) increased protein expression of $p75^{NTR}$ and of mesenchymal markers Fibronectin, N-Cadherin, α-SMA, Vimentin while reduced the expression of the epithelial marker E-Cadherin. This biological effect is significantly reversed in cells transfected with RNAi-$p75^{NTR}$ (Figure 1). Functional studies revealed that increased $p75^{NTR}$ protein expression was given to greater $p75^{NTR}$ mRNA stability.

Time course assays, performed in cells transfected with RNAi-$p75^{NTR}$ and TGFβ1-treated, demonstrated downregulation of pERK1/2 and pJNK, $p75^{NTR}$ downstream pathways and involved in the non-canonical TGFβ1 pathway promoting pro-fibrotic genes transcription Figure 2A).

Results of the analysis of SMAD pathway showed that SMAD3 was not significantly activated in cells untreated with TGFβ1. Moreover, selective ERK1/2 inhibition with PD98059 (10mM) reduced significantly the levels of mesenchymal markers N-Cadherin and α-SMA respect to the controls of untreated cells. Interestingly, in TGFβ1-treated cells in the presence of PD98059 the reduction of mesenchymal markers expression was minor respect to TGFβ1-untreated cells. These findings emphasize the importance of the ERK1/2 pathway in ADPKD. Our results revealed that the ERK1/2 pathway also plays a pivotal role in non-SMAD pathways downstream of TGFβ1 in fibrotic processes in ADPKD. Finally, Scratch and Trans-well migration assays showed a reduced cell motility in $p75^{NTR}$-knocked-down cells (Figure 2B).

Conclusion: Although more basic studies are clearly needed to understand the mechanism of action of $p75^{NTR}$, our results emphasized the crucial role of $p75^{NTR}$ in EMT changes in ADPKD cells which may contribute to the cystic phenotype and to fibrotic process.

RENAL DEVELOPMENT AND CYSTIC DISEASES

P0031 IS OXIDATIVE STRESS ASSOCIATED WITH TOTAL KIDNEY VOLUME IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE?

Ibrahim Dogan[1], Baris Eser[2], Nihal Aydemir[2], Huseyin Kayadibi[3], Oguzhan Ozcan[4], Nurdan Fidan[5], Sultan Ozkurt[6]

[1]Hitit University School of Medicine, Nephrology, Turkey, [2]Hitit University School of Medicine, Nephrology, Corum, Turkey, [3]Hitit University School of Medicine, Biochemistry, Corum, Turkey, [4]Mustafa Kemal University, School of Medicine, Biochemistry, Hatay, Turkey, [5]Hitit University, School of Medicine, Radiology and [6]Eskisehir Osmangazi University, School of Medicine, Nephrology, Eskisehir, Turkey

Background and Aims : Ischemia Modified Albumin (IMA) is a marker of cardiovascular risk factor associated with oxidative stress. In this study, our aim was to determine oxidative stress status in autosomal dominant polycystic kidney disease (ADPKD) and to evaluate its relationship with total renal volume.

Method : Seventy-two ADPKD (mean age 52 (41-64) years) and 33 healthy controls (mean age 54 (42-62) years) (P= 0.372) were included in the study. Total Oxidant Level (TOS) and Total Antioxidant Level (TAS) were measured using the colorimetric method. Oxidative Stress Index (OSI) was calculated. IMA level was measured by ELISA. Total renal volume was assessed by magnetic resonance imaging. The relationship between oxidative stress, inflammation and renal volume was evaluated by correlation analysis. P values <0.05 were considered significant for statistical analyses.

Results : Serum IMA level was higher in the patient group (158.46 ng/ml (85.98-246.70)) than in the control group (70.04 ng/ml (50.40-80.02); ($P< 0.001$). TOS level and OSI rate were significantly higher in the patient group compared to the control group, and TAS level was not different between the two groups ($P< 0.001$, $P< 0.001$, P= 0.576, respectively).Correlation analysis was performed between IMA, TAS and TOS levels, OSI rate and kidney volume. IMA level correlated with TOS level and OSI positively ($P< 0.001$), but there was no correlation between IMA level and TAS level and renal volume (P= 0.550, P= 0.286, respectively). IMA level was negatively correlated with GFR and positively correlated with proteinuria (P= 0.040, $P< 0.001$, respectively). There was no correlation between total renal volume and IMA, TAS, CRP and proteinuria. The correlation between volume and GFR and TOS level was borderline negative (P= 0.054, P= 0.051, respectively).

Conclusion : There is an increased level of oxidative stress in ADPKD. Increased IMA level may show oxidative stress in this population. Total renal volume in ADPKD is associated with loss of renal function but not sufficient to show oxidative stress.

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P0031A

URINE METABOLOMICS: AN EMERGING TOOL FOR DISSECTING BIOLOGICAL ABERRATIONS UNDERLYING RENAL DYSFUNCTION IN BARDET-BIEDL SYNDROME

Miriam Zacchia[1], Emanuela Marchese[2], Marianna Caterino[3], Margherita Ruoppolo[4], Giovambattista Capasso[5]

[1]Università della Campania L Vanvitelli, Dipartimento di Scienze Mediche Traslazionali, Naples, Italy, [2]Università della Campania L Vanvitelli, Dipartimento di Salute Mentale e Fisica e Medicina Preventiva, Naples, Italy, [3]Universit di Napoli, Federico II, [4]Università di Napoli, Federico II and [5]Università della Campania L Vanvitelli, Dipartimento di Scienze Mediche Traslazionali, Italy

Background and Aims: Bardet Biedl Syndrome (BBS) is a rare genetic disorder characterized by a wide range of organ dysfunction, including kidney disease. The severity of renal dysfunction is highly variable in this setting, ranging from tubular defects to the end stage renal disease, with poor genotype-phenotype correlation. Proteomics and metabolomics are powerful tools able to contribute to the better understanding of molecular basis of disease conditions. Our previous studies demonstrated that the urinary proteomic pattern of BBS patients differed from that of healthy subjects, with a set of deregulated proteins including cell adhesion and extracellular matrix organization proteins (1). The present study aims to characterize urine metabolomic profile of BBS patients, in order to identify both 1) potential disease biomarkers and 2) aberrant metabolic pathways underlying renal disease

Method: To this end, in the *pilot study* urine samples have been collected from 14 adult BBS patients and have been compared with healthy volunteers, using an untargeted strategy. In the *confirmation study*, 24 BBS patients with wide range of kidney dysfunction have been enrolled, and additional control groups, besides healthy subjects, were included: 1) age-gender-matched chronic kidney disease patients by other causes and 2) obese individuals.

Results: Several metabolites were de-regulated in BBS patients compared with normal subjects (lactic acid, glycolic acid,3-Hydroxypropionic acid, pyruvic acid, 3-hydroxyisobutyric acid, 2-ethyl-3-hydroxy-propionic acid, succinic acid, fumaric acid, erythropentonic acid, 2-hydroxyglutaric acid, 4-hydroxyphenyllactic acid, 3,4-pyridinedicarboxylic acid, retinoic acid, 4-hydroxyphenylacetic acid, palmitic acid, 9-Hexadecenoic acid, oleic acid and 9-Octadecenoic acid). The clusterization performed by MetaboAnalyst tool, revealed a possible deregulation of different metabolic pathways, including glycolysis, TCA cycle, pyruvate metabolism, lipids biosynthesis and glutamate metabolism (*p-value* <0.01) (**figure 1**); some of these pathways were described as de-regulated in other ciliopathies (2). In the confirmation study (on-going studies) some metabolites, including lactic acid and intermediates of Krebs cycle, correlated with kidney dysfunction only in the BBS group.

Conclusion: These findings suggest that urine metabolomic fingerprint of BBS patients is different from that of healthy subjects and indicate a possible deregulation of several metabolic pathways; some urinary molecules correlated with kidney dysfunction only in BBS patients, suggesting the specificity of these results.

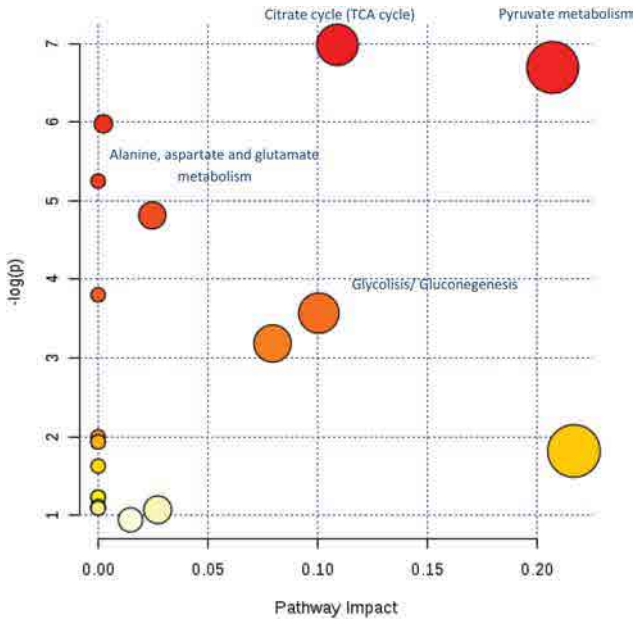


Figure 1. Deregulated metabolic pathways in BBS patients compared with healthy subjects (pilot study).

P0032

INCIDENCE OF GALLSTONES AND ASSOCIATED COMPLICATIONS WITH USE OF THE SOMATOSTATIN ANALOGUE LANREOTIDE FOR POLYCYSTIC KIDNEY AND LIVER DISEASE.

Sophie Aapkes[1], Robbert De Haas[2], Abigail Veldman[1], Lucas H.P. Bernts[3], Esther Meijer[1], Joost Ph Drenth[3], Ronald Gansevoort[1,4]

[1]University Medical Center Groningen, Nephrology, Groningen, Netherlands, [2]University Medical Center Groningen, Radiology, Groningen, Netherlands, [3]Radboud University Medical Center, Gastroenterology and Hepatology, Nijmegen, Netherlands and [4]On behalf of the DIPAK consortium

Background and Aims: Recently, we performed a large randomized-controlled trial to assess the effects of the somatostatin analogue lanreotide on kidney function and kidney and liver volume in autosomal dominant polycystic kidney disease (ADPKD), the DIPAK-1 trial. Lanreotide had no effect on rate of kidney function decline, but slowed kidney and especially liver growth and is used for this indication in clinical practice1,2. A higher incidence of gallstones has been suggested with lanreotide use, but the exact size and implications of this problem are unknown. Therefore, we systematically studied the incidence of gallstones with lanreotide in ADPKD patients.

Method: In the DIPAK-1 trial, 305 ADPKD patients (age 18-60 years and eGFR 30-60 ml/1.73m2/min) were randomized to lanreotide or standard of care. MRIs were performed at baseline and end of study (120 weeks). For this post-hoc study, patients with a medical history of cholecystectomy (n=7) or absence of a MRI at the end of study (n=28) were excluded. For the remaining study population (n=270), all MRIs were assessed for presence of gallstones by two trained investigators blinded for study treatment and study period and in case of disagreeing results, an abdominal radiologist was consulted for a final assessment. For patients with gallstones additional follow up after the end of the trial was obtained.

Results: In 2 baseline and 8 end-of -study MRIs, it was not possible to identify the gallbladder, due to multiple adjacent liver cysts. Of the remaining 260 patients (age 48.5 years, female 49.6%, eGFR 50.0 ml/min/1.73m^2), 14 patients (5,4%) had gallstones at baseline, of whom 5 were randomized to lanreotide and 9 to standard care. At the end of study, 32 patients (12,3%) had gallstones, of whom 21 patients had received lanreotide and 11 standard care. During the 120 week lasting study, new gallstones occurred in 17 out of 128 patients receiving lanreotide (13.3%) and 3 out of 132 patients receiving standard care (2.3%), rendering an adjusted Odds Ratio for gallstone formation with lanreotide use of 6.9 (95% Confidence Interval 1.9-24.7) $p<0.005$). The only other significant risk factor for gallstone formation was female gender (OR 3.5, CI 1.2-10.6, $p<0.05$). Age, body-mass-index and importantly liver volume were not associated with gallstone formation.

Of the 32 patients with gallstones at the end of study, seven experienced gallstone-associated complications. Three experienced a biliary pancreatitis (1 during and 2 after the study). Another one had signs of a chronic pancreatitis as accidental finding on imaging during the study, without having had symptoms. Furthermore, another 3 patients underwent a cholecystectomy for symptomatic gallstones after the study. Importantly, all patients with gallstone-associated complications were part of the subgroup of patients that developed *de novo* gallstones during lanreotide use in the study.

Conclusion: Lanreotide increases the risk of gallstone formation in ADPKD sevenfold. Gallstones were associated with severe complications, most occurring after the end of the trial. The benefit of somatostatin analogues to reduce kidney and liver size in ADPKD should therefore be weighed against the higher incidence of these adverse events, and patients and doctors should be aware of the risk of (symptomatic) gallstones with use of these drugs.

P0033

COMPARISON OF ANXIETY, DEPRESSION AND QUALITY OF LIFE IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: A CROSS-SECTIONAL, RANDOMIZED CONTROLLED PILOT STUDY

Tuba Elif Ozler[1], Cemal Alay[2], Egemen Cebeci[1], Sami Uzun[1], Serhat Karadag[1], Oktay Ozkan[1], Yagmur Bashan[1], Burcu Dag[1], Zeynep Karaali[2], Savas Ozturk[1]

[1]Haseki Training and Research, Department of Nephrology, Istanbul, Turkey and [2]Haseki Training and Research, Department of Internal Medicine, Istanbul, Turkey

Background and Aims: Patients with autosomal dominant polycystic kidney (ADPKD), in addition to uremic signs and symptoms, the need for renal replacement therapy and the risk of transferring the disease to their children put them under physical and mental stress. This may affect the psychosocial status of patients. In this study, we compared diabetic nephropathy (DN) patients who were expected to progress rapidly with early-stage ADPKD patients to reveal anxiety, depression and quality of life.

Method: In our cross-sectional, randomized controlled and single-center study, 55 adult patients with early stage ADPKD with eGFR $\geq$ 60 ml/min/1.73 m^2 and 50 patients with DN as control group were included. Both groups were applied to state trait anxiety inventory (STAI), patient health questionnaire 9 (PHQ-9), quality of life short form 36 and Beck depression inventory in order to evaluate their depression, anxiety and quality of life. Depression, anxiety and quality of life questionnaires' results, demographic and clinical characteristics, laboratory findings of the two groups were compared.

Results: Comparison of patients' and control groups demographic and clinical characteristics, and laboratory data were shown in Table 1. According to state trait anxiety inventory; moderate and high levels of anxiety were present in 94% patients with ADPKD and in 66% patients with DN ($p<0.001$). According to Beck depression inventory; depression is detected in 58.2% patients with ADPKD and in 26% patients with DN ($p=0.001$). When the PHQ-9 results were compared; depression is prevalent in 55.6% patients with ADPKD and in 34.7% patients with DN ($p=0.037$). Although ADPKD patients were at an early stage, we found anxiety and depression more frequent

Table 2: Comparison of patients' and control group anxiety, depression and quality of life questionnaire results

	ADPKD group (n=55)	Control group (n=50)	p
STAI			
State anxiety score tx-1, *mean± Std*	38.6±11.1	33.1±9.0	0.006
State anxiety score tx-1			
Low	11 (20)	21 (42)	
Intermediate	36 (65.5)	25 (50)	0.045
High	8 (14.5)	4 (8)	
Trait anxiety score tx-2, *mean± Std*	44.9±10.5	38.4±11.2	0.003
Trait anxiety score tx-2			
Low	3 (5.5)	17 (34)	
Intermediate	32 (58.2)	23 (46)	0.001
High	20 (36,4)	10 (20)	
PHQ-9, *median (IQR)*	6 (IQR 3-10)	3 (IQR 2-7.2)	0.02
Depression according to PHQ-9;			
None or minimal	24 (43.6)	32 (64)	
Mild	15 (27.3)	13 (26)	
Moderate	7 (12.7)	3 (6)	0.08
Moderately severe	8 (14.5)	1 (2)	
Severe	1 (1.8)	1 (2)	

Figure:

and severe than DN patients. While physical life quality was similar in both group; mental quality of life was lower in ADPKD patients according to quality of life short form 36 (p= 0.32 and p= 0.03 respectively) (Table 2). Independent variables affecting Beck depression inventory score; being a woman, smoking and being diagnosed with ADPKD; independent variables affecting PHQ9 score; being female and the excess of the number of medical tablets used daily; independent variables affecting personal trait anxiety score; being a woman, smoking, being diagnosed with ADPKDD, and presence of hypertension.

Table 1: Comparison of patients' and control groups clinical characteristics, and laboratory data

	ADPKD Group (n=55)	Control Group (n=50)	p
Gender (female)	34 (61.8)	29 (58)	0.69
Age (years)	42.2±10.4	55.9±8.4	<0.001
Age of diagnosis (years),	31.9±10.2	42.2±11.0	<0.001
Marital status (single)	6 (10.9)	10 (20)	0.27
Level of education			
Primary school or no education	32 (58.2)	33 (66)	0.16
Unemployed	28 (50.9)	26 (52)	0.91
Smoker	13 (23.6)	4 (8)	0.03
Total monthly household income (Turkish liras)	3000 (IQR 2000-4625)	3000 (IQR 2075-3500)	0.45
Number of medical tablets taken by the patient per day	1 (IQR 0-3)	6 (IQR 3.75-8)	<0.001
Number of people living in the same household	4 (IQR 3-4)	3 (IQR 2-4)	0.07
History of RRT in first and/or second degree relative	36 (65.5)	7 (14)	<0.001
Depression diagnosis in first and/or second degree relative	10 (18.2)	11 (22)	0.63
Mean blood pressure (mm Hg)	85.5±8.6	87.4±11.4	0.34
DM	5 (9.1)	50 (100)	<0.001
HT	26 (47.3)	41 (82)	<0.001
Urea (mg/dL)	32 (IQR 28-35)	40.5 (IQR 32.2-51)	<0.001
Creatinine (mg/dL)	0.79 (IQR 0.63-0.97)	0.97 (IQR 0.82-1.14)	<0.001
eGFH (ml/min/1.73m^2)	100 (IQR 73-115)	68 (IQR 64-86)	<0.001
Hemoglobin (gr/dL)	13.4±1.6	13±1.6	0.21
Albumin (g/dL)	4.3±0.2	4.2±0.3	0.11
CRP (mg/L)	2.9 (IQR1.3-3.8)	4.5 (IQR 2-8.5)	*0.03*
Spot urine proteinuria (mg/g)	100 (IQR 80-140)	375 (IQR 260-750)	*<0.001*

Conclusion: In ADPKD patients, anxiety, depression and decrease in quality of life can be seen more frequently than other uremic patients even in the early period when renal functions are preserved. This group of patients should be evaluated in this respect from the early stages of the disease.

P0034

IDENTIFICATION OF FACTORS ASSOCIATED WITH PROGRESSION, PROGNOSIS AND TOLVAPTAN INDICATION IN POLYCYSTIC KIDNEY DISEASE PATIENTS

Myrto Kostopoulou[1], Michaela Louka[1], Stavros Fokas[1], Eirini Tigka[1], Angelos Drakopoulos[1], Vasiliki Gkika[1], Mihail Tsagkatakis[2], George Tsirpanlis[1]

[1]General Hospital of Athens "G. Gennimatas", Department of Nephrology, Athens, Greece and [2]Geniki Apeikonistiki, Medical Imagining, Athens, Greece

Background and Aims: The identification of possible risk factors for the progression of Autosomal Dominant Polycystic Kidney Disease (ADPKD) is an emerging field especially after the introduction of the first disease-specific treatment. The present study aims to explore the associations between epidemiological, clinical and imagining data in a large cohort of ADPKD patients.

Method: This study was from a single outpatient clinic following patients with ADPKD. Patients were included in the study if they had a recent Magnetic Resonance Imaging (MRI) for measurement of Total Kidney Volume (TKV), a validated biomarker for disease progression. For all patients, the Mayo Clinic Imagining Category (MCIC) and the respective prediction for End Stage Renal Disease (ESRD) were calculated. Patients eligible for tolvaptan treatment (MCIC 1C, 1D, 1E, age < 55 years old and estimated-glomerular filtration rate (e-GFR) ≥ 25 ml/min) were identified. Characteristics including individual medical history, clinical and laboratory data were examined for possible associations with renal and imagining parameters using linear regression models.

Results: A total of 158 patients were included. Based on measurements of height-adjusted TKV (ht-TKV) and age, 5% of the patients were classified as 1A, 20% as 1B, 34% as 1C, 25% as 1D and 16% as 1E, MCIC. In multivariable analysis, patient's age ($p = 0.01$), male sex ($p < 0.001$), parent's age at which ESRD was reached (adjusted for patient age) ($p < 0.001$) and proteinuria ($p = 0.04$) were associated with ht-TKV. Parent's age at ESRD differed significantly between the MCICs of the offspring (mean$\pm$(SD)), 70.83 (12.90) in 1A, 63.79 (11.39) in 1B, 57.32 (10.42) in 1C, 51.42 (9.18) in 1D and 47.94 (5.73) years old in 1E, ($p < 0.001$). Similarly, there were significant differences in the presence and the age of hypertension onset ($p = 0.004$ and $p = 0.003$, respectively). In 104 patients (50 females, 54 males) who were eligible for tolvaptan treatment age at ADPKD diagnosis, age at hypertension onset and parent's age reaching at ESRD were all significantly lower ($p < 0.001$ for all) when compared to non-eligible patients. Finally, factors associated with the prediction score of ESRD (e-GFR 10/ml/min) were hypertension, uric acid and the age at ESRD of the affected parent ($p = 0.001$, 0.02 and 0.01, respectively).

Conclusion: The age at which an affected parent had reached ESRD, as heritability estimator, was significantly associated with a worst phenotype, prognosis and tolvaptan indication. Early diagnosis of the disease, hypertension and its early onset, proteinuria and male sex are also possible risk factors for the progression of ADPKD.

P0035

URINARY CITRATE AS A MARKER OF RENAL FUNCTION IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Francisco-Jose Borrego-Utiel[1], Isidoro Herrera[2], Enoc Merino Garcia[1], Clara Moriana Dominguez[1], Victoria Camacho Reina[2], Esther Ocaña Perez[2]

[1]UGC DE NEFROLOGIA. HOSPITAL UNIVERSITARIO DE JAEN, Spain and [2]UGC ANALISIS CLINICOS. HOSPITAL UNIVERSITARIO DE JAEN, Spain

Background and Aims: In autosomal dominant polycystic kidney disease (ADPKD) is frequent to find low urinary citrate levels. Recently it has been suggested that urinary citrate could be a marker of covert metabolic acidosis. Our aim was to analyze relationship between urinary citrate levels and renal functionality in ADPKD patients.

Method: We determined citrate, calcium and uric acid in 24-hour collected urine from 91 ADPKD patients

Results: Urinary citrate/creatinine ratio was 214±158 (range 5.3-678) mg/g Cr with levels significantly higher in females. When considering chronic kidney disease (CKD) stages we observed a progressive decrease in urinary osmolality and in urinary citrate, calcium and uric acid elimination. Low levels of citrate (<300 mg/g Cr) were present in 40% in CKD-1 stage, in 69.7% in CKD-2 stage, 92% in CKD-3 stage and 100% in CKD-4 + 5 stages. Urinary citrate was correlated with serum creatinine ($r = -0.66$, $p < 0.001$) and eGFR ($r = 0.56$, $p < 0.001$). Urinary citrate significantly correlated with urinary calcium but correlation with urinary uric acid was weaker. We did not find any correlation with serum bicarbonate. Using multiple lineal regression analysis we found as predictors of urinary citrate to glomerular filtration rate, female gender and urinary calcium levels. In a subgroup of patients we measured total kidney volume and we found an inverse correlation with urinary citrate levels that dissappeared when it was corrected with glomerular filtration rate. We did not also find a relationship between urinary elimination of calcium or uric acid and TKV after adjusting with eGFR.

Conclusion: Urinary citrate is very frequently reduced in ADPKD patients being present from very early CKD stages. Their levels are inversely correlated with glomerular filtration rate and directly with urinary calcium excretion. We did not found a relathionship with serum bicarbonate. We think that it would be interesting to study urinary citrate in other nephropathies and verify if it could be a marker of covert metabolic acidosis.

P0036

THE EFFECT OF CKD ASSOCIATED SNPS ON THE PROGRESSION OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Marlene Louise Nielsen[1], Dorte Launholt Lildballe[2], Mads Jørgensen[2], Maria Rasmussen[2], Henrik Birn[1,3]

[1]Department of Biomedicine, Aarhus University, Denmark, [2]Department of Clinical Genetics, Vejle Hospital and [3]Department of Renal Medicine, Aarhus University Hospital

Background and Aims: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most frequent, inherited, cystic kidney disease. It is characterized by formation and growth of renal cysts obstructing normal tubules leading to a decline in renal function and eventually end stage renal disease (ESRD). The disease is mainly caused by mutations in either *PKD1* or *PKD2*. Both the involved genes and the type of mutation have been shown to provide significant prognostic information in relation to the risk of early progression to ESRD. However, even within families, progression of disease varies widely between individuals with the same disease causing mutation. This variation might be explained by other genetic components. Previous studies have suggested genetic components affect the progression of Chronic Kidney Disease (CKD) and ESRD.

To explain the variation in disease progression, not accounted for by the disease causing gene, 15 Single Nucleotide Variants (SNPs) associated to CKD and/or ESRD were chosen for further analysis. In addition, 3 SNPs within *CFTR* was included, since variants within this gene is known to affect the progression of ADPKD.

Method: A cohort of 120 Danish individuals suffering from ADPKD was sequenced using targeted Next Generation Sequencing (NGS). The targeted NGS panel included *PKD1, PKD2*, rs13538, rs12460876, rs17319721, rs10109414, rs653178, rs267734, rs1260326, rs347685, rs11959928, rs6420094, rs7805747, rs4744712, rs626277, rs881858, rs12917707, rs213950, rs213965, rs1042180. If no causative variant was identified using the NGS panel, Multiplex Ligation-dependent Probe Amplification was performed to identify larger deletions and duplications. In addition, clinical information was obtained to divide patients into two established or predicted progression groups; fast or slow.

Results: Based on clinical information we identified 39 patients with established or predicted fast progression and 81 with slow progression. The distribution of SNPs in the fast progression group was compared to the distribution within a European population. Out of 18 SNPs, one was significantly different distributed among the fast progressive ADPKD patients, rs13538 ($p=0.01$); however, in contrast to expected the frequency of the SNP was lower in the fast progression group compared to the European population. To examine if the shift could be associated to a specific disease causing mutation type, the distribution of each SNP within different mutation types were analysed. The mutations were divided into three groups; PKD1 truncating, PKD1 nontruncating and PKD2. A significant difference was observed in all three groups.

Conclusion: A single SNP associated to progression of CKD was observed to have a different distribution in the fast progressive ADPKD patients. The distribution differed for all analysed mutation types, thus no specific mutation type or gene could explain the shift in distribution alone. Hence, none of the analysed SNPs seem to influence the rate of progression in the analysed cohort of ADPKD patients.

P0037

POPULATION CHARACTERISTICS ACROSS AN EXPANDED POOLED DATABASE OF MULTIPLE AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE CLINICAL STUDIES

Xiaolei Zhou[1], Eric Davenport[1], John Ouyang[2], Molly Hoke[2], Diana Garbinsky[1], Indra Agarwal[2], Dorothee Oberdhan[2]

[1]RTI Health Solutions, Research Triangle Park, NC, United States of America and [2]Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD, United States of America

Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disease and the fourth-leading cause of kidney failure. Over the past two decades, various studies have been conducted to characterize the natural history of ADPKD and investigate impacts of potential treatments on disease progression. Previously, we created a pooled longitudinal database of unique subjects from nine studies to evaluate and analyze outcomes. The database was expanded to include data from two recent tolvaptan (TOL) trials (156-13-210 and 156-13-211). Here, we describe the baseline characteristics of the expanded pooled population.

Method: Data from 11 ADPKD studies (from 2001 to 2018, sponsored by Otsuka or National Institutes of Health) were combined and divided into two groups: TOL and standard of care (SOC). TOL consisted of trial subjects initiating treatment in one of seven trials (156-04-250, 156-04-251, 156-06-260, 156-09-284, 156-09-290, 156-08-271, and 156-13-210); SOC included subjects from placebo arms of two TOL randomized trials (156-04-251 and 156-09-290), all standard blood pressure control arms in the HALT-PKD trials, and subjects from two observational studies (156-10-291 and CRISP). Subjects in the placebo arm of study 156-13-210 received TOL for 5 weeks before randomization and were therefore included in the TOL group. Eligible subjects who completed an early TOL study continued TOL treatment in the extension study 156-08-271 and/or in a second extension study 156-13-211. Estimated glomerular filtration rate (eGFR) was calculated in all studies using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Total kidney volume (TKV) was measured by magnetic resonance imaging and available in all studies except 156-13-210, 156-13-211, and HALT-PKD study B.

Results: The pooled analysis included 7,117 eligible subjects (TOL: 2,928; SOC: 4,189) from the United States (47.5%) and other countries. The two cohorts had similar age (mean age, 43.6 vs. 44.1 years) and sex distribution (50.5% male vs. 45.2% male). The TOL group had more white subjects (90.5% vs. 80.7%) and fewer Hispanic subjects (4.0% vs. 12.6%), a lower baseline mean eGFR (60 vs. 70 mL/min/1.73 m^2), more in chronic kidney disease (CKD) stage 3 or above (58.1% vs. 41.0%), and more frequent history of signs of rapid disease progression (e.g., nephrolithiasis, hematuria, urinary tract infection). Among 4,917 subjects with TKV assessments, mean baseline TKV was higher in the TOL group (1,817 mL) compared with SOC (1,627 mL).

Conclusion: In this large, longitudinal database of unique subjects with ADPKD, distinct differences exist in some baseline characteristics of the TOL and SOC groups. Compared with the previous database, the expanded database doubled the size of the TOL group and included more subjects who were older and with advanced chronic kidney disease stage. This database provides a diverse ADPKD population to assess outcomes.

P0038 **WATER RESTRICTION INDUCES THE SHORTENING OF PRIMARY CILIA IN KIDNEY TUBULAR CELLS**

Kwon Moo Park[1], Min Jung Kong[1]

[1]*Kyungpook National University, Anatomy, Daegu, Korea, Rep. of South*

Background and Aims: The primary cilia play a key role in the maintenance of cell homeostasis by sensing and transducing extracellular signals into the cell and are associated with several kidney diseases including ADPKD. Here, we investigated whether water restriction affects the length of primary cilia of kidney tubule cells and its underlying mechanisms.

Method: Some mice were not supplied with water for 2 days and then the length of primary cilia were determined by immunostaining using acetylated-α-tubulin (ac-α-tubulin) antibody. Madin-Darby canine kidney (MDCK) cells were exposed to high concentration of NaCl or mannitol and the lengths of primary cilia were determined under microscope.

Results: Water restriction shortened primary cilia length in kidney tubular cells along with the increase of urine osmolality. Water restriction lowered the expression of acetylated-α-tubulin (ac-α-tubulin), EXOC5, one of the components of exocyst complex, and α-tubulin transferase in the kidney. In MDCK cells, high concentration of NaCl or mannitol treatments shortened primary cilia length and decreased the expression of ac-α-tubulin, EXOC5, and α-tubulin transferase.

Conclusion: These findings demonstrate that water restriction induces the shortening of primary ciliua in kidney tubule cells along with increased urine osmolality, suggesting that primary cilia are involved in the urine concentric process.

P0039

IS A NEPHRECTOMY POLYCYSTIC KIDNEY DISEASE NECESSARY FOR PATIENTS WITH END-STAGE CHRONIC KIDNEY DISEASE?

Dmitriy Perlin[1], Ivan Dymkov[1]

[1]*Volgograd, Department of Urology, Volgograd, Russia*

Background and Aims: In the structure of end-stage CKD polycystic kidney disease is about 8-10 %. These patients often required preparation for transplantation. In addition, enlarged kidneys are reducing the volume of the abdominal cavity, negative impact on the peritoneal dialysis (PD).

Method: In 2005-2019 41 nephrectomies were performed in patients with end-stage CKD with polycystic kidney disease: 11 patients have undergone open nephrectomy, 13 patients laparoscopic nephrectomy and 17 retroperitoneoscopic nephrectomy. We analyzed postoperative period and complications, method of treatment end-stage CKD selected in future. In particular, we evaluated the effectiveness of peritoneal dialysis depending on the operating access.

Results: Complications: intraoperative bleeding was in 3 cases, damage of the spleen was in one. The significantly lower blood loss was in the group of operations performed endoscopic access. Subsequently, 16 patients were treated with hemodialysis (HD), 25 patients PD. The effectiveness of PD was estimated by 3 months and 1 year after start treatment by kt/v. In the group of patients with open nephrectomy, the effectiveness on average was 1.61 and 1.44 respectively. Patients underwent laparoscopic nephrectomy the efficiency is in average of 1.72, and 1.60, retroperitoneoscopic nephrectomy 1.88, 1.72 respectively. The conversion method of PD-treatment to the HD within 6 months after surgery was required in 5 patients (open nephrectomy technique), 2 patients (laparoscopic technique), no one patient (retroperitoneoscopic technique) was not required for the conversion PD to HD.

Conclusion: Our experience of nephrectomies in patient with end-stage CKD indicate the safety and effectivity of the endoscopic technique and its applicability to patients on PD. Retroperitoneoscopic access has less impact on the effective area of the peritoneum, which is reflected in the subsequent course of PD.

P0040

BASELINE CHARACTERISTICS AND ASSOCIATIONS WITH RENAL FUNCTION IN A GREEK COHORT OF POLYCYSTIC KIDNEY DISEASE

Myrto Kostopoulou[1], Michaela Louka[1], Konstantina Kanellopoulou[1], Vasiliki Gkika[1], Stavros Fokas[1], Anastasia Koutsogianni[2], Konstantinos Lymperopoulos[2], George Tsirpanlis[1]

[1]General Hospital of Athens, "G. Gennimatas", Nephrology Department, Athens, Greece and [2]General Hospital of Athens "G. Gennimatas", Magnetic Resonance Department, Athens, Greece

Background and Aims: Recent advances in the treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD) highlight the interplay between the clinical and the laboratory profile of the disease. This study aims to present the baseline characteristics of patients followed in a large ADPKD cohort from a single center in Greece, and explore possible associations between demographic, clinical and laboratory parameters.

Method: Patients followed in a specialized outpatient PKD clinic from December 2018 up to December 2019 were recruited in this study. At enrollment, demographics, medical and family history and laboratory data were recorded using a standardized form. Estimated glomerular filtration rate (eGFR) was calculated and Magnetic Resonance Imagining for total kidney volume (TKV) measurement was performed.

Results: One-hundred three females and 83 males with a mean age $\pm$ SD of 41.4 $\pm$ 13 years (18.8 % $<$ 30 years) were enrolled. Overall, 60.8% of them were classified as Chronic Kidney Disease, (CKD) stage 1 and 2. The ADPKD was diagnosed at a mean age $\pm$ SD of 26.5 $\pm$ 12.5 years. Thirty four percent out of 186 patients were diagnosed before the age of 20 and 9% of them before the age of 10. A positive family history was present in 89% of patients. In this subgroup, the median age of the affected parent that reached end stage renal disease (ESRD) was 55 (range 28-87) years. Hypertension was diagnosed in 89% at a mean $\pm$ SD age of 37.2 $\pm$ 10.5 years. Hepatic cysts were present in 79.3% of patients, urinary tract infections, nephrolithiasis, macroscopic hematuria and pain in 44.3%, 42.5%, 24.8% and 54.4% respectively. A history of intracranial bleeding in family was positive in 21.5%. In multivariable analysis, lower eGFR was associated with younger age at the time of APKD diagnosis ($p < 0.002$), younger age at hypertension diagnosis ($p < 0.08$) and greater values of TKV ($p < 0.001$), height adjusted TKV ($p < 0.001$) and Body Mass Index (BMI) ($p = 0.02$).

Conclusion: In this study, patients with ADPKD were diagnosed at a young age and hypertension developed early on the course of the disease. Both these factors together with higher values of BMI and TKV were independently associated with low eGFR.

P0041 **CHARACTERISTICS OF URINE-DERIVED RENAL EPITHELIAL CELLS (UREC) FROM CHILDREN WITH POLYCYSTIC KIDNEY DISEASE (PKD).**

Wolfgang H. Ziegler[1], Sarah Lüdiger[1], Charlotte Mett[1], Fatema Hasan[1], Birga Soetje[1], Dieter Haffner[1]

[1]*Hannover Medical School, Paediatric Kidney, Liver and Metabolic Diseases, Hannover, Germany*

Background and Aims: In hereditary PKD, epithelial cell defects are mostly caused by mutation of proteins of the cilia-centrosome complex. Use of primary cells from patients allows to study specific cell characteristics and altered activation of signal pathways in epithelial cell function-related culture models. In this *ex vivo* approach, comparison of cell properties is based on defined genetic origin and can be related to kidney function at the time of UREC collection, revealing consequences of genetic disposition and kidney-stress related changes on cell function.

Method: The study considers patients with genetically confirmed causes of PKD, autosomal recessive polycystic kidney disease (ARPKD), nephronophtisis (NPH), Bardet-Biedl syndrome (BBS), and age-matched controls with normal kidney function. UREC are grown from cellular urine sediment using selective growth conditions. Primary cells are cultured up-to 21 days (passages 2 & 3) and tested with respect to their proliferation, tubular origin and epithelial properties in 2D/3D culture conditions. To allow pathway analysis and improve control conditions, immortalized UREC lines are also included.

Results: UREC preparations of cohorts from ARPKD, NPH, and BBS patients, and controls were studied quantitatively to determine specific epithelial cell properties. Considering basic characteristics of each primary culture including cell morphology, expression of epithelial markers, and formation of cell-cell adhesions, the potential of UREC cells to polarize and generate liquid-filled epithelial spheroids was measured. The capacity of lumen formation in 3D culture strongly varies among individual cell preparations and appears to reflect the genetic origin of UREC cells, whereas no correlation to (remaining) kidney function (eGFR) is observed.

Conclusion: Determining specific, quantitative UREC cell properties related to genetics and kidney function, we expect to gain a better mechanistic understanding of cellular and renal epithelial defects in PKD patients. *Ex vivo* analysis based on UREC cells may provide options for testing of personalized pharmaceutical intervention.

P0042 SPECTRUM OF RENAL INVOLVEMENT IN CHILDREN WITH HNF1B NEPHROPATHY

Svetlana Papizh[1], Larisa Prikhodina[1]

[1]*Research and Clinical Institute of Pediatrics, Russian National Research Medical University, Moscow, Russia*

Background and Aims: Hepatocyte nuclear factor 1 gene (*HNF1B*) encodes for HNF-1ß, a transcription factor that is expressed early in embryonic development and plays a key role for tissue-specific regulations of gene expression in various organs such as the kidneys, urogenital tract, liver, biliary ducts and pancreas. *HNF1B* disease (MIM 137920) is recognized to represent an autosomal dominant syndromal disorder comprising variable phenotype with renal and extrarenal manifestations. Renal phenotype in *HNF1B* nephropathy is highly heterogeneous. The aim of the study was to evaluate the clinical characteristics of renal involvement in children with genetically proven *HNF1B* nephropathy.

Method: Five children (2M/3F) from unrelated families with heterozygous *HNF1β* mutations and kidney disorders were examined. We evaluated serum levels of electrolytes, magnesium (Mg), phosphorus (P), uric acid, acid-base composition; urinary excretion of Ca, P, creatinine (Cr); fractional excretion (FE) of Mg, urate (Ur), Na, K; tubular maximum phosphate reabsorption per GFR (TmP/GFR), and urinary β-2 microglobulin. Molecular genetic analysis was performed using by next generation sequencing.

Results: Cortical or medullary bilateral renal cysts were detected in all five children with *HNF1B* nephropathy. Kidney hypoplasia, medullary nephrocalcinosis, and low-grade proteinuria (<0.5 g/m^2/d) revealed in 2\5 (40%) of cases. One child had vesicoureteral reflux. All patients with *HNF1B* nephropathy had normal serum level of uric acid and all electrolytes, including Mg. Increased FE of Mg and urinary excretion of β-2 microglobulin was found in all cases. Increased FE of Ur, Na and K revealed in 4\5 (80%) of subjects. Decreased TmP/GFR had 3\5 (60%) of cases. At the first examination of patients aged 1.0 (IQR: 1.0; 2.0) years all of them already had decreased eGFR to CKD stage 2-3.

Conclusion: The present study demonstrates that patients with *HNF1B*-associated disease had wide spectrum of renal involvement. The most prevalent features of *HNF1B* nephropathy in our children were bilateral renal cysts, defects of proximal tubular function with wasting of electrolytes and progression to CKD stage 2-3 at early age.

P0043

SYMPTOMS IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: FINDINGS FROM QUALITATIVE PATIENT INTERVIEWS

Pronabesh DasMahapatra[1], Jennifer Cline[2], Ruth Pulikottil-Jacob[1], Manish Maski[3], Sarah Cantor[4], Ali Hariri[5], Robert Krupnick[6], Vijay Modur[5]

[1]Sanofi Genzyme, Health Economics & Value Assessment, Cambridge, United States of America, [2]IQVIA, Pittsburgh, United States of America, [3]Sanofi Genzyme, Medical Affairs, Cambridge, United States of America, [4]IQVIA, New York, United States of America, [5]Sanofi Genzyme, Clinical Development, Cambridge, United States of America and [6]IQVIA, Boston, United States of America

Background and Aims: Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) experience various symptoms due to increasing kidney volume and its associated complications. To understand symptom burden, qualitative interviews were conducted to characterize the ADPKD patient experience pertaining to the most common and disturbing symptoms.

Method: Combined concept elicitation and cognitive debriefing interviews were performed by trained interviewers following a preliminary conceptual model based on a targeted literature review. We currently report on the concept elicitation component, which explored relevant and bothersome symptoms in ADPKD patients, due to either the disease or associated treatments. Nineteen telephone interviews were conducted in four waves of 5, 4, 6, and 4 patients, respectively.

Results: The mean age of patients was 47 years (SD: 9 years); 68% (*n*=13) were female, and the mean estimated glomerular filtration rate (eGFR) was 41 ml/min/1.73m^2 (SD: 25 ml/min/1.73m^2), with the majority 47% (*n*=9) in stage 3 chronic kidney disease (CKD). The classes of treatments included antihypertensives (74%, *n=14*), vasopressin receptor antagonists (21%, *n=4*); diuretics (16%, *n=3*), analgesics (16%, *n=3*) and erythropoietin (5%, *n=1*). The most frequently mentioned symptoms were fatigue (89%, *n*=17), pain (84%, *n*=16), and nocturia (74%, *n*=14); all were considered at least moderately disturbing to patients' lives. Most patients experienced constant fatigue (74%, *n*=14) that worsened over time. Patients' descriptions of pain were variable, including back and side pain, severe cystic pain, and muscle pain; a few patients also mentioned shoulder pain, or pain due to kidney stones. Among patients reporting nocturia (*n=14*), about half (57%, *n*=8) rated nocturia on the upper end of the disturbance scale, regardless of number of voids per night, often accompanied by sleep disruption. While less frequently occurring, itchy skin, muscle cramping, abdominal swelling, and inability to eat were spontaneously mentioned among the most disturbing symptoms.

Conclusion: The novel component of this study is the significant disruption of nocturia in patients with ADPKD even in the absence of vasopressin receptor antagonist administration. In addition, it confirms the findings of the literature review and highlights the patient experience in ADPKD, most notably fatigue, nocturia, and pain as the most frequent and bothersome symptoms experienced by patients. Subjective evaluation of the ADPKD patient experience is critical to understand symptom severity and the burden of disease, to potentially quantify disease progression, and to assess the impact of emerging therapies.

GENETIC DISEASES AND MOLECULAR GENETICS

P0047 PREVALENCE OF FABRY DISEASE IN DIALYSIS PATIENTS IN FRANCE (FABRYDIAL STUDY)

Florence Sens[1,2], Laure Guittard[3,4], Bertrand Knebelmann[5], Olivier Moranne[6,7], Gabriel Choukroun[8], Valérie De-Précigout[9], Cécile Couchoud[10], Estelle Bravant[3,4], Mohammed A. Chakir[3], Léa Lancelot[3], Dominique P. Germain[11], Laurent Juillard[1,2]

[1]Hospices Civils de Lyon, Edouard Herriot, Service de néphrologie et d'explorations fonctionnelles, Lyon, France, [2]Univ Lyon, Université Claude Bernard Lyon 1, CARMEN UMR INSERM 1060, Lyon, France, [3]Hospices Civils de Lyon, Pôle Santé Publique, Service Recherche et Epidémiologie cliniques, Lyon, France, [4]Univ Lyon, Université Claude Bernard Lyon 1, HESPER EA 7425, Lyon, France, [5]Assistance Publique Hôpitaux de Paris, Hôpital Necker, Service de néphrologie, Paris, France, [6]Nimes University Hospital, Service de Néphrologie, Nimes, France, [7]Université Montpellier-Nimes, Montpellier, France, [8]CHU Amiens, Site Sud, Service de néphrologie, Amiens, France, [9]CHU Bordeaux, Hôpital Pellegrin Tripode, Service de néphrologie, Bordeaux, France, [10]Agence de la biomédecine, Coordination Nationale Réseau Epidémiologique et Information en Néphrologie, Saint-Denis-La-Plaine, France and [11]APHP Université Paris Saclay, Hôpital Raymond-Poincaré, Service de génétique médicale, Garches, France

Background and Aims: Fabry Disease (FD) is an X linked lysosomal storage disease due to pathogenic α-galactosidase A (GLA) variants. It leads to damage in kidney and other organs. Numerous prevalence studies have been conducted over the past twenty years in ESRD patients in different countries. However, many screening studies did not perform confirmatory GLA variant analyses, and included recently recognized 'benign/likely-benign' variants, thereby inflating prevalence estimates. Thus, the prevalence of Fabry disease in patients with end-stage renal disease remains controversial.

The FABRYDIAL study aimed to measure the prevalence of Fabry disease in patients aged 18 to 75 years and treated by chronic dialysis, either hemodialysis or peritoneal dialysis.

Method: The study was conducted in France in 5 geographic sectors (Aquitaine, Ile-de-France, Rhône-Alpes and Picardie regions, and the Gard department). One hundred and twenty-four dialysis centers participated in the study, which targeted patients undergoing chronic dialysis during the week of November 20, 2017. The exclusion criteria were the existence of a proven nephropathy unrelated to FD (polycystic kidney disease, type 1 diabetes or biopsy-proven IgA nephropathy, membranous glomerulonephritis or ANCA-associated vasculitis), the absence of health insurance coverage or guardianship or tutelage. α-galactosidase A in men, and both α-galactosidase A and lyso-GL3 in women, were measured on a drop of dried blood during the usual care of patients. GLA gene sequencing was performed in patients in whom one biological value was outside normal values. If a genetic variant was identified, a multidisciplinary Diagnosis Validation Committee (DVC) concluded, based on precise literature, clinical, biological and genetic data, as to the reality of Fabry disease.

Results: Among the 6,032 patients aged 18 to 75 years under chronic dialysis during the period considered, 714 were no longer treated in the participating centers when the research staff visited for eligibility assessment. 1,121 had non-inclusion criteria, which in 89% of cases were a confirmed diagnosis of kidney disease (by renal biopsy or other means) making the existence of Fabry disease very unlikely. 4,197 patients met the inclusion criteria, of which 3,088 were included (1,888 men and 1,200 women). Valid biological analyzes were available for 2815 patients (1721 men and 1094 women), and a genetic test was indicated for 91 patients (52 men and 39 women). Ninety-seven percent of the samples were analyzed with a unique assay technique in a unique laboratory. Five patients had a genetic variant (4 men and one woman). After discussion in the DVC, one male patient was considered to have a confirmed Fabry disease. He presented early signs of the disease (first-degree family history of cardiac or unexplained death, hypohidrosis, heat intolerance, tendency to chronic diarrhea, angiokeratoma, hypoacousia and tinnitus) which could have been identified earlier. The GLA variant was c.1185dupG / p.Phe396Glyfs, a clearly pathogenic frameshift variant. The prevalence of FD in included patients with biological data was 0.035% [0.006; 0.201] (0.058% [0.010; 0.33] in men, 0.000 % [0,000; 0.350] in women). If we consider that patients who were not included because of a specific renal diagnosis unrelated to FD did not have FD, the estimated prevalence decreased to 0.028% [0.006; 0.121].

Conclusion: The estimated prevalence of FD in a cohort of French dialysis patients is 0.035% [0.006; 0.201], and by sex 0.058% in men [0.010; 0.328] and 0,000% in women [0,000; 0.35]. Although it appears extremely low, it remains justified to bring up this diagnosis in the event of an evocative sign, whether for the patient or his relatives as FD benefit of effective specific treatments.

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P0048

THE EFFECT OF GENOTYPING ON THE NUMBER OF PHARMACOTHERAPEUTIC GENE-DRUG INTERVENTIONS IN CKD3-5 PATIENTS

Marieke Kerskes[1], Carien Van den Eijnde[2], Birgit Deiman[3], Albert-Jan Aarnoudse[4], Rene Grouls[1], Maarten Deenen[1]

[1]Catharina Hospital, Clinical Pharmacy, Eindhoven, Netherlands, [2]Utrecht University, Pharmaceutical Science, Utrecht, Netherlands, [3]Catharina Hospital, Clinical Chemistry, Eindhoven, Netherlands and [4]Catharina Hospital, Nephrology, Eindhoven, Netherlands

Background and Aims: Most patients with CKD (Chronic Kidney Disease) 3-5 are polypharmacy patients (i.e. use of $\geq$5 drugs). As renal function is important for the clearance of many drugs, dose adjustment is often necessary and some drugs are even contra-indicated in patients with CKD. Many of these drugs are metabolized by cytochrome P450 (CYP-enzymes) in the liver. Several genetic mutations in these CYP enzymes are known to result in an altered metabolism capacity of drugs. Knowledge of the patients CYP450 genotype may thereby be of added value in reducing the incidence of supratherapeutic concentrations of drugs and reducing side effects, especially in this patient population with already reduced renal function. The aim of this study was to determine the added value of pharmacogenetic testing to the routine medication evaluation in polypharmacy patients with CKD3-5 disease, defined as the total number of pharmacotherapeutic interventions based on a relevant gene-drug interaction as assessed by the nephrologist and hospital pharmacist.

Method: This was a prospective single-centre study in adult polypharmacy patients with CKD3-5 disease not on dialysis who visited the outpatient clinic of the Catharina Hospital Eindhoven, the Netherlands. In each patient enrolled in the study we determined a pharmacogenetic profile consisting of *CYP1A2*, *CYP2B6*, *CYP2C9*, *CYP2C19*, *CYP2D6*, *CYP3A4*, *CYP3A5* and *VKORC1*. A gene-drug interaction was considered as relevant based on the DPWG (Dutch Pharmacogenetics Working Group) guideline. Of all these according to the DPWG guideline relevant gene-drug interactions the treating nephrologist and hospital pharmacist assessed the clinical relevance and necessity of a pharmacotherapeutic intervention in the individual patient. Primary endpoint of the study was the total number of applied pharmacotherapeutic interventions based on a relevant gene-drug interaction.

Results: A total of 61 patients were enrolled. Median eGFR in the study population was 18 ml/min. Patients used a median (range) number of 12 (5-20) drugs. Genotyping resulted in a total of 172 altered phenotypes based on a pharmogenetic mutation. We observed a total of 66 gene-drug interactions, of which 56 were considered relevant and resulted in 26 applied pharmacotherapeutic interventions in 20 (32.8%) patients. These interventions consisted of 10 dose adjustments (38.5%), 7 drug stops (26.9%) and 9 drug changes (34.6%).

Conclusion: Pharmacogenetic testing leads to additional pharmacotherapeutic interventions based on relevant gene-drug interactions. This study shows that pharmacogenetic testing in CKD3-5 patients can be of added value to the routine medication evaluation, and may further optimize pharmacotherapy in this population.

P0049 **IDENTIFYING HUB GENES ASSOCIATED WITH CLINICAL CHARACTERISTICS IN IGA NEPHROPATHY BYWGCNA**

Chengyu Yang[1], Yan Xu[2]

[1]The Affiliated Hospital of Qingdao University, Department of Nephrology, Qingdao, P.R. China and [2]The Affiliated Hospital of Qingdao University , Department of Nephrology, Qingdao, P.R. China

Background and Aims: Clinically, IgA nephropathy has a variety of symptoms including paroxysmal gross hematuria, nephritic syndrome and nephrotic syndrome. This study aimed at investigating hub geneand genes modular related to IgA nephropathy clinical characteristics by using weighted gene co-expression network analysis combining clinical, microarray and network database parameters.

Method: We collected 32 human samples from the European Renal cDNA Bank and used RMA method to preprocess the raw data and utilize the limma package to obtain differentially expressed gene in renal interstitium and glomeruli. And then, we used the WGCNA package to construct the gene co-expression of differential expression genes and identify the hub genes associated with clinical characteristics in renal interstitium and glomeruli, respectively. Gene ontology enrichment analysis and KEGG analysis for hub genes which associated with clinical characteristics were performed by DAVID, and PPI information was acquired from STRING with visualization by Cytoscape.

Results: For glomeruli, 1470 genes differentially expressed between IgA nephropathy patients and healthy control, containing 10 hub genes associated with age, 8 hub genes associated with sex, 48 hub genes associated with Bp enrichd in ERK1 and ERK2 cascade and Rap1 signaling pathway, 223 hub genes associated with BMI enrich in organic acid catabolic process and fatty acid degradation pathway, 136 hub genes associated GFR enriched in immune response and PI3K-Akt signaling pathway, 82 hub genes associated with proteinuria enriched in extracellular matrix organization and PI3K-Akt signaling pathway. In tubulointerstitium, there were 480 genes differentially expressed between IgA nephropathy patients and healthy control. Among 480 DEGs, 6 hub genes associated with age, 15 hub genes associated with sex, 35 hub genes associated with Bp enrichd in positive regulation of apoptotic process, 87 hub genes associated with GFR enriched in negative regulation of macromolecule metabolic process and RNA transport, 33 hub genes associated with proteinuria enriched in regulation of apoptotic process and FoxO signaling pathway. PPI enrichment analysis shown that all hub genes sets are biologically connected cluster.

Conclusion: We made a preliminary investigation on molecular mechanisms of relationship between IgA nephropathy and clinical characteristics and identified hub genes and pathways closely related with BMI, GFR and Proteinuria in IgA nephropathy by a series of bioinformatics analysis.

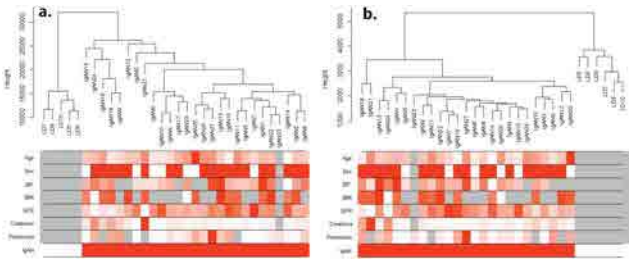


Fig.1 Sample of dendrogram and trait heatmap

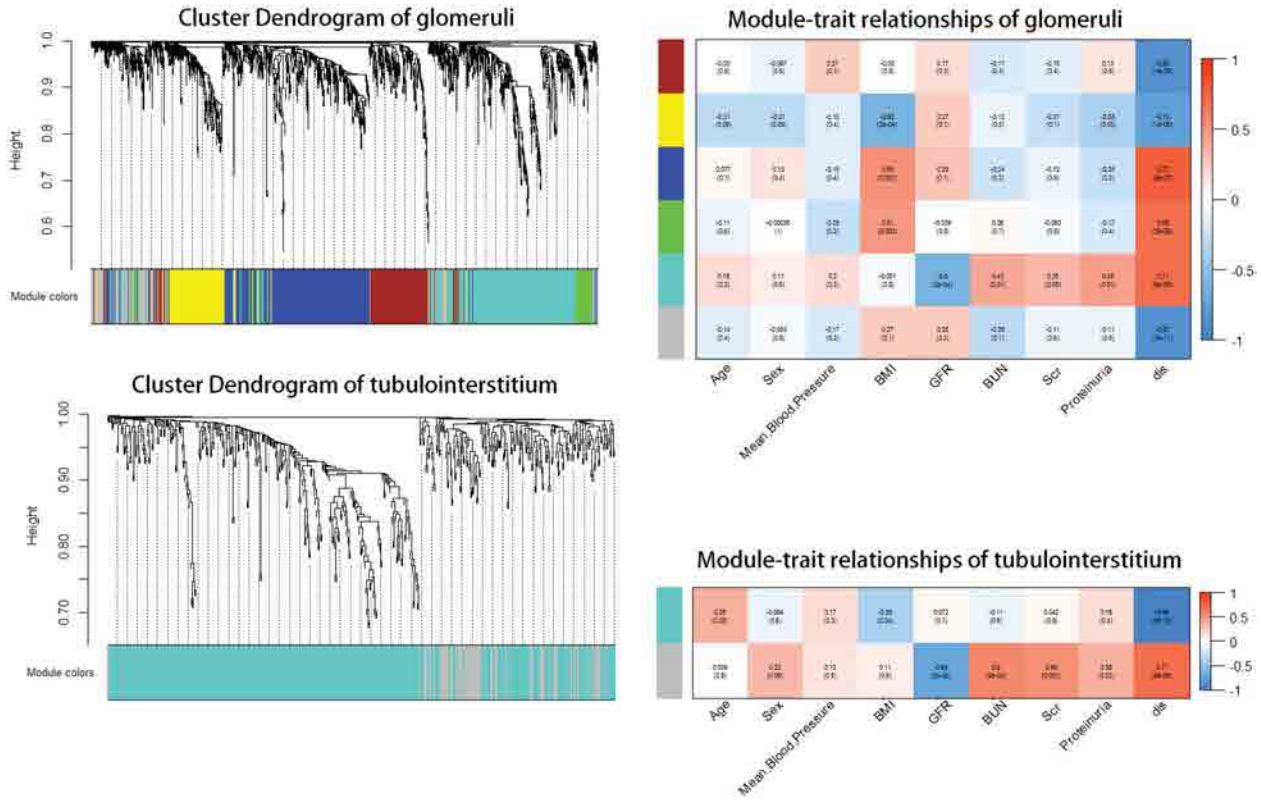


Fig.2 Weighted gene co-expression network analysis in IgA nephropathy glomeruli and tubulointerstitium

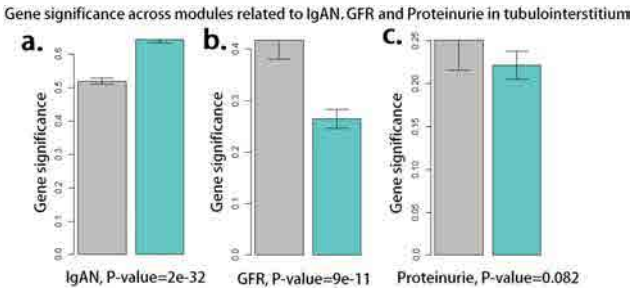


Fig.4 Module significance related to clinical characteristics in IgA nephropathy glomeruli

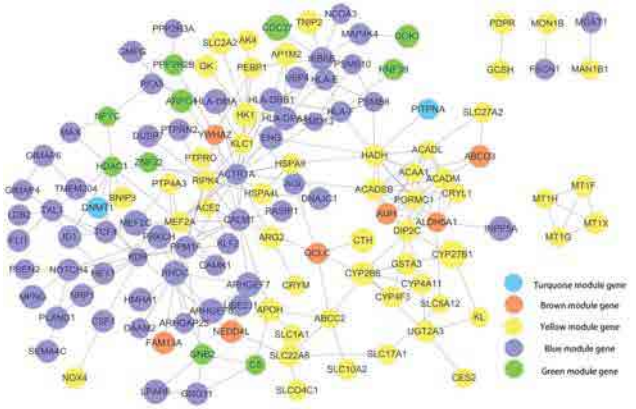


Fig.5 PPI enrichment analysis of hub genes associated with BMI in glomeruli

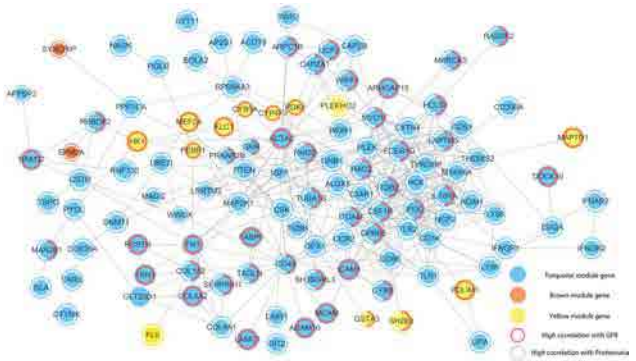


Fig.6 PPI enrichment analysis of hub genes associated with GFR and Proteinuria in glomeruli

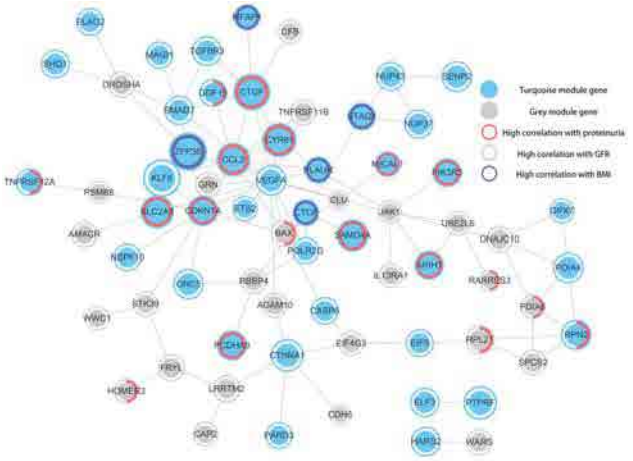


Fig.7 PPI enrichment analysis of hub genes associated with BMI in tubulointerstitium

Colors of nodes represent the module that genes belong to and the colors of circle represent gene relevant clinical characteristics. Genes that not display connections with other genes were not shown in the network. PPI enrichment analysis parameters: number of nodes: 111; number of edges: 94; average node degree: 1. 69; avg. local clustering coefficient: 0.361; expected number of edges: 62; PPI enrichment p-value: 7. 33e-05.

P0050

PRE-IMPLANTATION GENETIC TESTING FOR MONOGENIC KIDNEY DISEASE: TWENTY-FIVE YEAR EXPERIENCE IN THE NETHERLANDS

R Snoek[1], Marijn F. Stokman[1], Klaske D. Lichtenbelt[1], Cindy E. Simcox[2], Theodora C. Van Tilborg[2], Aimee D.C. Paulussen[3], Jos C.M.F. Dreessen[3], Franka Van Reekum[4], Nine Knoers[1,5], Christine De Die-Smulders[3], Albertien M. Van Eerde[1]

[1]University Medical Center Utrecht, Department of Genetics, Utrecht, Netherlands, [2]University Medical Center Utrecht, Department of Fertility, Utrecht, Netherlands, [3]Maastricht University Medical Center+, Department of Genetics, Maastricht, Netherlands, [4]University Medical Center Utrecht, Department of Nephrology, Utrecht, Netherlands and [5]University Medical Center Groningen, Department of Genetics, Groningen, Netherlands

Background and Aims: Due to the fast-paced developments in human genetics, a genetic cause can now be identified for an increasing number of pediatric and adult-onset kidney diseases. A monogenic kidney disease (MKD) can impact prognostication and therapy decisions. It also provides patients with options regarding family planning such as preimplantation genetic testing (PGT), a reproductive technology that helps prospective parents prevent passing on a disease-causing mutation to their offspring.

There are limited reports on PGT for MKD and most are focused on severe pediatric-onset diseases. The Dutch system of insurance reimbursement and nationwide regulation is unique, and it has allowed the Netherlands to be one of a handful of countries where couples have the option to choose PGT for MKD, including adult-onset forms of kidney disease. Here we provide the 25-year Dutch experience with PGT for MKD.

Method: We performed a retrospective cohort study of all couples counselled on PGT for MKD in the Maastricht University Medical Center+, the expert centre where all Dutch single cell genetic testing on embryos is performed, from January 1995 until June 2019.

Results: 99 couples were counseled for PGT, of which currently 15% is waiting for the genetic test to be validated. In the early years of PGT for MKD, referrals were incidental and only for couples at risk for offspring with paediatric-onset disease. From 2009 onwards, the number of referrals has steadily increased as has the number of couples referred for adult-onset MKD. Overall, the most frequent indications for referral for PGT were ADPKD (37%), X-linked Alport syndrome (25%) and ARPKD (9%).

After counselling, 36% of n=99 couples started PGT treatment. In total n=80 cycles with oocyte retrieval were performed (median 2 cycles [range 1-4]). These cycles led to a median of n=10 embryos (range 2-31) suitable for biopsy and a median of n=3 embryos (range 1-14) being genetically unaffected. Seventy-five percent (n=) of couples achieved at least one live birth.

Of n=99, 48% did not proceed with PGT, for various personal and technical reasons. Major reasons for opting out of PGT were that prospective parents did not want to wait for the lengthy PGT procedure (9%) or had a wish for natural conception with prenatal genetic testing (11%). Live birth rate was 40% (n=19) in the non-PGT group, with notably a similar duration to a live birth as the PGT group (2 years, range 0-5 years).

Conclusion: We provide the largest overview to date of the indications, uptake and results of PGT for MKD. Referrals for PGT, including adult-onset disease, have increased steadily over the past decade. PGT has favorable outcomes, with 75% of couples having at least one live birth, though this is likely due to our small sample size. Genetic and reproductive counseling, including information on PGT, should be provided to all patients and prospective parents from families with MKD to enable informed decision making.

P0051 **NOVEL AND KNOWN MUTATIONS IDENTIFIED BY CLINICAL EXOME SEQUENCING FOR THE DIAGNOSIS OF POLYCYSTIC KIDNEY DISEASE**

Tiziana Vaisitti[1], Monica Sorbini[1], Martina Callegari[1], Silvia Kalantari[1], Valeria Bracciamà[1], Francesca Arruga[1], Silvia Bruna Vanzino[1], Alessandra Pelle[2], Daniela Giachino[3], Enrico Cocchi[4], Simone Baldovino[5], Cristiana Rollino[6], Roberta Fenoglio[6], Michela Tamagnone[7], Maurizio Gherzi[7], Giorgio Soragna[8], Corrado Vitale[8], Valentina Berta[9], Giovanni Calabrese[9], Gianluca Leonardi[10], Luigi Biancone[10], Emanuela Strampelli[11], Serena Maroni[11], Sonia Santi[12], Loredana Funaro[13], Maurizio Borzumati[13], Patrizia Bertinetto[14], Giusto Viglino[14], Bruno Gianoglio[4], Licia Peruzzi[4], Dario Roccatello[5], Antonio Amoroso[1], Silvia Deaglio[1]

[1]Transplant Regional Center-Piedmont region, Immunogenetics and Transplant Biology, AOU Città della Salute e della Scienza & Department of Medical Sciences, University of Turin, Torino, Italy, [2]AOU San Luigi Gonzaga, Orbassano, Turin, Torino, Italy, [3]AOU San Luigi Gonzaga, Orbassano, Turin & Department of Clinical and Biological Sciences, University of Turin, Torino, Italy, [4]Nephrology Dialysis and Transplantation, Regina Margherita Children's Hospital, Turin, Torino, Italy, [5]Department of Clinical and Biological Sciences, University of Turin & SCU Nephrology and Dialysis (ERKnet member) - CMID, Center of Research of Immunopathology and Rare Diseases, San Giovanni Hospital, Turin, Torino, Italy, [6]SCU Nephrology and Dialysis (ERKnet member) - CMID, Center of Research of Immunopathology and Rare Diseases, San Giovanni Hospital, Turin, [7]Nephrology and Dialysis Unit ASL CN1, Cuneo, Cuneo, Italy, [8]Nephrology and Dialysis Unit Mauriziano Hospital, Turin, Torino, Italy, [9]Nephrology and Dialysis Unit of Casale Monferrato, Alessandria, Alessandria, Italy, [10]Nephrology and Dialysis Unit, Città della Salute e della Scienza, Turin, Torino, Italy, [11]Nephrology and Dialysis Unit ASL TO4, Turin, Torino, Italy, [12]Nephrology and Dialysis Unit of Chivasso ASL TO4, Turin, Torino, Italy, [13]Nephrology and Dialysis Unit of Verbania ASL VCO, Verbano Cusio Ossola, Verbania, Italy and [14]Nephrology and Dialysis Unit of Alba ASL CN2, Alba, Alba, Italy

Background and Aims: Autosomal dominant PKD determines formation of multiple cysts predominantly in the kidneys and usually becomes symptomatic during adulthood and can lead to renal failure. In contrast, in autosomal recessive PKD cysts occur in both the kidneys and the liver and usually presents an earlier onset. Obtaining genetic diagnosis is important to confirm clinical diagnosis and is required before treating with vasopressin 2 receptor blockers, which are the only drugs known to slow down the disease. Furthermore, in the case of kidney transplant from a living family member it is essential to exclude the presence of the mutation in the donor. We used clinical exome sequencing to provide genetic diagnosis to a cohort of patients with a clinical suspicion of PKD.

Method: 175 patients were referred to the Immunogenetics and Transplant Biology Service of the Turin University Hospital through a network of nephrology centers operating in the Piedmont region. Some patients were referred following genetic counseling. All patients signed an informed consent and the referring physicians provided relevant clinical data. DNA from eligible patients was extracted, checked for integrity, quantified and used for library preparation. A clinical exome sequencing (CES) kit by Illumina was used, allowing the analysis of 6,700 clinically relevant genes.

Results: Out of the 175 recruited patients eligible for CES, 38 (21.7%) had a clinical suspicion or diagnosis of PKD, with 50% of them presenting family history. The majority of the cohort was represented by male subjects (60.5%) and included both children (34.2%) and adults. The analytical approach was based on initial analysis of genes responsible for PKD (*PKD1*, *PKD2* and *PKHD1*). If no mutation could be identified, analysis was then extended to a panel of 99 genes responsible for ciliopathies. This approach led to the identification of causative variants in 33/38 (86.8%) of the PKD cohort, while no variant could be identified in 5/38 patients. In 5/33 (15.2%) patients, mutations were inconclusive as found in heterozygosity in genes known to have an autosomal recessive mode of inheritance, while 27/33 (81.8%) were in line with the initial clinical suspicion/diagnosis. Of these, the majority was represented by missense mutations (12), followed by frameshift and nonsense mutations (6 each) and 3 splicing variants. As expected, the majority of mutations were found in *PKD1* 17/27 (63%), *PKD2* 3/27 (11.1%) and *PKHD1* 2/27 (7.4%). In these two latter patients, variants were found as compound heterozygosity. We also found mutations in other genes known to cause cysts, including *TSC2* and *CPT2*. Of note, in 7 patients carrying *PKD1* mutations, we found a second variant in *PKD1* or *PKHD1*. Interestingly, when looking at patients characterized by kidney failure but lacking a clinical suspicion at recruitment or diagnosed with other phenotypes (66/175), we found variants in *PKD1* and in *PKD2* in 11 patients (9 and 2, respectively).

Of all identified variants in *PKD1*, *PKD2* and *PKHD1* genes, 17.6% were annotated as pathogenic (C5), 41.2% were likely pathogenic (C4) and 41.2% were variants of unknown significance (C3). 19 variants in these genes were not previously reported. All the variants found in genes responsible for PKD were validated and confirmed by Sanger sequencing. Family segregation studies are ongoing.

Finally, it is worth mentioning that in a portion of cases (5/38) with clinical and phenotypic features of PKD, supported also by a positive family history, we could not detect mutations in causative genes. These results may be explained by the presence of intronic variants, in line with data reported in literature.

Conclusion: These results demonstrate that CES may be applied to PKD patients to identify causative variants during their routine diagnostic flow. Furthermore, CES may be a useful tool to detect mutations in PKD-related genes in patients with undiagnosed diseases, considering its rapidly decreasing costs.

P0052 **EMERGING CONCEPTS IN KIDNEY ATTR AMYLOIDOSIS: CHRONIC ADMINISTRATION OF TAFAMIDIS**

Joana Tavares[1,2], Andreia Campos[1,2], Ana Rocha[3], Idalina Beirão[1,2,3], Isabel Fonseca[1,2,3], Ana Silva[2,3,4], Márcio Cardoso[2,5], Cristina Alves[2,4], Ana Sousa[2,4], Teresa Coelho[2,5], Luísa Lobato[1,2,3]

[1]Hospital de Santo António, Centro Hospitalar Universitário do Porto, Nephrology, Porto, Portugal, [2]Unidade Corino de Andrade, Hospital de Santo António, Centro Hospitalar Universitário do Porto, Porto, Portugal, [3]Instituto de Ciências Biomédicas Abel Salazar, University of Porto, Unit for Multidisciplinary Research in Biomedicine - UMIB, Porto, Portugal, [4]Hospital de Santo António, Centro Hospitalar Universitário do Porto, Neurology, Porto, Portugal and [5]Hospital de Santo António, Centro Hospitalar Universitário do Porto, Neurophysiology, Porto, Portugal

Background and Aims: Transthyretin (TTR) amyloidosis is a disease characterized by destabilization of the native TTR tetramer. It can be caused by aging or due to pathogenic mutations, and its diagnosis is often missed. Hereditary transthyretin amyloidosis (ATTRv), due to Val50Met mutation, is frequently linked with polyneuropathy but it can cause nephropathy too, causing wide range levels of albuminuria and renal dysfunction. Tafamidis, a TTR tetramer stabilizer, has been associated with significant decrease of albuminuria in ATTRv. However, TTR nephropathy is not an approved indication for its use. Plus, the renal effects of chronic oral administration of this TTR stabilizer are yet to be understood. This study evaluated longitudinal changes of eGFR-EPI within 72 months of therapy with tafamidis and identified factors associated with these changes.

Method: A retrospective cohort, single centre study was conducted. We have followed consecutive ATTRv Val50Met patients on tafamidis therapy from July 2012 to March 2019. Men and women aged 18-85 years were eligible if they had neuropathy stage I, were anti-amyloid treatment-naïve patients that accomplished at least 60 months of tafamidis therapy and had eGFR over 45 ml/min/1.73m^2 with any grade of albuminuria. Exclusion criteria were: pregnancy, malignancies, diabetes and concurrent etiologies for nephropathy. Statistical analyses included Mann-Whitney test and linear mixed models to analyze the longitudinal changes in eGFR of the two groups of patients (albumunuric/ non-albuminuric at baseline), by controlling for variables that could be associated with eGFR EPI Cystatin C course.

Results: From 366 patients, biopsy-proven ATTR amyloidosis, treated with tafamidis, 122 patients met our criteria (56 males, 66 females) and had a median age of 36 (IQR: 32-46) years old. Twenty-eight had pathological urinary albumin-to-creatinine ratio (ACR), defined by ACR >30 mg/dL, and ACR >300 mg/dL was only found in females. In univariate analysis no significant differences were found between median eGFR decline in albuminuric versus non-albuminuric patients (p=0.330). At all time points, mean eGFR levels were significantly lower in baseline albuminuric patients. According to our estimation, eGFR at baseline was 11.2 mL/min/1.73 m^2 lower in baseline albuminuric patients, adjusted for age at the disease onset and time between symptom onset and tafamidis initiation. Baseline albuminuria status (p=0,005), age at the disease onset (p<0,001) and time between initiation of symptoms and initiation of tafamidis (p=0,016) were the only independent factors associated with longitudinal changes of eGFR (higher age at the disease onset and higher time between symptom onset and tafamidis initiation were associated with lower levels of eGFR). Figure 1 shows the predicted eGFR EPI trajectories over time for baseline albuminuric/ non-albuminuric subjects.

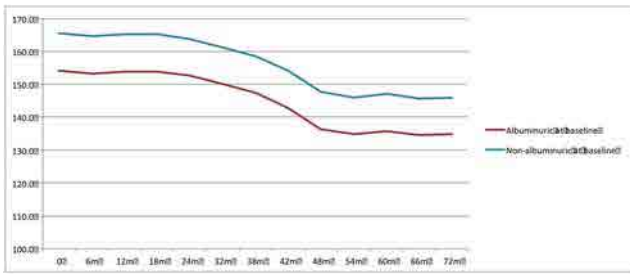


Figure 1 - Predicted eGFR EPI trajectories over time according baseline albuminuria

Conclusion: This study represents a real-life experience of oral chronic administration of tafamidis and its effects on ATTR nephropathy, concerning albuminuria reduction and renal function decline. Our analysis had shown similar decline rates in eGFR, irrespectively the degree of albuminuria at baseline, differently from what would be expected, since higher grades of albuminuria are related with more rapidly kidney function deterioration. Besides its capacity of stabilizing TTR tetramers, tafamidis could have an enhancing role in the podocyte regeneration process through potential cofactors for amyloid fibrils toxic effect, that could be present in the glomerular basement membrane and mesangium. This nephroprotector effect should be considered when a switch of therapy is demanded by the neuropathy status and a second line treatment is considered. Presence of renal disease may be an indication for tafamidis maintenance and combined therapy.

P0053 A METHOD FOR THE ISOLATION OF FLUORESCENT GLOMERULI FROM ZEBRAFISH LARVAE

Anna Iervolino[1,2], Tim Lange[1], Florian Siegerist[1], Maximilian Schindler[1], Giovambattista Capasso[2,3], Karlhans Endlich[1], Nicole Endlich[1]

[1]University Medicine Greifswald, Department of Anatomy and Cell Biology, Greifswald, Germany, [2]Biogem S.c.a.r.l., Department of Translational Nephrology, Ariano Irpino, Italy and [3]University of Campania "Luigi Vanvitelli", Department of Translational Medical Sciences, Napoli, Italy

Background and Aims: The zebrafish is a powerful animal model to study the glomerular morphology and the function of the permselectivity of the glomerular filtration barrier. Since zebrafish larvae develop quickly and can be bred to transparency, *in vivo* observation of these animals is possible. At 48 hours post fertilization (dpf), zebrafish develop a single filtering glomerulus which is attached to a pair of renal tubules. Like in mammals, the glomerular filtration barrier consists of a fenestrated endothelium, the glomerular basement membrane (GBM) and interdigitating podocyte foot processes bridged by a molecularly conserved slit diaphragm. By the use of genetically modified zebrafish strains with fluorescently labeled podocytes, it is possible to study alterations of the glomerulus during the development of renal disease directly *in vivo* and *in vitro*. As an injury model we used the nitroreductase/metronidazole (NTR/MTZ) zebrafish line to induce podocyte apoptosis and detachment from the GBM. Moreover, treatment of these larvae with MTZ induces glomerular injury that mimics focal segmental glomerulosclerosis (FSGS). The aim of our study was to establish a glomeruli isolation method which allows us to identify deregulation of miRNAs and mRNAs in the injured glomeruli by sequencing.

Method: The transgenic zebrafish strain *Cherry* (Tg(*nphs2*:Eco.nfsB-mCherry); *mitfa*$^{w2/w2}$; mpv17$^{a9/a9}$) which expresses the prokaryotic enzyme nitroreductase (NTR) fused to mCherry, a red fluorescent protein, under the control of the podocyte-specific podocin (*nphs2)* promoter in a transparent zebrafish strain, was used. The NTR/MTZ is a model of cell ablation to mimic podocyte injury. The prodrug MTZ (80 μM) is converted into a cytotoxin by NTR leading to a dose-dependent apoptosis exclusively in NTR-expressing podocytes. To induce podocyte injury, we treated *Cherry* larvae at 4 days post fertilization with MTZ (80 μM) freshly dissolved in 0.1% DMSO-E3 medium for 48 hours. Control larvae were treated with 0.1% DMSO-E3 medium. The treatment was stopped by a MTZ washout at 6 dpf.

In order to perform the miRNA and mRNA sequencing on glomeruli isolated from MTZ-treated and control larvae we tried to establish a method to obtain total RNA samples of good quality. For this purpose, three different approaches were tested and validated: 1) Sieving method, 2) Fluorescence-Activated Cell Sorting method (FACS), and 3) manual isolation of glomeruli by using a micropipette.

Results: Zebrafish larvae developed a glomerular damage similar to FSGS after MTZ-treatment. MTZ-treated larvae showed severe pericardial edema, a reduction of the nephrin and podocin expression, proteinuria and an increased mortality rate at 8 dpf.

After many tests we showed that glomeruli isolation using the sieving method and FACS were not efficient due to contaminations with other organs (sieving) and a loss of a large amount of cells per sample (FACS), respectively. Samples of the required quality for sequencing resulted only from the manual glomeruli isolation.

Conclusion: Here we describe methods to isolate fluorescent glomeruli from transgenic zebrafish larvae. For our studies, we used the NTZ/MTR kidney disease model in order to identify mRNAs and miRNAs regulated in response to glomerular damage. This technique will further allow to screen for healing drugs in high-throughput experiments.

P0054 **ACQUIRED DIFFERENTIAL EXPRESSION IN ACUTE KIDNEY INJURY OF GENES RESPONSIBLE FOR HEREDITARY NEPHROPATHIES.**

Sol Carriazo[1], Maria Dolores Sanchez-Nino[1], Maria Vanessa Perez Gomez[1], Laura Castañeda-Infante[1], Teresa Stock da Cunha[1], Guillermo Gonzalez-Martin[1], Alejandro Avello[1], Elena Gomá[1], Raul Fernandez-Prado[1], Emilio González-Parra[1], Alberto Ortiz[1]

[1]*Hospital Universitario Fundación Jiménez Díaz, Nephrology, Madrid, Spain*

Background and Aims: Gene sequencing is becoming an important diagnostic tool in a great number of medical specialties. Despite its interpretation is still a challenge, allows the identification of genes related to hereditary diseases and bild a base for the study of acquired nephropathies. We hypothesize that those genes responsible for hereditary nehpropathies could contribute to the pathogenesis of acquired nephropathies.

Method: In a murine model of acute kidney disease induced by folic acid, we analyzed the kidney transcriptomic after 24 hours of damage. In this database we evaluated if 625 genes described as responsible for hereditary nephropathies were expressed significantly. Later, we evaluated the correlation between diferentially expressed genes and glomerular filtration, using transcriptomic databases of human nephropathies (Nephroseq), so that, we could identify those relevant in acquired human nephropathies and in experimental settings. A functional enrichment analysis was done using the software Gorilla, and some of the genes were validated in our laboratory using RT-PCR.

Results: In acute kidney disease, the renal expression of 3906/25051 (15.59%) genes increased and the expression of 3537 (14.11%) decreased significantly ($p<0.05$). The percentage of genes expressed diferentially was higher when analysing the 625 genes responsible of familiar nephropathies. We identified 615 of those in the murine model and 105/615 (17.07%) increased it expression, and 155 (25.20%), decreased it ($p<0.05$ when compared with the database with 25051 genes). 241 of those 260 diferentially expressed genes (92.69%) where associated significantly with glomerular filtration rate in human nephropathies. The most enriched GO process were "complement activation", "protein activation cascade", "activation of immune response" and "RNA processing". We have validated the expression of 7 of the genes in acute kidney injury (SLC34A1, SLC34A3, Klotho, MAGED2, NLRP3, FN1, COL4A1), which supports the relevance of the transcriptomic results.

Conclusion: Genes involved in familiar nephropathies are overexpressed between genes diferentially expressed in acquired nephropathies, suggesting that they could play a role in the pathogenesis of the last, throught the regulation of the RNA processing, protein activation or immune response and complement regulation. The analysis of the functioning of genes responsible for familiar nephropathies in acquired nephropaties could identify new therapeutic targets in kidney damage.

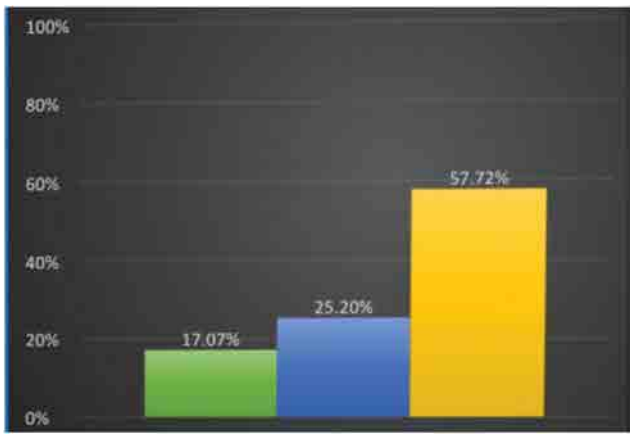


Figure:

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P0055 **GALECTIN-3 STRONGLY ASSOCIATES WITH RENAL FUNCTION, CARDIOMYOPATHY AND FIBROSIS IN PATIENTS WITH FABRY DISEASE**

Christiane Drechsler[1], Rudolf De Boer[2], Daniel Oder[3], Lena Gutjahr-Lengsfeld[1], Nurcan Üçeyler[4], Claudia Sommer[4], Christoph Wanner[1], Peter Nordbeck[3]

[1]University Hospital Wuerzburg, Dept of Internal Medicine 1, Div of Nephrology, Wuerzburg, Germany, [2]University of Groningen, Dept of Cardiology, Groningen, Netherlands, [3]University Hospital Wuerzburg, Dept of Internal Medicine 1, Div of Cardiology, Wuerzburg, Germany and [4]University Hospital Wuerzburg, Dept of Neurology, Wuerzburg, Germany

Background and Aims: Patients with Fabry disease frequently develop cardiac hypertrophy and progressive Fabry nephropathy. The progress of cardiac hypertrophy can lead to replacement fibrosis and heart failure.

Galectin-3 is expressed in the heart, kidneys, blood vessels, and macrophages. It marks activated macrophages in failure-prone hypertrophied hearts and contributes to cardiac dysfunction. Experimental data suggest that galectin-3 is involved in fibrosis and inflammation also associated with renal failure. Galectin-3 inhibitor therapy tested in a phase 2 clinical trial in chronic kidney disease lead to an improvement of the estimated glomerular filtration rate. Given the role of Galectin-3 in cardiac hypertrophy, heart and renal failure, we hypothesized that it may be of potential relevance particularly for Fabry disease patients.

Method: This study investigated the galectin-3 concentrations in 172 patients with genetically proven Fabry disease. We studied the association of galectin-3 concentrations with renal function, left ventricular mass, and adverse clinical symptoms in patients with Fabry disease. Galectin-3 was measured by FDA-approved ELISA. GFR was determined by DTPA clearance. Left ventricular mass and cardiomyopathy were assessed by magnetic resonance imaging and echocardiography. In cross-sectional analysis, associations with adverse clinical outcomes were determined by correlation analysis and linear and binary logistic regression analysis, respectively. Data was adjusted for age and sex.

Results: Patients had a mean age of 39 ± 14 years and 41% were male. The mean galectin-3 concentration was 17 ± 12 ng/mL (normal value is approx. 11 ng/mL). Patients had a mean BMI of 23.7 ± 4.5 kg/m^2 and a mean GFR of 92 ± 38 ml/min. Galectin-3 was strongly correlated with GFR, creatinine and urea. With higher galectin-3 concentrations of the patients, their GFR was lower ($r=-0.63$, $p<0.001$) and creatinine and urea were higher ($r=0.68$ and $r=0.53$, respectively, both $p<0.001$). Furthermore, cardiac hypertrophy was significantly higher with higher concentrations of galectin-3. The correlation coefficient for septal hypertrophy was $r=0.43$ ($p<0.001$) and for posterior hypertrophy $r=0.39$ ($p<0.001$), respectively. Similarly, cardiac fibrosis was significantly higher with higher galectin-3 levels ($r=0.34$, $p<0.001$). Patients of the highest galectin-3 tertile furthermore had significantly higher risks of adverse clinical symptoms. The adjusted odds ratio to suffer from angina pectoris was increased $>$ 6-fold and the odds ratio to suffer from neuropathic pain was increased $>$ 3-fold for patients of the highest galectin-3 tertile as compared to patients of the lowest galectin-3 tertile.

Conclusion: Increased galectin-3 concentrations were strongly associated with cardiac hypertrophy, cardiac fibrosis, decreased renal function, and adverse clinical symptoms in patients with Fabry disease. Galectin-3 can be useful as biomarker for cardiac and renal complications in Fabry disease. Galectin-3 inhibitor treatment may reduce complications of Fabry disease, and requires a randomized controlled trial.

P0056

USE OF CLINICAL EXOME SEQUENCING IN THE DIAGNOSTIC FLOW OF MONOGENIC KIDNEY DISEASES: THE PIEDMONT EXPERIENCE

Tiziana Vaisitti[1], Monica Sorbini[1], Martina Callegari[1], Silvia Kalantari[1], Valeria Bracciamà[1], Francesca Arruga[1], Silvia Bruna Vanzino[1], Alessandra Pelle[2], Daniela Giachino[3], Enrico Cocchi[4], Simone Baldovino[5], Cristiana Rollino[6], Roberta Fenoglio[6], Licia Peruzzi[4], Dario Roccatello[5], Antonio Amoroso[1], Silvia Deaglio[1]

[1]Transplant Regional Center-Piedmont region, Immunogenetics and Transplant Biology, AOU Città della Salute e della Scienza & Department of Medical Sciences, University of Turin, Torino, Italy, [2]AOU San Luigi Gonzaga, Orbassano, Turin, [3]AOU San Luigi Gonzaga, Orbassano, Turin & Department of Clinical and Biological Sciences, University of Turin, Torino, Italy, [4]Nephrology Dialysis and Transplantation, Regina Margherita Children's Hospital, Turin, Torino, Italy, [5]Department of Clinical and Biological Sciences, University of Turin & SCU Nephrology and Dialysis (ERKnet member) - CMID, Center of Research of Immunopathology and Rare Diseases, San Giovanni Hospital, Turin, Torino, Italy and [6]SCU Nephrology and Dialysis (ERKnet member) - CMID, Center of Research of Immunopathology and Rare Diseases, San Giovanni Hospital, Turin

Background and Aims: next-generation sequencing (NGS) technologies are becoming a powerful diagnostic tool in precision medicine. Specifically, exome sequencing can help in the diagnosis of selected diseases, in their medical management and therapeutic choices. Inherited kidney diseases (IKD) are among the major causes for kidney failure, both in children and adults, resulting in increased mortality, high health care costs and need for organ transplantation. In addition, it is worth mentioning that a significant proportion of patients in the kidney transplant lacks a clear diagnosis. This subset of diseases may thus benefit from the application of NGS technology, as the simultaneous investigation of hundreds of genes can lead to the identification of causative variants in a vast population of patients.

The aim of this study is to validate the use of a clinical exome sequencing approach in the diagnostic flow for kidney diseases leading to organ failure to i) confirm the clinical diagnosis, ii) find the genetic cause of previously unrecognized diseases and iii) improve the outcome of organ transplantation by excluding live-donors carrying the same mutational burden.

Method: 160 patients were recruited, directly or following a genetic counseling, exploiting a network of 21 nephrology centers spread across the Piedmont region, coordinated by the "Centro Regionale Trapianti (CRT)" of Torino. Patients were then evaluated for NGS eligibility. DNA extracted from blood samples was checked for integrity, quantified and used for library preparation. A clinical exome sequencing (CES) kit by Illumina was used, allowing for targeted capture, enrichment and sequencing of 6700 clinically relevant genes. Reads were aligned to hg37 reference genome using the Isaac enrichment tool and variants filtered using an *ad-hoc* set up pipeline of analysis.

Results: clinical exome sequencing was performed on a diagnostic cohort of 138 patients, both children (37.7%) and adults (62.3%), with a prevalence of male subjects (56.5%). The majority of the cohort (51.5%) presented a positive family history for kidney disease, while 22 patients were excluded from the study as organ failure was most likely the result of secondary events. The cohort was highly heterogeneous with 21% of patients presenting with ciliopathies, 18.1% with glomerular disease, 7.2% with tubular disease while the remaining cohort presented other diseases or was undiagnosed (44.3%). An *ad hoc* analytical pipeline was designed, based on selected genotype-phenotype correlation database, filter-in metrics, inheritance model and annotation of variants based on public databases and *in-silico* prediction tools. By adopting well defined criteria of recruitment and analysis, causative genes were identified in 61.6% of cases and in the 57.3% of cases results were in line with the original diagnostic hypothesis. Moreover, 50.8% of cases with organ failure for unknown reasons were solved with the identification of causative genes. Out of the 133 total variants found in the cohort, 63 were classified as pathogenic or likely pathogenic. The remaining 70 identified variants were annotated as variant of unknown significance and will be further investigated.

Conclusion: Taken together, these results show that CES is a powerful non-invasive tool for the genetic diagnosis of IKD. Identification of disease causative variants may represent a critical step for the diagnosis, clinical management of the patients, and potentially for optimal live-donor selection.

P0057

ADPKD: COMPLEX GENOTYPES MAY EXPLAIN SEVERE PHENOTYPE AND INTRAFAMILIAL PHENOTYPIC VARIABILITY

Claudia Izzi[1], Elisa Delbarba[2], Laura Econimo[3], Chiara Dordoni[1], Gianfranco Savoldi[4], Cinzia Mazza[4], Nadia Dallera[5], Francesco Scolari[6]

[1]Asst-Spedali Civili of Brescia, Division of Nephrology and Department of Obstetrics and Gynecology, Brescia, Italy, [2]Asst-Spedali Civili of Brescia, Division of Nephrology, Italy, [3]Asst-Spedlai Civili of Brescia, Division of Nephrology, Italy, [4]Asst-Spedali Civili of Brescia, Medical Genetics Laboratory, Italy, [5]ASST-Spedali Civili, Montichiari, Division of Nephrology, Italy and [6]University of Brescia, Asst-Spedali Civili of Brescia, Division of Nephrology, Italy

Background and Aims: Discordant affected relative-pairs are seen in ∼10% of families with Autosomal Dominant Polycystic Kidney Disease (ADPKD); <1% of patients exhibit very early onset (VEO) disease. Complex genotypes may result in renal disease variability beyond that predicted by the sole effect of a single PKD mutant allele, leading to the discovery of biallelic or digenic disease. Here we illustrate such complexity in 6 ADPKD pedigrees.

Method: Among our single-center ADPKD cohort (186 index patients), we selected pedigrees (P) in which marked familial phenotypic variability or severe and early onset disease was investigated by NGS and MLPA analysis of PKD1 and PKD2 genes and NGS analysis of other cystogenes. Segregation analysis by Sanger sequencing of PKD variants was performed in available affected and unaffected family members.

Results: In P1 and P2, the index cases (IC), presented with very early onset (VEO) disease characterized by prenatal/neonatal enlarged and hyperechogenic kidneys mimicking autosomal recessive polycystic kidney disease (ARPKD). In P1, with neonatal onset, the ADPKD affected father transmitted a PKD1 PT variant p.Gln4231*, whereas the mother, without renal cystic phenotype, transmitted a PKD1 *hypomorphic* variant p.Asp1332Asn.

In P2, the ADPKD-PKD2 mother's pregnancy was complicated by Potter sequence. Parent's PKHD1 gene analysis was negative. Two missense NT variants in PKD1/PKD2 genes were detected in the healthy father, respectively p.Gly1944Arg and p.Thr203Ile. Therefore, a complex PKD inheritance was supposed in the fetus. Fetus DNA was not available.

In P3 early onset (EO) ADPKD in two monozygous twins was underpinned by a PKD1 NT variant (p.Arg1951Gln) inherited by the ADPKD mild affected father and worsened by a de novo PKD1 truncating variant p.Arg2402*.

In P4 and P5 a digenic ADPKD (PKD1 +PKD2 and PKD1 +PKHD1) was diagnosed in severe ADPKD IC. In P4 the two most severely affected siblings carried a PKD2 T variant (p.Ala365fs) and a PKD1 NT variant p-Cys259Tyr.

In P5 the IC presented with EO ADPKD, a de novo splicing variant c.2097 + 5_+6insT in PKD1 gene was discovered but the phenotype was probably worsened by the presence of biallelic variant in a second cystogene PKHD1: one paternally inherited: p.Gly1712Arg and one maternally inherited: p.Asp3088Asn .

Elderly parents in P6 had mild ADPKD with bilateral few kidney cysts and preserved eGFR, whereas IC showed moderate/severe CKD due to ADPKD biallelic variants. The IC carried a homozygous PKD1 NT variant (p.Arg4154Cys): each mutant allele inherited from the mild ADPKD affected parents.

Conclusion: Our study illustrates the genetic complexity in an otherwise "simple" Mendelian disorder, providing insights into the genetic basis of severity of ADPKD cases and into ADPKD intrafamilial disease variability. In our pedigree all cases with more severe clinical picture in the family presented at least two PKD variants. In P5 we found for the first time an EO ADPKD due to both PKD1 and PKHD1 variants.

PKD1 and PKD2 sequence analysis together with cystic kidney disease gene panel analysis is recommended in those patients with discordant phenotype compared to family members. Molecular study of PKD patients is expected to be a good prognostic tool together with clinical and renal imaging data to better manage disease therapy, follow-up and reproductive issues.



Figure:

P0058 THE ROLE OF GENETICS IN INCOMPLETE DISTAL RENAL TUBULAR ACIDOSIS IN NEPHROLITHIASIS

Viola D'Ambrosio[1,2], Eugenio Sangiorgi[2], Bernhard Hess[3], Giovanni Gambaro[4], Pietro Manuel Ferraro[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Nefrologia, Roma, Italy, [2]Università Cattolica del Sacro Cuore, Roma, Italy, [3]Klinik Im Park and University of Zurich, Internal Medicine and Nephrology, Zurich, Switzerland and [4]University of Verona, Renal Unit, Division of Nephrology and Dialysis, Department of Medicine, Verona, Italy

Background and Aims: Distal renal tubular acidosis (dRTA) is characterized by an impairment of urinary acidification resulting in a hyperchloremic non-anion gap metabolic acidosis, hypokalemia and inappropriately elevated urine pH. If not treated, this chronic condition eventually leads to nephrocalcinosis and recurrent nephrolithiasis, impaired renal function and bone demineralization due to reabsorption of bicarbonate and phosphate complexed with calcium from the bone as a buffer for metabolic acidosis. Distal RTA is therefore a well-defined entity that can be diagnosed by genetic testing of five genes known to be disease-causative (ATPV1B1 and ATPV0A4, FOXi1, SLC4A1 and WDR72).

Incomplete distal renal tubular acidosis (idRTA) is defined as impaired urinary acidification that does not lead to overt metabolic acidosis and therefore can be diagnosed if patients fail to adequately acidify urine after an ammonium chloride (NH4Cl) challenge or other acid load tests. It is observed in 10-20% of calcium stone formers. It is still uncertain whether idRTA represents a distinct entity or it is part of the dRTA spectrum and whether it is caused by mutations in the same genes of overt dRTA. Heterozygous ATP6V1B1 pathogenic variants have been linked to idRTA, as well as mutations in SLC4A1.

Method: In this cross-sectional study we investigated a group of 23 stone formers whose clinical features were suspicious of idRTA: a history of nephrolithiasis or nephrocalcinosis with morning urinary pH $>$ 5.8 in the absence of overt metabolic acidosis. They therefore underwent a simplified NH4Cl challenge and were found to have impaired urinary acidification ability. These patients were then analyzed by genetic testing with sequencing of 4 genes: SLC4A1, ATP6V1B1, ATP6V0A4 and FOXi1.

Results: Two unrelated individuals were found to have mutations in SLC4A1: 2 different variants in heterozygosis that had never been described before. The first patient was a 47-year old man, recurrent stone former (mainly apatite, but also some calcium oxalate), with hypercalciuria but normal bone mineral density (BMD). His family history revealed 1 uncle with kidney stones. The second patient was a 56-year old woman with a diagnosis of osteogenesis imperfecta, a history of reduced BMD and severe restrictive ventilation disorder and passed 1 stone (35% apatite, 65% CaOx). She was found to have bilateral nephrocalcinosis and hypocitraturia. Her family history revealed a sister with kidney stones.

Conversely, 21 patients did not show any mutations for the genes sequenced, leading to a prevalence of genetic mutations of 8.7%. This is a much lower figure compared with overt dRTA, in which only 30% of patients with a clinical diagnosis of hereditary dRTA have no identified causative mutations in the currently known genes.

Conclusion: This suggests the involvement of other genes (WDR72 or others) or non-genetic tubular dysfunction in the pathogenesis of idRTA in stone formers.

P0059 **CLINICAL AND IMAGING FEATURES OF A NOVEL DNAJB11 MUTATION COMPARED TO PKD1-PKD2 ADULT POLYCYSTIC KIDNEY DISEASE (ADPKD). TWO DIFFERENT DISEASES?**

Lucio Manenti[1], Isabella Pisani[1], Marco Allinovi[2], Micaela Gentile[1], Maria Teresa Farina[1], Francesco Peyronel[1], Paola Zanelli[3], Paola Sebastio[3], Viviana Palazzo[4], Sabrina Giglio[4], Sara Giuliotti[5], Enrico Fiaccadori[1]

[1]Azienda Ospedaliero-Universitaria di Parma, UOC Nefrologia,, Parma, Italy, [2]Careggi University Hospital, SOD Nefrologia, Dialisi e Trapianto, Firenze, Italy, [3]Azienda Ospedaliero-Universitaria di Parma, SSD Immunogenetica dei trapianti, Parma, Italy, [4]Azienda Ospedaliero-Universitaria Meyer, SOD Complessa di Genetica Medica, Firenze, Italy and [5]Azienda Ospedaliera Universitaria di Parma, UOC Radiologia, Parma, Italy

Background and Aims: ADPKD is characterized by the progressive development of bulky renal cysts, often resulting in end-stage renal disease (ESRD). Among this group 85% of cases recognize a genetic mutation concerning *PKD1/PKD2* genes (ADPKD). Among the remaining 15% of ADPKD patients, *DNAJB11* mutations (DNAJB11-PKD) has been recently recognized. [Cornec-Le Gall E, Olson RJ, Beesse W t al. Monoallelic Mutations to DNAJB11 Cause Atypical Autosomal-Dominant Polycystic Kidney Disease. Am Journ Hum Gen 2018, 102:832-844.]

DNAJB11 encodes a co-chaperone of the endoplasmic reticulum (ER) also called ERdj3. It is part of the HSP40 protein family and plays a central role in both intracellular and extracellular proteomic homeostasis (proteostasis). In the intracellular compartment it acts as a co-chaperone in the pathway of the unfolded protein response (UPR) in which it binds misfolded proteins which have to be secreted and activates BiP an HSP70 of ER whose function is to correct the misfolding. In our Nephrology Unit we collected the largest cohort of patients with a new stop codon mutation (p.Arg34*) of *DNAJB11*. All patients are relatives of different ranks and were born in a small village in the mountains of the Parma province.In this study we compare clinical features of DNAJB11-PKD with ADPKD to define differences between the two groups.

Method: We identified retrospectively from outpatient and dialysis databases of the Nephrology Unit of Parma patients carrying pArg34* *DNAJB11* or *PKD1-PKD2* mutations. We collected the clinical features and the available diagnostic imaging of all identified patients.

Results: We collected 19 patients with DNAJB11-PKD and 37 with ADPKD. The clinical characteristics are reported in Figure 1 . Our DNAJB11-PKD cohort vs ADPKD presented significantly a normal renal size (median value 10.5cm vs 16cm respectively) and smaller cysts size (median value 2cm vs 5cm respectively). Interestingly 5/19 DNAJB11 patients had type 2 diabetes vs no cases in the ADPKD group ($p<0.05$). ADPKD patients presented ESRD about 10 years before DNAJB11-PKD and renal survival resulted significantly worse (Figure 2).We revised also the previous diagnosis of our DNAJB11-PKD patients; 3/19 DNAJB11-PKD cases were diagnosed as having ADPKD. The remaining were classified as medullary sponge kidney disease (7/19), diabetic nephropathy (3/19) or nephroangiosclerosis (6/19).

Conclusion: *DNAJB11* mutations were reported as a cause of ADPKD for the first time in May 2018 by Cornec-Le-Gall and colleagues. In their study were reported 7 different mutations in 23 patients and they identified 2/23 patients with type II diabetes. We here report the larger single *DNAJB11* mutation cohort in the literature and compared it with genetic proven ADPKD. We documented differences in pathognomonic clinical features of ADPKD like renal survival, enlarged kidneys and bulky cysts. Moreover about 30% of DNAJB11-PKD patients present Type II diabetes that would be related to altered proteostasis in the ER. Since DNAJB11-PKD appears to differ in relevant aspects from well known ADPKD, it would be less confusing to classify DNAJB11-PKD indipendently from ADPKD.

Figure 1. Clinical features of our DNAJB11 or ADPKD patients.

Variable	DNAJB11-PKD	ADPKD	p values
Patients (n°)	19	37	-
Gender (M/F)	9/10	24/13	NS
ESRD (y/n)	7/12	11/26	NS
Age; min-max(at ESRD)	72; 54-80	61; 47-76	NS
Renal size;min-max (cm)	10.5;7-11	16;12-22	**<0.001**
Bigger renal cyst;min-max (cm)	2;1-10	5;1-13	**0.004**
Associated diseases			
Tipe II diabetes(y/n)	5/14	0/20	**0.04**
Neoplasms (at diagnosis)(y/n)	4/15	1/19	NS

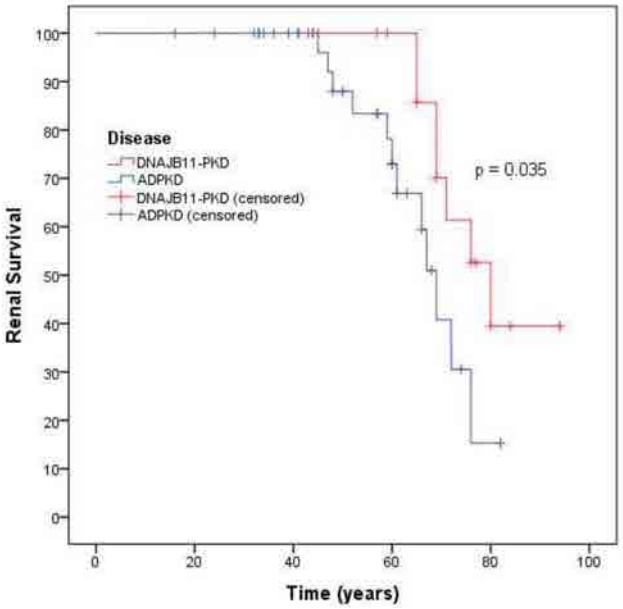


Figure:

P0060 **COMBINED NOVEL PBX1 AND RET VARIANTS IN AN ADULT WITH SYNDROMIC RENAL HYPOPLASIA: A CASE REPORT.**

Friederike Petzold[1], Jan Halbritter[1]

[1]*University Hospital Leipzig, Division of Nephrology, Department of Internal Medicine, Leipzig, Germany*

Background and Aims: Congenital abnormalities of the kidney and urinary tract (CAKUT) represent the main cause of pediatric end-stage renal disease with vast pheno- and genotypic heterogeneity. However, its contribution to adult chronic kidney disease (CKD) is less well characterized. We here report on an adult who underwent genetic testing for previously unrecognized CAKUT.

Method: Phenotypic characterization of a family with mild syndromic form of kidney hypoplasia. Panel-based genetic analysis for CAKUT associated genes in DNA from peripheral blood cells, oral mucosa, and urinary cells.

Results: A 20-year-old male presented with bilateral hypoplastic kidneys, first diagnosed with nocturnal enuresis at the age of ten. For CKD stage 2 (eGFR 72ml/min/1.73㎡), hypertension, and moderate albuminuria (300mg/d) he was treated with Ramipril. Additionally, facial dysmorphism with low-set microtia, slight micrognathia, and slightly impaired intelligence was apparent. Bilateral audiograms did not reveal any hearing impairment. His father showed slightly reduced kidney size without any laboratory anomalies or extrarenal symptoms. Further family history including his mother and three half siblings presented unremarkable.

Genetic analysis revealed the following two variants:

First, a novel heterozygous truncating variant, absent from patient and population databases, was found in *PBX1* c.992C>A p.Ser331* (NM_002585.3). As this variant was detected in 25% of NGS reads, we tested for potential mosaicism by direct sequencing in DNA obtained from oral mucosa and urinary epithelia. While the latter showed no *PBX1* variation, mucosa cells revealed the mutated allele in 50% of reads. Segregation analysis of the father showed *PBX1* wild-type. The mother was not available for genetic testing.

Additionally, we identified a novel heterozygous splice site variant in *RET*: c.1760-5C>A (NM_020975.4), absent from both patient and population databases. This substitution is predicted to affect splicing at the acceptor site of exon 10. Sanger sequencing demonstrated paternal inheritance.

Conclusion: Pathogenic *PBX1* variants were recently associated with CAKUTHED (Congenital Abnormalities of the Kidney and Urinary Tract with or without Hearing loss, abnormal Ears, or Developmental delay) syndrome (Heidet 2017), characterized by highly variable phenotypes. PBX1 encodes a homeodomain transcription factor taking part in transcriptional regulation during embryonic development. Functional studies suggest disturbed PBX1-dependent transactivation ability and altered nuclear translocation, resulting in abnormal interactions between PBX1 proteins and cofactors (Slavotinek 2017). Prevailing PBX1 expression in embryonic compared to adult kidneys support an important function in development (Le Tanno 2017).

An aberrant splicing effect of the identified *RET* variant is supported by the fact that the father, who carries the same variant but *PBX1* wild-type, has slightly reduced kidneys. Associations between abnormal kidney development and alterations of RET were first described in stillborn fetuses with renal agenesis (Skinner 2008), but also in patients with vesicoureteral reflux (Yang 2008). RET encodes for a receptor tyrosine-protein kinase, which while binding ligands such as GDNF (glial cell-line derived neurotrophic factor) is involved in signaling pathways and plays an important part during organ development. Particularly, the RET/GDNF signaling pathway plays a crucial role during development of the kidneys (Costantini 2010). Functional analyses indicate an altered phosphorylation status of RET as possible causative mechanism.

To the best of our knowledge, this case is the first to report on combined *PBX1* and *RET* gene variants associated with mild syndromic renal hypoplasia, likely mitigated by genetic mosaicism.

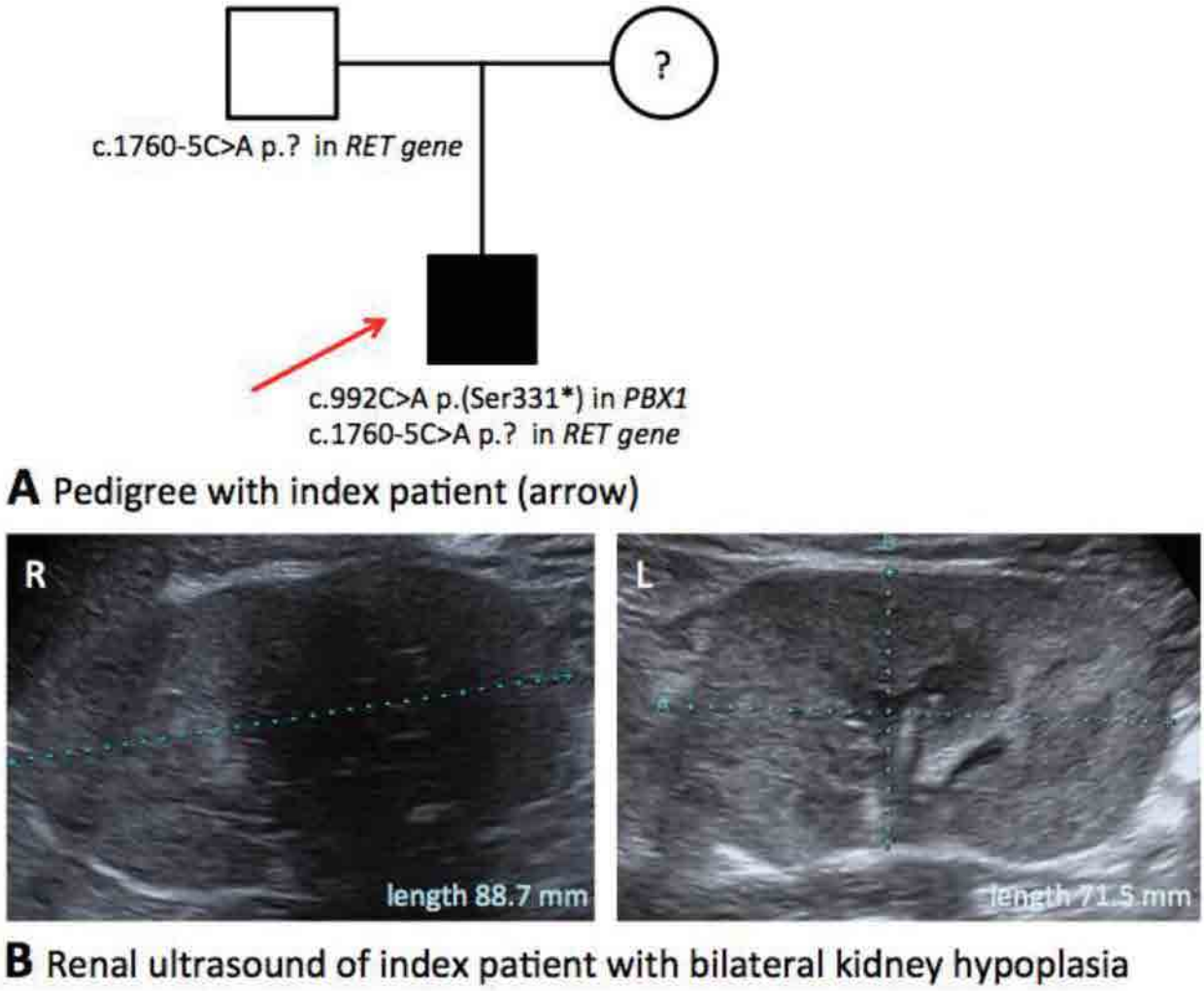


Figure:

P0061 LOSS OF UBIQUITIN SPECIFIC PROTEASE-40 CAUSES PODOCYTE DETACHMENT AND CONTRIBUTES TO THE DISEASE PROGRESSION OF GLOMERULOSCLEROSIS

Naoaki Mikami[1], Eriko Tanaka[1], Ichiro Hada[1], Kunimasa Yan[1]

[1]*Kyorin University, Pediatrics, Tokyo, Japan*

Background and Aims: We reported that the ubiquitin specific protease-40 (USP40) is expressed in podocytes beyond the species and plays a crucial role in glomerulogenesis in zebrafish (Takagi H, Am J Physiol Renal Physiol 2017). However, the role of USP40 in podocytes and its functional downstream after birth is largely unknown. Recent report indicated that other USP family: USP10 regulates integrin beta1 and fibrotic wound healing in myofibroblasts (Gillespie SR, J Cell Sci 2017). The present study aimed to explore the biological role of USP40 in the acquired podocyte injury and to determine the interacting partner by focusing on podocyte detachment.

Method: We generated USP40-knockout mice (USP40KO); however, they showed no apparent kidney abnormality. Therefore, to explore the biological role of USP40 in acquired podocyte injury, we crossed USP40KO with NEP25 mice, in which selective podocyte injury can be induced by injection with an immunotoxin, LMB2. Urinary protein was analyzed until day 9 after LMB2 injection, and then kidney tissues were subjected to light microscopy, immunohistochemistry of p57, and immunofluorescence microscopy of integrin beta1. The glomeruli were isolated and subjected to immunoblot analysis of integrin beta1. The effect of USP40 knockdown on integrin beta1 expression was studied in cultured mouse podocytes. Finally, the protein binding of integrin beta1 with USP40 was determined by immunoprecipitation using cultured mouse podocytes.

Results: NEP-USP40KO mice developed earlier and higher levels of proteinuria compared with NEP mice. Light microscopy and immunohistochemistry showed higher levels of kidney injury in NEP-USP40KO mice compared with NEP mice in terms of hyalinosis ($p<0.01$), crescent formation ($p<0.01$), and cell proliferation ($p<0.01$) in the glomeruli, podocyte loss ($p<0.05$), and tubulointerstitial injury ($p<0.01$). Immunoblot analysis and immunofluorescence revealed decreased expression of integrin beta1 in podocytes of NEP-USP40KO mice compared with NEP mice. Gene knockdown of USP40 in cultured podocytes decreased the protein expression of integrin beta1. Finally, apparent protein binding of USP40 with integrin beta1 was observed.

Conclusion: Integrin beta1 is known to play a crucial role as the adhesion molecule that connects the podocytes with the extracellular matrix of the glomerular basement membrane. It is also known that the lack of integrin beta1 causes podocyte detachment, which is involved in the disease progression of glomerulosclerosis. Therefore, the present study suggests that USP40 may be involved in a self-defense mechanism in podocyte injury probably through interacting with the regulatory machinery of integrin beta1 in podocytes.

P0062

GLUCOSYLCERAMIDE SYNTHASE INHIBITION WITH VENGLUSTAT IN CLASSIC FABRY DISEASE PATIENTS LEADS TO PROGRESSIVE REDUCTION OF ENDOTHELIAL CELL GLOBOTRIAOSYLCERAMIDE INCLUSION VOLUME

Michael Mauer[1], Ozlem Goker-Alpan[2], Dominique P. Germain[3], William Wilcox[4], Robert J. Hopkin[5], Elena Lukina[6], Tarekegn Geberhiwot[7], Patrick Deegan[8], Anna Tylki-Szymanska[9], Charlotte Sensinger[10], Atef Zaher[10], Eric Hailman[10], Vijay Modur[10], Behzad Najafian[12]

[1]University of Minnesota, Department of Pediatrics and Medicine, Minneapolis, United States of America, [2]LDRTC, Fairfax, United States of America, [3]University of Versailles, Paris-Saclay University, French Referral Center for Fabry Disease, Division of Medical Genetics and INSERM U1179, Montigny, France, [4]Emory University School of Medicine, Atlanta, United States of America, [5]Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Division of Human Genetics, Cincinnati, United States of America, [6]National Research Center for Hematology, Moscow, Russia, [7]University of Birmingham, Birmingham, United Kingdom, [8]Addenbrooke's Hospital, Lysosomal Disorders Unit, Cambridge, United Kingdom, [9]The Children's Memorial Health Institute, Department of Pediatrics, Nutrition and Metabolic Diseases, Warsaw, Poland, [10]Sanofi Genzyme, Cambridge, United States of America and [12]University of Washington, Department of Pathology, Seattle, United States of America

Background and Aims: Fabry disease (FD) is a rare, X-linked, genetic disorder caused by mutations in the gene for the lysosomal enzyme alpha-galactosidase A (αGal-A). The progressive accumulation of glycosphingolipids, most notably globotriaosylceramide (GL-3), in lysosomes of a variety of organs and cell types leads, over decades, to renal, cardiovascular, and other clinical manifestations. In a phase 2 study, glucosylceramide synthase inhibition with venglustat led to a progressive reduction in plasma GL-3 to low-normal levels. Scoring by light microscopy showed a reduction in lysosomal GL-3 inclusions in skin capillary endothelial cells (EC) after 3 years of therapy, although not after 6 months. To further characterize the effect of venglustat using more precise methods, we applied unbiased stereological methods to quantitate GL-3 inclusions in skin ECs.

Methods: Skin biopsies were obtained from classic male Fabry disease patients (N = 11) at baseline and during daily treatment with venglustat in a phase 2 study (NCT02228460, NCT02489344). Images from at least 50 superficial skin capillaries were obtained using transmission electron microscopy at 7,500 X magnification. The fraction of the volume (Vv) of cytoplasm occupied by GL-3 inclusions [Vv(Inc/Endo)] in all ECs in these capillaries was estimated using point counting by a masked reader. Two-sided paired t tests were used to evaluate differences between baseline and post-treatment values at each time point.

Results: Venglustat therapy led to a significant reduction from baseline in Vv(Inc/Endo) of 21.1% after 6 months and 38.7% after 3 years of treatment (Figure).

Conclusions: Treatment with venglustat led to a reduction in GL-3 inclusion fractional volume in skin capillary ECs which was detectable after 6 months using precise quantitative methods. This was followed by further reduction over the next 2 1/2 years. We posit that, in the absence of αGal-A activity, inhibition of GL-3 production with venglustat allowed other enzymatic or non-enzymatic mechanisms to progressively reduce EC lysosomal GL-3 content, and that long-term venglustat therapy may therefore prevent or reverse progressive tissue injury in Fabry disease.

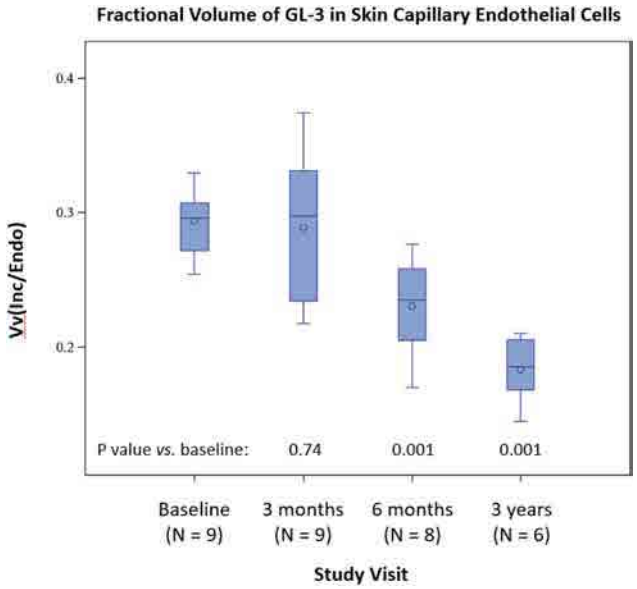


Figure:

P0063 CLINICAL CHARACTERISTICS OF PATIENTS WITH GENETICALLY CONFIRMED ALPORT SYNDROME

Gulsah Ozdemir[1], Bora Gulhan[1], Emine Atayar[2], Nur Canpolat[3], Oguz Soylemezoglu[4], Z. Birsin Ozcakar[5], Fehime Kara Eroğlu[6], Cengiz Candan[7], Belde Kasap Demir[8], Alper Soylu[9], Selcuk Yuksel[10], Harika Alpay[11], Ayse Agbas[12], Ali Duzova[1], Mutlu Hayran[13], Fatih Ozaltin[1,2], Rezan Topaloglu[1]

[1]Hacettepe University Faculty of Medicine, Pediatric Nephrology, Ankara, Turkey, [2]Hacettepe University Faculty of Medicine, Nephrogenetic Laboratory, Ankara, Turkey, [3]Istanbul University Cerrahpaşa Faculty of Medicine, Pediatric Nephrology, İstanbul, Turkey, [4]Gazi University Faculty of Medicine, Pediatric Nephrology, Ankara, Turkey, [5]Ankara University Faculty of Medicine, Pediatric Nephrology, Ankara, Turkey, [6]Dr. Sami Ulus Maternity and Children's Health Hospital, Pediatric Nephrology, Ankara, Turkey, [7]Istanbul Medeniyet University Göztepe Training and Research Hospital, Pediatric Nephrology, İstanbul, Turkey, [8]Tepecik Training and Research Hospital, Pediatric Nephrology, İzmir, Turkey, [9]Dokuz Eylül University Faculty of Medicine, Pediatric Nephrology, İzmir, Turkey, [10]Pamukkale University Faculty of Medicine, Pediatric Nephrology, Denizli, Turkey, [11]Marmara University Faculty of Medicine, Pediatric Nephrology, İstanbul, Turkey, [12]Haseki Training and Research Hospital, Pediatric Nephrology, İstanbul, Turkey and [13]Hacettepe University Faculty of Medicine, Preventive Oncology, Ankara, Turkey

Background and Aims: Alport syndrome (AS) is an inherited glomerular basement membrane disease caused by mutations in *COL4A3, COL4A4* or *COL4A5* genes. Recently, it has been reported that focal segmental glomerulosclerosis (FSGS) can be seen in AS and *COL4A* mutations can be detected in FSGS. In this study, we aimed to define the clinical characteristics of patients with genetically confirmed AS, in order to establish genotype-phenotype correlation and investigate the effects of different treatment regimes.

Method: A total of 87 pediatric AS patients included in this multicenter study. We retrospectively collected data from medical records and requested other centers to fill out a questionnaire, which included data regarding patient demographic features, family history, clinical and laboratory characteristics at first presentation, histopathological (if available) and genetic tests results, treatments and yearly follow-up results.

Results: A total of 87 (41 female, 46 male) genetically confirmed AS patients (*COL4A5*, n=43; *COL4A3*, n=25; *COL4A4*, n=19) were studied. Mean age at first presentation was 7.6±4.1 years and the median follow-up duration was 4.3 years (IQR 1.9–7.3). 14 (16.1%) of 87 patients presented with nephrotic syndrome (NS); renal biopsy findings showed FSGS in 11 (79%) of 14 patients with NS, and *COL4A3* mutations were the most common (n=7, 50%) in this group. Of 14 NS patients, 12 received steroid, 11 received cyclosporine (CsA) and 4 received other immunosuppressives prior to genetic diagnosis. The inheritance pattern of the patients with NS was consistent with ARAS in 10 patients (71.4%), XLAS in 3 patients (21.4%), and ADAS in 1 patient (7.2%). During follow up, glomerular filtration rate (GFR) decreased below 90 ml/min/1.73 m^2 in 24 of 87 patients (27.5%). *COL4A3* mutations (n=14, 58.3%) were the leading genetic abnormality in patients who progressed to chronic kidney disease (CKD). At the last visit, GFR loss was significantly higher in patients with *COL4A3* mutations when compared to patients with *COL4A4* and *COL4A5* mutations (p=0.04). Among patients with NS, 9 of 14 (64.2%) progressed to CKD. Genetic results of patients with NS who progressed to CKD were *COL4A3* in 6 (66.7%), *COL4A4* in 2 (22.2%) and *COL4A5* in 1 (11.1%) patients. In survival analysis, renal survival rate without CKD was 12.1 years (95% CI: 6.7-17.5). After the first presentation, the 5-year cumulative risk of CKD was 51.8%, 12.6%, and 12.9% in patients with *COL4A3, COL4A4* and *COL4A5* mutations, respectively (p=0.001). We observed that patients with *COL4A3* mutations, ARAS inheritance pattern, histopathology of FSGS or NS presentation progressed to CKD earlier ($p<0.001$ for *COL4A3*, p=0.01 for ARAS, $p=<0.001$ for FSGS, p=0.01 for NS presentation) when compared to those without. CsA treatment did not improve renal survival.

Conclusion: Detailed analyses of data from genetically confirmed Turkish patients with AS provided important clues regarding to the presentation, course and outcomes of the disease. *COL4A3* mutations, ARAS inheritance pattern, NS presentation and FSGS finding in renal biopsy are major risk factors for progression to CKD. We recommend genetic testing for patients suspected of having AS. Furthermore, *COL4A* mutations should be considered in patients with FSGS and steroid resistant NS. This approach will shed light on the prognosis of patients and help with definitive diagnosis, preventing unnecessary and potentially harmful medications.

P0064 RENAL PHENOTYPES IN A GROUP OF PATIENTS WITH MITOCHONDRIAL DISEASES

Letizia Zeni[1,2], Matteo Bargagli[3], Guido Primiano[3,4], Giuseppe Grandaliano[1,3], Serenella Servidei[3,4], Pietro Manuel Ferraro[1,3]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Nefrologia, Roma, Italy, [2]Università degli Studi della Campania "Luigi Vanvitelli", Caserta, Italy, [3]Università Cattolica del Sacro Cuore, Roma, Italy and [4]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Neurofisiopatologia, Roma, Italy

Background and Aims: Mitochondrial diseases (MDs) are one of the most common inherited metabolic disorders caused by mutations of either mitochondrial or nuclear genes involved in the oxidative phosphorylation pathway.

Tissues with high energy demand (i.e. brain and skeletal muscle) are preferentially affected, and MDs are not rarely referred to as mitochondrial encephalomyopathies. However, one of the hallmarks of MDs is multisystemic involvement, with large clinical variability and severity due to different mitochondrial DNA heteroplasmy levels. Given the possibility of multisystemic phenotype of MDs, renal involvement has been suggested, based on renal cells vulnerability to poor energy supply. A specific mitochondrial kidney disease is thought to underlie renal manifestations, therefore theoretically every district of the nephron might be affected by MDs. Regarding tubular involvement, we suggested a possible association between nephrolithiasis and MDs, based on data of 3 related stone formers with reduced urinary citrate excretion and MELAS syndrome. The aim of this study is to provide a clinical description of the renal phenotypes of patients with MDs.

Method: In 2019, 6 patients with MDs routinely followed by the Neurology outpatient clinic of our Institution were randomly asked to perform renal screening. Genetic tests, blood and 24-hour urine analyses were assessed in the whole population. The main comorbidities were recorded. Glomerular filtration rate (GFR) was estimated using creatinine clearance.

Results: Half of the patients were female, the average age at renal evaluation was 48±15 years; diabetes, hypertension and neurosensorial hypoacusia occurred in 4, 1 and 2 subjects, respectively. Five patients had m.3243A>G mutation, responsible for more than 85% of maternal inherited diabetes and deafness (MIDD) and syndrome of mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS). The remaining patient carried the m.8363G>A variant, reported to be associated with a multisystem MDs known as Leigh syndrome (subacute necrotizing encephalomyelopathy). Median serum creatinine was 0.6 mg/dL (IQR: 0.5-1.1) with median GFR of 92 mL/min/1.73 m^2 (IQR: 40-117). Three patients exhibited signs of kidney disease: one had both reduced GFR and proteinuria (eGFR 37 mL/min/1.73 m^2 and 750 mg/day respectively), one had renal impairment (58 mL/min/1.7 $3m^2$) and severe hypocitraturia (22 mg/day), one showed increased urinary calcium excretion (348 mg/day). In one patient, evaluation of the type of proteinuria has not been performed yet. Serum lactate was 3.1±1.9 mmol/L, urinary pH 5.8±0.3 and median urinary citrate excretion 593 mg/24h (IQR: 310-923). No relevant results were found on serum and/or urinary levels of sodium, potassium, magnesium, phosphorus, urate, chloride, oxalate, parathyroid hormone and 25-OH vitamin D.

Conclusion: These results confirmed the presence of renal disease and its heterogeneity in patients with MDs. A complete renal screening is necessary in these subjects in order to early recognize renal involvement and carefully select candidates for further diagnostic work-up including renal biopsy. A consensus on the optimal renal screening for these patients has yet to be established.

P0065 DOUBLE MUTATION INHERITANCE IN PATIENTS WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS AND ALPORT SUNDROME

Jingyuan Xie[1]

[1]*Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Nephrology Department, Shanghai, P.R. China*

Background and Aims: Focal segmental glomerulosclerosis (FSGS) and Alport syndrome (AS) are the leading causes of ESRD globally. FSGS and AS are clinically heterogeneous nephropathies and mainly genetic causes are the mutations in genes expressed in podocytes and glomerular basement membrane (GBM) respectively. A simple Mendelian model fail to explain the genetic control of both nephropathies completely because of the heterogeneous nature and presence of incomplete penetrance. Therefore, here we investigated the possible digenic control of FSGS and AS.

Method: To detect the double mutational (mono- or di-genic) cause of FSGS and AS, we conducted whole exome sequencing (WES) and panel sequencing in 67 kidney patients during the period of four years (2015 to June 2019). Inclusion criteria was the proband's clinical symptoms confirming the FSGS or AS based on clinical symptoms and renal biopsy. Clinical and genetic analyses were implemented to correlate the phenotypes with genotypes.

Results: Genetic analysis discovered that 35 out of 67 (52.23%) had genetic cause of selected nephropathies and 24 out of 35 (68.57%) had mutations in COL4A (3,4 & 5) genes and 11 (31.42%) in other genes. Interestingly, we found 7 out of 35 patients (20%) with double mutations (mono- or di-genic) in COL4A3/COL4A4 genes. After the mentioned period, during routine genetic screening, we also found another patient having double mutations in COL4A3 gene. Subsequently, Sanger sequencing confirmed that the identified mutations were co-segregating with the disease(s) in an incomplete penetrance fashion within the family. Lastly, we found 16 mutations in 8 patients having either monogenic or digeneic double mutations in COL4A3 and/or COL4A4 genes. In sum, we found 12 (75%) mutations in COL4A3 and 4 in COL4A4 (25%), and5 probands (62.5%) had compound heterozygous mutations in COL4A3, 1 proband (12.5%) had in COL4A4 and 2 probands (25%) had digenic (COL4A3/COL4A4) mutations. Last of all, among all the mutations, 10 were novel and 6 have been described previously.

Conclusion: This genetic analysis provides the first evidence for digenic inheritance of FSGS. The nephrologists and clinical geneticists should keep this possibility in mind for the accuracy in diagnosis, disease management and genetic counseling in future. Additionally, we are also adding 10 novel mutations in COL4A3 and COL4A4 genetic pools.

P0066 KIDNEYCODE: A GENETIC TESTING PROGRAM FOR PATIENTS WITH CHRONIC KIDNEY DISEASE

Prasad Devarajan[1], Geoffrey Block[2], Keisha Gibson[3], Jim McKay[4], Colin Meyer[5], Kristina Robinson[6], Bradley Warady[7], Alexander Chang[8]

[1]Cincinnati Children's Hospital Medical Center, Department of Pediatrics, Cincinnati, United States of America, [2]Reata Pharmaceuticals, Clinical Development, Plano, United States of America, [3]University of North Carolina at Chapel Hill, Department of Medicine, United States of America, [4]Reata Pharmaceuticals, Inc., Medical Affairs, Plano, United States of America, [5]Reata Pharmaceuticals, Product Development, Plano, United States of America, [6]INVITAE, San Francisco, United States of America, [7]Children's Mercy Kansas City, Department of Nephrology, Kansas City, United States of America and [8]Geisinger Medical Center, Department of Nephrology, Danville, United States of America

Background and Aims: Knowledge about genetic causes of chronic kidney disease (CKD) is one of the key gaps in global kidney research and recent International Society of Nephrology recommendations encourage the adoption of genetic testing to enable a goal of providing precision medicine based on individual risk (1). A recent whole-exome sequencing study showed that genetic inheritance may be responsible for up to 10% of CKD diagnoses, many of which may be previously undiagnosed or mis-diagnosed (2). Continued advances in DNA sequencing technology have made genetic testing, even whole-exome sequencing, applicable to routine clinical diagnoses. In order to test the hypothesis that genetic testing can provide valuable information to increase the accuracy and precision of diagnosis in CKD, we designed a gene panel to prospectively provide genetic testing in a subset of patients with CKD defined by a specific set of inclusion criteria.

Method: Reata Pharmaceuticals is partnering with Invitae on a program called KidneyCode, which provides no-charge genetic testing to enable diagnosis of three specific rare monogenic causes of CKD: Alport syndrome (AS), autosomal dominant polycystic kidney disease (ADPKD) due to PKD2 mutations, and focal segmental glomerulosclerosis (FSGS), as well as detection of variants in one of the autosomal recessive polycystic kidney disease gene, PKHD1. Invitae's renal disease panel includes 17 genes (ACTN4, ANLN, CD2AP, COL4A3, COL4A4, COL4A5, CRB2, HNF1A, INF2, LMX1B, MYO1E, NPHS1, NPHS2, PAX2, PKD2, PKHD1, and TRPC6), and its assay includes both full-gene sequencing and intragenic deletion/duplication analysis using next-generation sequencing (NGS). The assay targets the coding exons and flanking 10bp of intronic sequences. Invitae's method of variant classification uses a systematic process for assessing evidence based on guidelines published by the American College of Medical Genetics (3). Patients in the US at risk for hereditary CKD (eGFR $\leq$ 90 mL/min/1.73m2 plus hematuria or a family history of CKD) or with a known diagnosis of AS or FSGS are eligible. Family members of those with suspected or known AS or FSGS are also eligible. All participants in the KidneyCode program have access to genetic counseling follow-up at no additional charge.

Results: In the first five months of the KidneyCode program, 152 genetic tests have been completed. A genetic variant was reported in 87 patients. Of those 87 patients, 67 patients had 75 variants in COL4A3, 4, or 5 genes (34 Pathogenic/Likely Pathogenic (P/LP), 41 Variants of Uncertain Significance (VUS)), 20 patients had 24 variants in genes associated with FSGS (3 P/LP, 21 VUS), 15 patients had 20 variants in PKHD1 (1 P/LP, 19 VUS), and 2 patients had variants in PKD2 (1 P/LP, 1 VUS).

Of the 34 patients with Pathogenic or Likely Pathogenic COL4A variants, 19 reported a previous diagnosis of Alport syndrome. Other diagnoses in patients with COL4A mutations included FSGS, thin basement membrane disease, and familial hematuria. Extra-renal manifestations such as hearing loss and eye disease were reported in 7 of the 34 patients with COL4A variants.

Conclusion: Initial results with the KidneyCode panel demonstrate the utility of NGS and support the hypothesis that combining genetic testing with clinical presentation and medical history can significantly improve accuracy and precision of diagnosis in patients with hereditary CKD.

P0067 **PREDICTORS OF LONG-TERM OUTCOME IN A SPANISH COHORT OF PATIENTS WITH FABRY DISEASE ON ENZYME REPLACEMENT THERAPY**

Marian Goicoechea[1,2], Francisco Gomez-Preciado[3], Silvia Benito[4], Joan Torras[2,3], Roser Torra[2,4], Ana Huerta[5], Alejandra Restrepo[6], Jessica Ugalde[7], Daniela Astudillo[8], Irene Agraz[9], Manuel Lopez-Mendoza[10], Gabriel De Arriba[11,12], Elena Corchete[13], Borja Quiroga[14], Maria Luisa Martin-Conde[15], Maria Jose Gutierrez[16], Vanessa Lopes[17], Carmela Ramos[18], Irene Mendez[19], Mercedes Cao[8], Fernando Dominguez[6], Alberto Ortiz[2,20]

[1]Hospital General Universitario Gregorio Marañon, Nephrology, Madrid, Spain, [2]Spanish Kidney Research Network (REDINREN), FEDER FUND, Madrid, Spain, [3]Hospital Bellvitge, Nephrology, [4]Fundacion Puigvert, Nephrology, [5]Hospital Universitario Puerta de Hierro, Cardiology, [6]Hospital Universitario Puerta de Hierro, CIBERCV, Heart Failure and Inherited Cardiac Diseases Unit, Madrid, , [7]Hospital Clinic, Nephrology, [8]Complejo Hospitalario Universitario A Coruña, Nephrology, [9]Hospital Vall d'Hebron, Nephrology, [10]Hospital Universitario Virgen del Rocio, Nephrology, [11]Hospital Universitario de Guadalajara, Nephrology, [12]Universidad de Alcala de Henares, Medicine , [13]Hospital Infanta Leonor, Nephrology, [14]Hospital Universitario La Princesa, Nephrology, [15]Hospital Universitari Arnau Lleida, Nephrology Unit, LLeida, , [16]Hospital Universitario del Tajo, Nephrology, [17]Hospital Universitario Ramon y Cajal, Nephrology, [18]Hospital Universitario y Politecnico La Fe, Nephrology Unit, Valencia, Spain, [19]Hospital Universitario Gregorio Marañon, Cardiology and [20]Fundación JImenez Diaz, Nephrology

Background and Aims: Fabry disease may be treated by enzyme replacement therapy (ERT), but the impact of chronic kidney disease (CKD) on the response to therapy remains unclear. The aim of the present study was to analyse the incidence and predictors of clinical events in Fabry disease patients on ERT.

Method: Multicentre retrospective observational analysis of patients diagnosed and treated with ERT for Fabry disease. The primary outcome was the first renal, neurological or cardiological events or death during a follow-up of 60 months (24-120).

Results: In 69 patients (42 males, 27 females, mean age 44.6 ±13.7 years), at the end of follow-up, eGFR and the left ventricular septum thickness remained stable and the urinary albumin: creatinine ratio tended to decrease, but this decrease only approached significance in patients on agalsidase-beta (242 to 128 mg/g ($p = 0.05$).

At the end of follow-up, 21 (30%) patients had suffered an incident clinical event: 6 renal, 2 neurological and 13 cardiological (including 3 deaths). Events were more frequent in patients with baseline eGFR ≤60 ml/min/1.73 m2 (log Rank 12.423, p=0.001), and this remained significant even after excluding incident renal events (log Rank 4.086, p=0.043), being these differences more relevant in females (log Rank 18.514, $p<0.001$) than males (logRank: 3.442, p=0.064). Lower baseline eGFR was associated with a 3- to 7-fold increase in the risk of clinical events in different Cox models.

Conclusion: GFR at the initiation of ERT is the main predictor of clinical events, both in males and in females, suggesting that start of ERT prior to the development of CKD is associated with better outcomes. For the first time, we show that initiation of ERT in women before renal function deteriorates has a similar or even larger impact as in Fabry males to prevent clinical events.

P0068 APABETALONE, A CLINICAL STAGE BET INHIBITOR, REDUCES THE PRO-INFLAMMATORY RESPONSE IN PBMCS FROM FABRY DISEASE PATIENTS ON ERT THERAPY

Li Fu[1], Sylwia Wasiak[1], Brooke Rakai[1], Stephanie Stotz[1], Norman Wong[1], Jan Johansson[2], Michael Sweeney[2], Connie Mohan[3], Aneal Khan[3,4], Ewelina Kulikowski[1]

[1]Resverlogix, Calgary, Canada, [2]Resverlogix, San Francisco, United States of America, [3]Cumming School of Medicine, Alberta Children's Research Institute, University of Calgary, Calgary, Canada and [4]Professor of Medical Genetics and Pediatrics, University of Calgary

Background and Aims: Fabry disease (FD) is a rare X-linked recessive genetic disorder caused by mutations in the α-galactosidase A gene. Absence or defects of this lysosomal enzyme lead to globotriaosylceramide (Gb3) accumulation. Gb3 disrupts basic cellular metabolic processes, inducing oxidative stress and promoting inflammation. Systemically, Gb3 accumulation leads to organ damage throughout the body with an increase in renal, cardiac, cerebrovascular and skin complications. Enzyme replacement therapy (ERT) is current standard of care. This therapy may reduce Gb3 deposits but the impact on cardiac and kidney function is unclear based on the limited studies. Further, ERT is less effective in the late phases of FD, partially due to the development of uncontrolled inflammation and fibrosis. Apabetalone is a clinical stage orally administered bromo and extra terminal domain inhibitor (BETi) that has beneficial effects on vascular inflammation and vascular calcification through an epigenetic pathway. Based on its mechanism of action and impact on multiple disease drivers in both preclinical and clinical studies, apabetalone has therapeutic potential to modulate inflammation in FD patients on ERT therapy.

Method: PBMCs and neutrophils were isolated from fresh blood of FD patients ± ERT therapy using density gradient centrifugation. The baseline immune status of PBMCs was compared in naïve FD patients (without ERT, n=3) and ERT treated patients (n=8) via flow cytometry. PBMCs or neutrophils from ERT patients were treated ex vivo with 5μM or 20μM apabetalone ± LPS stimulation. Expression of key pro-inflammatory mediators was analyzed with real time quantitative PCR. The production of reactive oxygen species (ROS) in neutrophils was assessed by flow cytometry.

Results: The PBMC inflammatory profile in baseline showed monocytes from ERT patients produced lower amounts of pro-inflammatory mediators (TNFα and IL6) than naïve patients (∼60%, trending $p \leq 0.06$ and $p \leq 0.08$ respectively). However, surface abundance of CCR2, a chemokine receptor for the MCP1 chemokine that promotes monocyte recruitment to local inflamed tissue during inflammatory process, was ∼2-fold greater on monocytes from ERT subjects than the naïve controls (trending $p \leq 0.06$). Gene expression of *MCP1* was approximately 5-fold higher in PBMC from ERT patients versus naïve controls ($p=0.01$). In response to ex vivo LPS stimulation, PBMCs from FD patients on ERT showed a robust induction of pro-inflammatory responses with increases in gene expression of *MCP1*, *IL12B*, *TNFA* and *IL6*. Ex vivo treatment with apabetalone (5μM) blocked the LPS-induction of *MCP1* gene expression (∼90%, $p<0.0001$), and suppressed the upregulation of *IL12B*, *TNFA* and *IL6* by 85%, 27% and 17%, respectively ($p<0.0001$,$p=0.04$,$p=0.004$). In response to LPS stimulation, neutrophils induced reactive oxygen species (ROS), an indicator of oxidative damage caused by intracellular Gb3 deposit in FD patients, by ∼6 fold. Apabetalone treatment reduced this induction by 32% and 62% at 5μM and 20 μM, respectively ($p=0.01$, $p=0.0007$).

Conclusion: Monocytes from FD patients on ERT therapy display an enhanced expression of the CCR2-MCP-1 axis as compared to naïve controls, indicating the potential for immune cell tissue infiltration and local inflammation. Apabetalone counters this increase by preventing *MCP1* gene transcription. Apabetalone also reduces PBMC mediated pro-inflammatory gene transcription (*TNFA*, *IL12B*, *IL6*) and neutrophil mediated ROS production in response to LPS stimulation. Therefore, apabetalone treatment may reduce pathological inflammation in FD patients and thus complement ERT to optimize patient outcomes, which will be tested further with warranted clinical studies.

P0069 MICRO RNA 155, 210, 494, 29B AND 34A EXPRESSION PROFILE IN PREECLAMPSIA AND NORMAL PREGNANCIES

Ali Ghafari[1], Mahboob Lessan pezeshki[2], Mojtaba Saffari[2]

[1]Tehran University of medical sciences, Internal medicine, Tehran, Iran and [2]Tehran University of medical sciences, Genetic, Tehran, Iran

Background and Aims: Preeclampsia (PE) is a complex disorder that is characterized by hypertension and proteinuria after the 20th week of pregnancy, and it causes most neonatal morbidity and perinatal mortality. Despite many efforts, the knowledge acquired regarding its pathogenesis and pathophysiology does not allow us to treat it efficiently. It is not possible to arrest its progressive nature, and the available therapies are limited to symptomatic treatment.

MicroRNAs (miRNAs) are small non-coding RNAs of approximately 19–23 nucleotides that can bind to the 3' untranslated region of target mRNAs resulting in the degradation and translation inhibition of the mRNA, thereby regulating gene expression at the post-transcriptional level. Many studies have confirmed deregulated miRNA in pregnant patients with PE, and the function and mechanism of these differentially expressed miRNA are gradually being revealed.

Method:

Sample collection

Among the patients in the maternity ward, Department of Obstetrics and Gynecology. pregnant women who carried fetuses from 26 to 40 weeks of gestation were selected for study. Plasma samples were obtained from a total of 90 women in two groups; 48 being preeclamptic and 42 being healthy pregnancies, forming the control group. None of these subjects had undergone an invasive procedure. A volume of 5 mL maternal venous blood was drawn and collected in an ethylenediamine tetraacetic acid (EDTA) tube. The blood samples were centrifuged initially at 1200 g for 10 min and a second time at 10,000 g for 10 min, and 500 mL from the supernatant layer were used. The supernatant layer of the plasma was taken to Department of Molecular Biology and Genetics, Molecular Diagnosis Laboratory for storage at -80°C until the time of study.

Total RNA extraction

Total RNA was isolated from plasma using Trizol (Invitrogen, Carlsbad, CA) following the manufacturer protocol. Total RNA was analyzed using the commercially available Bioanalyzer Agilent RNA 6000 picoassay.

MicroRNA isolation from maternal plasma

MicroRNAs were obtained with the High-Specificity miRNA QRT-PCR detection kit (Stratagene-an Agilent Technologies Company, USA-Canada) according to manufacturer recommendations. Micro RNAs were subjected to a polyadenylation reaction as previously described. Next, using an oligo dT primer harboring a consensus sequence, reverse transcription was performed using an Affinity Script RT/RNase Block Enzyme mixture (Stratagene). miRNA was anayzed using the Bioanalyzer 2100- Agilent Small RNA assay.

QRT-PCR platform

The cDNA was amplified by real-time PCR. The real-time PCR analysis was performed on a Stratagene Mx3005P. This reaction contained a microRNA-specific forward primer, a TaqMan probe complementary to the 3ëžŒ of the specific microRNA sequence, as well as part of the polyA adaptor sequence, and a universal reverse primer complementary to the consensus 3ëžŒ sequence of the oligodT tail.

Results were recorded in clinic sheets and were analyzed using SPss version 22.

Results: G1 consist of 48 and G2 42 pts. There were no differences in two group in respect to age (mean age was 28± 9.5 and 27± 5.23 in G1 and G2 respectively). Micro RNA155, 210 and 494 were significantly higher in plasma of G1 (Pv 0.001, 0.0001, 0.005 respectively). Micro RNA 29b was significantly lower in G1 (Pv 003). And there was no difference between two groups in respect to Micro RNA 34a (Pv 0.09). And also PE patients with higher plasma creatinine have more plasma level of Micro RNA155 and 210. There was a significant correlation between Micro RNA 494 and anemia in PE patients

Conclusion: In this study we showed that Micro RNA155, 210 and 494 increased and Micro RNA 29b decreased in PE and after clarifying by further studies may use as a predictor in clinical practice.

P0070

ARE BIOMARKERS OF AGEING IN THE FORM OF TELOMERE LENGTH AND/OR THE DNA METHYLATION STATUS ASSOCIATED WITH FRAILTY PHENOTYPE IN PATIENTS WITH END STAGE KIDNEY DISEASE ON DIALYSIS?

Vasantha Muthuppalaniappan[1], Kieran McCafferty[1], Muhammad Yaqoob[1]

[1]*William Harvey Research Institute, Queen Mary University of London, London, United Kingdom*

Background and Aims: There appears to be an accelerated ageing process seen among patients with end stage kidney disease. They often exhibit prematurely aged phenotypes which include frailty, sarcopenia and protein energy wasting. These phenotypes are associated with increased morbidity and mortality. The exact reason for premature ageing in this cohort is poorly understood. We hypothesised that biomarkers of cellular senescence and biological age may be associated with phenotypes of ageing observed in dialysis patients; in particular the frailty phenotype. Both telomere length (TL) and DNA methylation (DNAm) status have been recognised as predictors of biological age. The aim of the study was to investigate the relationship between TL and DNAm status with frailty phenotype among patients on dialysis.

Method: This was a single centre prospective observational study among eligible haemodialysis (HD) and peritoneal dialysis (PD) patients as per the inclusion and exclusion criteria. All recruited patients had their DNA extracted from peripheral leucocytes and frailty was measured by using the Fried Frailty Phenotype criteria. Extracted DNA was used to measure TL by quantitate polymerase chain reaction according to the modified Cawthon protocol. DNAm status was measured by sodium bisulphite conversion with targeted sequencing of 48 CpG sites. All baseline demographic data were obtained from electronic patient record.

Results: Between the period of December 2015 to July 2018, 239 dialysis (125 HD, 114 PD) patients were recruited. The age range of the study recruits were 23 to 83 years of age with a mean age of 54.3 years. There were 44 and 43 females in the HD and PD group respectively. All patients had TL measured and 228 patients (118 in HD, 110 in PD) had DNAm status measured successfully. Frailty assessments at baseline were completed in 213 patients (110 in HD, 103 in PD). A decrease in mean TL ($p<0.001$) and increased mean DNAm age ($p<0.001$) was observed in the frail group. TL and DNAm status were significantly associated with frailty in a univariate analysis, $p=0.010$ and $p=0.014$ respectively but only TL remained significant in a multivariate analysis to predict frailty, $p=0.018$. Increased frailty was observed in dialysis patients with shorter TL which remained significant following multivariate logistic regression analysis. A receiver operating characteristic curve analysis demonstrated that TL was a significant predictor of frailty, $p<0.001$ with an area under the curve of 0.64. A decrease of TL by one standard deviation was associated with a 52.2% increase risk of frailty when adjusted for age and gender in this dialysis cohort.

Conclusion: The study supports the hypothesis that TL; a biomarker of ageing is better associated with frailty, an ageing phenotype in comparison to DNAm status in dialysis patients. This is the first study to show a significant association between TL and frailty status in the dialysis patients. DNAm status is derived from an individual's chronological age and may not be the best surrogate for chronological age. Therefore, to use this measure seems rather counter intuitive as the incorporation of chronological age might mask clinically significant associations that exist when the DNAm status is considered in isolation. These findings provide a preliminary proof of concept validation that TL is associated with frailty and may provide the basis of future research. The use of targeted methylation CpG sites may be a better predictor of frailty in this cohort which is an area that has sparked an interest.

P0071 MOLECULAR ALTERATIONS AND THE SEARCH FOR GENETIC MODIFIERS IN BRANCHIOOTORENAL SYNDROME

Sebastian Sewerin[1], Katalin Dittrich[2], Ria Schönauer[1], Brigitte Mayer[3], Jan Halbritter[1]

[1]University Hospital Leipzig, Division of Nephrology, Leipzig, Germany, [2]University Hospital Leipzig, Division of Pediatric Nephrology, Leipzig, Germany and [3]University Hospital Dresden, Division of Pediatric Nephrology, Dresden, Germany

Background and Aims: Branchiootorenal (BOR) syndrome (MIM# 113650) is an exceedingly rare disorder of autosomal-dominant inheritance that describes the combination of branchial anomalies, structurally defective ears with associated hearing loss, and congenital anomalies of the kidney and urinary tract (CAKUT). Pathogenic variants in the developmentally important gene *EYA1* have been found to underlie most instances of BOR syndrome. Given the high inter- and intrafamilial variability of phenotypic traits in BOR syndrome, renal involvement varies significantly. However, distinct somatic, genetic, or environmental factors underlying this phenomenon remain elusive. Moreover, the precise role of EYA1 in renal development and pathogenesis of BOR related kidney disease remains ill-defined. Here, we sought to investigate molecular alterations as well as genetic modifiers of renal involvement in a family segregating a previously reported (Rodríguez-Soriano et al. Pediatr Nephrol 2001) heterozygous canonical splice site variant in *EYA1* (c.1698 + 1G>A, NM_000503.5). Remarkably, structural kidney anomalies led to end-stage renal disease in a two-year old boy while his father exhibited normal renal function.

Method: For analysis of the splice site *EYA1* variant, cDNA was obtained from primary patient fibroblasts. Immunofluorescence microscopy was employed to assess the intracellular distribution of EYA1 in both patient and control fibroblasts. Semiquantitative data on cellular EYA1 abundance were obtained from immunoblotting of whole protein extracts from patient and control fibroblast cultures. As for the investigation of genetic modifiers of renal involvement in BOR syndrome, identification of candidate genes was based upon whole exome sequencing data in all four family members (the parental couple and both affected children). Analysis of variants was restricted to *de novo* variants and those inherited from the non-affected mother.

Results: The splice site *EYA1* variant that was assumed to be disease-causing turned out to be pathogenic. Mutant transcript variants result from exon skipping, leading to the translation of an aberrant C-terminus. This affects the highly conserved C-terminal EYA domain that is crucial for interaction with several transcription factors (e.g., from the SIX family). In line with these findings, our imaging data demonstrate a reduced nuclear enrichment of EYA1 in the mutant case, suggesting an impaired nuclear translocation process. Immunoblotting showed an increased EYA1 abundance in mutant fibroblasts, possibly indicating compensation of gene dose effects. Data from immunofluorescence microscopy and immunoblotting are preliminary. Finally, our search for genetic modifiers of renal involvement in BOR syndrome yielded a promising candidate variant in *CYP51A1* in both affected children and their mother. CYP51A1 is an essential enzyme of cholesterol synthesis and has been shown to be indispensable for embryonic development.

Conclusion: Here, we sought to define the molecular basis of BOR syndrome in a family segregating a canonical splice site variant in *EYA1*. Analysis of the splice site demonstrates pathogenicity of this very variant. Further *in vitro* functional analyses show reduced nuclear localization of EYA1 in mutant fibroblasts, albeit we detected an increase in EYA1 abundance. Our findings are compatible with the notion that the interaction of mutant EYA1 with various transcription factors in the cytosol is impaired, preventing nuclear translocation of the protein complex. We propose that an increase in EYA1 abundance in mutant cells constitutes a compensatory mechanism. In searching for genetic modifiers of renal involvement in BOR syndrome, we identified a candidate variant in *CYP51A1*. Both *CYP51A1* and *EYA1* are developmentally important and concurrence of pathogenic variants in both genes may impair normal renal development.

P0072 GENERATION OF A C. ELEGANS MODEL TO STUDY THE INTERALLELIC INTERACTIONS OF PODOCIN

Regina Légrádi[1], Magdolna Tália Keszthelyi[1], Tímea Köles[1], Kálmán Tory[1]
[1]MTA-SE Lendület Nephrogenetic Laborary, Budapest, Hungary

Background and Aims: *NPHS2* is the most frequently mutated gene in steroid-resistant nephrotic syndrome. *NPHS2* encodes podocin, a key component of the glomerular filtration barrier. Podocin is a 42 kDa integral membrane protein, which accumulates in lipid raft microdomains at the podocyte slit diaphragm and is known to form oligomers.

The c.686G>A, p.R229Q is the most common non-silent variant of *NPHS2*. We formerly described that R229Q is pathogenic only when trans-associated to specific 3' missense mutations on the other parental allele. These C-terminal podocin mutants exert a dominant negative effect on R229Q podocin and retain it in intracellular compartments. As such, R229Q is the first variant in human genetics with a mutation-dependent pathogenicity. Based on FRET analysis and structural modeling, we formerly showed that the dominant negative effect is mediated by an altered oligomerization. However, the pathogenicity of several [mutation];[R229Q] associations is still in question and the identification of other rare *NPHS2* variants with a mutation-dependent pathogenicity require an *in vivo* model. We therefore aimed to generate a *Caenorhabditis elegans* model, deficient for the homologous gene of *NPHS2* (*mec-2*) and coexpressing differently (GFP- and mCherry-) tagged human podocin pairs. MEC-2 shares 45% identity and 83% similarity over 275aa (72%) of podocin (383aa). Expressed in six neurons, it is responsible for gentle-touch mechanosensation. The *mec-2* mutants are insensitive to gentle touch in the center part of the body.

Method: Vectors encoding C-terminal GFP- or mCherry-tagged MEC-2 or human podocin with *C. elegans* codon optimization under *mec-2* promoter and a selection marker (*unc-119*) were generated. Double (*mec-2* and *unc-119*) mutant strains were established. Mutant strains were transformed by microparticle bombardment. The gentle-touch mechanosensation was examined by cat's whiskers in a blinded experiment.

Results: The expression pattern of GFP and mCherry under *mec-2* promoter corresponded to the six neurons responsible for gentle-touch sensation, indicating the proper functioning of the promoter. Strains with extrachromosomal MEC-2 or podocin coding vectors were successfully established (GFP-tagged MEC-2: n= 55 strains, GFP-tagged podocin: n= 81, mCherry-tagged podocin: n= 18). However, we found no rescue of the gentle touch sensation in any of them in blinded experiments. We hypothesized that either the fluorescent tag or the lack of chromosomal integration prevents the rescue effect of MEC-2. We therefore aimed to achieve self-cleaving of MEC-2 and the fluorescent tag, and inserted a T2A self-cleaving peptide-encoding sequence between them. To achieve chromosomal integration, we are implementing the MosSCI (Mos1-mediated Single Copy Insertion) technique.

Conclusion: Once the rescue with MEC-2 is achieved, the rescue effect of wild type and next different human podocin variant(s) will be aimed to analyze. The generation of the first animal model to study human interallelic interactions is challenging.

P0073 EVALUATION OF BLOOD PRESSURE CONTROL AMONG PATIENTS WITH ANDERSON-FABRY DISEASE

Federica Rossi[1], Sara Auricchio[2], Agnese Binaggia[3], Letizia Roggero[1], Federico Pieruzzi[1]

[1]University of Milano-Bicocca, School of Medicine and Surgery, Monza, Italy, [2]ASST Monza, Nephrology and Dialysis Unit, Desio, Italy and [3]ASST Monza, Nephrology and Dialysis Unit, Monza, Italy

Background and Aims: Anderson-Fabry disease (AFD) is a rare X-linked sphingolipid disorder caused by deficient activity of the enzyme α-galactosidase A leading to a progressive lysosomal accumulation of globotriaosylceramide and a consequent organ failure. Data on blood pressure (BP) values in AFD patients are scanty, however those available have revealed a significant prevalence of high blood pressure, especially in case of moderate to severe kidney impairment, becoming more prevalent with the progression of the renal disease.

High blood pressure and hypertension major risk factors prevalence were analysed among a single Fabry cohort.

Method: Between January 2015 and May 2019, 32 AFD patients, 24 (75%) female and 8 (25%) male, referred to the Fabry Disease Unit, Nephrology Division of San Gerardo Hospital (Monza, Italy), were enrolled. All patients were Caucasian with an average age of 50±12.2 years old.

Data regarding hypertension were obtained by 24h ambulatory blood pressure monitoring (ABPM), home self-monitoring, and repeated ambulatory measurements (Table 1). Patients were defined hypertensive according to 2018 ESC/ESH Guidelines. The severity and the stability of AFD were assessed in each patient with the Fabry Stabilization Index (FASTEX). Major risk factors for hypertension were also evaluated (Table 2).

Results: The 24h ABPM revealed uncontrolled high blood pressure in 6 (18.7%) patients with consensual home and office BP alterations. All patients were female with an average age of 58±9.9 years old. They had mostly a sedentary life-style, half of them had a diagnosis of dyslipidaemia and one was obese (BMI > 30). In the normotensive group, half of the patients were sedentary, less than a half of them was affected by dyslipidaemia and the average BMI was between the normal ranges. Other known risk factors for hypertension were scanty represented between the two groups. No one had history of transient ischemic attack or stroke. In the normotensive group the majority of patients had a normal or near-normal renal function, while in the hypertensive group one-third showed mild proteinuria and renal impairment with a moderate reduction in glomerular filtration rate. The FASTEX index showed that 84.6% of the normotensive group were stable, while 66.6% of the hypertensive group were not. In 9 (34.6%) patients of the normotensive group ACE-inhibitors/angiotensin-receptor blockers were previously introduced for the treatment of proteinuria in normal blood pressure values, while 2 (33.3%) patients of the hypertensive group received antihypertensive drugs.

Conclusion: In this observational study, the majority of AFD patients were normotensive. The prevalence of hypertensive patients was lower than 20%. Overall patients had a low prevalence of well-known risk factors associated with the development of hypertension.

The link between AFD disease and the development of hypertension has not been fully studied yet. Hypertension in AFD patients might be due to Fabry associated vascular or renal disease or because of an associated essential hypertension.

Arterial blood pressure seems to be relatively well controlled among AFD patients presenting with a low prevalence of risk factors for hypertension and a mild and stable organ involvement. In contrast, unstable patients with a high prevalence of well-known hypertension risk factors, particularly renal impairment, should be followed carefully, because they have a major risk of developing uncontrolled blood pressure.

Further prospective studies with a larger sample size are needed to better investigate the pathophysiology of hypertension in AFD patients.

Category	Overall			Normotensive			Hypertensive		
	Pts	SBP (mmHg)	DBP (mmHg)	Pts	SBP (mmHg)	DBP (mmHg)	Pts	SBP (mmHg)	DBP (mmHg)
Ambulatory BP	32			26			6		
Daytime (or awake) mean		118±11.7	72±8.9		115±10.2	69.3±7.2		132±7.3	82.8±5.7
Night-time (or asleep) mean		106±13.2	63±7.7		103.4±12.1	60.7±5.2		116.8±13.2	73.3±9
24 h mean		117±13.6	69±8.2		112.4±9.9	66.7±6.4		138.1±4.8	81.1±3.6
Office BP	32	124±15	78±10.3	26	119.8±11.2	74.6±8.4	6	144.1±13.9	91.6±4
Home BP	32	119±14.2	71±11	26	115.5±11.7	66.7±6.9	6	133.3±16.3	89.1±4.9

Figure:

P0074 **EXPANDING THE VARIABILITY OF THE ADPKD-GANAB CLINICAL PHENOTYPE: A NEW FAMILY OF ITALIAN ANCESTRY**

Elisa Delbarba[1], Laura Econimo[2], Chiara Dordoni[3], Eva Martin[2], Barbara Gnutti[3], Gianfranco Savoldi[3], Cinzia Mazza[3], Nadia Dallera[2], Francesco Scolari[4], Claudia Izzi[3]

[1]Spedali Civili, Nephrology, Brescia, Italy, [2]Ospedale di Montichiari, Montichiari, Italy, [3]Spedali Civili, Brescia, Italy and [4]Università di Brescia Medicina, Brescia, Italy

Background and Aims: Causative GANAB mutations have been described in only 123 families, 98 diagnosed with late-onset mild ADPKD and 35 with ADPLD. We describe a new family with mild, late-onset ADPKD due to p. R839W GANAB mutation, previously reported in an ADPLD patient requiring liver transplantation.

Method: Mutation analysis of PKD1, PKD2, GANAB genes was performed by targeted NGS analysis. To analyze GANAB gene we developed a custom panel of 11 kidney cystogenes (GANAB, PKDH1, TSC1, TSC2, UMOD, HNF1B, REN, OFD1, PARN, DNAJB11, SEC61A1) designed using Ion Ampliseq Designer. Sanger sequencing was performed in order to validate all the variants classified as pathogenic, likely pathogenic and VUS. Raw sequence data analysis, including base calling, demultiplexing, alignment to the hg19 human reference genome, was performed using the Torrent Suite Software version 5.5; the average depth of total coverage was set at 500X and for variant calls at minimum of 30X. Deletion and duplication analysis of PKD1 and PKD2 was performed using MLPA P351-C1 and P352-D1 probemixes, MRC-Holland.

Results: Diagnosis of ADPKD was made in a 45-year old man during pre-surgical screening for umbilical and inguinal hernia repair. The patient's clinical course was characterized by several complications pertaining to the ADPKD spectrum: nephrolithiasis (20 yo); umbilical/bilateral inguinal hernia repair, hypertension and mild aortic root dilation (45 yo) and AKI due to ureteral obstruction (50 yo). Abdomen CT scan showed bilateral renal cysts (TKV 565 cc), nephrolithiasis, normal-sized liver with multiple cysts, and sigmoid colon diverticulosis. Renal function was normal (SCr 0.69 mg/dL, CKD-EPI 115 ml/min). In the index case, NGS and MLPA analysis of PKD1 and PKD2 genes did not detect variants. We then use the abovementioned multigene NGS panel and identified a missense heterozygous c.2515C>T (p.R839W) variant in the GANAB gene. Screening was then extended to family members. No family members displayed renal function impairment. Both the 80 yo mother and the 84 yo father were found to have multiple bilateral kidney cysts (HtTKV of 239 ml and 435 ml, respectively), no liver cysts were found in either of them. Parents segregation analysis identified the GANAB variant p.R839W in the mother and in the maternal aunt. The father tested negative for all the abovementioned cystogenes.

Conclusion: we confirm that the renal phenotype caused by mutations in GANAB is very different from those due to mutations in PKD1 and PKD2, giving rise to a mild form of renal cystic disease, usually not progressing to ESRD. Despite the mild renal cystic burden, the index case showed a plethora of renal and extrarenal manifestations of ADPKD. The finding that patients with GANAB mutation can present with renal and liver cystic phenotype is intriguing, indicating a commonality between pathogenic background of two different inherited disorders, ADPKD and ADPLD. The missense GANAB mutation identified in our ADPKD family was first described in a pedigree reported by Porath et al. and diagnosed as ADPLD. This suggests that, beyond the effect of the shared mutation on GII subunit α, other modifier loci and environmental factors may influence the course of liver disease development and progression. Our study illustrates the important diagnostic role of a broader genetic testing, able to screen not only for PKD1 and PKD2 variants, but also for pathogenic variants in other cystogenes.

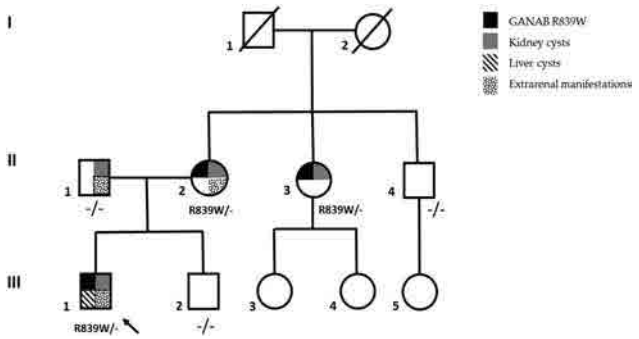


Figure: Pedigree and clinical data of the family; the Index case (III-1), the mother (II-2) and the aunt (II-3) carry the R839W GANAB variant.

P0075

EXPERT OPINION ON THE MULTIDISCIPLINARY MANAGEMENT OF CYSTINOSIS IN ADOLESCENT AND ADULT PATIENTS

Nicholas Webb[1], Anibh M. Das[2], Sally Hulton[3], Elena Levtchenko[4], Aude Servais[5], Christoph Wanner[6]

[1]Manchester University NHS Foundation Trust, Manchester, United Kingdom, [2]Klinik für Päd. Nieren-, Leber- und Stoffwechselerkrankungen, Hannover, Germany, [3]Birmingham Children's Hospital NHS Foundation Trust, Birmingham, United Kingdom, [4]KU Leuven, Leuven, Belgium, [5]APHP - Hôpital Necker Enfants Malades Néphrologie, Paris, France and [6]Universitätsklinikum Würzburg, Würzburg,, Germany

Background and Aims: Cystinosis is a rare autosomal recessive lysosomal storage disorder caused by mutations in the *CTNS* gene on chromosome 17p13. It affects between 1:150,000–1:200,000 live births, with a prevalence of approximately 1.6 per million. It is a life-long progressive disease which results in an abnormal lysosomal accumulation of the amino acid cystine in multiple organs and tissues of the body. The most common presentation of cystinosis (95%) is the infantile nephropathic form, with renal symptoms developing in the first few months of life. Over the next 10–20 years, extra-renal manifestations of cystinosis become apparent, which require multidisciplinary care. Here we describe a consensus-based programme with the objective of creating clinical recommendations to support HCPs with the management of adolescents and adults living with the multi-organ effects of cystinosis.

Method: The programme was led by a Steering Committee (SC) of European clinicians with expertise in managing cystinosis. Recommendations were developed using a quasi-Delphi methodology. The SC identified and prioritised a list of key questions. An Extended Faculty (EF) of additional specialists with extensive experience managing cystinosis in patients of all ages, were invited to answer the questions via an online digital platform. The consolidated answers of expert opinion were summarised into recommendations that were supported by evidence-based guidance and additional published data where possible. The EF were invited to agree / disagree with the draft clinical recommendations. Where there was disagreement, the SC members amended the recommendations and the EF re-voted on the revisions. This process continued until consensus was achieved on all final recommendations.

Results: The expert-agreed clinical recommendations reflect the multi-organ effects of cystinosis. Thus, advice on factors relating to the nervous system, muscle involvement, ophthalmology, cardio-respiratory system, dental care and nutrition, dermatology, endocrine system, and gastrointestinal and hepatological involvement, are given, along with renal considerations. Guidance on fertility and family planning that reflect some of the major advances in recent years, are also provided. Ideas on improving psychological well-being and adherence includes recommendations on the use of validated screening tests, increasing access to occupational therapy, and interacting with patient groups. The programme has also produced an online checklist to support HCPs in their daily clinical practice by providing a focus to guide regular consultations with the patient.

Conclusion: These expert recommendations offer HCPs relevant advice that support them in the management of adolescents and adults living with the multi-organ effects of cystinosis. The recommendations complement existing international and local guidance and aim to improve patient outcomes.

P0076 HOMOARGININE ASSOCIATES WITH RENAL AND CARDIAC FUNCTION IN FABRY DISEASE

Christiane Drechsler[1], Andreas Menitzer[2], Winfried Maerz[3], Lena Gutjahr-Lengsfeld[1], Daniel Oder[4], Nurcan Üçeyler[5], Claudia Sommer[5], Peter Nordbeck[4], Christoph Wanner[1]

[1]University Hospital Wuerzburg, Dept of Medicine 1, Div of Nephrology, Würzburg, Germany, [2]Medical University of Graz, Clinical Institute of Medical and Chemical Laboratory Diagnostics, Graz, Austria, [3]Synlab Academy, Mannheim, Germany, [4]University Hospital Würzburg, Dept of Medicine 1, Div of Cardiology, Wuerzburg, Germany and [5]University Hospital Wuerzburg, Dept of Neurology, Wuerzburg, Germany

Background and Aims: Patients with Fabry disease frequently develop progressive Fabry nephropathy, hypertrophic cardiomyopathy with arrhythmias and subsequent death, transient ischemic attacks and early cerebral stroke. Homoarginine is an amino acid derivative, mainly produced in the kidney from its precursor lysine. Homoarginine may increase nitric oxide availability, decrease the release of cytokines, modulate the renin-angiotensin-aldosterone system and improve cardiac contractility. We hypothesize that high homoarginine levels associate with less clinical symptoms and better renal function in patients with Fabry disease.

Method: This study investigated the homoarginin status and its association with renal function, left ventricular (LV) mass and adverse clinical symptoms in patients with Fabry disease. Homoarginine was measured by high-performance liquid chromatography in 162 patients who were genetically proven to have Fabry disease. GFR was determined by DTPA clearance. LV mass and cardiomyopathy were assessed by magnetic resonance imaging and echocardiography. In cross-sectional analyses, associations with adverse clinical outcomes were determined by linear and binary logistic regression analyses, respectively, and were adjusted for age, sex, and BMI.

Results: Patients had a mean age of 39±14 years and 41% were male. The mean homoarginine concentration was 2.0±1.0 µmol/l. Patients had a mean BMI of 23.7±4.5 kg/m^2 and a mean GFR of 93±37 ml/min. Homoarginine was significantly correlated with GFR and proteinuria. The better the homoarginine status of the patients, the higher was their GFR (r=0.20, p=0.04) and the lower proteinuria (r=-0.21, p=0.03). Furthermore, LV mass was significantly higher with lower homoarginine levels (r=-0.30, p<0.01). Patients of the lowest homoarginine tertile had a 4-fold higher risk of myocardial hypertrophy (OR 4.17, 95% CI 1.44-12.02), especially with septal and posterior hypertrophy, compared to those of the upper tertiles. Similarly, patients of the lowest homoarginine tertile had a higher rate of angina pectoris (OR 4.2, 95% CI 1.3-13.3) and chronic pain (OR 4.1, 95% CI 1.7-10.1), compared to patients of the upper tertiles. At lower homoarginine status, the median levels of proteinuria increased, as well as the prevalence rates of heart failure and the need for analgesic therapy.

Conclusion: In conclusion, low homoarginine status was strongly associated with cardiomyopathy, renal function and adverse clinical symptoms in patients with Fabry disease. Whether homoarginine supplementation improves complications of Fabry disease, requires a randomized controlled trial.

P0077

A NEW MUTATION OF DNAJB11 AS A CAUSE OF CYSTIC KYDNEY DISEASE: THE FOURTH GENE OF ADPKD

Isabella Pisani[1], Marco Allinovi[2], Viviana Palazzo[3], Micaela Gentile[4], Sabrina Giglio[3], Enrico Fiaccadori[1], Lucio Manenti[1]

[1]UO Nefrologia, Azienda Ospedaliero-Universitaria di Parma, Dipartimento di Medicina e Chirurgia, Parma, Italy, [2]SOD Nefrologia Dialisi e Trapianto, Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy, [3]SOD complessa di Genetica Medica, Azienda Ospedaliero-Universitaria Meyer, Firenze, Italy and [4]UO Nefrologia, Azienda Ospedaliero-Universitaria di Parma, Scuola di Specializzazione in Nefrologia, Università di Parma, Dipartimento di Medicina e Chirurgia, Parma, Italy

Background and Aims: Monogenic inherited diseases are an underestimated but important cause of chronic kidney disease (CKD). Despite the increasing knowledge about their inheritance, they are identified in fewer than 10% of CKD patients. Among monogenic causes of CKD, polycystic kidney diseases (PKD) represent a group of disorders with a clinical and genetic heterogeneity and a variable phenotype (from early manifestations during pregnancy or childhood to the absence of clinical manifestations until adulthood). We here present a PKD family with 5 members displaying the disease (Figure 1).

Method: We revised patients clinical history, laboratory data and imaging exams. An accurate family history was recovered. Blood samples were collected from living patients to perform an exome analysis using next generation sequencing to analyze all possible genes involved in PKD.

Results: Each patient presented a clinical history of nephrolithiasis, a variable degree of CKD (from normal kidney function to renal transplant), urinary and blood parameters compatible with distal renal tubular acidosis (hypercalciuria, low urinary citrate excretion and hypokalemia). Imaging exams showed several renal cysts in the medulla or at the cortico-medullary junction with intracystic calcifications (Figure 2). Some patients displayed also large cortical renal cysts and also hepatic and pancreatic cysts. The genetic analysis performed using next generation sequencing in four patients showed a new mutation on the gene DNAJB11; the mutation introduced a stop codon and was identified as pathogenic by prediction programs. It was present in heterozygosity in all subjects and had an autosomal dominant pattern of inheritance.

Conclusion: DNAJB11 mutations were reported as a cause of PKD for the first time in 2018 by Cornec-Le-Gall and colleagues. The nephropathy derived from these mutations need to be differentiated from ADPKD (autosomal dominant polycystic kidney disease), from ADTKD (autosomal dominant tubulointerstitial kidney disease) and from medullary sponge kidney. DNAJB11 encodes a co-chaperone of the endoplasmic reticulum (ER) also called ERdj3. It is part of the HSP40 protein family and plays a central role in both intracellular and extracellular proteomic homeostasis (proteostasis). In the intracellular compartment it acts as a co-chaperone in the pathway of the unfolded protein response (UPR) in which it binds misfolded proteins which have to be secreted and activates BiP an HSP70 of ER whose function is to correct the misfolding. In the kidney it is mainly expressed in the thick ascending limb of Henle's loop, in the distal tubule and in the collecting duct justifying the clinical presentation of nephropathy and differentiating the disease from ADPKD (Figure 3).

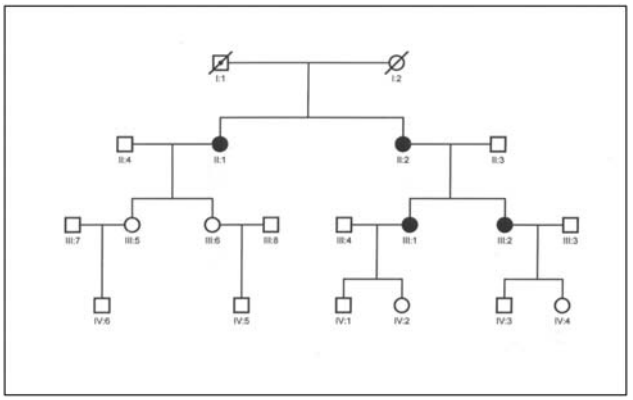


Figure 1

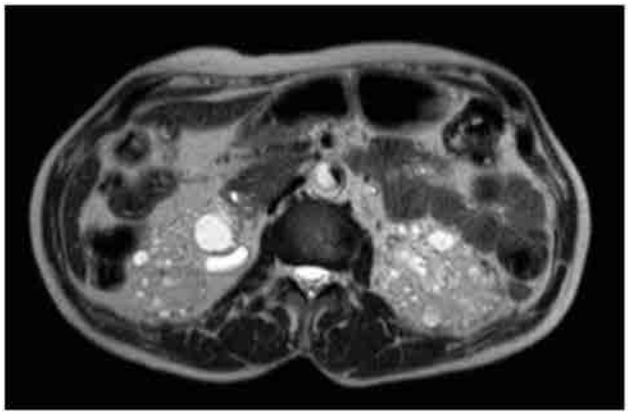


Figure 2

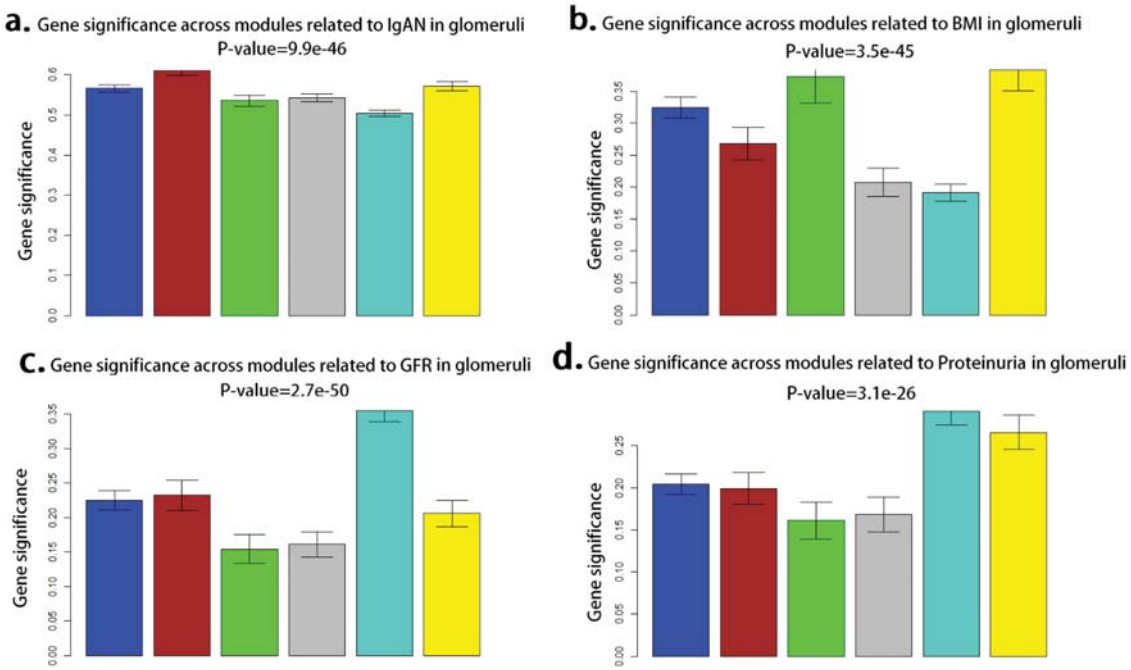


Fig.3 Module significance related to clinical characteristics in IgA nephropathy glomeruli

P0078 **INVESTIGATION THE VARIANTS AT THE BINDING SITE OF INFLAMMATORY TRANSCRIPTION FACTOR IN PATIENTS WITH ESRD**

SUI-LUNG SU[1]

[1]*Taipei, SCHOOL OF PUBLIC HEALTH, TAIPEI, Taiwan, R.O.C.*

Background and Aims: Inflammation is an important factor for enhancing the disease process from chronic kidney disease (CKD) to end-stage renal disease (ESRD). Nuclear factor-kappa B (NF-κB) is a transcription factor that regulates the expression of genes involved in inflammation.

We investigated the potential association with the gene polymorphism of transcription factor binding site of NF-κB in ESRD patients.

Method: We used the Taiwan Biobank database, University of California, Santa Cruz, reference genome, chromatin immunoprecipitation sequencing database to find the SNPs at potential binding sites of NF-κB. In addition, we performed a case–control study and genotyped 847 patients with ESRD and 846 healthy controls at Tri-Service-General-Hospital from 2015 to 2016. Further we used ChIP-assay and Luciferase reporter assay to identify the binding activity at different genotype.

Results: Results of biometrics screening in the databases revealed 15 SNPs with the potential binding site of NF-κB. Genotype distributions of rs9395890 were significantly different in ESRD cases and healthy controls (P = 0.032). In the Dominant model, rs9395890 with T allele had a higher risk of ESRD (P = 0.032; odds ratio [OR] = 1.32, 95% confidence interval [CI] = 0.99–1.76). The ChIP assay reveals that around 1.49 times enrichment of NF-κB of the variant type TT when compared to that of the wild type GG in the rs9395890 ($P<0.027$; TT=3.20±0.16, GT=2.81±0.20, GG=1.71±0.18,) and the luciferase activity curve showed T allele was higher than G allele.

Conclusion: In conclusion, we demonstrate that rs9395890 may be associated with ESRD in the Taiwanese population.

P0079

STRATEGIC ACTION FOR POLYCYSTIC KIDNEY DISEASE IN GALICIA. POPULATION APPROACH MODEL EXPORTABLE TO OTHER AUTONOMOUS COMMUNITIES

Lara Besada Cerecedo[1], Nisrine Arhda[2], Ana Maria Barcia de la Iglesia[1], Maria Garcia Murias[3], Noa Carrera Cachaza[1], Consorcio Investigadores GalCYST[1], Miguel Garcia Gonzalez[4]

[1]Health Research Institute of Santiago de Compostela (IDIS), Group of Genetics and Developmental Biology of Renal Diseases, Santiago de Compostela, Spain, [2]University Hospital Complex of Santiago de Compostela, Department of Nephrology, Santiago de Compostela, Spain, [3]Health Research Institute of Santiago de Compostela (IDIS), Group of Genetics and Developmental Biology of Renal Diseases., Santiago de Compostela, Spain and [4]Health Research Institute of Santiago de Compostela (IDIS)/Galician Public Foundation of Genomic Medicine, Group of Genetics and Developmental Biology of Renal Diseases, Santiago de Compostela, Spain

Background and Aims: The Strategic Action for Polycystic Kidney Disease (PKD) in Galicia was started in 2016, as a population strategy model (genetic cascade study) coordinated between the reference hospitals in this region, with the objective of diagnosing cost-effectively Galician families with the disease

Method: We develop panels for the simultaneous study of the currently known candidate genes, using ultrasequencing technologies (NGS). Each index case is analyzed by NGS and in the rest of the family members, the presence / absence of the eventual mutation identified is analyzed by Sanger Sequencing.Patient clinical data were collected to establish the genotype-phenotype correlation

Results: NefroCHUS has a historical record of 224 Galician families with PKD. Since January 1, 2016, 306 new PKD families have been identified from hospitals belonging to the three Galician health areas: Coruña - Ferrol (CHUAC (67 families), CHUF (17 families)), Vigo - Ourense (CHOP (44 families), CHUOU (43 families), CHUVI (32 families) and Povisa (18 families)) and Santiago-Lugo (HULA (35 families), HCB (22 families) and CHUS (28 families)), for a total record of 530 PKD families identified based on clinical criteria. Carrying out genetic studies allowed the calculation of gene mutagenicity rates for each health area: Coruña-Ferrol (58% PKD1, 36% PKD2 and 6% GANAB), Vigo-Ourense (80% PKD1, 15% PKD2 and 5 % other genes) and Santiago-Lugo (53% PKD1, 44% PKD2 and 3% GANAB). Taking into account the families of the historical record, mutagenicity rates in the Galician population are distributed as follows: 70% PKD1, 28% PKD2 and 2% other genes. So far 446 patients have been phenotypically characterized. The average age of diagnosis was 38 years, the main reason being family history (59%; n = 264). 73% of the patients presented arterial hypertension (AHT) with an average detection age of 42 years (range 6-82 years). 21% of the patients (n = 92) iniciated renal replacement therapy with a mean age of 49 years (38-80 years). The presence of liver cysts proved to be a very frequent extrarenal manifestation (67.9%; n = 303). Other manifestations to highlight are: low back pain (27%; n = 119), cystic kidney infection (7.4%; n = 33) or the presence of intracranial aneurysms (3.1%; n = 14)

Conclusion: It has been established the genetic map of the Autosomal Dominant Polycystic Kidney Disease in Galicia and at the same time a model of population approach in hereditary diseases that is exportable to other autonomous communities.

P0080 **INTERLEUKIN-17A GENE POLYMORPHISM (RS2275913G>A) IN SLE PATIENTS.**

Nehal Atef elshabrawy[1], Hussein Sheashaa[2], Adel L Abdelsalam[3], Ahmed Mohammed Abd El Wahab[4]

[1]Mansoura university hospital, Nephrology and Dialysis, EL MANSOURA, Egypt, [2]Mansoura university (UROLOGY AND NEPHROLOGY CENTER), Nephrology, Mansoura, Egypt, [3]Mansoura university (MHU), Rheumatology and Immunology, Mansoura, Egypt and [4]Mansoura university hospital, Nephrology and Dialysis, Mansoura, Egypt

Background and Aims: There are six IL-17-family ligands [IL-17A, IL-17B, IL-17C, IL-17D, IL-17E (IL-25) and IL-17F]. Interleukin-17A (IL-17A) also commonly called IL-17, is produced by the T helper17 (Th17) subset of CD4+ T cells.Interleukin-17 and other Th17 cytokines are linked to the pathogenesis of diverse autoimmune and inflammatory diseases. IL-17A is detected in synovial fluids and synovium from RA patients and induces proinflammatory cytokine production from synoviocytes, also expression of IL-17A was higher in SLE patients and its level positively correlated with the severity of lupus nephritis, because of its contribution to increasing anti-double-stranded DNA (dsDNA) antibody production in SLE. The aim of the present study is to determine the IL-17A gene polymorphism (rs2275913 G>A) frequency in patients with SLE and lupus nephritis, and to determine the association of this polymorphism with the disease activity.

Method: This cross-sectional, observational, case control study was carried out on 50 females patients, with their age ranged from 15 to 50 years (mean 25.67±9.29 years) with SLE attending Mansoura University Hospital .A control group of 50 healthy females of matched age were also included. The patient group was subdivided into patients with and those without lupus Nephritis (35 and 15 patients, respectively). Lupus nephritis was confirmed by renal biopsy. All patients were subjected to a thorough clinical evaluation and routine laboratory tests. SLEDAI score was calculated for all patients to determine the degree of lupus activity. DNA extraction was performed for all patients as well as controls, One SNPs of IL-17A (rs2275913G>A) was genotyped utilizing PCR- RFLP technique.

Results: The frequency of rs2275913 A allele was significantly higher in SLE patients than the control group (34.0% vs. 21.0%, respectively; p=0.04, OR =1.9, 95%CI =1.03-3.65). While G allele was significantly higher in control group, (P=0.04)). Moreover, AA genotype was significantly higher in the SLE patients than in the control group (8.0% vs. 0.0%, respectively; p=0.036) and associated with higher SLEDAI, ANA, and anti-dsDNA antibodies titer, (P=0.03, P=.039, P=0.047 respectively).on the other hand there was no significant difference in GG and GA genotypes in the SLE patients versus the control group. The frequency of both genotype GA and AA was higher in the SLE patients than the controls (60% vs. 42%, respectivley; OR=2.07, CI-95%=0.9-5.59); although the difference was not statistically significant (P= 0.07).Although A allele was numerically higher in lupus nephritis group versus non nephritis group(37.0% vs 27.0%, respectively), the Analysis of the frequency of IL-17A rs2275913 alleles and genotypes showed no statistical differences between the two groups. Moreover there was no statistical significance between different genotypes in cases of nephritis regard lupus nephritis class (P=0.9) and no statistical significance between different genotypes (GG-GA-AA) regarding activity indices (AI) or chronicity indices (CI) in lupus nephritis group (P=0.18, P=0.56 respectively).

Conclusion: We suggest that there was a significant association between IL-17A rs2275913 G>A polymorphism and SLE, as A allele and AA genotype were increased in SLE patients, lupus nephritis especially those with high activity

P0081 **IMPACT OF RENAL FAILURE ON OVERALL SURVIVAL OF PATIENTS WITH FABRY DISEASE**

Ekaterina Karovaikina[1], Sergey Moiseev[1,2], Nikolay Bulanov[1], Alexey Moiseev[2], Agunda Kuchieva[1], Viktor Fomin[3]

[1]Sechenov First Moscow State Medical University, Tareev Clinic of Internal diseases, Moscow, Russia, [2]Moscow State University, Faculty of Fundamental Medicine, Moscow, Russia and [3]Sechenov First Moscow State Medical University, Moscow, Russia

Background and Aims: End-stage renal disease (ESRD) is associated with significant morbidity and mortality among patients with Fabry disease (FD). The aim of our study was to evaluate impact of renal failure on overall survival of patients with FD.

Method: We recruited 117 adult (>18 years) patients with FD that was confirmed by enzymatic and genetic studies. ESRD was defined according to the KDIGO guidelines (2012). Kaplan-Meyer analysis and Log Rank test were used to estimate overall survival of patients with FD.

Results: Thirty-seven (36 males and 1 female) of 117 patients had ESRD. Thirty-three of them were treated with chronic hemodialysis, whereas four patients have undergone renal transplantation. Among patients with ESRD eleven (29.7%) patients died at the median age of 43 (37; 46) years. All deceased patients were males. The median time from dialysis initiation to death was 32 (6; 67) months. The causes of death included sudden cardiac death (n=9), stroke (n=1) and peritonitis (n=1). Only 2 deceased patients received enzyme replacement therapy over 3 and 11 months. There were deaths only in the ESRD group (Table). There was a decline in survival function after the age of 30 years in patients with ESRD. In Kaplan-Meyer analysis overall survival was 51.2 years (95% Confidence interval 47.7-54.7) and was lower in patients with ESRD (Log Rank (mantel-Cox) $\chi 2=17.5$, df 1, $p<0.0001$, Figure). Five- and 10-year survival after dialysis initiation was 72.5% and 54.1%, respectively.

Table. C linical characteristics of patients with and without ESRD

Parameters	ESRD "+" (n=37)	ESRD "–" (n=80)	p-value
Age, years; Me (IQR)	43 (36; 50)	34 (28; 48)	0.005
Males, n (%)	36 (97.3)	39 (48.8)	<0.0001
Enzyme replacement therapy, n (%)	7 (18.9)	26 (32.5)	0.185
Classic phenotype, n (%)	34 (91.9)	70 (87.5)	0.753
Neuropathic pain	28 (75.7)	58 (72.5)	0.823
Angiokeratomas	18 (48.6)	32 (40.0)	0.425
Hypohidrosis/anhidrosis	29 (78.4)	36 (45.0)	0.001
Vortex keratopathy	11 (50.0)	51 (70.8)	0.079
Brain involvement, n (%)			
Lesions on MRI	26/30 (86.7)	34/76 (44.7)	<0.0001
Stroke	11 (29.7)	11 (13.8)	0.046
Heart involvement on MRI, n (%)			
Left ventricular hypertrophy	19/20 (95.0)	28/73 (38.4)	<0.0001
Fibrosis	9/20 (45.0)	13/73 (17.8)	0.017
Death, n (%)	11 (29.7)	0	<0.0001

Conclusion: ESRD was the major factor associated with low survival of patients with FD in Russia. One out of every 3 dialysis patients died in 5 years after dialysis initiation.

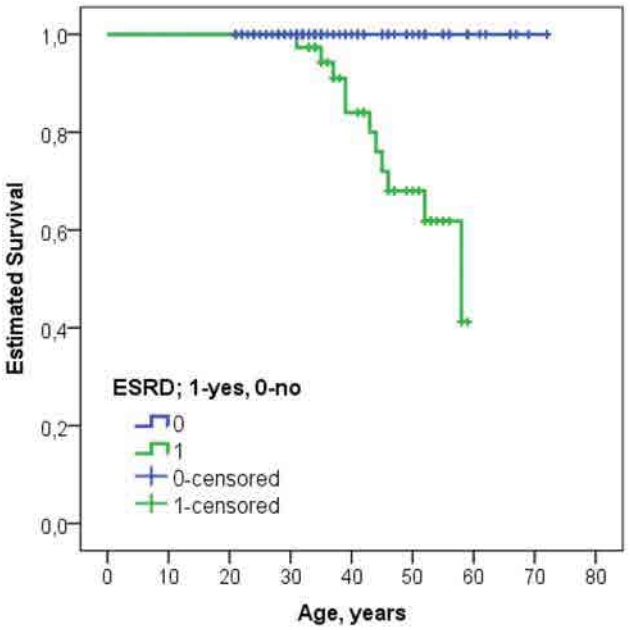


Figure: Overall survival of patients with FD with respect to the presence of ESRD (Log Rank (mantel-Cox) $\chi 2=17.5$, df 1, $p<0,0001$).

P0082 CHARACTERISTICS OF ADULT PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME IN RUSSIA

Kseniya Demyanova[1], Natalia Kozlovskaya[1], Yuia Korotchaeva[2]

[1]Peoples' Friendship University of Russia, Internal Medicine, Moscow, Russia and [2]I.M. Sechenov First Moscow State Medical University, nephrology department, Moscow, Russia

Background and Aims: Atypical hemolytic uremic syndrome (aHUS) is complement mediated thrombotic microangiopathy (TMA), caused by genetic abnormalities in the complement gene cluster. Information about the course of aHUS in the adult population in Russia is not enough accumulated. This study presents the characteristics of Russian adult patients (pts) with aHUS.

Aim: To assess the characteristics of adult pts with aHUS in Russia.

Method: statistical analysis of retrospective and prospective data

The study included 243 pts with acute TMA (microangiopathic hemolytic anemia, thrombocytopenia, decreased haptoglobin and / or blood schizocytosis, kidney damage) from different regions of Russia. All patients were tested for ADAMTS-13 activity, and there were no accidents of TTP in our study. Cases of acute TMA associated with pregnancy and childbirth (n=134), systemic diseases (n=10), anticancer drugs treatment (n=1) and sepsis (n=13) were excluded. 85 pts with diagnosis of aHUS were selected for further analysis.

Results: Characteristics of pts are presented in table 1. The average age at the time of acute episode was 32.4 years, the disease was equally common among men and women. Relapsing course was rare (n=11, 13%), the maximum number of relapses – 5. In the debut, 67.8% of pts had signs of kidney damage, in 21% - gastrointestinal tract, 4.8% - CNS, 4.8% - pulmonary thromboembolism, 1.6% - visual impairment. During the acute episode, extrarenal manifestations were detected in 70% of pts, while in 38 cases (44.7%), multiple organ failure (MOF) developed with simultaneous damage from 3 to 7 organs. The most commonly observed symptoms of gastrointestinal lesions (n = 39, 45%), CNS (n = 32, 37%), heart (n = 18, 21%), less often - the organ of vision (n = 10, 12%). Kidney damage was characterized by the development of AKI in 70%, in the rest - urinary syndrome, arterial hypertension, the initial signs of renal dysfunction in various combinations. A morphological examination of kidney was performed in 40 pts (kidney biopsy - 35, autopsy - 5): acute TMA was detected in 28 pts (70%), chronic TMA - in 7 (17.5%), a combination of acute and chronic TMA - in 2 (5%), a combination of IgA-nephropathy and TMA - in 1 case (2.5%) and in 2 patients a membrane-proliferative glomerulonephritis pattern with TMA. Genetic analysis was performed in 19 pts (22%), in 7 of which (37%) identified gene variants associated with the development of aHUS (C3 in 3 pts, CFHR5 in 2 pts, CFH in 2, in 1 case - MCP and in 1-DGKE). In addition, variants of genes of the complement system with an unclear clinical value were found in all pts (n = 19). 72% of pts (n = 61) needed renal replacement therapy, almost all pts received plasma therapy (83%) and anticoagulants (85%). Only 13 pts (15%) received complement-blocking therapy with eculizumab. In the outcome of the acute episode in 12 cases (14%) renal function fully recovered, in 20 pts (23%) signs of renal dysfunction persisted (CKD 2–4 stages), 53 pts (62.3%) reached ESRD, 10 pts died (12%).

Conclusion: The features of aHUS in our cohort were:

1. Severe course with the development of MOF in 45% of cases
2. High frequency of ESRD in the outcome of aHUS (62.3%)
3. The incidence of genetic mutations (37%) is comparable to foreign cohorts

Table 1. Characteristics of adult pts with aHUS

	statistical value	aHUS pts (N=85)
Age	Mean (SD)	32.4 (13.1)
Gender male/female	n (%)	43(51)/42 (49)
Number of TMA relapses	Mean (SD)	1.3 (0,72)
	Min, Max	1, 5
Hв g/l	Mean (SD)	69 (14,1)
LDH U/l	Median	854 [550;7500]
Plt (thousand in 1 μl)	Mean (SD)	84 (21,6)
Cr umol/l	Mean (SD)	567 (141,6)

Figure:

P0083 **HLA-DRB1*1301-DQB*0603-DRB3*0202 HAPLOTYPE IS INDEPENDENTLY ASSOCIATES WIHT POOR PROGNOSIS IN PLA2R-RELATED MEMBRANOUS NEPHROPAHTY**

Weibo Le[1], JingSong Shi[1], Qin Hou[1]

[1]*National Clinical Research Center of Kidney Diseases, Jinling Hospital, Nanjing University School of Medicine, Nanjing, P.R. China*

Background and Aims: The susceptibility of Idiopathic membranous nephropathy (MN) is associated with HLA alleles. We previously found almost all (98.7%) patients with PLA2R-related MN carry either or both of the HLA-DRB1*1501 and DRB3*0202 risk alleles. However, the associations of HLA alleles and renal outcome is not known.

Method: we investigated the associations between HLA alleles and renal outcome in 392 PLA2R-related MN patients.

Results: We found that HLA-DRB1*1301 and DQB1*0603, which are in high linkage disequilibrium ($R^2 = 1.0$, D'=1.0), are associated with at least 30% eGFR decline during follow-up (HR 2.2, $p<0.001$). HLA-DRB1*1301 and DQB1*0603 are not a susceptible HLA allele for PLA2R-related MN. Neither HLA-DRB1*1501 nor DRB3*0202 is associated with renal outcome. After adjusting age, gender and the two susceptible HLA alleles, DRB1*1301 haplotype remains significant associated with renal outcome. Compared those patients with negative DRB1*1301, patients with positive DRB1*1301 showed a similar eGFR level at baseline, but a significant lower eGFR at the last follow up. There were 12 PLA2R-related MN patients with positive DRB1*1301, eight of them (66.7%) showed more than 30% eGFR decline during follow-up. Among the 12 patients carrying DRB1*1301, all (100%) had DRB3*0202, four (33.3%) had DRB1*1501, and none (0%) had DRB1*0301. Linkage disequilibrium analysis showed the susceptible allele DRB3*0202 was highly linked with DRB1*0301 and DRB1*1301, while HLA-DRB1*0301 was not associated with renal outcome.

Conclusion: HLA-DRB1*1301-DQB*0603-DRB3*0202 haplotype is independently associated with Poor Prognosis in PLA2R-related Membranous.

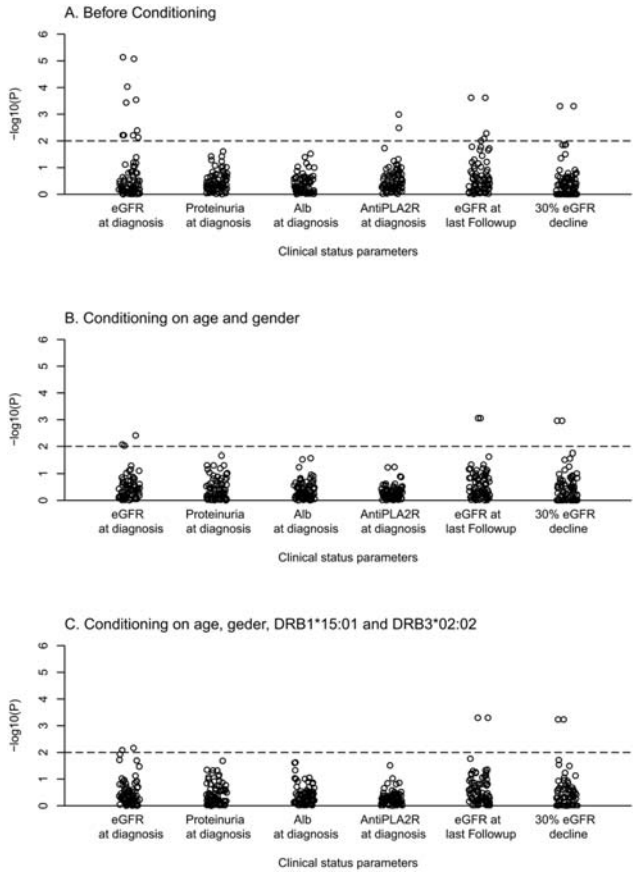


Figure 1 HLA-DRB1*1301-DQB*0603 Haplotype is independently Associates with Poor Prognosis in PLA2R-related Membranous

P0084 DIGENIC INHERITANCE: TWO RARE CASES OF GITELMAN SYNDROME

Franca Anglani[1], Elisa Pagnin[1], Giovanni Bertoldi[1], Lisa Gianesello[1], Matteo Rigato[1], Leonardo Salviati[2], Lorenzo Calò[1]

[1]University of Padua, Deapartment of Medicine DIMED, Division of Nephrology, PADOVA, Italy and [2]University of Padua, Department of Women's and Children's Health, Clinical Genetics Unit, PADOVA, Italy

Background and Aims: The clinical implementation of whole-exome sequencing (WES) as molecular diagnostic tool allows investigation of the pathogenic variants interplay in multiple genes resulting in complex spectrum of phenotypes in a same patient. The phenotypic complexity of genetic disease in patients with multiple molecular diagnoses is a challenge. The blending of two distinct disease phenotypes in a same patient may suggest an apparently new clinical phenotype, while molecular diagnoses with two overlapping disease phenotypes may result in phenotypic expansion of a single disease. We present two autosomal recessive Gitelman syndrome (GS) patients whose pathogenic variants in two different genes challenged us for clinical interpretation and therapeutic intervention.

Method: Case 1: GS diagnosis at 4 years of age, severe clinical phenotype (appearance at unusual early age, hypochloremia, borderline hypomagnesemia resembling Bartter syndrome (BS), need of more complex therapy. Case 2: The diagnosis of GS was made at the age of 45 years. The patient presented classical signs of GS, with less marked metabolic alkalosis and unusual chronic renal insufficiency (CRI). Exome sequencing panel was used for mutational screening of Bartter (BS) and GS genes. Sanger sequencing and Multiplex Ligation-dependent Probe Amplification (MLPA) were also applied.

Results: Case 1: We detected in the SLC12A3 gene the frameshift p.(Thr7Arfs) and the missense p.(Gly264Ala) variants, the first a known disease-causing mutation, the second associated with a severe form of GS in a patient. Another known disease-causing mutation p.(Met357Thr) was detected in the KCNJ1 gene encoding renal outer medullary K+ channel, ROMK1. It is one BS gene and was never associated with GS. The SLC12A3 p.(Gly264Ala) variant's high frequency makes it uncommon polymorphism although functional because it alters NCC activity but makes questionable its causative effect on GS phenotype. Our patient severe GS phenotype may be determined by the mutations in either SLC12A3 and KCNJ1 genes inherited respectively from mother and father. If the hypomorphic SLC12A3 variant is causative, hence the heterozygous KCNJ1 pathogenic variant might be a modifier allele responsible of the GS severe presentation. Case 2: We detected two novel variants in the SLC12A3 gene [p.(Lys894fs):p.(Pro331Leu)]. Both are pathogenic according to ACMG guidelines. Another very rare missense variant p.(Val245Met) was identified in the SLC4A1 gene, whose mutations cause distal tubular acidosis type I (dRTA). The missense mutation, never associated with dRTA, is predicted pathogenic by in silico tools. Its presence questions on phenotype interpretation: blended phenotype due to a concomitant presence of a dual molecular diagnosis? Or an expansion of a single phenotype (GS) due to the presence of a modifier gene variant? dRTA and GS have overlapping features such as hypokalemia, hypercalciuria. In the patient the less marked metabolic alkalosis, and the presence of CRF points to the latter.

Conclusion: Digenic inheritance in GS was reported in only one other instance. These two cases demonstrate how our understanding of the complexity of genetic heterogeneity of rare diseases is far to be completed. It becomes essential to shed light on how combinations of variants in different genes are responsible for a disease phenotype

P0085 MAYO AND PRO-PKD SCORE CONCORDANCE FOR PROGRESSION OF RENAL FALIURE EVALUATION IN ADPKD PATIENTS

Irene Capelli[1], Valeria Aiello[1], Elisa Carretta[2], Claudio Graziano[3], Nicola Sciascia[4], Cristiana Corsi[5], Vilma Mantovani[6], Francesco Monteduro[4], Marco Seri[3], Gaetano La Manna[1]

[1]Nephrology, dialysis and renal transplant unit, S. Orsola Hospital University of Bologna, Depertment of experimental diagnostic and specialty medicine (DIMES), Bologna, Italy, [2]Rizzoli Orthopedic Institute, Bologna, Italy, [3]Unit of Medical Genetics, S. Orsola Hospital University of Bologna, Depertment of experimental diagnostic and specialty medicine (DIMES), Bologna, Italy, [4]Department of Radiology, S. Orsola Hospital University of Bologna, Depertment of experimental diagnostic and specialty medicine (DIMES), Bologna, Italy, [5]Department of Electrical, Electronic, and Information Engineering "Guglielmo Marconi," University of Bologna,, Bologna, Italy and [6] Center for Applied Biomedical Research (CRBA), St. Orsola University Hospital, Bologna, Italy, Bologna, Italy

Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is a multisystemic disease characterized by the progressive development of bilateral renal cysts, resulting in enlargement of the kidney volume due to cystic formations, hypertension, haematuria, and loss of renal function. Recent advances in genomics have contributed to have a better understanding of the pathogenesis of the disease suggesting new treatment strategies to inhibit or delay cysts formation and expansion.Since 2015, the European Medicines Agency approved Vaptans as therapy to slow the growth of kidney volume and the decline in kidney function in patients defined rapid progressors.

In 2016 European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Working Groups on Inherited Kidney Disorders and European Renal Best Practice (WGIKD/ ERBP) published a position statement for definition of rapid progression. These recommendations included two algorithms to assess indications for initiation of ADPKD treatment. They selected three criteria based on: 1) the relationship between TKV(total kidney volume) and the decline in renal function according CRISP study, using Mayo Clinic Score 2) eGFR slope with an average $\geq$2.5 mL/min/ 1.73 m2/ yearly loss of renal function over a period of 5 yearsor 3) the link between genetic mutation and clinical information study using Propkd score.A 5 –years follow-up is not always available to achieve the criteria for rapid progressor, therefore the use of scores in clinical practice is widespread.In this scenario both scores (MAYO and PRO-PKD) are able to define rapid progressor patients and it is possible to use them alternatively as reported in literature.

The aim of this study is to evaluate the prognostic scores in a real life experience.

Method: All ADPKD patients in follow-up in our Nephrology Unit from January 2017 to July 2019 were included in the study. Descriptive statistics were used to summarize demographic and clinical characteristics. Therefore we classified them for TKV, genetic mutation, renal function, Mayo score and Propkd score.

Rapid progression was defined as 1C-D-E Mayo and high risk PRO PKD while non rapid progressors was 1A-1B mayo and low and intermediate PRO-PKD. Kappa statistic was used to determinate the concordance between Mayo and PROPKD score. Change in renal function within patients with the same class of score where analysed using Paired Wilcoxon signed rank sum test.

Results: We examined75 patients, 78% between 18-50 years, equally distributed for sex. The results shown thatdisease was more frequent familiar (88 %) witha percentage of mutations of PKD1 versus PKD2 mutation (90,7%/9,3%). 31patients (41%) had a GFR between 45-89 ml/min, 52patients (69%) achieved the criteria for nephromegaly according guideline (TKV $>$ 750CC). Respectively 76% (57pt) and 21%(16pt) were defined as rapid progressors for Mayo score ad Propkd score.

The slope of GFR was worse in patients defined rapid progressor in spite of non rapid-progressor according MAYO score (-2,8 ml/min vs 0,3 ml/min) as for propkd classification (-3 vs - 1,75ml/min).

Only for 15 patients the results were concordant for this two scores,43 patients identified as rapid progressor for Mayo score were non rapid progressor for Propkd score, in the same way 2 patients classified for Propkd were not rapid progressor for Mayo score. K of Coen of 0,07.

Conclusion: High risk patients present a significant decline in renal function in the first year with both score systems, confirming results of previous studies. Currently the scores used to define rapid progressors select patients differently. Concordance between scores il low (K of Cohen 0,076). The Propkd score is more selective compared to Mayo score. NeverthelessProPKD allows to identify some rapid progressor patients excluded from the use of the Mayo score only. The combined use of scoring may however increases the ability to identify progressive patients.

P0086

FOCAL SEGMENTAL GLOMERULOSCLEROSIS AND TROMBOCYTOPENIA WITHOUT BLEEDING DIATHESIS: WHEN GENETICS MATTER.

Elisa Olivo[1], Sabina Leonardi[1], Vittorio Di Maso[1], Mary Louise Artero[1], Francesco Bianco[1]

[1]*Trieste, Nephrology, Trieste, Italy*

Background and Aims: A 45-year old patient presented to our renal unit because of increased serum creatinine (2 mg/dL), proteinuria (2g/24h collection) and haematuria; platelets were 12000/mcL. His family history was negative. He had already undergone cataract surgery and was wearing a hearing device. Alport syndrome was suspected and kidney biopsy performed. Light microscopy showed focal segmental glomerulosclerosis (FSGS), while immunofluorescence was negative. Electron microscopy was not available. No specific treatment was undertaken and he progressed to end-stage renal disease (ESRD) in 10 years. The patient chose peritoneal dialysis. He was considered at high risk of bleeding but the Tenchkoff catheter was inserted without problems. After 3 months he received kidney transplant and again no pathological bleeding occurred.

Method: A genetic test was requested using next generation sequencing (NGS).

Results: A mutation of myosin heavy chain 9 (MYH9) gene which encodes the non-muscle myosin heavy chain-IIA (NMMH-IIA) was found. This mutation is associated with thrombocytopenia and proteinuria; platelets are giant and display normal aggregation, even in those patients who have a very low count. Proteinuria can be mild or in the nephrotic range, with or without microhaematuria. Kidney involvement is highly heterogeneous and leads to ESRD in half of the cases. Light microscopy shows FSGS as the prevalent pattern whereas electron microscopy is characterized by podocyte foot process effacement. In fact, NMMH-IIA is expressed in podocytes and controls cytoskeleton and cell migration. The differential diagnosis with Alport disease is challenging because additional features of MYH9 mutation are sensorineural deafness and presenile cataract. For all these reasons, accurate kidney biopsy study, family history and genetics are decisive.

Conclusion: Genetic testing has a pivotal role in understanding kidney diseases and should be more and more used.

RENAL PATHOLOGY. EXPERIMENTAL AND CLINICAL

P0087 TRAF3 MODULATION: A NOVEL MECHANISM OF THE ANTI-INFLAMMATORY EFFECTS OF VITAMIN D RECEPTOR AGONIST PARICALCITOL IN RENAL DISEASE

Sandra Rayego-Mateos[1], Jose Luis Morgado Pascual[2], José M. Valdivielso[3], Ana Sanz[4], Enrique Bosch panadero[4], Raul Rodrigues Diez[2], Jesus Egido[5], Alberto Ortiz[4], Emilio Gonzalez Parra[4], Marta Ruiz-Ortega[2]

[1]Instituto Maimonides de investigación Biomedica de Cordoba (IMIBIC), GE-06 Pathophysiology of Renal and Vascular Damage Laboratory, Cordoba, Spain, [2]IIS-Fundación Jiménez Díaz. Universidad Autónoma Madrid., Molecular and Cellular Biology in Renal and Vascular Pathology., Spain, [3]Institut de recerca biomedica de Lleida (IRBLleida), Vascular and Renal Translational Research Group, Lleida, Spain, [4]IIS-Fundación Jiménez Díaz-UAM/IRSIN, Division of Nephrology and Hypertension., Spain and [5]CIBER in Diabetes and Associated Metabolic Disorders (ISCIII, Ministerio de Economía y Competitividad), Spain

Background and Aims: Tumor necrosis factor receptor-associated factors (TRAFs) are critical signaling adaptors downstream of pro-inflammatory receptors, involved in canonical and non-canonical nuclear factor-κB (NF-κB) activation. Vitamin D receptor agonists (VDRAs) exert beneficial effects in renal disease and possess anti-inflammatory properties, but the underlying mechanism remains unknown. Our aim was to investigate TRAF3 involvement on renal disease and its potential modulation by VDRAs.

Method: Studies were done in isolated peripheral blood mononuclear cells (PBMCs) from end-stage renal disease (ESRD) on haemodialysis (treated or not with VDRAs) patients, healthy donors or cultured renal cells. Preclinical models of renal damage were: unilateral ureteral obstruction (UUO), acute renal damage induced by Folic acid (FA) administration and TWEAK-induced renal inflammation. The effect of VDRA (paricalcitol) was tested in vitro and in vivo.

Results: In PBMCs isolated from ESRD, TRAF3 protein levels were downregulated compared to healthy controls, associated to activation of non-canonical NF-κB2 (downregulation of RelB or p52/NF-κB2 protein levels) and altered pro-inflammatory cytokine profile. Interestingly, treatment of those patients with the VDRA paricalcitol restored all the described features. In vitro experiments in PBMCs and tubular epithelial cells exposed to inflammatory stimuli showed that paricalcitol prevented TRAF3 downregulation, NF-κB2 activation and proinflammatory genes upregulation. Moreover, immunoprecipitation studies showed that paricalcitol diminished TRAF3 ubiquitination in the K48-linked chains and CIAP1-TRAF3 interaction. TRAF3 overexpression by CRIPS/cas9 technology mimics VDRAs effects. In preclinical models of renal damage paricalcitol inhibited renal NF-κB2 activation, reducing p52 and RelB nuclear accumulation and transcriptional activity associated to lower renal inflammation. In TWEAK-induced renal injury in VDR knockout mice, paricalcitol prevented TRAF3 downregulation and NF-κB2-dependent gene upregulation, suggesting a VDR-independent anti-inflammatory effect of paricalcitol.

Conclusion: The present studies identify TRAF3 downregulation as a key feature promoting inflammation in CKD identifying non-canonical NF-κB activation as a key driver of inflammation in this context. The fact that the VDR is not required for paricalcitol actions suggests novel-signaling pathways involved in the anti-inflammatory effect of paricalcitol. This may allow the design of drugs that restore TRAF3 levels but are devoid of VDR-dependent effects on mineral bone metabolism, which may limit the use of VDRAs as anti-inflammatory agents.

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P0088

THE INFILTRATION OF T AND B LYMPHOCYTES AND NK CELLS IN KIDNEY BIOPSIES OF PATIENTS WITH FABRY DISEASE UNDER ENZYME REPLACEMENT THERAPHY

Kultigin Turkmen[1], Hasan Esen[2], Mehmet Ali Karaselek[3], Seyma Celikbilek Celik[3], Ismail Baloglu[1], Sukru Guner[3], Ismail Reisli[3], Sevgi Keles[3]

[1]Necmettin Erbakan University, Meram Medical School, Nephrology, Konya, Turkey, [2]Necmettin Erbakan University, Meram Medical School, Pathology, Konya, Turkey and [3]Necmettin Erbakan University, Meram Medical School, Pediatric Allergy and Immunology, Konya, Turkey

Background and Aims: Fabry Disease (FD) is a lysosomal glycosphingolipid storage disorder. Kidneys are affected in FD. Despite enzyme replacement theraphy (ERT), some patient still have an ongoing deterioration of renal functions probably secondary to inappropriate immune responses. There is no data regarding NK cell subtypes and the exact relation with B-T lymphocytes and NK cells in patients with FD. We aimed to analyze subtypes of NK cells in patients with FD and compared these results with healthy subjects. Additionally, we analyzed the renal biopsy (RBx) materials of our patients prior to ERT in terms of B, T and NK cell infiltration and compared these cells in some of our FD patients after 4 years of ERT.

Method: 15 patients with FD and 10 healthy controls were included in the study. Of 15 patients, 8 patients were receiving agalsidase alfa or beta. Blood samples obtained from both group were taken into 2 ml EDTA tube to evaluate peripheral NK cell subgroups according to CD56 and CD16 expression and CD3, CD4, CD8 expression to determine subtypes T cells. These cells were evaluated by flow cytometry technique. The RBx of 10 patients with FD were evaluated before ERT and 3 were reevaluated after 4 years of ERT in terms of T-B, NK and plasma cells infiltration of kidney. The paraffin blocks of specimens were examined with HE, PAS, Masson-trichrome and toluidine blue staining and frozen blocks were examined with red-oil 10 staining

Results: The characteristics of patients with FD and healthy controls are depicted in Figure 1. Except proteinuria, there were no significant differences in terms of biochemical parameters between two groups. According to flow-cytometric analyses, total percentage of NK and T helper 1, 2, 17 and Treg cells of FD patients are similar to controls (Fig 1). When we analyzed subgroups of NK cells and determined that $CD56^{dim}CD16^{dim}$NK cells were increased, however, $CD56^{dim}CD16^{bright}$NK cells were decreased in patients with FD compared to controls (Fig1). We performed RBx of 10 patients. The percentages of CD3, 4, 8 positive Tcells, CD19, CD20 positive B cells, CD 16, 56 positive NK cells and CD 138 positive plasma cell infiltration are shown in Fig 2. According to RBx findings prior to ERT, all patients had interstistial fibrosis (IF),

Parameters	Healthy subjects (n=10) Mean±SD or Median (IQR)	Patients with Fabry disease (n=15) Mean±SD or Median (IQR)	P value
Age (Age)	29± 7.02	34.93± 15.06	0.200
Female/Male	5/5	7/8	0.878
Glucose (mg/dL)	94.5±13.15	91.46±9.64	0.541
eGFR (ml/min)	97.5 (23.75)	106 (54)	0.698
Creatinine (mg/dL)	0.83 ±0.21	0.82 ±0.38	0.946
Uric acid (mg/dL)	4.82 ±1.28	4.11 ± 1.51	0.237
Albumin (g/L)	4.5± 0.49	4.29± 0.40	0.288
Proteinuria	87.5 (48.25)	185 (218)	0.003
CRP (mg/L)	2.4 (5.15)	0.9 (3.4)	0.133
Th1	17.6 (6.9)	14.5 (16.62)	0.897
Th17	4.38 (2.69)	4.12 (7.27)	0.796
Th2	8.07 (2.89)	7.56 (5.53)	0.202
Treg	7.13±2.01	7.83±1.87	0.395
CD56positive	10.8±7	11.6±3.7	0.495
$CD56^{bright}CD16^{neg}$	6.1±2.6	13.4±10	0.109
$CD56^{dim}CD16^{neg}$	3.5±3.3	3.4±2.7	0.951
$CD56^{dim}CD16^{dim}$	38±21	59±26	0.041
$CD56^{dim}CD16^{bright}$	49±25	19±28	0.008

Patients		MORPHOLOGICAL FINDINGS								IMMUNOLOGICAL FINDINGS							
		TG	SS	GS	NSG	IF(%)	AS	PV	PI	CD3 (%)	CD4 (%)	CD8 (%)	CD16 (%)	CD56 (%)	CD19 (%)	CD20 (%)	CD138 (%)
1	Patient 1 (First Bx)	12	0	0	12	5	0	3	2	60	30	20	10	5	0	0	0
2	Patient 1 (Second Bx)	18	1	1	16	10	2	3	3	70	20	10	10	5	0	0	0
3	Patient 2 (First Bx)	3	1	1	1	10	1	3	3	70	30	40	10	10	0	1	1
4	Patient 2 (Second Bx)	7	0	4	3	40	1	3	4	60	30	10	10	5	0	10	2
5	Patient 3 (First Bx)	6	1	1	3	20	2	3	2	60	30	10	20	10	0	0	0
6	Patient 3 (Second Bx)	1	0	0	1	40	2	3	3	70	30	20	10	5	0	20	10
7	Patient 4	1	0	0	1	10	0	2	2	80	20	40	20	10	0	0	0
8	Patient 5	14	0	0	14	10	0	3	4	60	30	10	10	5	0	0	0
9	Patient 6	17	0	1	16	5	1	3	3	60	20	40	20	10	0	0	0
10	Patient 7	8	0	0	8	10	0	3	2	60	20	10	10	5	0	0	0
11	Patient 8	2	0	0	2	5	0	2	2	60	30	20	20	10	0	1	0
12	Patient 9	39	1	2	36	5	1	2	3	50	20	30	30	10	0	1	0
13	Patient 10	10	0	0	10	5	0	3	3	60	30	10	10	5	0	0	0

Figure:

podocyte vacuoles (PV), podocyte inclusion (PI), CD3, CD4, CD16, CD56 positivity at different levels. In contrast, almost none of the patients had CD19, CD20, CD138 positivity. We rebiopsied 3 patients after 4 years of ERT and reevaluated specimens in terms of IF, global and segmental sclerosis (SS), PV, PI and the percentages of CD3, CD4, CD16, CD56, CD 19, CD 20, CD 138 positivity. 2 rebiopsied patients from the same family had increased serum creatinine and proteinuria despite 4 years of regular ERT. In the second biopsy of these two patients, we found that global sclerosis (GS), IF and PI are increased and abundant CD19, CD20 and CD 138 positive cells were seen which were almost absent in the first biopsy. The other patient from another family, had mildly increased proteinuria and had no creatinine increment after 4 years of ERT. In this patient, we found that GS, SS, IF, PI and arterial sclerosis were increased, however CD 3, 4, 8 positive T cells were decreased and no changes in the percentage of CD16, 56 positive NK cells. We could not demonstrate CD 19, 20, 138 positivity in the latter patient.

Conclusion: Our group, for the first time, demonstrated that $CD56^{dim}CD16^{dim}$subtype of NK cells is increased in FD which is closely associated with cellular cytotoxity in normal population. Additionaly, CD 19 and CD 20 positive B cell infiltration are increased and glomerular and interstitial changes are advanced in some patients with ongoing kidney function deterioration despite 4 years of regular ERT. Hence, infiltration of Bcells in the kidneys of patients under ERT might change our therapeutic approaches in the near future. Further studies are needed to clarify the exact roles of B T and NK cells in FD.

P0089

KEAP1/NRF2 PATHWAY REGULATES GFR BY INCREASING THE GLOMERULAR EFFECTIVE AREA WITHOUT AFFECTING THE AFFERENT/EFFERENT ARTERIOLE RATIO

KENGO KIDOKORO[1], Yoshihisa Wada[1], Megumi Kondo[1], Atsuyuki Tokuyama[1], Seiji Itano[1], Tamaki Sasaki[1], Chris Wigley[2], Joel Proksch[2], Colin Meyer[2], Naoki Kashihara[1]

[1]Kawasaki medical school, Nephrology and hypertension, Kurashiki Okayama, Japan and [2]Reata Pharmaceuticals Inc., Irving, TX, United States of America

Background and Aims: The Keap1/Nrf2 pathway regulates the expression of a series of cytoprotective, anti-inflammatory and antioxidant genes. The Nrf2 activator, bardoxolone methyl (BARD), has consistently increased estimated GFR (eGFR) in clinical studies in patients with chronic kidney disease. BARD demonstrated improvement of renal function assessed by inulin clearance, the clinical gold standard for measuring GFR, in diabetic kidney disease patients. These findings suggest the Keap1/Nrf2 system is deeply involved in the regulatory mechanisms of GFR. However, the precise mechanisms are not fully elucidated. We pharmacologically and genetically investigated the mechanisms of GFR regulation by Keap1/Nrf2 system using in vivo multiphoton microscope (MPM) imaging techniques.

Method: C57BL/6 (Cont), Nrf2 knockout (Nrf2-KO), and Nrf2-activated Keap1-knockdown mice (Keap1-KD) were used. The mice were treated the synthetic triterpenoid RTA dh404 (10 mg/kg/day by gavage) which is a Nrf2 activator for rodents, for a week. We successfully developed the technique to evaluate single-nephron GFR (SNGFR) using MPM (Circulation 2019). The glomerular hemodynamics, diameter of the afferent/efferent arterioles and glomerular permeability were also evaluated. The calcium influx into cells in response to ATP and angiotensin II stimulation and the effect on [Ca2+]i by RTAdh404 were evaluated using Fluo 4 and Fura red in cultured mesangial cells and podocytes. Production of reactive oxygen species and nitric oxide (NO) availability were assessed by fluorescent method using CellROX® Deep Red and diaminofluorescein-FM diacetate (DAF-FM DA) upon the exposure to these stimuli.

Results: SNGFR in Keap1-KD mice was significantly higher than in the control (9.13±0.55 vs 4.40±0.39 nl/min, Figure 1). RTA dh404 increased SNGFR in the control but not in the Nrf2-KO mice (6.00±0.40 vs 4.66±0.35 nl/min, Figure 1). There was no significant change in the ratio of the glomerular afferent/efferent arteriole diameter in all groups. RTA dh404 treatment increased glomerular volume but did not affect the glomerular permeability of albumin and 40kd-dextran. RTA dh404-treatment inhibited calcium influx into cultured podocytes and mesangial cells induced by angiotensin II or ATP, thereby affecting contractile responses. Oxidative stress and NO-bioavailablity were also ameliorated with RTA dh404.

Conclusion: The Keap1/Nrf2 pathway plays a pivotal role in controlling GFR and presumably underlies the effect of BARD on GFR in patients.

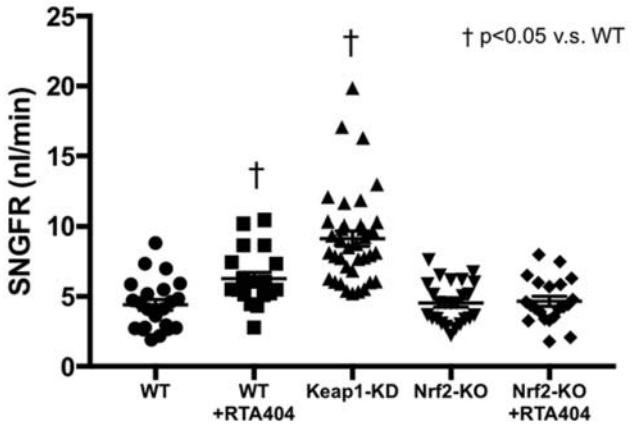


Figure 1:

P0090 SPIRONOLACTONE ALLEVIATES ISCHEMIC STROKE SEVERITY IN MALE MICE WITH CHRONIC KIDNEY DISEASE

Mathilde Lando[1,2,3], Maria Grissi[1], Cedric Boudot[1], Sabrina Poirot[1], Agnès Boullier[1,2,4], Gaëlle Lenglet[1], Carine Avondo[1], Gabriel Choukroun[1,2,3], Saïd Kamel[1,4,5], Jean-Marc Chillon[1,5,6], Lucie Henaut[1]

[1]University of Picardie Jules Verne, UR UPJV 7517 MP3CV, Amiens, France, [2]University of Picardie Jules Verne, Faculty of Medicine, Amiens, France, [3]Amiens University Hospital, Division of Nephrology, Amiens, France, [4]Amiens University Hospital, Department of biochemistry, Amiens, France, [5]University of Picardie Jules Verne, Faculty of Pharmacy, Amiens, France and [6]Amiens University Hospital, Direction of clinical research, Amiens, France

Background and Aims: Ischemic stroke is highly prevalent in patients with chronic kidney disease (CKD) and has been associated with poor outcomes. In experimental studies, CKD mice display wider and more inflammatory ischemic lesions as well as poorer functional outcomes than mice with normal renal function. In rodents with normal renal function, treatment with a mineralocorticoid receptor antagonist decreases brain ischemic lesion and improves functional outcomes. The goal of this study was to investigate the impact of a treatment with spironolactone, a mineralocorticoid receptor antagonist, on stroke outcomes in CKD mice.

Method: Male C57BL/6J mice were randomly assigned to CKD or SHAM groups. CKD was induced through right kidney cortical electrocautery in 8 week-old mice followed 2 weeks later by left total nephrectomy. Mice received spironolactone (50 µg/kg/day) or placebo (subcutaneous tablets, Innovative Research of America) for 6 weeks until stroke induction by transient middle cerebral artery occlusion (tMCAO). Neurological deficits were monitored daily, 3 days before and 1 day after stroke induction. Mice were euthanized 24 hours after tMCAO. Total infarct volumes and apoptosis were determined by cresyl violet staining and TUNEL respectively. Immunohistochemical detection of neurons was performed using an anti-NeuN antibody. To characterize the pro-inflammatory polarization of microglia/macrophages, M1 signature genes' expression (CD-32, IL-1β and IL-6) was analyzed by qPCR.

Results: Untreated CKD mice displayed wider ischemic lesions (40.3 ± 4.5 versus 23.8 ± 3.9 mm^3; $p < 0.05$) and poorer neurological score, grip strength and prehensile abilities compared to untreated sham mice. Pro-inflammatory M1 signature genes' expression (CD-32, IL-1β and IL-6) was significantly increased in the ischemic hemisphere of CKD mice compared to the non-ischemic hemisphere. Treatment with spironolactone decreased ischemic lesion (19.3 ± 5.1 mm^3; $p < 0.05$) and improved neurological score, grip strength and prehensile abilities in CKD mice. Treatment with spironolactone also reduced apoptosis, neuronal loss and microglia/macrophages pro-inflammatory M1 signature genes' expression in CKD mice. In contrast, treatment with spironolactone had no effect in sham mice.

Conclusion: These data demonstrate that the mineralocorticoid receptor could be a promising therapeutic target to decrease brain inflammation and improve stroke recovery in CKD.

P0091

DEEP LEARNING-BASED IMMUNOFLUORESCENCE ASSESSMENT OF GLOMERULAR DISEASES

Peng Xia[1], Zhilong Lv[2], Yu-bing Wen[1], XueSong Zhao[1], ChuanPeng Wang[1], Hua Zheng[1], Wei Ye[1], Yan Qin[1], Xuemei Li[1], FEI REN[2], Limeng Chen[1]

[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Nephrology Division, Beijing, P.R. China and [2]Institute of Computing Technology, Chinese Academy of Sciences, Beijing, P.R. China

Background and Aims: Immunofluorescence (IF) tests of renal tissue are of great value in diagnosing most of the glomerular diseases. However, high quality IF tests and results interpretation by experienced pathologists are not universally available in different areas of China. The development of deep neural networks has been used to facilitate digital analysis of pathologic images recently. We proposed a novel Convolutional Residual Dense Network (CR-DenseNet) to facilitate IF assessment of renal biopsy samples.

Method: A dataset with 725 IF images, including 312 images of IgA nephropathy (IgAN), 319 images of idiopathic membranous nephropathy (IMN) and 94 images of type V lupus nephritis (LN V) diagnosed in Peking Union Medical College Hospital (PUMCH) from November, 2016 to March, 2018 were used for training and validation of CR-DenseNet. All the images were photographed using ANDOR, ZYLA, Japan. The resolution was 2560 × 2160 pixels. These images were carefully annotated for the distribution characteristics and final diagnosis by two renal pathologists independently. IgAN showed mesangial predominating deposition. IMN showed glomerular basement membrane (GBM) predominating deposition. LN V showed positive depositions in both mesangial area and GBM. These three groups were used for IF distribution identification training. In CR-DenseNet, convolutional residual dense blocks were introduced, each of them consisted of a dense block with a convolutional skip connection to fully exploit the dense local features. To identify the deposition location, we imposed a switch in the proposed model to handle an additional input for different types of tasks, which can provide glomerular contours approximated from the IF image foreground (Figure 1). Performance was evaluated using overall accuracy and F1 score. F1 was computed as 2×True Positive / (2×True Positive + False Positive + False Negative). The whole protocol was approved by Institutional

Review Board of PUMCH (No. S-K913).

Results: Experimental results showed that the proposed CR-DenseNet model outperformed the state-of-the-art method. In identification of segmental and glomerular IF positive images, our model showed overall accuracy of 92.0%. The true positive rate and F1 score of segmental positive samples recognition were 90.1% and 0.889. The true positive rate and F1 score of glomerular recognition positive samples were 94.1% and 0.938. Furthermore, the overall accuracy of our model in identifying mesangial predominating deposition (IgAN), GBM predominating deposition (IMN) as well as positive depositions in both mesangial area and GBM (LN V) was 91.2%. The true positive rates of each above-mentioned deposition classification were 93.1%, 90.5% and 88.9%, respectively. The corresponding F1 scores were 0.964, 0.905 and 0.889.

Conclusion: Our preliminary data showed that CR-DenseNet model was quite powerful in making IF diagnosis of typical glomerular diseases for the first time.

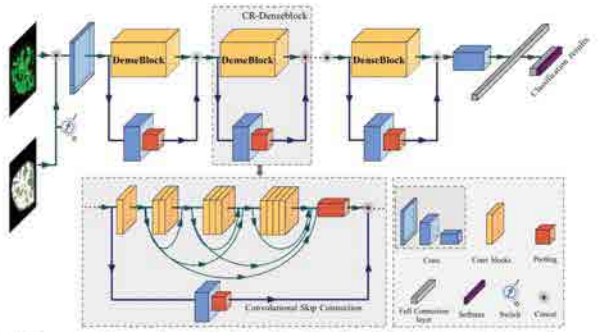


Figure 1. The overview of the proposed Convolutional Residual DenseNet (CR-DenseNet). The inputs consist of the immunofluorescence image and corresponding glomerular contours approximated from the foreground, which can be controlled by a switch according to tasks. The convolutional residual dense blocks (CR-Denseblock) is composed of dense blocks with a convolutional skip connection.

Figure:

P0092

GEMPREDICT: AN HISTOLOGICAL AND BIOLOGICAL COMBINED CRITERIA TO DIAGNOSE PRIMARY MEMBRANOUS NEPHROPATHY

Camille Roger[1], Viviane Gnemmi[2], Claire Cartery[3]

[1]CHRU Lille, Nephrology, Lille, , [2]CHRU Lille, Pathology, Lille, and [3]CH Valenciennes, Nephrology, Valenciennes,

Background and Aims: Membranous nephropathy (MN) is a frequent cause of nephrotic syndrome of non-diabetic origin in adults, and a leading cause of end stage renal disease. Its origin is primary in up to 80% of cases but can also be secondary to underlying diseases such as cancer, lupus or other systemic disease, infections or drugs. Important recent advances have been made in our understanding of primary MN physiopathology with the identification of various antibodies such as PLA_2R, THSD7A, Exostosin 1,2 suggesting autoimmunity. However, distinction between primary and secondary MN remains difficult and can lead to numerous and expensive complementary exams and postpone treatment. Some authors (Cambier, Ronco, CJASN 2012) proposed an algorithm based on histological and biological features in order to distinguish primary from secondary MN. Yet this algorithm has never been tested. The main objective of our study was to evaluate the efficiency of a combined histological and biological criterion in order to establish the diagnosis of primary MN.

Method: We conducted a pluricentric retrospective cohort study in Northern France. All patients with histological proved membranous nephropathy between January 2010 and December 2016 were included. All kidney biopsies were re-analysed in order to specify the predominant IgG subclass and PLA_2R staining. The combined criterion was considered present if: PLA_2R was detected (in biopsy or serum), with no endocapillary proliferation and an IgG4 subclass predominance (or co-predominance) on kidney biopsy. The gold standard to diagnose primary MN was the exclusion of other causes of MN after biological and radiological investigation, in particular the absence of cancer detected after at least 2 years of following. We tested the sensitivity, specificity, and predictive values of this combined criterion in order to diagnose primary MN.

Results: 173 patients were included. 66 (38.2%) patients were women. At the time of diagnosis mean age was 52.1 years old (SD: 17.4), mean albumine and creatinine were respectively 25.2 g/L (9.02) and 14 mg/L (17.7). Mean protein to creatinine ratio was 5.75 g/g. 119 (68.8%) patients had primary membranous nephropathy. Secondary membranous nephropathy were due to lupus, other auto immune disease and cancer in respectively 25 (14.5%), 14 (8.0%), and 15 (8.0%) cases. 59 patients had a positive combined criterion. Sensitivity of the criterion was: 0.50 [95%CI: 0.40-0.59], Specificity was: 0.90 [95%CI: 0.80-0.98] compared to a specificity of 0.50 [95%CI 0.34-0.54] for single criterion PLa_2R on biopsy. Negative predictive value was 0.45 [95%CI: 0.31-0.59] and positive predictive value was 0.92 [95%CI: 0.84-0.99]. Histological features associated with primary membranous nephropathy were: no extracapillary proliferation ($p=0.003$), presence of PLA_2R ($p<0.001$), IgG4 predominant staining ($p<0.001$) and low Ig1 staining (2.24 + in secondary MN versus 1.86 + in MN) $p=0.011$.

Conclusion: Our histological combined criterion had a high specificity: 0.90 [95%CI 0.80-0.98] and positive predictive value 0.92 [95%CI: 0.84-0.99]. Presence of this combined criterion could allow the clinician to reduce the number of complementary analyses and help conclude faster to the primary etiology of the MN.

P0093

IMPROVED INTEROBSERVER AGREEMENT IN BANFF SCORING OF RENAL ALLOGRAFT BIOPSIES WHEN ROUTINELY USING CD3/PAS STAIN

Neil Abrahams[1,2], Lauren Abrahams[1], Katherine Freeman-Costin[3], Cecilia Obregon[1], Mandolin Ziadie[1,4]

[1]Memorial Healthcare System, Hollywood, Florida, USA, Department of Pathology, Division of Renal Pathology, Holllywood, United States of America, [2]Florida Atlantic University, Charles E. Schmidt College of Medicine, Boca Raton, United States of America, [3]Florida Atlantic University, Charles E. Schmidt College of Medicine Biostatistics Core, Boca Raton, United States of America and [4]Memorial Healthcare System, Division of Pediatric Pathology, Hollywood, United States of America

Background and Aims: The BANFF Classification of renal allograft rejection consists of scores for cellular and antibody mediated rejection. The scores for tubulitis (t), interstitial inflammation (i), glomerulitis (g), total inflammation (ti), and endotheliatis (v) have direct prognostic and therapeutic significance as they contribute to a diagnosis of renal allograft rejection. The original BANFF scoring was developed using hematoxylin and eosin (H&E) stain only. This study examines the level of interobserver agreement using H&E and a combination CD3/PAS stain that highlights T lymphocytes and basement membranes.

Method: 50 consecutive renal allograft biopsies were retrieved and on each case H&E and CD3/PAS stains (Ventana/Roche Tissue Diagnostics clone 2GV6 for CD3) were performed. CD3/PAS and H&E slides were matched and blinded for two reviewers [reviewer (R1) and reviewer 2 (R2)]. Each case was graded in an identical manner following criteria designated for (t),(i),(g) and (ti) as previously described in the Banff Classification for Renal Allograft Biopsies. Cases were not graded for (v) as there were too few cases with endothelialitis to allow for statistical evaluation. The matched scores were analyzed using weighted Kappa statistics for interobserver agreement within each group. Agreement levels were characterized using Landis and Koch descriptions for level of agreement. All p values were two-tailed, values of <0.05 were considered statistically significant. Statistical analyses was performed using SAS Version 9.4, Cary NC.

Results: Mean age was 44 years with a range of 9 -75 years. Standard deviation (SD) for age was 18 years. Gender distribution was 20% female and 80% male. Agreement between R1 and R2 for (t) scores was moderate (Weighted Kappa 0.5276) as opposed to fair for H&E group (Weighted Kappa 0.4189). Similarly, interobserver agreement was moderate for scores of (i) and (ti) in the CD3/PAS group and fair in the H&E group. For both CD3/PAS and H&E interrater evaluations, agreement was fair to poor for (g) with weighted Kappa of 0.3928 and 0.3559 respectively.

Conclusion: This study showed increased levels of interobserver agreement when using a CD3/PAS combination stain to score allograft biopsies for (t), (i) and (ti). Since (t), (i) and (ti) scores directly affect a diagnosis of rejection, we propose routine use of CD3/PAS in addition to H&E when reviewing renal allograft biopsies. Glomerulitis (g) shows poor interobserver agreement regardless of the stain used and further studies to refine the criteria for (g) in Banff revisions of the classification may be of value.

P0094

KLOTHO DECLINE IS ASSOCIATED WITH PRO-HYPERTROPHIC SIGNALING IN MYOCARDIUM OF NEPHRECTOMIZED SPONTANEOUSELY HYPERTENSIVE RATS (PILOT SYUDY)

Evdokia Bogdanova[1], Vladimir Dobronravov[1], Natalia Semenova[2], Irina Zubina[1], Olga Galkina[1], Olga Beresneva[1], Galina Ivanova[3], Marina Parastaeva[1], Ivan Kayukov,[1], Alexei Smirnov[1]

[1]Pavlov University, Research Institute of Nephrology, St Petersburg, Russia, [2]Russian Research Institute of Hematology and Transfusiology, St Petersburg, Russia and [3]Pavlov Institute of Physiology, Laboratory of cardiovascular and lymphatic systems physiology, St Petersburg, Russia

Background and Aims: Klotho deficiency is suggested to be involved in cardiac complications in chronic kidney disease (CKD) through modulation of intracellular pro-hypertrophic signaling pathways.

The aim of this study was to investigate the molecular mechanisms of myocardial remodeling in the settings of Klotho decline in experimental CKD.

Method: Systolic blood pressure (BP), myocardial mass index (MMI), serum and urinary creatinine (Cr), serum urea (Ur), inorganic phosphate (Pi), 25-hydroxyvitamin D (25OHD), parathyroid hormone (PTH), fibroblast growth factor 23 (FGF23), Klotho, myocardial Klotho, calcineurin/ NFAT and beta-catenin expression (IHC), quantitative morphometry of cardiomyocite (CM) thickness and nuclei area (hematoxylin and eosin), myocardial perivascular (PF) and interstitial fibrosis (IF), renal fibrosis (RF) (Masson's trichrome) and Klotho expression (rKl, IHC) were analyzed in spontaneously hypertensive rats with 3/4 or 5/6 nephrectomy (Nx) and duration of experimental exposure 1 and 2 mo (Nx1, n = 9; Nx2, n = 8). Controls were sham operated (SO) animals (SO1, n = 9; SO2, n = 9).

Results: The experimental model was corresponded to the initial stages of CKD (Ur level was between 6.64 and 13.36 mmol/L, serum Cr increased less than 50% vs SO, RF did not exceed 22 % FOV). Serum concentration of Klotho and rKl expression decreased, while MMI, CM thickness increased in both Nx1 and Nx2 (Table). There were no differences in serum Pi, FGF23 and PTH levels in Nx1 vs SO (Table). In Nx2 Klotho decline was accompanied by the development of IF and PF, serum 25OHD decrease, Pi and FGF23 increase vs SO2 (Table). In multiple regression analyzes including SO and Nx animals rKl was independently associated with MMI ($\beta = -0.38 \pm 0.16$, $p = 0.026$), and CM thickness ($\beta = -0.64 \pm 0.14$, $p < 0.001$). Myocardial fibrosis was associated with rKl level (IF: $\beta = -0.87 \pm 0.19$, $p = 0.001$) and serum 25OHD (PF: $\beta = -0.34 \pm 0.15$, $p=0.032$). According to pilot data of IHC, in Nx rat myocardium Klotho protein expression decreased, cytoplasmic calcineurin and nuclear NFAT in CM were observed (Figure), suggesting an increase in the activity of the calcineurin / NFAT signaling pathway. An intracellular redistribution of β-catenin from the cytoskeleton to the cytoplasm and nuclei were observed in CM of Nx rats (Figure), likely corresponding to increase in the activity of Wnt signaling.

Conclusion: Associations of CM hypertrophy, myocardial fibrosis and Klotho decline in CKD may be mediated by calcineurin / NFAT and Wnt signaling in myocardium.

P0095

MOLECULAR MECHANISMS OF THE CARDIOVASCULAR EFFECTS OF LANTHIONINE, A NEW UREMIC TOXIN, AND ITS INTERACTIONS WITH THE REDOX MICROENVIRONMENT

Carmela Vigorito[1], Eugenia Anishchenko[2], Annapaola Coppola[2], Patrizia Lombari[1], Diego Ingrosso[2], Alessandra Perna[1]

[1]University of Campania Luigi Vanvitelli, Translational Medical Sciences, Napoli, Italy and [2]University of Campania Luigi Vanvitelli, Precision medicine, Napoli, Italy

Background and Aims: The non-proteinogenic amino acid lanthionine is a byproduct of the biosynthesis of hydrogen sulfide (H2S), an endogenously produced gas with cardiovascular properties). Lanthionine concentration is increased in uremia and it has been proposed as a new uremic toxin. In the zebrafish model, lanthionine induces effects on cardiac embriogenesis, arrhythmia, and locomotor alterations. Some effects are counteracted by glutathione, the well known antioxidant. In a human endothelial cell model, lanthionine significantly reduces H2S release, both protein content and glutathionylation of cystathione beta-synthase (CBS), one of the main H2S-producing enzymes, miR-200c and miR-423 levels, as well as vascular endothelial growth factor expression, while it also increases intracellular calcium levels. We investigated in the present abstract the actions of glutathione on some of lanthionine effects on zebrafish and endothelial cells. We utilized what is considered to be a more stable form of glutathione, acetylglutathione (AcGSH).

Method: Zebrafish behavior and heart size were analyzed by the Danio Vision system and confocal microscopy, respectively. Gene and protein expression were analyzed usimg qPCR and Western Blot, respectively. CBS glutathionylation has been assessed by immunoprecipitation with a magnetic beads-coated anti-GSH. Interleukins levels were evaluated by ELISA. Lanthionine acetylation was evaluated by LC/MS.

Results: In zebrafish, we demonstrated that AcGSH significantly increases heart size and the expression of atrium specific proteins. Increased heart rate and heart rhythm plasticity determined by AcGSH were partially counteracted by lanthionine. Monitoring of larval movements showed that this behavior was affected by AcGSH supplementation. In endothelial cells, AcGSH increased H2S release, and, utilized in combination with lanthionine, it was able to partially counteract its effects on H2S release. AcGSH was able to increase CBS glutathionylation and to offset lanthionine effects on glutathionylation. In addition, it increased tubulin, histone, and NFKB acetylation and IL-8 and IL-13 levels. We also demonstrated with mass spectrometry that lanthionine was non-enzymatically acetylated by AcGSH, suggesting a possible mechanism.

Conclusion: In conclusion, our findings support the notion that lanthionine is a uremic toxin, which is strongly modified in its effects by the redox microenvironment.

P0096 **RENAL EXPRESSION AND CIRCULATING LEVELS OF CANONICAL WNT PATHWAY INHIBITORS IN THE EXPERIMENTAL MODEL OF EARLY CHRONIC KIDNEY DISEASE**

Evdokia Bogdanova[1], Olga Beresneva[1], Olga Galkina[1], Irina Zubina[1], Galina Ivanova[2], Marina Parastaeva[1], Vladimir Dobronravov[1]

[1]Pavlov University, Research Institute of Nephrology, St Petersburg, Russia and [2]Pavlov Institute of Physiology, Laboratory of cardiovascular and lymphatic systems physiology, St Petersburg, Russia

Background and Aims: Molecular mechanisms implicated in the initial stages of inorganic phosphate (Pi) imbalance in chronic kidney disease (CKD) remain poorly understood.

The aim of the study was to evaluate whether canonical Wnt pathway inhibitors (iWnt) involved in early response to Pi retention in CKD.

Method: Mild CKD was induced by 3/4 nephrectomy (NE, n=10) in spontaneously hypertensive rats (SHR) fed rat chow diet containing 0.8 % phosphate. Controls were sham operated SHR (SO, n=9). Duration of experimental exposure (NE or SO) was 4 months. Creatinine (Cr), albumin/ creatinine ratio (Alb/Cr), inorganic phosphate (Pi), fractional (FEPi) and daily Pi excretion (uPi24), intact parathyroid hormone (PTH), fibroblast growth factor 23 (FGF23), Klotho protein, sclerostin (SOST) and Dickkopf-1 (DKK1), *SOST* and *DKK1* mRNA expression in kidney, renal interstitial fibrosis (RF) were analyzed.

Results: Levels of Alb/Cr, serum Cr, RF and indices of Pi exchange in the experimental model corresponded to mild CKD with Pi retention (Table). No differences were observed in serum levels of Klotho, FGF23 and PTH in experimental group vs controls (Table). Serum SOST and DKK1 concentrations were significantly higher in NE group while the kidney expression of *SOST* and *DKK1* mRNAs decreased compared to SO (Table).

Conclusion: Early stages of experimental CKD are characterized by increased serum concentrations of sclerostin and Dickkopf-1 in the absence of Klotho, FGF23 or PTH levels alterations. The increase of circulating iWnt levels seems not to be associated with their renal biosynthesis and likely have a bone origin.

P0097

IDENTIFICATION OF TWO NOVELS SINGLE NUCLEOTIDE VARIANTS OF THE COMPLEMENT GENES IN A PATIENT WITH THE ASSOCIATION OF PREGNANCY ATYPICAL HEMOLYTIC UREMIC SYNDROME AND C3 GLOMERULOPATHY

GUSTAVO GRELONI[1], Federico Varela[1], Griselda Bratti[1], Guillermo Rosa Diez[1], Celia Dos Santos[2], Analia Sanchez Luceros[3]

[1]Hospital Italiano Buenos Aires, Nephrology, Buenos Aires, Argentina, [2]Academia Nacional de Medicina, Hemathology, Buenos Aires, Argentina and [3]Academia Nacional de Medicina, Hemathology, Buenos Aires, Argentina

Background and Aims: Advances in the past 2 decades have shown atypical hemolytic uremic syndrome (aHUS) to be a disorder of the alternative pathway of complement. Most aHUS cases involve sequence variations in genes encoding complement proteins The term pregnancy associated aHUS (P-aHUS) refer to the thrombotic microangiopathy (TMA) that result from uncontrolled complement activation during pregnancy or the postpartum period. P-aHUS is a devastating systemic disease, with high maternal mortality and morbidity rates, in the pre-eculizumab era. The term 'C3 glomerulopathy' (C3GN) encompasses a heterogeneous spectrum of immune-mediated nephropathies that share a common pathological feature, glomerular deposition of C3. This entity may progress to advanced stages of chronic kidney disease and shares a common genetic risk factors with aHUS. Even more, some authors even suggest that C3GN and aHUS represent two forms of a disease spectrum with a common pathogenic principle. Here, we report this rare association and describe the family genetic variants that could cause it

Method: We describe the clinical and laboratoy data of a patient with the association of aHUS and C3 Glomerulopathy. A genetic study was performed and her available relatives were also screened for mutations/polymorphisms in aHUS-associated complement genes. After extracting gDNA from whole blood (Wizard Genomic DNA Purification Kit, Promega), PCR products of coding sequences and intronic flanking regions of complement genes were sequenced by ABI PRISM 310 Genetic Analyzer (Applied Biosystems). In silico analysis for pathogenicity was completed with Polyphen2-HDIV, PhyloP/Phastcons (MutationTaster), SIFT and PANTHER. All the participants provided informed written consent

Results: In 3/2012 a 27-year-old patient, with no family history, started his current illness one month after his first natural birth, with acute renal failure and microangiopathic hemolytic anemia, demonstrating a severe TMA in a renal biopsy. Laboratory results showed low C3 serum levels, but C4 were normal, haptoglobine was undetectably low, and all ADAMTS13 parameters were normal. Her urine tests showed also glomerular hematuria and proteinuria in the nephrotic range. She was treated with plasmapheresis and fresh frozen plasma with hematological improvement, but hemodialysis was required for more than 3 months. Despite partial recovery of renal function, six months later reappeared anemia and developed severe arterial hypertension, congestive heart failure and progressive renal insufficiency. Diagnosis of aHUS was made and start treatment with eculizumab with progressive recovery of renal function in the following months. Nevertheless the C3 serum levels persisted low and the proteinuria and hematuria did not change even after long term treatment with eculizumab. Retrospectively, her urynalisis before the pregnant showed proteinuria and hematuria, and a revision of a renal biopsy revealed the presence of dominant C3 deposits in the immunofluorescence, and electrondense deposits in the electronic microscopy, suggesting the diagnostic of C3GN. In a genetic study two novel single nucleotide variants were founded (**CFH** c.575G>A, p.C192Y (exon 5) (NM_000186), predicted to be pathogenic by 4 of 5 available pathogenicity prediction programs; and **CFI** c.1189G>T, p.V397L (exon 11) (NM_000204), predicted pathogenic by 0 of 6 available pathogenicity prediction programs). (Figure 1)

Conclusion: We present here the family genetic bases of a patient who developed a C3GN and a aHUS with a different response to treatment with eculizumab. In this case we identified two novel genetic variants in the CFH and CFI genes in a patient with aHUS, who inherited one variant from each parent. Although the CFI variant is predicted to be benign, the CFH variant is predicted to be damaging. It is located in exon 5, which encodes a portion of the factor H protein implicated in binding to C3b

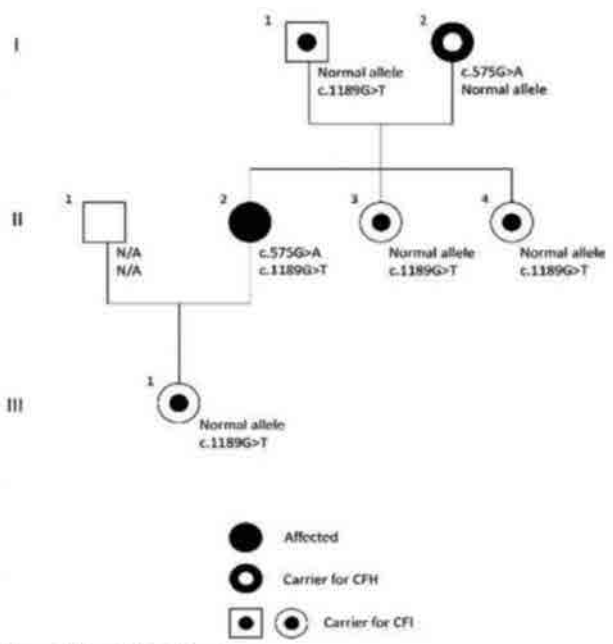


Figure 1 Family's pedigree.

Figure:

P0098 **CHANGES OF PERICYTE IN AGING KIDNEY**

Hyung Duk Kim[1], Eun Nim Kim[1], YONGJIE JIN[1], Ji Hee Lim[1], Yaeni Kim[1], Tae Hyun Ban[1], Cheol Whee Park[1], Bum Soon Choi[1]

[1]*Division of Nephrology, Department of Internal Medicine, The Catholic University, SEOUL, Korea, Rep. of South*

Background and Aims: In aging kidney, oxidative stress and inflammation lead to a decrease in renal function. Recent studies related to the aging process of the kidneys have shown that pericyte is a progenitor cell of myofibroblast, and the relationship between renal fibrosis and pericyte has been reported. In this study, we investigated the pericytes changes in aging kidneys and mechanism of aging-related pericyte changes.

Method: In vivo study, 2, 24-months-old mice and 18-month-old mice treated with pentoxifylline for 6 months were analyzed with western blot. And renal biopsy from KT donors were analyzed. Donors under age 25 were assigned to young group and donors over age 60 to old group.

Results: Changes of pericytes in mice and human renal tissues were consistent with those in the aging model. In the old age group, pericytes were decreased and interstitial fibrosis was increased. Western blot analysis in mice kidney revealed that IL-1β, IL-6 and TNF-α were significantly increased in old age and significantly decreased in pentoxifylline group. Angiopoietin 2 was increased in old age group and decreased in pentoxifylline group.

Conclusion: In aging kidney, pericytes have been shown to exhibit numerical reduction and loss of perivascular location as in the aging mice model. These changes in pericytes are thought to be induced by angiopoietin 2 excretion.

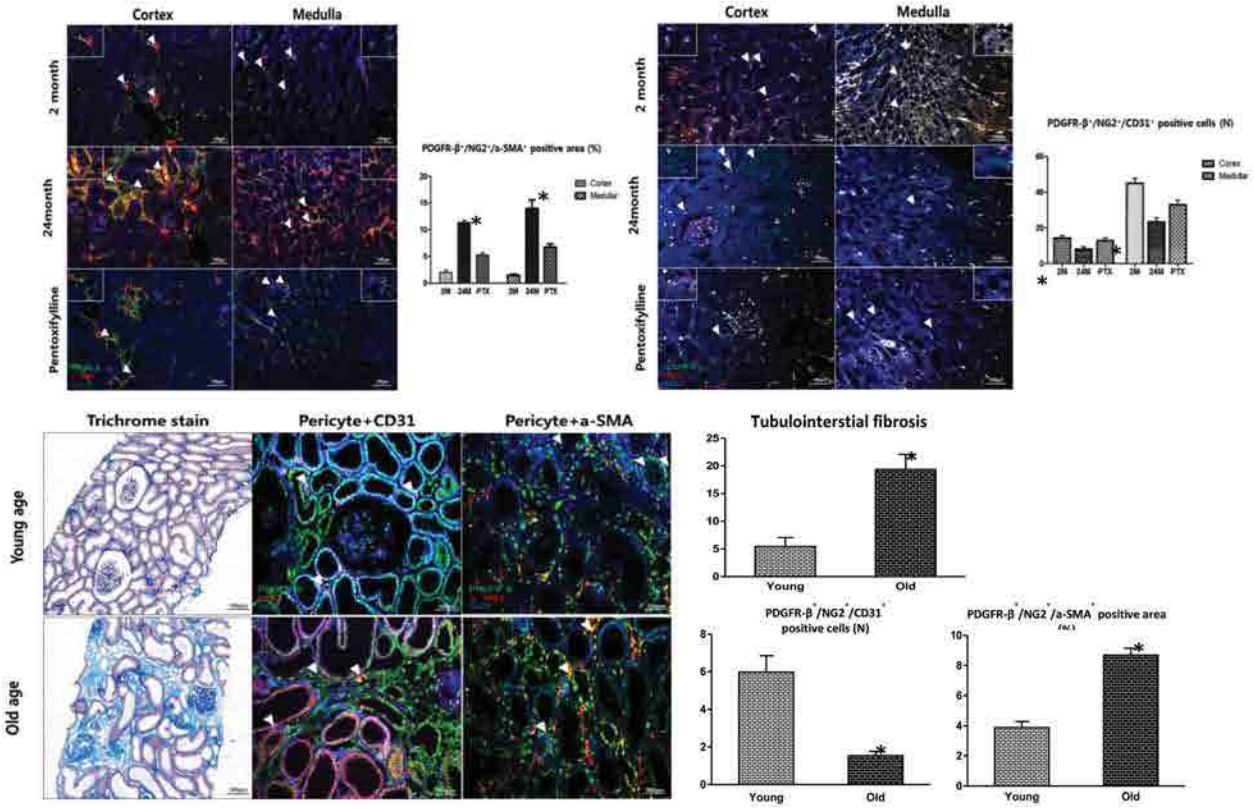


Figure:

P0099

CALCINEURIN INHIBITION, BUT NOT DEHYDRATION, IN RATS MIMICS HUMAN RENAL HISTOPATHOLOGY OF PATIENTS WITH CHRONIC INTERSTITIAL NEPHRITIS IN AGRICULTURAL COMMUNITIES (CINAC)

Gerd Schreurs[1], Cynthia Nast[2], Stuart Maudsley[3], Patrick D'Haese[1], Marc De Broe[1], Benjamin Vervaet[1]

[1]University of Antwerp, Laboratory of Pathophysiology, Antwerp, Belgium, [2]Cedars-Sinai Medical Center, Los Angeles, United States of America and [3]University of Antwerp, Receptor Biology Lab, Antwerp, Belgium

Background and Aims: CINAC patients present a newly discovered constellation of proximal tubular lysosomal lesions which is also observed in patients experiencing calcineurin inhibitor (CNI) nephrotoxicity, suggesting that CINAC is a toxin-induced nephropathy involving calcineurin inhibition. An alternate hypothesis advocates chronic heat stress/dehydration as the major etiological factor for CINAC. Here, we evaluated in rats to what extent heat stress/dehydration versus CNI exposure reflects proximal tubular CINAC histopathology.

Method: Wistar rats were divided in 3 groups. Group 1 (n=6) was given water ad libitum (control group). Group 2 (n=8) was water deprived for 10 hours per 24h, 5 days/week and were placed in an incubator (37°C) for 30 min/hr of water deprivation. Group 3 (n=8) underwent daily oral gavage with cyclosporine (50mg/kg body weight). Animals were weighed daily and urine was collected at day 3, 17 and 28. After 28 days, rats were sacrificed. Kidneys were collected for light (LM) and electron microscopic (EM) histopathological analysis as well as for cortical renal tissue proteomics.

Results: Cyclosporine rats developed focal cortical lesions mimicking those of CINAC patients: i.e. atrophic proximal tubuli with thickened basement membranes and associated tubulo-interstitial fibrosis, PASM staining demonstrating enlarged argyrophyllic granules in the affected proximal tubuli, LAMP1 immunofluorescent staining identifying a subset of these granules as lysosomes, and EM confirming the presence of enlarged lysosomes, some dysmorphic approaching CINAC lysosomes. In dehydrated rats, confirmed by urinary osmolality and fluctuating body weight associated with water deprivation, none of the cyclosporine features were observed. Proteomic analysis confirmed cellular toxicity by cyclosporine, whereas the dehydration group lacked any markers of such.

Conclusion: The histopathological analogy between CNI nephrotoxicity in rats and humans and CINAC suggests a toxicological etiology for CINAC. In rats, dehydration/heat stress alone does not lead to the constellation of proximal tubular lesions as observed in CINAC patients.

P0100

CALORIC RESTRICTION ALLEVIATES AGING-RELATED FIBROSIS OF KIDNEY THROUGH MIR-21 DOWNREGULATION IN EXTRACELLULAR VESICLES

Guang-Yan Cai[1]

[1]*Chinese PLA General Hospital, Department of Nephrology, State Key Laboratory of Kidney Diseases, National Clinical Research Center for Kidney Diseases, Beijing, P.R. China*

Background and Aims: The mechanism of renal interstitial fibrosis occurs with kidney aging is unknown. Caloric restriction and caloric restriction mimetics (CRM) alleviate aging-related-fibrosis. The aim of this study is to investigate whether extracellular microvesicles (EVs) derived from senescent cells facilitate fibrosis development in aging kidney and the potential signalling pathway involved in the process.

Method: In this study, animal experiments included 3-mon-old ad libitum(YAL) rats, 24-mon-old ad libitum(OAL) rats and 24-mon-old caloric restriction(OCR) rats, which was given 70% of OAL's for 8 months. Senescent cells were induced in proximal tubular epithelial cells(PTCs) by high glucose and further treated with resveratrol as CRM. The expression of miR-21, peroxisome proliferator-activated receptor(PPARα), hypoxia-inducible factor(HIF1α) in the kidney of rats and PTCs were examined. Epithelial to mesenchymal transition (EMT) and the related signalling pathway were detected by up- or down-regulation of miR-21, respectively.

Results: Long-term caloric restriction ameliorated senescent changes and aging-related fibrosis in aged ad libitum rat kidney. Caloric restriction blunted the increased expressions of miR-21 and HIF1α, the decreased expression of PPARα in renal tissue of old rats. High glucose induced PTCs senesence phenotype and EMT. miR-21 was detected in extracellular vesicles secreted by senescent PTC cells. CRMs resveratrol prevented EMT through downregulation of miR-21 in extracellular vesicles from the senescent PTC cells. Further, inhibiting miR-21 of donor senescent cells prevented the occurrence of EMT in recipient PTC cells. Finally, miR-21 induced EMT mainly through targeting PPARα protein and enhancing HIF1α expression.

Conclusion: This study demonstrated that miR-21-containing extracellular microvesicles derived from the senescent cells could facilitate tubular phenotype transition of neighbouring PTC cells via PPARα-HIF1α signalling pathway. Long-term caloric restriction and caloric restriction mimetics alleviate aging-related renal fibrosis through downregulation of miR-21 excretion.

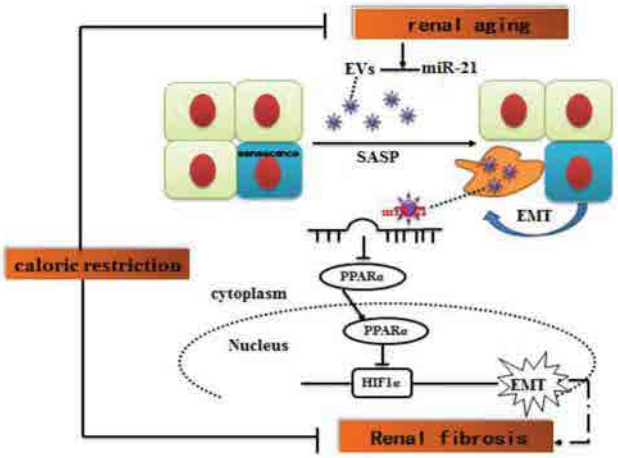


Figure:

P0101 **INHIBITION OF TUMOR NECROSIS FACTOR ALPHA ENHANCED ANTIFIBROTIC EFFECT OF EMPAGLIFLOZIN IN AN ANIMAL MODEL WITH RENAL INSULIN RESISTANCE**

Mohammed Keshawy[1,2], Hoda Mohammed[3]

[1]faculty od medicine, internal medicine, Ismailia, Egypt, [2]faculty od medicine, internal medicine, ismailia, Egypt and [3]faculty of pharmacy, biochemistry, zagazig, Egypt

Background and Aims: Insulin resistance (IR) has emerged as one of the main risk factors for renal fibrosis (RF) that represents a common stage in almost all chronic kidney disease. The present study aims to investigate the inhibitory effect of empagliflozin (EMPA "a sodium-glucose co-transporter 2 inhibitor") and infliximab [IFX "a tumor necrosis factor-α (TNF-α) antibody"] on RF in rats with induced IR.

Method: IR was induced by adding 10% fructose in drinking water for 20 weeks. Thereafter, fructose-induced IR rats were concurrently treated with EMPA (30 mg/kg), IFX (1 dose 5 mg/kg), or EMPA + IFX for 4 weeks, in addition to IR control group (received 10% fructose in water) and normal control (NC) group.

Results: Rats with IR displayed hyperglycemia, deterioration in kidney functions, glomerulosclerosis, and collagen fiber deposition in renal tissues as compared to NC. This was associated with downregulation of the renal sirtuin 1 (Sirt 1) expression along with higher renal tissue TNF-α and transforming growth factor-β1 (TGF-β1) levels. Both EMPA and IFX significantly modulated the aforementioned fibrotic cytokines, upregulated the renal Sirt 1 expression, and attenuated RF compared to IR control group. Of note, IFX effect was superior to that of EMPA. However, the combination of EMPA and IFX alleviated RF to a greater extent surpassing the monotherapy. This may be attributed to the further upregulation of renal Sirt 1 in addition to the downregulation of fibrotic cytokines.

Conclusion: These findings suggest that the combination of EMPA and IFX offers additional benefits and may represent a promising therapeutic option for RF.

P0102 A REVIEW OF RENAL BIOPSIES IN A LARGE UK RENAL CENTRE- A 20 YEAR EXPERIENCE

Amy Hudson[1], Smeeta Sinha[1]

[1]*Salford Royal NHS Foundation Trust, United Kingdom*

Background and Aims: Percutaneous renal biopsy is the mainstay of renal pathological diagnosis. Not only does it secure an accurate diagnosis, but also lends itself to guiding the prognosis of a myriad of renal disorders. An important diagnostic modality for nephrologists, they have contributed greatly to the field of nephrology, both in terms of the classification of diseases and assisting in understanding their pathogenesis. Adequacy of the tissue samples of at least ten to fifteen glomeruli is generally preferred. The aim of our retrospective study was to review the renal biopsies done in one large UK renal centre, namely Salford Royal Foundation Trust, over the last twenty years. This Trust covers a catchment area that serves approximately 1.5 million people.

Method: A list of all renal biopsies performed at Salford Royal Foundation Trust between January 2000 to January 2020 was generated by our pathology department. Following this, each individual biopsy report was reviewed. In addition to this, certain information was collated from individual patient records; namely patient demographics, the indication for biopsy, tissue type (native or transplant), histological diagnosis and outcomes. Our centre has an excellent electronic patient record (EPR). This enabled us to analyse full clinical data retrospectively for each case.

Results: Between January 2000 and January 2020 a total of 3555 renal biopsies were performed at Salford Royal Foundation Trust. These biopsies were performed solely by nephrology specialists and supervised trainees, under ultrasound guidance. 177.5 biopsies were performed on average, per year, ranging between 140 – 203.

90% of biopsies were performed on native kidneys, with 10% being performed on transplanted kidneys.

10% of biopsies had normal histology morphologically when reviewed by light microscopy. There diagnoses of these included entities minimal change disease and thin basement membrane disease most commonly.

IgA nephropathy was the most common glomerular pathology identified, in keeping with the wealth of published literature. There were over 525 biopsies done confirming IgAN as the primary pathology.

7% of biopsies had a crescentic glomerular pathology when examined histologically. The main causes included crescentic IgA nephropathy and anca-associated vasculitis.

Conclusion: Kidney biopsies have long been regarded as safe, minimally invasive procedures are of paramount importance to our diagnostic armamentarium. Our data echoes that of already published pathology series, IgAN being the most common glomerular pathology in our series. We further plan to analyse the various conditions and their outcomes in further detail.

P0103 **ANALYSIS OF GLOMERULAR IGG SUBCLASSES SWITCH IN IDIOPATHIC MEMBRANOUS NEPHROPATHY CLASSIFIED BY GLOMERULAR PHOSPHOLIPASE A2 RECEPTOR ANTIGEN AND SERUM ANTIBODY**

Haoyuan Cui[1], Chao Li[1], Hang Li[1], Yu-bing Wen[1], Xi-wei Yan[1], Yu-ting Hu[1], Xuemei Li[1], Limeng Chen[1], Yan Qin[1], Xuewang Li[1]

[1]*Peking Union Medical College Hospital, Nephrology division, Beijing, P.R. China*

Background and Aims: IgG subclass switch phenomenon in early pathological stage of idiopathic membranous nephropathy (IMN) was reported recently. However, the profile of serum anti-phospholipase A2 receptor (PLA2R) antibody and glomerular PLA2R antigen was not reported in previous studies. The objective of our study was to testify whether glomerular IgG subclass switch phenomenon was present in PLA2R-related and PLA2R-unrelated IMN, respectively.

Method: This was a retrospective study including 157 Chinese patients with biopsy-proven IMN in a tertiary referral hospital between September 2017 and November 2019. IMN patients were classified into PLA2R-related (n = 132) and PLA2R-unrelated (n = 25) subgroups. We compared the immunofluorescence intensity of glomerular IgG subclass between two groups among different electron microscopic (EM) stages.

Results: Positive rate of anti-PLA2R antibody was 56.0% (88/157) and glomerular PLA2R deposition was 75.8% (119/157). The intensity of IgG4 deposition in PLA2R-related group was stronger than that in unrelated group (2.1 ± 0.6 vs. 1.6 ± 0.7, P = 0.001). In stage I, IgG4 showed difference in predominant or co-dominant rate (pre/co rate) between two groups (P = 0.015). IgG4 was predominant in early stage (stage I) of both groups (pre/co rate 97% vs 57%). IgG1 was the less predominant subtype in stage I (pre/co rate 39% vs 43%). Pre/co rate of IgG3 declined with EM stage (P = 0.013).

Conclusion: IgG subclass switch were not found in PLA2R-related or unrelated IMN. IgG4 was the predominant IgG subtype in all stages of PLA2R-related IMN. The positive rate of glomerular PLA2R antigen was higher than serum PLA2R antibody.

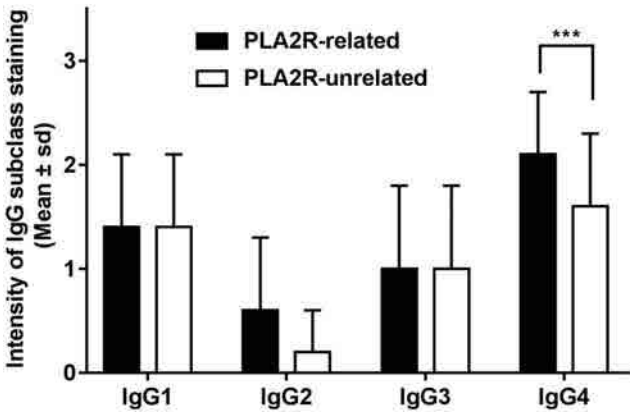


Figure. 1 The fluorescence intensity of IgG subclasses between PLA2R-related and PLA2R-unrelated group

*** P = 0.001

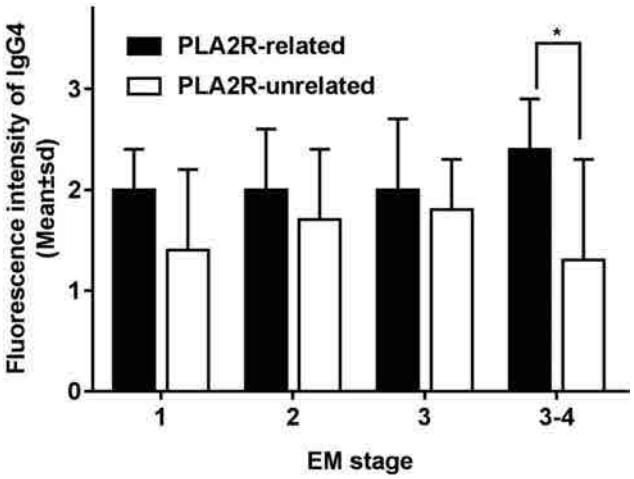


Figure 2. The fluorescence intensity of IgG4 between PLA2R-related and PLA2R-unrelated group

* P = 0.032

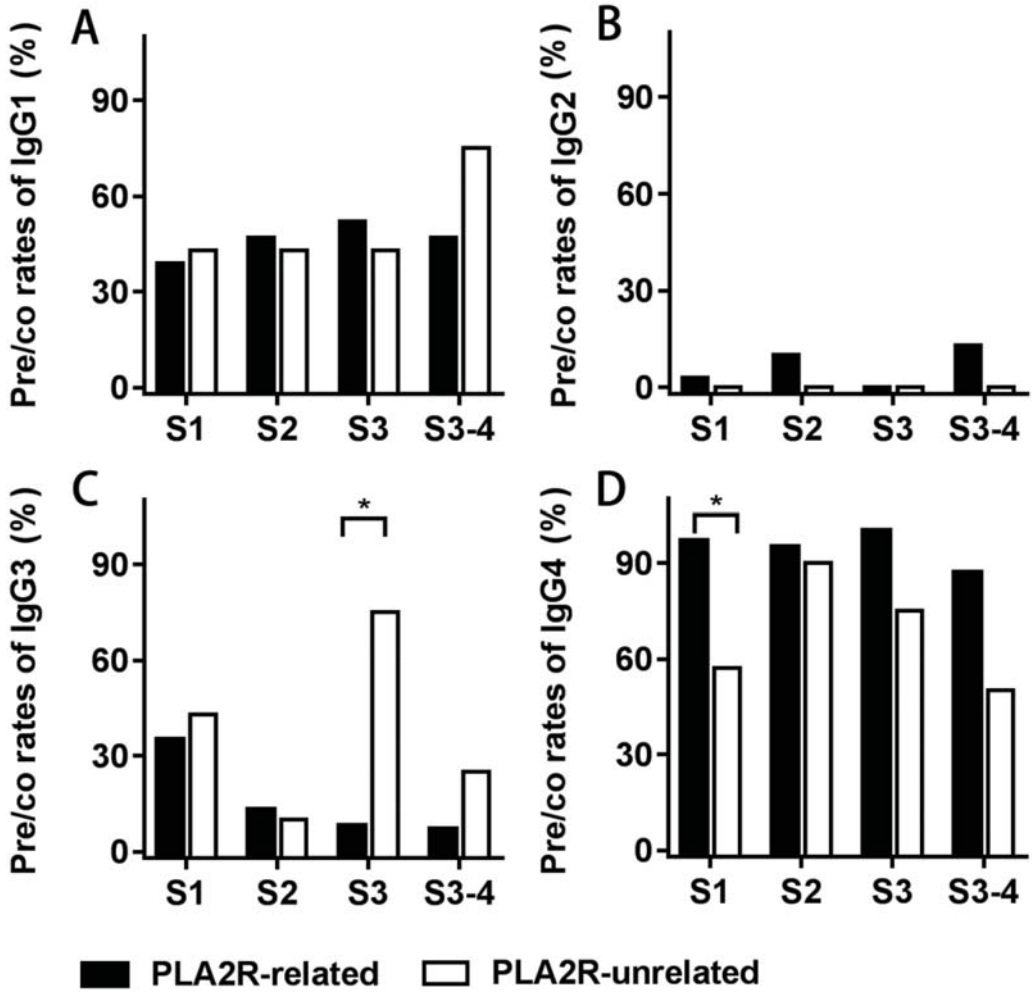


Figure 3. Predominant/co-dominant deposits of IgG subclasses in different EM stages S1: Stage 1; S2: Stage 2; S3: Stage 3; S3-4: Stage 3-4. * $P < 0.05$

P0104 THERAPEUTIC METFORMIN TREATMENT IS ABLE TO HALT THE PROGRESSION OF CHRONIC KIDNEY DISEASE IN RATS

Raphaelle Corremans[1], Benjamin Vervaet[1], Patrick D'Haese[1], Anja Verhulst[1]
[1]*University of Antwerp, Biomedical Sciences, Wilrijk, Belgium*

Background and Aims: Metformin, a biguanide drug, is the first-line oral antidiabetic agent used by 200 million patients suffering from type 2 diabetes mellitus. In the last decades, it has become clear that metformin exerts benign pleiotropic actions beyond its prescribed use and emerging data show protective effects against different age-related diseases. Additionally, recent preclinical and clinical data point towards a beneficial impact of metformin on the kidney. Current treatment strategies for chronic kidney disease (CKD) mainly focus on controlling important risk factors, such as high blood pressure and diabetes. To date, effective treatment directly targeting the kidney is lacking. Here, the ability of metformin to attenuate progression of already established CKD, independent from its effects on diabetes, was investigated.

Method: A rat model of adenine-induced CKD (n=64) was used. Metformin (200 mg/kg) or vehicle (1% carboxymethylcellulose) treatment, by daily oral gavage (7 days/week), was initiated after 4 and 5 weeks of adenine (0.25%) administration; *i.e.* after CKD had developed. Treatment was continued during 4 weeks until the end of the study (*i.e.* week 8 and 9, respectively). A constant dose volume of 10 mL/kg was used. The effect of metformin on renal function and histopathology was studied.

Results: Serum creatinine levels dramatically rose in vehicle-treated CKD rats: from 0.6 $\pm$ 0.1 mg/dL (week 0) to 1.3 $\pm$ 0.2 mg/dL (week 4) and 2.6 $\pm$ 1.2 mg/dL (week 5) and further to 5.7 $\pm$ 0.6 mg/dL (week 8) and 4.8 $\pm$ 1.1 mg/dL (week 9). Metformin treatment, which started after 4 and 5 weeks, prevented almost completely further increases in serum creatinine levels after 8 (2.0 $\pm$ 0.5 mg/dL) and 9 (2.9 $\pm$ 0.5 mg/dL) weeks compared to vehicle-treated CKD rats ($p<0.05$). The calculation of creatinine clearance confirmed these results. Histological examination of periodic acid–Schiff (PAS)-stained renal sections revealed less tubular dilation, epithelial flattening, brush border loss and, basement membrane thickening in metformin-treated CKD rats in comparison to vehicle-treated animals. The renal tubulointerstitial area percentage was significantly lower in metformin-treated CKD rats, as compared to vehicle treatment (from 35% and 41% tubulointerstitial area after 4 and 5 weeks, respectively, to 50% and 53% in vehicle-treated CKD rats and 34% and 41% in metformin-treated CKD rats after 8 and 9 weeks, respectively). Leukocyte common antigen (CD45)-staining revealed significantly less infiltration of inflammatory cells in metformin-treated CKD rats after 9 weeks (8%) as compared to the vehicle-treated CKD rats (12%). Semiquantitation of proliferating cell nuclear antigen (PCNA)-staining at 9 weeks showed that the amount of tubules containing more than 50% proliferating cells were increased, whereas PCNA-negative tubules were decreased in metformin-treated CKD rats compared to vehicle-treated CKD rats ($p<0.05$) .

Conclusion: Therapeutic metformin treatment is able to attenuate the progression of pre-existing adenine-induced CKD in rats.

P0105 THE ROLE OF PROTEOGLYCANS IN GLOMERULAR PHYSIOLOGY AND PATHOPHYSIOLOGY

Alina Khramova[1], Kerstin Ebefors[1], Jenny Nyström[1]

[1]*University of Gothenburg, Physiology, Gothenburg, Sweden*

Background and Aims: Damage to the filtration barrier in the kidney may result in proteinuria, a hallmark of kidney disease. The glomerular filtration barrier consist of 3 layers: the endothelial cells with their endothelial surface layer (ESL), the glomerular basement membrane and podocytes. The ESL is rich in negatively charged molecules, such as proteoglycans (PGs). The negatively charged molecules restrain the flow of charged molecules, as albumin, over the barrier. Loss of ESL has been shown to lead to proteinuria without damage to the other structures of the filtration barrier. In order to gain further knowledge about the function and composition of the glomerular ESL we eluted the glomerular ESL from rats and analyzed the PG content as well as the effect of loss of the ESL on the function of the glomerular filtration.

Method: The basic principles of ion exchange chromatography were applied in this study. In order to elute highly negatively charged proteoglycans of the ESL, we used 1 M NaCl solution (HS). 1 M mannitol (HO) was included to evaluate osmotic effects. A control fraction was eluted with normal saline solution (0,15 M NaCl) (NS). Solutions were introduced intraarterially to rat kidneys under anesthesia *in vivo*. Venous effluent was collected and analyzed using proteomics and mass spectrometry. Fractional clearance of albumin was measured as well as GFR. Electron microscopy (EM) was used to investigate changes to the filtration barrier and the thickness of the glomerular ESL. Immunohistochemistry was used to confirm the presence of identified PGs in human tissue.

Results: We identified 15 PGs and PG candidates in ESL as well as hyaluronan. The most abundant PGs were lumican, glypican-1, syndecan-4, perlecan, podocan, decorin, serglycan, agrin and biglycan. In general, PGs were found in in all HS, NS and HO fractions, but in higher yields in the HS samples. EM demonstrated that the glomerular ESL thickness was significantly reduced in HS perfused rats – 28% ($p<0.05$) compared to rats perfused with NS. Rats perfused with HS also had increased fractional clearance of albumin compared to NS and HO, and a large reduction of GFR 10 minutes after perfusion.

Conclusion: The ESL itself represents a dynamic structure with significant molecular turnover and is formed by PGs, glycosaminoglycans, glycoproteins and soluble proteins. In our study, we identified several PGs in the glomerular endothelial ESL. We show that loss of ESL leads to increased albumin fractional clearance and reduction in GFR after perfusion, strongly suggesting that the ESL is important for preventing proteinuria. Characterizing the composition of the glomerular ESL is therefore of great importance, and can give new possible targets for treatment of proteinuria.

P0106 **URINE COMPLEMENT FRAGMENTS ARE ASSOCIATED WITH KIDNEY FUNCTION AND DISEASE ETIOLOGY**

Tianlin He[1], Joachim Beige[2,3], Justyna Siwy[1], Igor Golovko[2], Martin Pejchinovski[1], Jochen Metzger[1], William Mullen[4], Antonia Vlahou[5], Harald Mischak[1,4]

[1]Mosaiques Diagnostics GmbH, Hannover, Germany, [2]Hospital St. Georg, Department of Nephrology and Kuratorium for Dialysis and Transplantation Renal Unit, Leipzig, Germany, [3]Martin-Luther-University Halle/Wittenberg, Germany, [4]University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom and [5]Biomedical Research Foundation Academy of Athens, Athens, Greece

Background and Aims: Changes in complement factors have been associated with chronic kidney disease, most prominently in the context of C3 glomerulopathy. Based on these reports, the hypothesis was generated that specific urine complement fragments are associated with kidney disease etiologies, and progression of the disease may be reflected by changes in these proteins or peptides. In this study, we aimed at investigating the occurrence of complement fragments in urine, and their association with kidney function in general and disease etiology in particular.

Methods: Urine samples from patients with kidney disease of different etiologies and control subjects with normal kidney function were investigated using tandem mass spectrometry coupled with capillary electrophoresis and liquid chromatography to identify complement derived peptides based on their amino acid sequence. Subsequently, distribution of these peptides in the different kidney disease etiologies and normal kidney function was investigated via analysis of datasets recorded in the human proteome/peptidome database. All datasets, where eGFR was available and at least one of the complement peptides detected, were included.

Results: Twenty one different urinary peptides derived from complement could be identified. These peptide fragments originated from the complement factors C3, C4A and C4B, and CFB. Further investigation of 4557 datasets recorded in the urine proteome/peptidome database meeting the aforementioned inclusion requirements (eg available eGFR values and with at least one of the complement peptides detected), revealed, for most C3-derived peptides, an inverse, while for the majority of peptides derived from CFB, a positive association with eGFR.

Sequence	Complement X	rho	p	n
EGVQKEDIPPADLSDQVP	C3	-0.13	0.034	258
EGVQKEDIPPADLSDQVPDTESETRIL	C3	-0.10	<0.0001	1564
EGVQKEDIPPADLSDQVPDTESETRILLQ	C3	0.13	0.0002	906
LQGTPVAQMTEDAVDAERLKHL	C3	-0.25	<0.0001	833
IGGLRNNNEKDMALT	C3	-0.09	0.21	395
LTTAKDKNRWEDPGKQLYNVEAT	C3	-0.16	<0.0001	643
QALAQYQKDAPDHQELN	C3	-0.32	<0.0001	257
YQKDAPDHQELNLDVS	C3	-0.29	0.005	91
TLTKAPVDLLGVAHNNL	C4A	0.07	0.52	87
APVDLLGVAHNNL	C4A	-0.36	0.0004	91
LGVAHNNL	C4A	0.04	0.29	402
TLTKAPADLRGVAHNNL	C4B	0.01	0.95	95
TKAPADLRGVAHNNL	C4B	-0.28	<0.0001	360
DELPAKDDPDAPLQPVTP	C4B	-0.05	0.1	802
FLSSLTETIEGVDAEDGHGPGEQQ	CFB	-0.38	0.0203	37
LSSLTETIEGVDAEDGHGPGEQ	CFB	0.01	0.17	1285
LSSLTETIEGVDAEDGHGPGEQQ	CFB	-0.23	<0.0001	2159
LTETIEGVDAEDGHGPGEQQ	CFB	0.11	0.019	452
TETIEGVDAEDGHGPGEQ	CFB	0.04	0.0466	2170
TETIEGVDAEDGHGPGEQQ	CFB	0.19	<0.0001	505
SSLTETIEGVDAEDGHGPGEQQ	CFB	0.02	0.758	212

The table lists the detected complement derived peptides, the parental protein (Complement X), rho and p-value of the association with eGFR, and the number of samples (n) where the peptide was detected.

When investigating the urine complement fragments, as a result of disease etiology, disease-specific distribution was detected, indicating a distinct association of complement factors and associated proteases, depending on disease etiology. As an example, the peptide distribution in AKI, IgA-Nephropathy (IgA-N) and vasculitis is shown in the Figure.

Conclusion: Multiple complement-derived peptides are significantly associated with kidney function, and with certain kidney disease etiologies, such as AKI, IgA-N or vasculitis. Proteomic screening of these complement factors may provide a basis, not only for non-invasively assessing kidney disease, but also for an opportunity to develop novel drugs; the latter, via targeting the associated proteases responsible for the release of these complement-derived peptides, in a specific kidney disease manner, in urine.

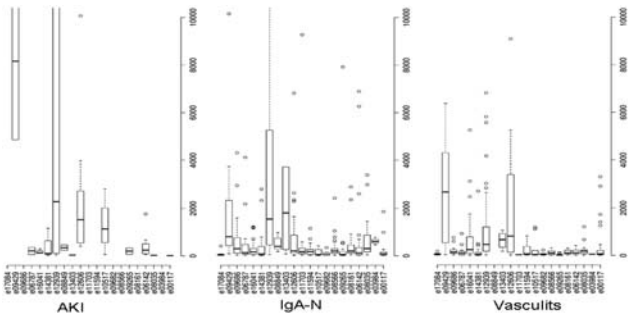


Figure: Distribution of specific complement fragments in Acute Kidney injury (AKI), IgGA-Nephropathy, and ANCA-associated vasculitis.

P0107 DIGITAL PATHOLOGY FOR THE ROUTINE DIAGNOSIS OF RENAL DISEASES: A STANDARD MODEL

Vincenzo L'Imperio[1], Franco Ferrario[1], Manuela Nebuloni[2], Federico Pieruzzi[3], Renato Alberto Sinico[3], Fabio Pagni[1]

[1]Universita' di Milano-Bicocca, Medicine and Surgery, Pathology, Monza, Italy, [2]Universita' di Milano (La Statale), Biomedical and clinical sciences (L. Sacco), Milan, Italy and [3]Universita' di Milano-Bicocca, Medicine and Surgery, Nephrology, Monza, Italy

Background and Aims: Whole-slide imaging (WSI) and virtual microscopy are useful tools implemented in the routine pathology workflow in the last 10 years, allowing second-opinion on definitive or frozen-section diagnosis (telepathology) and demonstrating a substantial role in multidisciplinary (MDT) meetings and education (Griffin et al, Histopathology. 2017;70(1):134-145). The FDA approval of the clinical employment of this technology led to the progressive digitalization of routine pathological practice. In this setting, a recent work explored the usefulness of this technology applied to renal biopsies, stressing the possibility to create integrate networks to share cases for diagnostic and research purposes (Barisoni et al, Clin Kidney J. 2017;10(2):176–187). Here is discussed the 5-years experience of an Italian Renal Pathology service in which telepathology is a definitive standard of care.

Method: Renal biopsies were collected in the Anatomic Pathology Department of San Gerardo Hospital, Monza, Italy from 14 different Italian Nephrology centers (9 from the North, 1 from the Center and 4 from the South of Italy) from January 2015 to December 2019. After the routing processing of the tissue, biopsies were scanned with Aperio CS2 device for light microscopy and Aperio ScanScope FL for immunofluorescence (Leica Biosystem, Illinois, USA, Figure 1A). Digital slides were then imported in the Spectrum platform along with the final report and additional pictures (eg. electron micrographs and special stains) such as shown in Figure 1B.

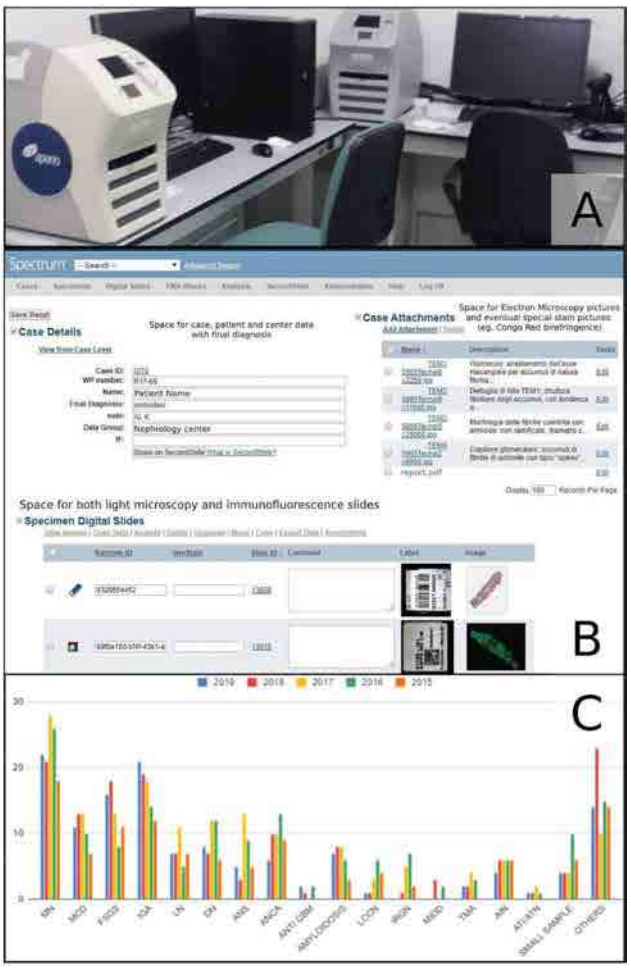


Figure 1: Legend: (A) Light microscopy (left) and immunofluorescence (right) scanners used in our service. (B) Example of the web page of a single renal biopsy case that can be accessed by authorized pathologists and nephrologists with appropriate credentials. (C) Trend of final diagnosis in the 5-years lapse of time.

Results: In 5 years, 704 renal biopsies (interval 110-160) were scanned and analysed with a turnaround time of around 2-3 working days. The most frequent diagnosis was represented by MN (16%, 115 cases, interval 18-28) followed by IgA nephropathy (12%, 84 cases, interval 12-21), FSGS (9%, 66 cases, interval 8-18), MCD (8%, 54 cases, interval 7-13), paucimmune crescentic GN (7%, 48 cases, interval 6-13), diabetic nephropathy (6%, 45 cases, interval 6-12), lupus nephritis (5%, 37 cases, interval 5-11), arterionephrosclerosis (5%, 35 cases, interval 5-13), amyloidosis (5%, 32 cases, interval 3-7) and tubulointerstitial nephritis (4%, 28 cases, interval 4-6). Only 4% of cases (28, interval 4-10) were suboptimal for the diagnosis and the remaining 19% (132 cases, interval 20-36) were characterized by rarer diseases, as detailed in Figure 1C.

Conclusion: In renal pathology the assessment of biopsies with different techniques (light and electron microscopy and immunofluorescence) is mandatory and can represent an obstacle in the routine employment of digital pathology. In the present experience we demonstrated the feasibility and sustainability of the digital switch in renal pathology routine, thanks to appropriate devices and platform. This led to store cases for teaching and MDT meetings, allowing to maintain the same short turnaround time for the diagnosis. Moreover, the employment of WSI technique can allow to couple the proteomic features of renal tissue with the classic morphological aspects of the diseased parenchyma (L'Imperio et al Proteomics Clin Appl. 2016 Apr;10(4):371-83). This approach, along with the possibility of a multicentric enrollment of patients, led to the publication of 6 scientific papers in highly impacted journals, further confirming the positive role of digital pathology in this field.

P0108 RESOLVIN D2 TREATMENT AMELIARATES ANGIOTENSINII-INDUCED RENAL INJURY

Raquel Rodrigues-Díez[1,2,3], Lucía Serrano Díaz del Campo[1,3], Ana García Redonde[1,2,3], Mercedes Salaices[1,2,3], Ana Briones[1,2,3]

[1]IdiPAZ, Madrid, Spain, [2]CIBERCV and [3]Facultad De Medicina, Pharmacology and therapeutic, Madrid, Spain

Background and Aims: Renal inflammation is a protective response to several types of renal insults. Resolution is the ideal outcome of acute inflammation, however fail in resolution leads to chronic inflammation, progressive renal fibrosis and finally to end-stage renal failure. Recently is has been established that resolution of inflammation is mediated not only by disappearance of pro-inflammatory signals (including lipid mediators such as leukotrienes and prostaglandins) but also by activation of specialized pro-resolving mediators (SPM) including lipid mediators such as protectins (PD) and resolvins (Rvs) derived from omega-3 fatty acids precursors.

Several authors have explored the role of different SPM in the treatment of experimental nephropathies. In the experimental model of bilateral ischemia/reperfusion pro-resolving mediators such as RvDs and PD1 were endogenously produced in the kidney in response to the injury. In this model, administration of RvD1 or PD1 before the ischemia or after the reperfusion showed a renoprotective effect. Moreover in the unilateral ureteral obstruction model RvE1 and RvD1administration inhibited interstitial fibrosis.

One of the key mediators of renal injury is Angiotensin II (AngII) that participates in the pathogenesis of renal diseases through the regulation of two key processes, inflammation and fibrosis. Therefore, the aim of this study was to investigate the effect of the pro-resolving mediator Resolvin D2 (RvD2) in AngII-induced renal injury

Method: We used C57BL/6 mice that were infused with AngII (1440 μg/kg/day o 1000 ng/Kg/min). After 7 days of AngII treatment, when hypertension was already established, mice were treated with RvD2 (100ng/mouse ip) every two days for additional 7 days. At day 14 mice were sacrificed and kidneys were removed for protein and gene expression analysis and for histological examination.

Results: In our experimental model RvD2 ameliorated renal injury assessed by expression of NGAL both at mRNA and protein levels. In addition AngII-treated mice presented significant reduction in glomerular size that was increased by RvD2 treatment reaching values comparable to control. In addition, RvD2 inhibited the activation of inflammatory markers including COX-2, IL-6 and MCP-1 induced by AngII and reduced the number of $F4/80^{+}$ infiltrated macrophages. We next evaluated the effect of RvD2 in the activation of NFκB, a key signaling pathway in inflammation. We observed that RvD2 inhibited AngII-induced NFkB activation. Moreover, RT-PCR analysis indicated that Ang II increased the expression of Tenascin C, a component of the fibrogenic niche in kidney fibrosis, as well as Type-I Collagen and Fibronectin and these levels were significantly reduced by the treatment with RvD2. These results were also confirmed by Masson-Goldner trichrome staining. Importantly, these effects were independent of changes in blood pressure. We finally studied whether the effects of RvD2 might be related to the modulation of RvDs endogenous biosynthesis pathway or RvD2 receptor GPR-18. mRNA analysis showed that AngII did not modified the expression levels of RvD2 biosynthesis enzymes including LOX-5 and LOX-15 nor GPR-18. However, RvD2 treatment increased the expression of LOX-15 and GPR-18 and down-regulated LOX-5 indicating a possible auto-regulatory mechanism of RvD2

Conclusion: Our results evidence a dual beneficial effect of the pro-resolvin mediator RvD2 in Ang II-induced renal injury as RvD2 treatment reversed not only renal inflammation but also tubulo-interstitial fibrosis. Hence, synthetic pro-resolving mediators would be an interesting therapeutic option for renal diseases.

P0109 EVALUATION AND COMPARISON OF TWO RENAL HISTOLOGICAL CLASSIFICATIONS OF IGA VASCULITIS.

Zhour EL OUAFI[1], Jason Shourick[2], Clement Danthu[1], Evangeline Pillebout[4], Alexandra Audemard[5], Eric Thervet[6]

[1]CHU limoges, Nephrologie, LIMOGES, France, [2]université paris sud, Bio informatiques/ statistiques, Paris, France, [4]Hopital Saint Louis, APHP, Nephrologie, paris, France, [5]CHU Caen, Medecine interne, Caen, France and [6]HEGP APHP, Nephrologie, paris, France

Background and Aims: Primary IgA nephropathy (IgAN) and IgA vasculitis nephritis (IgAVN) share common features e.g. clinical, histological, pathophysiological. Their prognosis assessment is usually considered to be dependent on histological findings which are therefore useful to establish therapeutic intervention.

The validated MEST-C classification is widely used for IgAN. Regarding IgAVN, various classifications are used in clinical practice. However, there is no consensus regarding their feasibility, correlations with renal outcome and their usefulness regarding therapeutic decisions. The aim of this study was to compare the Pillebout and Nochy French classification (PNC), created as a specific IgAVN prognosis scoring system MEST-C classification.

Method: Renal biopsies (RB) of patients with IgAVN were selected from two previous national IGAV cohorts and then reclassified according to the MEST-C and PNC classifications. For both classifications, the primary endpoint was the renal remission defined as a final glomerular filtration rate (GFR) greater than 60 ml / min. We also analyse: a) the renal survival defined as the absence of dialysis or transplantation; b) clinical-pathological correlation between the 2 classifications and c) the interobserver reproducibility.

Results: 372 RB from 316 patients were analysed, with 240 patients followed for at least 1 year. The median age was 48 yrs (14 to 86), with a sex ratio of 1.76 for men and a median follow-up of 4.3 years (range 1 to 22.7). Renal impairment was more severe over the age of 60 yrs. The presence of general signs, the initial GFR, and hypertension were significantly associated with renal survival. Proteinuria and albuminemia were associated with proliferative lesions (MEST-C score: E, C). The fibrous lesions (MEST-C: T and PNC stage V) were associated with GFR at the end of the follow-up. No significant association was found between the PNC stage and renal survival. Univariate analyses showed significant association with the primary outcome for the MEST-C T variable (p=0.02). However, by multivariate analysis, this association did not persist. The correlation between the observers was better for MEST-C compared with PNC (0.87 vs. 0.75).

Conclusion: Our results suggest that MEST-C classification has a good clinical and pathological correlation, a good reproducibility, and is interesting to evaluate the long-term renal outcome of patients with IgAVN. However, the correlation is still not perfect. Indeed, fibrosis was the only pathological feature independently associated with renal endpoints. We suggest that MEST-C is a scoring system which is not fully adapted due to the predominant inflammatory mechanism in IgAVN unlike IgAN. PNC should not be used because of the poor interobserver correlation. It is important to identify new specific IgAVN histological markers, taking into account the inflammatory mechanism, to ensure a more accurate prognostic classification, useful to guide therapeutic strategy.

P0110 DPP4- INHIBITOR LINAGLIPTIN ACCELERATES RESOLUTION OF CRESCENT FORMATION IN A RAT MODEL OF ANTI-GBM GLOMERULONEPHRITIS

Anna-Lena Mayer[1], Nadja Ebert[1], Thomas Klein[2], Kerstin Amann[1], Christoph Daniel[1]

[1]Friedrich-Alexander-Universität Erlangen-Nürnberg, Department of Nephropathology, Erlangen, Germany and [2]Boehringer Ingelheim Pharma GmbH & Co. KG, Cardio-metabolic Diseases, Ingelheim, Germany

Background and Aims: Crescent formation is a severe glomerular damage in the pathogenesis of different kidney diseases. However the exact pathomechanism of crescent formation is unclear up to now. In human kidney biopsies we observed high dipeptidyl peptidase 4 (DPP4) expression in early crescent formation. Therefore, we investigated the potential involvement of DPP4 in the pathogenesis of crescentic anti-GBM nephritis in a rat model using a DPP4- inhibitor independent of his present use in the treatment of type 2 diabetes.

Method: Anti-GBM nephritis was induced in Wistar Kyoto rats for investigation of short and long term effects of the DPP4- inhibitor linagliptin treatment (3 mg/kg bw). In the short term experiment (endpoint 2 weeks) linagliptin treatment was started either with model induction or one week later. In the long term experiment (endpoint 8 weeks) linagliptin treatment was started either on day 0 or on week 4. In both experiments we included an untreated healthy and anti-GBM nephritic group. All groups consisted of 11 animals. Kidney function was monitored on weeks 1, 2, 3, 5 and 8. Kidney tissue was used to determine DPP4 expression and activity, morphologic changes and mRNA expression.

Results: Similarly to our observation in human kidney biopsies the in situ DPP4 activity and DPP4 expression were both increased in nephritic glomeruli especially within the crescents. Linagliptin could almost completely inhibit all renal DPP4 activity without any effect on DPP4 expression. Short-term treatment had no significant effect on crescent formation. However, long-term preventive treatment resulted in reduced number of crescents (51±3% vs 65±3%), glomerulosclerosis (score 1.2±0.07 vs 1.6±0.1), tubulointerstitial injury (score 1.2±0.1 vs 1.8±0.2), renal fibrosis (score 1.3±0.13 vs 1.9±0.14) and proteinuria (265±29 vs 363±22 mg/24h) compared to untreated nephritic rats. Therapeutic intervention with linagliptin resulted in weaker amelioration of renal disease at week 8, but also significantly reduced renal fibrosis (score 1.4±0.13 vs. 1.9±0.14) and crescent formation (52±4% vs. 65±3%) compared with vehicle. About 20% of all glomeruli showed Pax8+ parietal epithelial cells (PECs) on the tuft in short term treatment, being significantly reduced by therapeutic linagliptin treatment on day 14. In the long term experiment the number of Pax8+ PECs on glomerular tuft was reduced by more than 50% in both treatment groups and confirmed by quantitative mRNA analysis using isolated glomeruli. Despite the number of Pax8-positive cells on glomerular tuft was reduced by linagliptin therapy, a subpopulation of PECs positive for the transcription factor SOX9 was significantly increased on glomerular tuft compared to healthy and non-treated rats on day 14.

Conclusion: DPP4- inhibition with linagliptin reduced Pax8+ cells on glomerular tuft, indicating accelerated resolution of formed crescents and improvement in renal injury. This DDP4 effect might be mediated by differential regulation of a subpopulation of PECs expressing the transcription factor SOX9.

P0111

AN UPDATE ON EPIDEMIOLOGY AND CLINICOPATHOLOGIC CORRELATION OF RENAL BIOPSY FINDINGS - A TERTIARY KIDNEY CENTRE REPORT

Hadia Bagherzadegan[1], Shahrzad Ossareh[2], Mitra Mehrazma[3,4]

[1]Iran University of Medical Sciences- Rasoul-Akram General Hospital, Internal Medicine-Nephrology, Tehran, Iran, [2]Iran University of Medical Sciences- Hasheminejad Kidney Center, Medicine- Nephrology, Tehran, Iran, [3]Iran University of Medical Sciences-Hasheminejad Kidney Center, Pathology, Tehran, Iran and [4]Iran University of Medical Sciences- Oncopathology research center, Pathology, Tehran, Iran

Background and Aims: Several studies have reported the results of renal biopsies from different registries and single centres. In most series focal and segmental glomerulosclerosis (FSGS), IgA nephropathy (IgAN), membranous glomerulopathy (MG) and lupus nephritis (LN) have been reported as the most common primary and secondary glomerulonephritis (GN). This study was conducted to update the reports of our hospital, as the main referral kidney centre of the country.

Method: Data from 4713 patients, who had undergone renal biopsy between Sept-1999 to Sept.-2019 were extracted from the GN data registry of our centre. Demographic data, renal syndrome at presentation and laboratory findings were studied. Almost all kidney specimens had been studied with light and immunofluoroscent microscopes and in selected cases with electron microscope. Nephrotic syndrome (NS) was defined as proteinuria >3.5 g/day or >3 g/day, if associated with hyperlipidemia, hypoalbuminemia and edema. Nephritic syndrome was defined as proteinuria >500 mg/day and hematuria, with or without hypertension and/or serum Cr (SCr) ≥1.4 mg/dl. Subnephrotic (SN) proteinuria was defined as proteinuria of 200 -3000 mg/day. Acute kidney injury (AKI) was defined as increase in SCr >1.4 during the past few days to weeks before admission.

Results: The most frequent type of renal pathology was MG (25.2%) followed by FSGS (13.6%), IgAN (12%), LN (8.9%), minimal change disease (MCD) (7%), crescentic GN (6.2%) and paraprotein associated GN (4.3%). The prevalence of different renal pathologies changed significantly over time (p-value:0.000) (figure).The most common clinical presentation was NS (60.2%), followed by SN proteinuria (15.2%), nephritic syndrome (12%) and AKI (7.5%). Age, sex, clinical syndrome at presentation and hypertension were significantly different between major pathological diagnostic groups (p=0.000). Table shows the detailed clinical features of the most important glomerulonephritides in our centre. Figure shows the changes in prevalence of each pathologic diagnosis over 21 years.

Conclusion: In our series the most common types of GN were MG, FSGS and IgAN, which are the most frequent glomerulonephritides in other biopsy series with various orders. Most of our patients presented with NS, followed by SN proteinuria. The relative frequency of MPGN and LN have reduced and FSGS has increased over time.

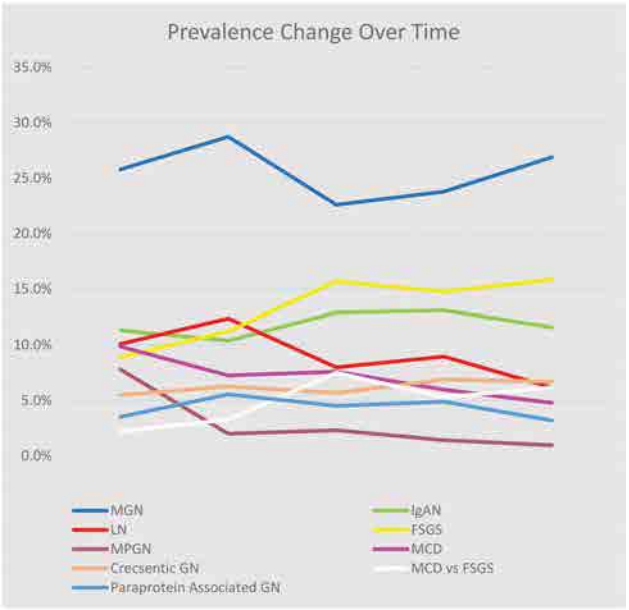


Figure:

Demographic and clinical manifestations of the main pathologic diagnoses

Pathologic Diagnosis	MGN	FSGS	IgAN	LN	MCD	Crescentic GN	MCD vs FSGS	Paraprotein Associated	MPGN	Others	Total	p-value
Frequency (%)	1189 (25.2%)	642 (13.6%)	567 (12%)	419 (8.9%)	328 (7%)	294 (6.2%)	241 (5.1%)	204 (4.3%)	128 (2.7%)	701 (14.9%)	4713 (100%)	
Mean age ±SD	40.8± 15.2	39.6±15.6	37.7±12.9	31.5±11.3	33.6±15.1	43.5±17.1	37.8± 15	54.6± 15.2	35.1± 17.8	44.5±17.3	40±16	<0.001
Male: Female	1.3: 1	1.5: 1	2.6: 1	1: 3.8	1:1	1.3: 1	1: 1	1.6: 1	1.5 : 1	1.5: 1	1.3: 1	<0.001
NS (%)	78.5	52.2	46	54.1	80.1	49.8	59.5	69.6	76.2	39.1	60.2	<0.001
SCr≥ 1.4 (%)	22.7	55	65.8	48.1	28.1	94.5	34.9	71.9	64.1	85.8	52.7	<0.001
Hypertension(%)	34.6	49.8	50.5	44.6	24.8	56.2	29.2	34.9	64.5	59.3	44.3	<0.001

P0112

BOWMAN'S CAPSULE RUPTURE ON RENAL BIOPSY IMPROVES THE OUTCOME PREDICTION OF ANCA-ASSOCIATED GLOMERULONEPHRITIS CLASSIFICATION

Vincenzo L'Imperio[1], Gisella Vischini[2], Fabio Pagni[1], Pietro Manuel Ferraro[2]

[1]*University of Milano - Bicocca, Medicine and surgery, Pathology, monza, Italy and* [2]*Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Nefrologia, roma, Italy*

Background and Aims: ANCA-associated vasculitis is the most common cause of rapidly progressive glomerulonephritis (GN) and can lead to ESRD or death, even after aggressive immunosuppressive therapies (Jones et al, N Engl J Med, 363(2010), 211-220). The histological assessment of renal tissue can help in predicting the outcome and a 4-tiered classification based on glomerular lesions has been proposed to stratify these cases (Berden et al, J Am Soc Nephrol, 21(2010), 1628-1636). Subsequent studies, however, failed to confirm its predictive value (Tanna et al, Nephrol Dial Transplant, 30(2015), 1185-1192), stressing the need of new prognostic markers of the disease. The present study investigates whether additional histological features can improve the performance of the current classification in predicting the outcome of these patients.

Method: A retrospective series of biopsy-proven paucimmune crescentic GN has been collected between January 2012 and June 2018 from two Italian centers (San Gerardo Hospital, Monza and Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma). After the exclusion of patients with negative/unavailable serum ANCA testing, lacking clinical data, less than 12 months of follow-up, less than 5 glomeruli per biopsy and coexisting glomerular diseases, a final cohort of 52 cases was selected. Demographic and clinical data at the time of the diagnosis are reported in Figure, panel A. Renal biopsies have been reviewed by two experts in renal pathology and scored for multiple glomerular, tubulointerstitial and vascular lesions, as well as classified following the 4-tiered schema. The outcome of interest was time to need for RRT or death, whatever occurred first. Cox proportional hazards regression models were constructed with time to composite event, loss to follow-up or censoring (06/30/2019). Time at risk started at the date of renal biopsy. Histologic predictors were collapsed into binary variables (0-1 = low; 2-3 = high) and tested in univariate models, with the association expressed as hazard ratios (HRs) and 95% confidence intervals (CI); those showing a significant association with the outcome (Figure, panel B) were included in a multivariable model together with a variable representing the Berden class. The prognostic performance of models including only the Berden class or the Berden class plus additional predictors was assessed using Harrell's c-statistic.

Results: During a follow-up of 1,828 person-months, 13 composite events developed (8 deaths, 5 RRT), corresponding to an incidence rate of 7.1 (95% CI 4.2, 12.2) per 1,000 person-months. Of the tested predictors, Bowman's capsule rupture (BCR, Figure, panel C) was significantly associated with the outcome (p = 0.023). Compared with a model including only Berden class (c = 0.67), the addition of this parameter significantly improved the prognostic performance (c = 0.76). In the multivariable model including Berden class, BCR remained significantly associated with the outcome (HR 3.61, 95% CI 1.15, 11.34; p = 0.028).

Conclusion: The present study demonstrated an improved performance of Berden classification in predicting patients' outcome after the implementation of BCR. This can allow a better stratification of these cases, leading to tailored therapeutic approaches. Further investigations on a larger prospective cohort are required to confirm these results.

A

Number of cases	52	
Male (n, %)	30	58%
Age (mean±SD)	64 ±	16
Proteinuria (g/24h, mean±SD)	1.7 ±	1.5
Serum creatinine (mg/dl, mean±SD)	3.1 ±	2.2
eGFR (EPI-CKD formula, mean±SD)	31.0 ±	29.1
ANCA MPO (N, %)	31	60%
Dialysis at diagnosis (N, %)	5	10%
Outcomes		
Need of RRT (N, %)	10	19%
Deceased patients (N, %)	8	15%
Any (N, %)	13	25%
Berden class (N, %)		
Focal	16	31%
Crescentic	8	15%
Sclerotic	4	8%
Mixed	24	46%

B

Predictor	HR	p value
Active lesions		
Endocapillary hypercellularity	1.47 (0.32 - 6.72)	0.62
Cellular/fibrocellular crescents	1.68 (0.55 - 5.15)	0.36
Glomerular fibrinoid necrosis	0.62 (0.14 - 2.78)	0.53
Bowman's capsule rupture	3.71 (1.20 - 11.44)	**0.02**
Chronic lesions		
Global glomerulosclerosis	1.49 (0.50 - 4.45)	0.47
Fibrous crescent	2.08 (0.63 - 6.84)	0.23
Segmenatal sclerosis	2.45 (0.79 - 7.58)	0.12
IFTA	1.26 (0.27 - 5.88)	0.77
Arteriosclerosis	2.79 (0.91 - 8.56)	**0.07**

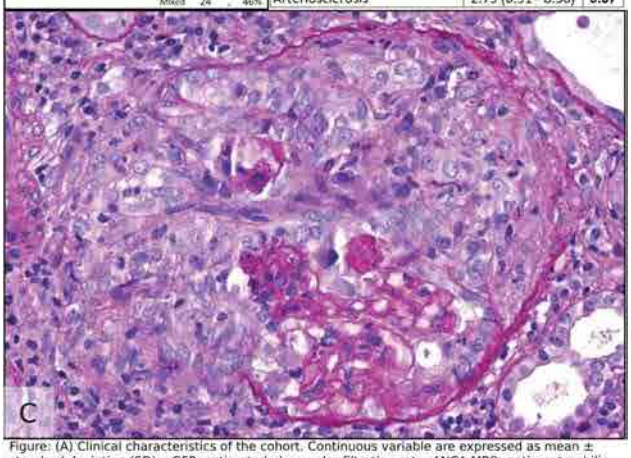


Figure: (A) Clinical characteristics of the cohort. Continuous variable are expressed as mean ± standard deviation (SD). eGFR, estimated glomerular filtration rate; ANCA MPO, anti-neutrophilic cytoplasm antibody to myeloperoxidase; RRT, renal replacement therapy. (B) Results of univariate analysis. Features with significant p-value in bold. HR, hazard ratio (95% confidence interval); IFTA, interstitial fibrosis and tubular atrophy. (C) Bowman capsule rupture in a glomerulus with circumferential cellular crescent (PAS, x20).

Figure:

P0113

STANDARDIZED GRADING OF CHRONIC CHANGES IN MINIMAL CHANGE DISEASE: A VALIDATION STUDY IN NATIVE KIDNEY BIOPSY SPECIMENS

Gabriel Stefan[1,2], Simona Stancu[1,2], Madalina Hoinoiu[2], Nicoleta Petre[1,2], Adrian Dorin Zugravu[1,2], Gabriel Mircescu[1,2]

[1]Nephrology Hospital Dr. Carol Davila, Nephrology, București, Romania and [2]Carol Davila University of Medicine and Pharmacy, București, Romania

Background and Aims: Recently, a group of pathologists and nephrologists devised a simple scoring system for chronic changes based on the grading of glomerulosclerosis (GS), tubular atrophy (TA), interstitial fibrosis (IF) and arteriosclerosis (AS). We aimed to validate for the first time this score in patients with minimal change disease.

Method: We included 79 adult patients (age 50.3 (46.3, 54.3) years, 57% male, eGFR 54.7 (44.2, 63.5) mL/min) with biopsy proven MCD between 2010-2015 who were followed up until January 1, 2017. The extent of GS, TA and AS was scored from 0 to 3, 0 to 3 and 0 to 1, respectively. The scores were then added (total renal chronicity score) to grade the overall severity of the chronic lesions into minimal (0–1 total score), mild (2–4 total score), moderate (5–7 total score) and severe (>8 total score). The outcomes were: patient survival; kidney survival defined as doubling of serum creatinine or ESRD; partial (proteinuria 0.3 to 3.5g/24h) or complete remission (proteinuria <0.3g/24h) - whichever came first. Variables related to renal outcome were further evaluated in a multivariate Cox proportional hazard (CPH) model.

Results: Minimal chronic lesions were found in 77%, mild in 18% and moderate in 5% of the studied patients. Fifty percent had a null score of chronicity; they were younger (44 (29-53) versus 62 (44-66) years, $p<0.001$), had higher eGFR (65.0 (42.1-83.2) versus 43.4 (25.8-63.9) mL/min, $p<0.01$) but similar proteinuria (4.8 (1.9-8.2) versus 4.5 (1.1-6.7) g/g, $p=0.3$). Patients with a score higher than one had higher mortality (18% versus 0%, $p<0.001$) and started RRT more often (15% versus 0%, $p=0.01$). There were no differences regarding the presentation as acute kidney injury, and in reaching complete or partial remission. Moreover, there were no clinical or pathology features that predicted remission. 17% of the patients reached the composite endpoint of kidney survival; mean kidney survival time was 5.7 (5.2, 6.3) years. In the CPH analysis the only independent predictors of decreased renal survival were elevated chronicity score (HR 1.56 (95%CI 1.14-2.14), $p<0.01$), lower serum albumin (HR 0.27 (95%CI 0.08-0.88), $p=0.03$) and the presence of hypertension (HR 0.18 (95%CI 0.03-0.93), $p=0.04$).

Conclusion: To the best of our knowledge, this is the first study to validate the standardized grading of chronic changes as an independent predictor of renal survival in patients with minimal change disease.

P0114 **BENEFITS AND CHALLENGES OF A RENAL BIOPSY REGISTRY AND NETWORK - FCGG EXPERIENCE**

Wim Laurens[1], Johan De Meester[1], Ben Sprangers[2], Steven Van Laecke[3], Dendooven Amélie[4], Lerut Evelyne[5], Johan Vande Walle[6], De Vriese An[7], Lissa Pipeleers[8], Maes Bart[9], Helbert Mark[10], Rachel Hellemans[11], Dejagere Tom[12]

[1]AZ Nikolaas, Nephrology & Dialysis, Sint-Niklaas, Belgium, [2]UZ Leuven, Nephrology, Dialysis & Transplantation, Leuven, Belgium, [3]UZ Gent, Nephrology, Dialysis & Transplantation, Gent, Belgium, [4]UZ Gent, Pathology, Gent, Belgium, [5]UZ Leuven, Pathology, Leuven, Belgium, [6]UZ Gent, Pediatric Nephrology & Dialysis, Gent, Belgium, [7]AZ Sint-Jan, Nephrology & Dialysis, Brugge, Belgium, [8]UZ Brussel, Nephrology, Dialysis & Transplantation, Jette, Belgium, [9]AZ Delta, Nephrology & Dialysis, Roeselare, Belgium, [10]ZNA Antwerpen, Nephrology & Dialysis, Antwerpen, Belgium, [11]UZ Antwerpen, Nephrology, Dialysis & Transplantation, Edegem, Belgium and [12]Jessaziekenhuis, Nephrology & Dialysis, Hasselt, Belgium

Background and Aims: End December 2016, a renal biopsy network in the Flemish region (Belgium) was founded as a collaboration between the renal pathologists and nephrologists. This FCGG network introduced a uniform renal biopsy request form, a well-structured report form of the renal pathology examination and a comprehensive list of renal pathology diagnoses.

Method: Following informed consent [99.5%] and in compliance with GDPR, the registration of the renal biopsies consists of basic categorical renal data, structured renal pathology information and the final clinical renal disease.

Results: In 2017 and 2018, 1385 renal biopsies were registered – 10.5 per million inhabitants per year; in addition, 28 patients had a repeat biopsy in the same time frame (2%). Of the pediatric patients (age < 18 years; N=92; 6.6%), 23 had IgA nephropathy, 20 a minimal change disease and 15 another type of glomerulonephritis. The biopsy was reported as normal or non-diagnostic in 15 patients (16%) – the majority was clinically considered as glomerulonephritis. The spectrum of the adult population was quite similar across gender and age groups: 56% glomerulonephritis [= IgA nephropathy [19%] + FSGS [8%] + pauci-immune glomerulonephritis [7%] + other GN [22%]), 10% tubulo-interstitial nephritis, 7% acute tubular necrosis [ATN], 7% diabetes mellitus, and 7% nephroangiosclerosis. Exceptions are pauci-immune glomerulonephritis as the most important renal disease in women aged 65 years and older, and lupus nephritis as the second most important glomerulonephritis in women aged 18-44 years. Only a small percentage of adult renal biopsies yielded no result (7%), clinically interpreted as glomerulonephritis in 50% of the cases.

Conclusion: The FCGG network has provided a more intense collaboration between renal pathologists and nephrologists mainly by standardizing the renal biopsy reading and reporting across all centers. More precise estimates of the prevalent renal diseases were provided for the first time; however, in order to get full information, renal diseases diagnosed by other techniques (serology, genetic analysis) should also be collected in the future. Efforts will be done to coordinate the clinical care of renal diseases, particularly the more rare renal diseases, and to offer access to new therapeutic molecules or new schemes, through this super-regional network.

P0115 EFFECT OF CARDIOPULMONARY BYPASS ON THE DEVELOPMENT OF ACUTE KIDNEY INJURY AFTER OPEN-HEARD SURGERY

Nikolai Molchan[1], Regina Akmalova[1], Dmitriy Sokolov[1], Olga Galkina[1], Yuri Polushin[1], Elena Levykina[1]

[1]*First Pavlov State Medical University of St. Petersburg, Saint Peterburg, Russia*

Background and Aims: Assessment of factors associated with cardiopulmonary bypass (CPB) in acute renal dysfunction in patients in the early postoperative period after cardiac surgery.

Method: Monocentric observational study in patients (n = 97) who underwent elective open-heart cardiac surgery (coronary artery bypass grafting -50.44%, aortic valve prosthetics - 31.04%, mitral valve prosthetics - 12.61%) using cardiopulmonary bypass. Inclusion criteria: the study included patients not younger than 18 years old, undergoing cardiac surgery with CPB lasting up to 95 minutes (coronary bypass surgery, valve replacement), without signs of end-stage chronic kidney disease (CKD).

Using nonparametric correlation analysis, we evaluated the effect on the development of acute kidney injury (AKI) of the following extracorporeal circulation factors: duration of CPB, aortic cross-clamp, mean arterial pressure (MAP), cardiac index (CI), perfusion flow rate (PFR), transport, consumption and oxygen extraction variables. The diagnosis of AKI was made on the basis of the KDIGO classification, the studied parameters were recorded initially (before the operation), 15 minutes after the start of general anesthesia, 30 minutes after the start of cardiopulmonary bypass and 15 minutes after the end of general anesthesia.

Results: The frequency of AKI in 24 hours after surgery was 56.3% (58 cases): including stage 1 in 37 (35.9%), stage 2 in 17 (16.5%), stage 3 - in 4 (3.9%) patients. In the 48th hour of the postoperative period signs of AKI regressed, and were presented in only 26 people (25.2%), including the stage 1 in 18 (17.5%), the stage 2 - in 5 (4.8%), stage 3 - in 3 (2.9%). Among the risk factors for AKI in cardiac surgery with CPB, the main effect of of the anemia was revealed, especially a decrease in hemoglobin levels of less than 90 g / l and hematocrit of less than 25%.

Conclusion: Hemodilution below the "threshold" values of hemoglobin and hematocrit during the CPB provoke acute kidney injury in patients undergoing open-heart surgery.

P0116 **DISCOVERY OF A NOVEL ANTIMICROBIAL COMPOUND AGAINST PSEUDOMONAS AERUGINOSA FROM URINE OF KTX PATIENTS**

Daniela Knafl[1], Goran Mitulovic[2], Peter Pichler[1], Thomas Reiter[1], Ludwig Wagner[1;3], Wolfgang Winnicki[3]

[1]Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria, [2]Medical University Vienna, Department of Laboratory Medicine, Vienna, Austria and [3]Medical University Vienna, Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria

Background and Aims: The urinary microbiome harbors a great repertoire of bacteria, which possess an immense potential for the biosynthesis of different biochemical products such as polyketide synthases. Traditionally such compounds have been utilized as pharmaceutical drugs, for example as antibiotics or cytostatic substances or agrochemical agents. While examining the urinary microbiome of KTX-patients during AKI and concomitant antibiotic treatment a remarkable decrease of *Candidatus solibacter usitatus* in one patient attracted our attention. Surprised about detecting a putative close relative of a bacterium, which originally has been found in Australian soil in our patient's urine, we examined the genome and protein coding regions of *Candidatus solibacter usitatus*. Thereby we identified a biosynthetic pathway, which allowed us to clone and produce an up-to-now unknown polyketide type 1 synthase, which we named Dananase.

Method: The *dananase* gene was synthesized, cloned into the pEX-A258 for replication and inserted into the p-TOPO-entry-D gateway vector following PCR amplification. The resultant insert was shifted into the pEXP1- DEST gateway vector. *E. coli* transformants were selected for *dananase* expression. BAP1-*E. coli* was transformed with the *dananase*-pEXP1- DEST expression plasmid and grown in liquid culture under induction with IPTG. The supernatant was filtered and utilized for antimicrobial activity testing against *Pseudomonas aeruginosa*. Metabolome analysis of BAP1- pEXP1-DEST-*dananase* following induction with IPDG was performed and compared to LB-media alone and supernatants of dummy plasmid transformed BAP1-*E. coli*. In addition, the molecular structure of *dananase* product was determined using trans-AT polyketide synthase predictor web application genome mining tool.

Results: The 1646 amino acid long polyketide synthase type 1 named *dananase* was cloned into pEXP1 expression vector and expressed in BAP1. The supernatant contained specific antimicrobial activity against clinical isolates of *Pseudomonas aeruginosa*. This highly active compound could be further purified by HPLC but not yet identified in its structure. In silico prediction analysis suggested a polyketide as follows CC(C(O)*)C=CC(CC(NC([K])C(CC(O)=O)=O)=O)=O. Mass spectrometric analysis revealed several Dananase-specific peaks representing most likely its product in the supernatant.

Conclusion: The *dananase* gene of *Candidatus solibacter usitatus* consists of 4941bp and encodes a polymodular polyketide synthase type-1, its product successfully inhibits growth of *Pseudomonas aeruginosa in vitro*.

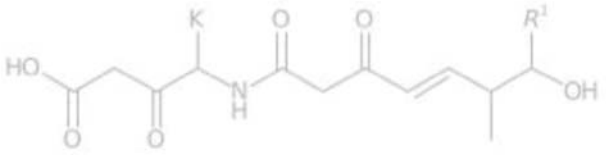


Figure:

P0117 **DOSE ESCALATING TOXICOLOGY STUDY OF ELP-VEGF, A NOVEL BIOLOGIC FOR RENAL THERAPEUTIC ANGIOGENESIS**

Gene Bidwell[1], Jamarius Waller[1], Jason Engel[2], Alejandro Chade[2]

[1]University of Mississippi Medical Center, Neurology, Jackson, MS, United States of America and [2]University of Mississippi Medical Center, Physiology, Jackson, MS, United States of America

Background and Aims: Chronic renal disease, irrespective of the etiology, is hallmarked by renal microvascular rarefaction. This rarefaction is associated with a reduced bioavailability of the pro-angiogenic cytokine vascular endothelial growth factor (VEGF). Recently, we developed a therapeutic intervention for ischemic renal conditions using therapeutic angiogenesis – supplementing renal VEGF levels. This was achieved by administration of a biopolymer-stabilized form of VEGF using a fusion protein between human VEGF-A_{121} and an elastin-like polypeptide carrier protein (ELP-VEGF). ELP-VEGF induced microvascular remodeling and increased microvascular density when administered intra-renally in swine models of unilateral renovascular disease (RVD) and chronic kidney disease (CKD), which was associated with improved renal function, reduced renal inflammation, and reduced renal fibrosis. Also, ELP-VEGF targeted the kidney when administered systemically and induced similar beneficial effects on renal function and renal vascular density. The therapeutic dose of ELP-VEGF in the swine models was 0.1 mg/kg when administered intra-renally and 1.0 mg/kg when administered intravenously. The aims of the present study were to determine the maximum tolerated dose of ELP-VEGF and assess its dose-related toxicity. We hypothesize that ELP-VEGF will not exhibit toxicity at therapeutic doses.

Method: A dose escalating toxicology experiment was performed in Sprague Dawley. Female rats were instrumented with either carotid catheters or carotid artery telemeters

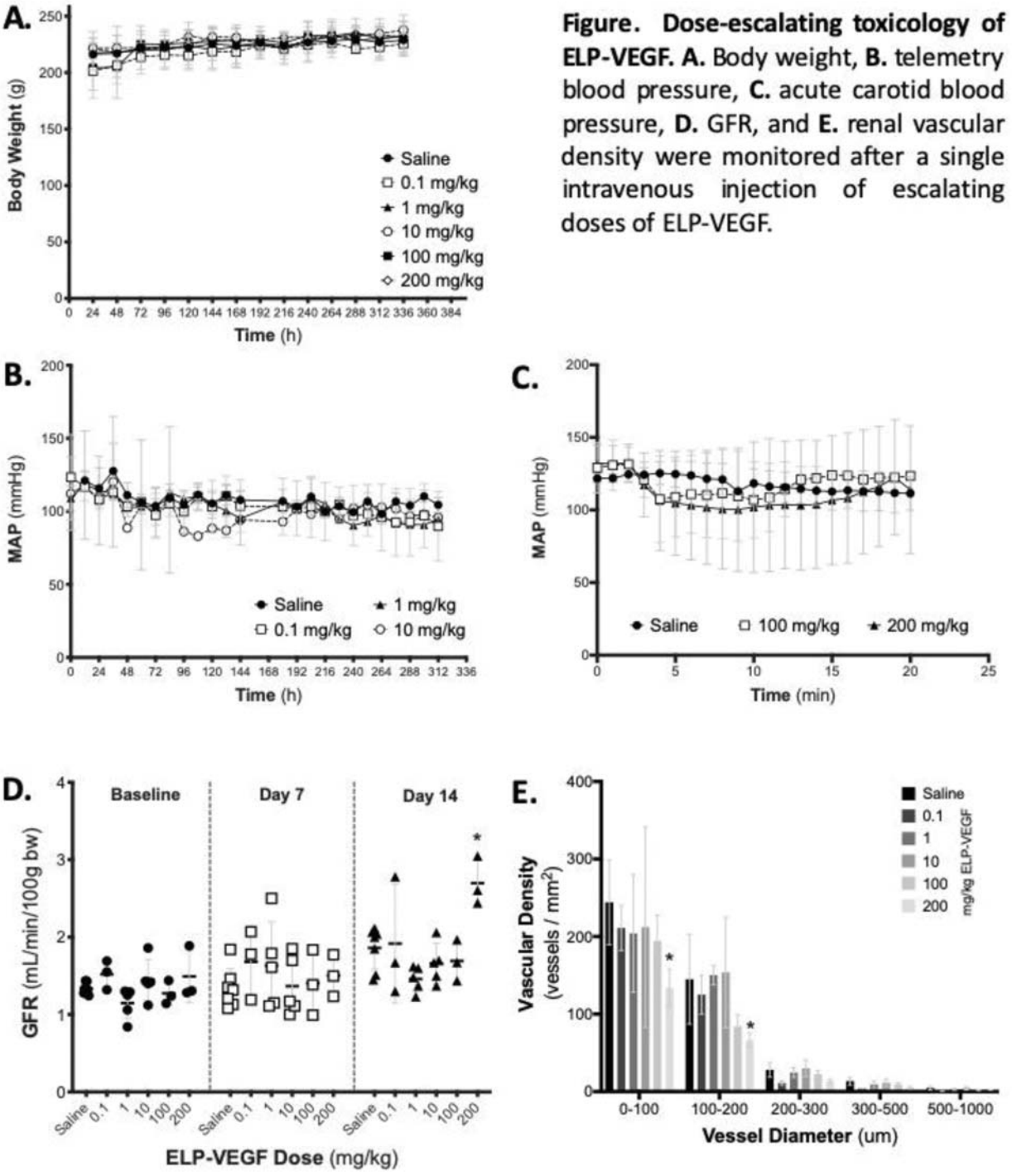


Figure. Dose-escalating toxicology of ELP-VEGF. A. Body weight, **B.** telemetry blood pressure, **C.** acute carotid blood pressure, **D.** GFR, and **E.** renal vascular density were monitored after a single intravenous injection of escalating doses of ELP-VEGF.

Figure:

for blood pressure monitoring. After a recovery period, a baseline 24-hour urine sample was collected, and baseline glomerular filtration rate (GFR) was measured by monitoring FITC-sinistrin clearance via transdermal fluorescence. A single injection of saline control or ELP-VEGF (0.1, 1, 10, 100, or 200 mg/kg) was administered, and blood pressure was monitored by telemetry or by direct carotid arterial pressure measurements. Body weights were monitored daily throughout the study, and 24-hour urine collections and GFR measurements were repeated 7 and 14 days after protein injection. On day 14 after injection, blood was collected, one kidney was collected and fixed for histological examination, and the second kidney was perfused with Microfil vascular contrast agent for quantification of renal vascular density by micro-CT.

Results: ELP-VEGF caused no significant changes in body weight at any dose. At the highest doses there was an acute drop in blood pressure (20 – 30 mm Hg at 100 and 200 mg/kg dose, respectively) for approximately twenty minutes post-injection which then normalized. GFR was unchanged by ELP-VEGF at doses up to 100 mg/kg. However, GFR was significantly increased 14 days after treatment with 200 mg/kg ELP-VEGF (1.5 +/- 0.3 versus 2.7 +/- 0.3 mL/min/100 g body weight, p=0.0021). Plasma toxicology revealed no changes in markers of liver or kidney toxicity (AST, ALT, BUN, creatinine, LDH, bilirubin) at any dose or time point. Renal vascular density was unaffected by ELP-VEGF at doses up to 10 mg/kg. However, at 200 mg/kg ELP-VEGF, renal vascular density was significantly decreased for small (0 – 100 micron, p=0.0007) and intermediate (100 – 200 micron, p=0.028) sized vessels

Conclusion: ELP-VEGF has a proven therapeutic potential for treatment of RVD and CKD at therapeutic doses ranging from 0.1 – 1.0 mg/kg in swine models. Dose escalating toxicity assessment in rats found no effect of ELP-VEGF on body weight, blood pressure, plasma markers of liver and renal toxicity, GFR, or renal vascular density at these therapeutic doses. ELP-VEGF doses of 100 – 200 mg/kg caused transient hypotension immediately after the injection and were associated with increased GFR and loss of renal vascular density, possibly indicating renal damage at ultra-high doses. We conclude that the therapeutic window for ELP-VEGF is 100 – 1,000 times the effective therapeutic dose.

P0118 ANEMIA AS A RISK FACTOR FOR CONTRAST-INDUCED NEPHROPATHY

Emna Chaabouni[1], Hela Jbali[1], Najjar Mariem[2], Mzoughi Khadija[3], Zouaghi Karim[1]

[1]La Rabta, Nephrology, tunis, Tunisia, [2]Charles Nicolle Hospital, Nephrology, tunis, Tunisia and [3]Habib Thameur Hospital, cardiology, tunis, Tunisia

Background and Aims: Contrast-induced nephropathy is a potentially serious complication following coronary angiography and percutaneous coronary intervention .

The association between severity of anemia and Contrast-induced nephropathy following coronary angiography is not well-established. In this prospective study, we aimed at assessing the association of anemia of various severity with the risk of Contrast-induced nephropathy in patients who underwent coronary angiography

Method: We prospectively enrolled 158 patients who underwent coronary angiography with or without percutaneous coronary intervention from December 2017 to February 2018 at a cardiology department .

CIN was defined as an increase in serum creatinine level >25% or 0.5 mg/dL after 48 hours and anemia was defined as a value of Hb level $\leq$ 13 g/dl in male patients or $\leq$ 12 g/dl in female patients.

Patients were stratified into three subgroups—mild (11.1 to 13.0 g/dL) in male patients and (11.1 to 12.0 g/dL) in female patients, moderate (9.1 to 11.0 g/dL) and severe anemia (7.0 to 9.0 g/dL).

we used a multivariable logistic-regression model.

Results: 158 patients (females = 36.1%, mean age 60.0 $\pm$ 11 years) who underwent coronary angiography, 15 (9,5%) developed Contrast-induced nephropathy .

Presence of anemia was associated with increased risk of developing Contrast-induced nephropathy (OR = 3.04, 95% confidence interval [CI] = 1.03 to 8.96, p= 0,043).

Risk of Contrast-induced nephropathy was increasingly higher with increasing severity of the anemia; mild (OR = 1.67, 95% CI = 1.38 to 2.17, p=0,036), moderate (OR = 3.3, 95% CI = 0.61 to 10.6, p=0,028) .There was no patient with severe anemia.

Conclusion: In conclusion, severity of anemia is a strong predictor of CIN following coronary angiography.

P0119 **ARTIFICIAL INTELLIGENCE IN RENAL PATHOLOGY: IBM WATSON FOR THE IDENTIFICATION OF GLOMERULOSCLEROSIS**

Paola Suavo-Bulzis[1], Federica Albanese[1], Davide Mallardi[1], Francesco Saverio Debitonto[2], Ruggero Lemma[2], Annalisa Granatiero[2], Marisa Spadavecchia[2], Giacomo Donato Cascarano[3], Vitoantonio Bevilacqua[3], Loreto Gesualdo[1], Francesco Pesce[1]

[1]University of Bari "Aldo Moro", Bari, Italy, Nephrology Dialysis and Transplantation Unit, Department of Emergency and Organ Transplantation, Bari, Italy, [2]IBM Client Innovation Center, Bari, Italy and [3]Polytechnic University of Bari, Department of Electrical and Information Engineering (DEI), Bari, Italy

Background and Aims: Artificial Intelligence (AI) is the branch of computer technology aimed at creating hardware and software systems solving problems similarly to human intelligence, whereas specifically machine learning (ML) is the "field of study that gives computers the ability to learn without being explicitly programmed". Our study was carried out taking advantage of the Watson Visual Recognition System by IBM, an advanced AI tool based on ML able to classify complex visual content. The aim of the study was to train and test the ability of the system in recognizing sclerotic and non-sclerotic glomeruli.

Method: A dataset of 26 renal biopsies performed at the Nephrology unit of the Department of Emergency and Organ Transplantation (DETO), University of Bari, Italy, was used for the analysis. All biopsies were stained with Periodic Acid-Schiff (PAS) staining. Each bioptic section was acquired using Aperio ScanScope; glomeruli were identified and sclerotic glomeruli were marked in yellow, non-sclerotic ones in green. Annotations were validated by two renal pathologists. The final dataset consisted of 2772 glomeruli: 428 with sclerosis, 2344 with no sclerosis (ratio 1/5.5).

The dataset was divided in three parts: training set (about 70% of the entire dataset), validation set (about 10%) and test set (about 20%).

Watson Visual Recognition Service is customizable and the system can be trained on recognizing any visual content. Classifiers are created and trained uploading both positive (in our study, sclerotic glomeruli) and negative (non-sclerotic glomeruli) classes. The IBM Watson learning algorithm is not open, therefore in order to improve the performance of the system, it is necessary to train it with different models and choose the best one.

Results: We created all the possible models derived from the arrangement of the following 4 variables: color of the image (PAS staining or grey scales), dimension (original or resized), number of images in order to balance the positive and negative classes, binary (one class containing sclerotic glomeruli) or multi-class (two classes: sclerotic and non-sclerotic glomeruli). Every test had a cut-off of 0.5: if >0.5, the system considered the glomerulus belonging to the tested class.

After validating all the models with all the variables considered, the best performing model was the following: grey scaled, resized and multi-class.

This model was then tested with a different number of input images (300, 600, 900, 1200, and 1600). The models with the most numerous dataset have been created using *data augmentation*, a technique that virtually increases the number of available samples.

Results show that the use of larger input datasets does not yield a better linear performance. In fact, models 900 and 1200 had worst performances than other models, the best performances of the system were reached with model 1600, both in recognizing sclerotic (positive class) and non-sclerotic (negative class) glomeruli (*Table 1, Figure 1 and 2*).

Conclusion: In our study, renal biopsy images were analyzed and classified using the IBM Watson Visual Recognition tool which was able to distinguish automatically and with very high accuracy between sclerotic and non-sclerotic glomeruli. This study focuses only on the glomerular compartment and the next step will be the recognition of intermediate lesions and other portion of renal tissue. Our results prove the potential of AI and ML techniques in supporting the activity of renal pathologists.

Table 1

	300	600	900	1200	1600
NEGATIVES	99.39%	99.39%	99.39%	99.04%	99.60%
POSITIVES	94.25%	94.25%	93.10%	90.80%	96.55%

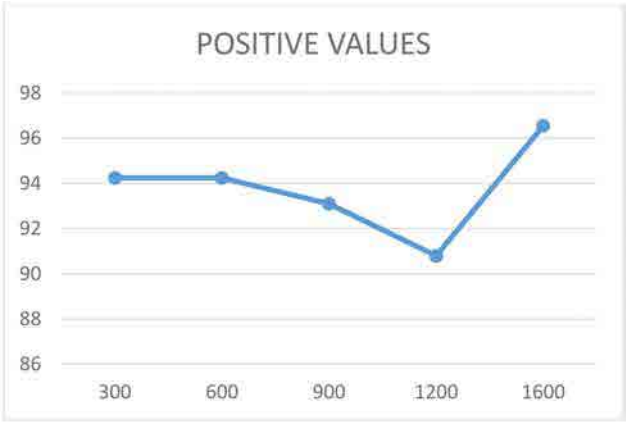


Figure 1

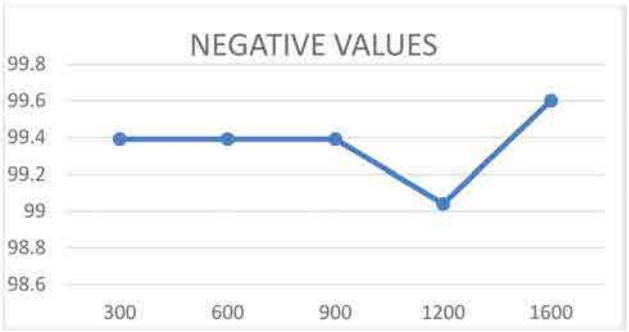


Figure 2

P0120

FEATURES OF ULTRASTRUCTURAL CHANGES IN KIDNEY TISSUE IN THE PATIENTS WHO HAVE PASSED AWAY AS A RESULT OF SEPSIS

Mehman Agayev[1], Shalala Ismayilova[1], Arzu Ibishova[2]

[1]Azerbaijan Medical University, Department of Nephrology and [2]Azerbaijan Medical University, Department of Pathological Anatomy

Background and Aims: It is believed that septicemia and septicopyemia can lead to functional failure of many organs, including the kidneys. In this regard, it is important to study the morphological features of ultrastructural changes in kidney tissue.

Method: Structural changes in renal tissue of 30 patients who died as a result of sepsis were investigated by electron-microscopy. The burial was carried out at an early stage (1-6 hours after death). The sections obtained for ultrasonic examination were examined on "James 100 S " electron microscope after contrasting with uranyl acetate and lead citrate solution.

Results: An ultrastructural study of the cells of the cortical and medial layers of the kidneys revealed that there are changes in extracellular contacts and cell fragmentation as a result of lysis of the cytoplasmic membrane of cells. The integrity of the basal membrane of epithelial cells of the proximal and distal tubules are preserved. However, the basal layer did not have a homogeneous structure, intersected and transparent in certain areas. Numerous vacuoles, lipid supplements and fragments of lysed intracellular proteins in the cytoplasm have been identified in the cytoplasm of cells. Most of the nucleus was in the collapse phase. The lumen of tubules is narrow and most of the microvilli of the brush border are destructed. It was revealed that in sepsis renal failure and severe destructive changes and the formation of necrosis sites in the structural elements of the nephron as a result of bacterial toxins were mainly observed in areas where bacteria were localized.

Conclusion: Abnormalities of podocytes, of endothelial cells, disruption of the basal membrane layers as a result of abnormal damage of organelles especially mitochondria, changes of proximal and distal tubules may be caused by severe renal failure due to sepsis.

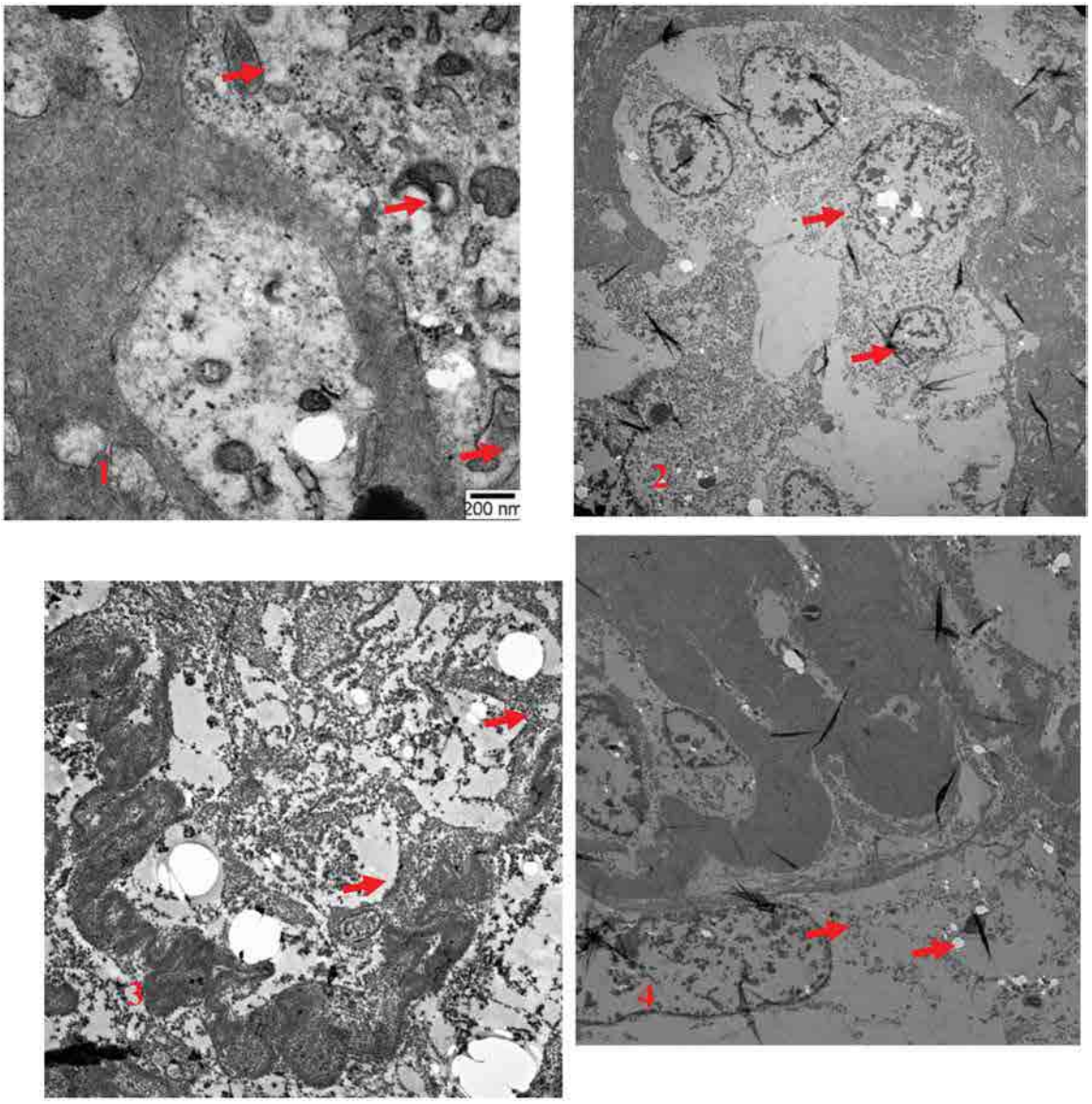


Figure 1–4. The destructed mitochondrias in the cytoplasm of proximal tubules

The lack of the brush border of the proximal tubules and the karyorrhexis of the nucleus are marked with red arrows.

Destruction of basal membrane of capillary loops and break of collagen fibers (marked with red arrow).

The signs of edema in the intracellular area (marked with red arrow)

P0121 KIDNEY BIOPSY FINDINGS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Elbis Ahbap Dal[1], Taner Basturk[1], Tamer Sakaci[1], Nuri Baris Hasbal[2], Mustafa Sevinç[1], Ayse Aysim Ozagari[3], Kamile Gulcin Eken[3], Abdulkadir Unsal[1]

[1]Sisli Hamidiye Etfal Education and Research Hospital, Nephrology, Istanbul, Turkey, [2]Hakkari State Hospital, Nephrology, Hakkari, Turkey and [3]Sisli Hamidiye Etfal Education and Research Hospital, Pathology, Istanbul, Turkey

Background and Aims: The aim of the study is to evaluate kidney biopsy findings other than renal diabetic changes in patients with type 2 diabetes mellitus.

Method: Diabetic patients with kidney biopsy between January 2003 and January 2020 were enrolled to the study. Kidney biopsy was performed to patients with suspicion of kidney disease other than diabetic nephropathy. The suspicious cases were patients without diabetic retinopathy, diabetes mellitus history less than 5 years, creatinine increase faster than expected course and hematuria. Demographic features, biopsy finding were all noted.

Results: Totally, 135 patients' data were evaluated in which 54.1% was male. Demographic characteristics of the patients and laboratory data are given in Table 1. Mean age was 55.4±11 years and mean diabetes duration was 6.9±6.3 years. Mean duration of diabetes was 5.3±5.5 years in patients with nondiabetic nephropathy whereas it was 10.2±6.4 and 11.2±7.6 years in patients with diabetic and/or nondiabetic pathologies respectively ($p<0.05$). Serum creatinine and proteinuria level were lower, and hemoglobin levels were higher in patients with nondiabetic nephropathy ($p<0.05$).C3 was low in 3.7% of patients. ANA and ANCA positivity were seen in 8.1% and 3.7% of the patients, respectively. Patients without diabetic retinopathy was 81.7% of the total cohort. Biopsy indications were renal insufficiency (8.9%), nephrotic syndrome (24.4%), non-nephrotic proteinuria (16.4%), renal insufficiency with nephrotic range proteinuria (25.9%), renal insufficiency with non-nephrotic proteinuria (24.4%). Mean glomeruli number was 19.3±11.1. Ten patients had macroscopic hematuria in which all resolved with conservative care. Early diabetic changes, diffuse and/or nodular glomerulosclerosis were present in 3.1% and 96.9% of diabetic patients, respectively. Biopsies with diabetic changes with other nondiabetic pathologies were 3% of the biopsies. Isolated nondiabetic nephropathy was found in 23.7% of patients. Pathologic findings other then diabetic changes were as follows in patients without diabetic nephropathy: focal segmental glomerulosclerosis (FSGS) 49.5%, membranous glomerulonephritis 14,1%, Ig A nephropathy 12,1%, membranoproliferative glomerulonephritis 5 %, crescentic glomerulonephritis 4,1%, acute tubular necrosis 4,1%, amyloidosis 3%, tubulointerstitial damage 2%, others 6,1%.

Conclusion: Biopsy in diabetic patients is beneficial to show both diabetic nephropathy and other kidney pathologies. Kidney biopsy may be performed if there is suspicion of other glomerular pathologies. Focal segmental sclerosis was the most common pathology in our patients without diabetic nephropathy

P0122 **THE MECHANISM OF DNA INJURY INDUCED COLLAGEN TYPE VI EXCRETION IN GLOMERULAR ENDOTHERIAL CELLS**

Fujii Ai[1], Yumi Sunatani[2], Furuichi Kengo[1], Keiji Fujimoto[1], HIROKI ADACHI[1], Kuniyoshi Iwabushi[2], Hitoshi Yokoyama[1]

[1]Ishikawa, Kanazawa medical univercity of nephrology, Ishikawa prefecture Kahoku gun, Japan and [2]Ishikawa, Kanazawa medical univercity of biology, Ishikawa prefecture Kahoku gun, Japan

Background and Aims: Collagen deposition is observed in various part of kidney tissue and is serious pathological damage in kidney. Nodular glomerulosclerosis is one of a phenotype of collagen deposition in glomerular lesion, which affects the prognosis of renal function, but there is no effective treatment at present. Recently, we identified that glomerular endothelial cells with DNA double-strand breaks (DSB) are involved in the long-term accumulation of ECM molecules, especially collagen type VI(COL6). However, the mechanism of glomerular COL6 accumulation is still unclear.

Method: We examined the phospho-histone H2AX (γ-H2AX) of the DSB marker and COL6 accumulation in biopsied human kidneys to investigate their association. In addition, we investigated *in vitro* the relationship between DSB and COL6 excretion and the intracellular signal pathways in human glomerular endothelial cells (HRGEc) using mitomycin C (MMc)-induced DNA damage. In this study, we focused on the expression of DSB response signal pathways, i.e. ATM, ATR and DNA-PK using their specific kinase inhibitors (KU55933, VE-821, Nu7441).

Results: COL6 deposits and γ-H2AX expression in nuclei were detected in human glomerular capillary loop and glomerular nodular lesions. The multiple regression analysis showed that γ-H2AX positive area is the most independent factor for COL6 accumulation in glomeruli (β: 0.539, t=2.668, p=0.014). Furthermore, COL6 was the independent factor of nodular lesion in various pathologic diseases such as diabetic nephropathy, hypertensive glomerulosclerosis and the long-term transplanted allografts (β: 0.373, t=2.268, p=0.032).

In vitro study, COL6 excretion detected by the decrease of COL6 positive cells was suppressed only in the ATR-inhibited group (control vs. kinase inhibitors; 2 h, 40.1 ± 23.5 vs. 59.0 ± 23.2%, $p < 0.01$; 24 h, 18.8 ± 23.6 vs. 56.3 ± 16.5%, $p < 0.001$).

Conclusion: This study suggested that nodular glomerulosclerosis is induced by DNA damage and COL6 deposition through ATR pathway in glomerular capillary endothelial cells. These findings will provide great insights into the development of new therapies that would suppress glomerularsclerosis in various kidney diseases.

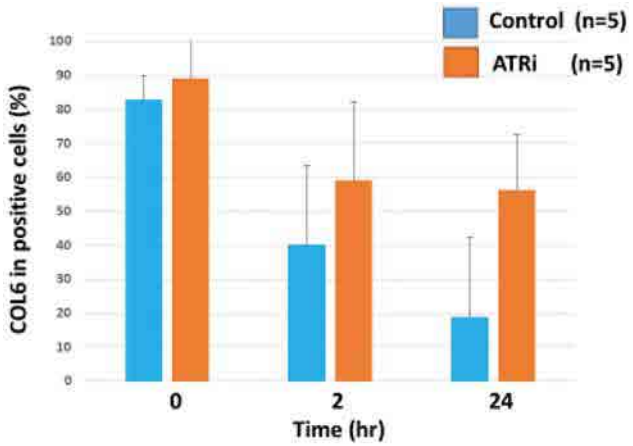


Figure. ATM and Rad3-related (ATR) is required for collagen type 6 secretion

Figure:

P0123 **THE IMPORTANCE OF PPAR-ALPHA IN AKI TO CKD TRANSITION IN NEPHROPATHY INDUCED BY FOLIC ACID**

Gabriel Estrela[1], Adriano Arruda[2], Leandro Freitas-Lima[2], Jonatan Barrera-Chimal[3], Ronaldo Araujo[2]

[1]Federal University of São Paulo Unifesp, Clinical and Experimental Oncology, São Paulo, Brazil, [2]Federal University of São Paulo Unifesp, Biophysics, São Paulo, Brazil and [3]Universidad Nacional Autónoma de México, Instituto de Investigaciones Biomédicas, mexico city, Mexico

Background and Aims: PPAR-alpha is a nuclear receptor which plays major role in the regulation of lipid metabolism, activation of PPAR-alpha has been shown to have beneficial effects in renal diseases. Acute kidney injury (AKI), even if followed by renal recovery, is a risk factor for the future development of chronic kidney disease (CKD) and end-stage renal disease (ESRD). Our main objective was to determine the importance of PPAR-alpha in AKI to CKD transition in folic acid induced nephropathy.

Method: Male C57/Bl6 and PPARKO (C57Bl6 background) mice were divided in 4 groups, Control, Folic Acid, Gemfibrozil + Folic Acid and PPARKO + Folic Acid. Animals has been treated with single dose of Folic Acid (250mg/kg i.p) and Gemfibrozil (150mg/kg gavage) euthanized after 48 hours for AKI assessment and 28 days for CKD. Renal parameters, histology, real time PCR were performed to investigate renal injury, inflammation and fibrosis.

Results: After 48 hours of folic acid inducing AKI, PPARKO mice showed decreased urea levels (Folic Acid: 178,9±25,2 PPARKO: 92,4±15,5), less tubular injury (Folic Acid: 0,61±0,05 PPARKO: 0,21±0,03), lower mRNA expression of NGAL (Folic Acid; 32,2±7,67 PPARKO 3,74±1,71), KIM-1 (Folic Acid: 671,8±170,2 PPARKO: 43,4±29,7) and TNF-alpha (Folic Acid: 2,81±0,58 PPARKO: 0,67±0,14), while PPAR-alpha activation with gemfibrozil showed to have no effects in AKI. After 28 days of folic acid inducing CKD. PPARKO showed same levels of injury than folic acid alone treated mice, however PPAR-alpha activation with gemfibrozil decreased urea levels (Folic Acid: 79,2±3,2 Gemfibrozil: 46,1±3,8), showed less tubulointerstitial fibrosis (Folic Acid: 0,60±0,05 Gemfibrozil: 0,18±0,02) and lower urine protein/creatinine ratio (Folic Acid: 5,48±0,58 Gemfibrozil: 2,53±0,12),

Conclusion: PPAR-alpha deletion protects against AKI induced by folic acid but did not showed protection in chronic phase, in the other hand ppar-alpha activation with gemfibrozil did not protect in AKI but show to be effective in CKD.

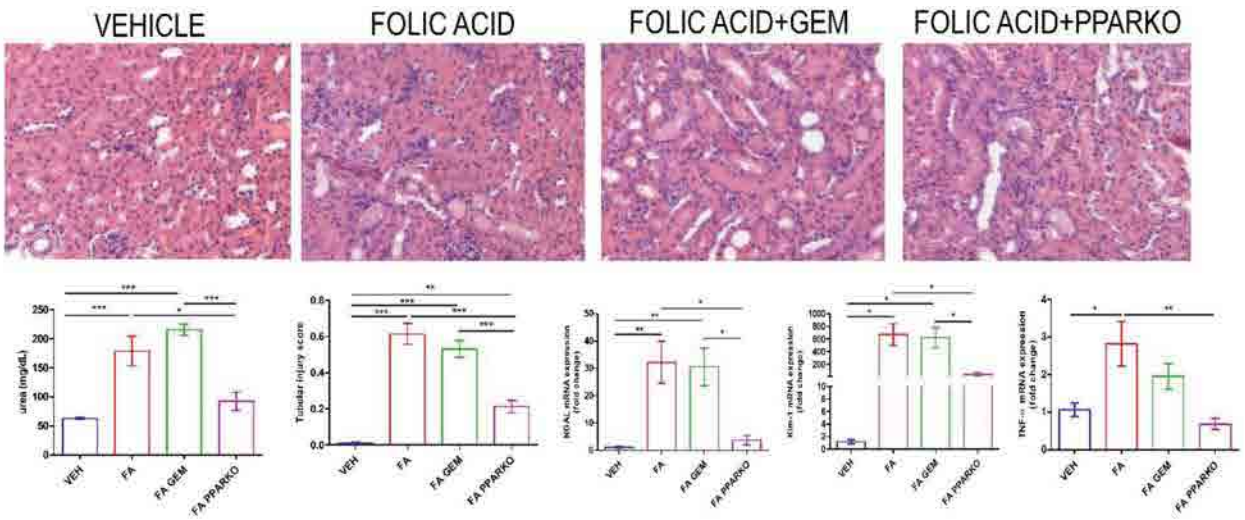


Figure:

P0124 **PREDICTIVE VALUE OF RENAL RISK SCORE AND CHRONICITY SCORE IN PREDICTING RENAL OUTCOME IN ANCA ASSOCIATED GLOMERULONEPHRITIS**

Yong-Xi Chen[1], Xiao-Ning An[1], Zhao-Nan Wei[1]

[1]Ruijin Hospital affiliated to Shanghai Jiaotong University, school of medicine, Department of nephrology, Shanghai, P.R. China

Background and Aims: Renal Risk Score (RRS) and Chronicity Score (CS) are both newly proposed tools to predict End stage renal disease (ESRD) which could be applicable in Antineutrophil cytoplasmic antibody (ANCA) associated glomerulonephritis (AGN) patients. Their predictive value has not been fully studied and compared.

Method: Patients with newly biopsy-proven AGN at Department of Nephrology, Ruijin Hospital were retrospectively studied. Patients were evaluated with RRS and CS for clinical factors, pathological lesions and outcome. Their predictive value of renal survival was also compared with 2010 histological classification.

Results: There were 252 AGN patients enrolled in current study, including 212 MPA, 12 GPA, 4 EGPA and 24 renal limited vasculitis (RLV). In current study, the median serum creatinine of patients at diagnosis was 245.5 μmol/L (IQR 128-487.5 μmol/L) and median eGFR was 20.3 ml/min (IQR 9-45.3 ml/min). Fifty (19.8%) patients required dialysis at disease onset. The median RRS score at diagnosis was 6 (IQR 0-9) and CS score was 4 (IQR 3-7).

During up to 217 months of follow-up (mean 63.9 months), 71(28.2%) patients progressed to end stage renal disease (ESRD) and required renal replacement therapy. Significant differences were found regarding dialysis dependency within RRS and CS groups ($p<0.001$ and $p<0.01$ respectively).

The C statistic of the predictive models was 0.828 (95% CI, 0.775-0.880) for developing ESRD required renal replacement therapy. The addition of RRS or CS scoring scheme to the model significantly improved discrimination.

Compared with the 2010 histopathological classification, RRS and CS both showed adequate and similar discrimination, but significantly greater discrimination than 2010 histopathological classification.

Conclusion: Among AGN patients, RRS and CS achieved similar discrimination, but the discrimination of RRS was superior.

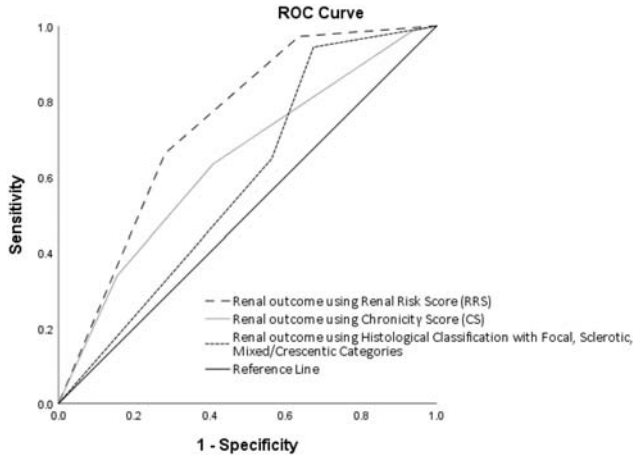


Figure:

P0125

ELECTRON MICROSCOPIC DESCRIPTION OF A SENSITIVE DIAGNOSTIC PROXIMAL EPITHELIAL LYSOSOMAL LESION IN PATIENTS WITH CINAC/CKDU/MEN AND CNI NEPHROTOXICITY

Benjamin Vervaet[1], Cynthia Nast[2], Channa Jayasumana[3], Gerd Schreurs[1], Frank Roels[4], Chula Herath[5], Nika Kojc[6], Vahid Samaee[7], Sonali Rodrigo[5], Swarnalata Gowrishankar[8], Christiane Mousson[9], Rajeewa Dassanayake[10], Carlos Orantes[11], Vincent Vuiblet[12], Claire Rigothier[13], Patrick D'Haese[1], Marc De Broe[1]

[1]Laboratory of Pathophysiology, University of Antwerp, Antwerp, Belgium, [2]Cedars-Sinai Medical Center, Los Angeles, United States of America, [3]Rajatrata University of Sri Lanka, Faculty of Medicine, Anuradhapura, Sri Lanka, [4]Ghent University, Department of Pathology, Ghent, Belgium, [5]Sri Jayewardenepura General Hospital, Department of Nephrology, Colombo, Sri Lanka, [6]University of Ljubljana, Institute of Pathology, Faculty of Medicine, Ljubljana, Slovenia, [7] University of Antwerp, Electron Microscopy for Materials Science (EMAT), Antwerp, Belgium, [8]Apollo Hospitals, Department of Pathology, Hyderabad, India, [9]Centre Hospitalier Universitaire de Dijon, Department of Nephrology, Dijon, France, [10]General Hospital, Renal Unit, Polonnaruwa, Sri Lanka, [11] Ministry of Health of El Salvador, National Institute of Health, San Salvador, El Salvador, [12]Centre Hospitalier Universitaire de Reims, Departments of Nephrology and Renal Pathology, Reims, France and [13]Centre Hospitalier Universitaire de Bordeaux, Service Néphrologie, Transplantation, Dialyse et Aphérèses, Bordeaux, France

Background and Aims: In CINAC patients from Sri Lanka, we recently observed a sensitive constellation of proximal tubular cell findings including cellular/tubular atrophy, cell fragment shedding and, by electron microscopy (EM), the presence of an increased number of enlarged lysosomes. Here we focused on precisely defining the EM lysosomal phenotype and evaluating its presence in CINAC/MeN/CKDu cases and controls from other countries.

Method: Thirthy-two renal biopsies (18 Sri Lanka, 10 El Salvador, 1 India, 3 France) of patients with a diagnosis of CINAC (CKD 1-3A, 3B) were examined by electron microscopy (EM) in comparison to renal biopsies of normal kidneys at implantation, patients with calcineurin inhibitor (CNI) toxicity (n=17), proteinuric nephropathies (n=15), light chain disease (n=4), several cases on nephrotoxic drugs (lomustine, clomiphene, lithium, tenofovir, cisplatinum) and patients with reduced renal function of various causes (n=20).

Results: The aberrant lysosomal phenotypes can be defined as enlarged (>1.2μm) and dysmorphic with a light-medium electron-dense matrix containing dispersed dark electron-dense non-membrane bound round to irregular shaped "aggregates". In addition, indicative clusters of 4-6 smaller lysosomes with the same features could be observed. No cristae or other features of mitochondria, autophagic vacuoles, lipofuscin/ceroid droplets, peroxisomes (marginal plate), lysosomal myeloid bodies (aminoglycoside nephropathy) or electron dense laminated lysosomal inclusions (Fabry disease) were observed. Patients with calcineurin inhibitor nephrotoxicity and several cases on nephrotoxic drugs (lomustine, clomiphene, lithium) and a subset of patients with light chain disease, all conditions that can either directly or indirectly be linked to calcineurin inhibition, presented the same lesions. We present an image set demonstrating the phenotypical consistency of the diagnostic lysosomal lesion versus similar features that are non-diagnostic.

Conclusion: A rather sensitive constellation of lysosomal lesions in renal proximal tubular cells was detected associated with CINAC/CKDu/MeN and CNI nephrotoxicity in several countries, suggesting a common new pathomechanistic paradigm where CINAC patients are experiencing a tubulotoxic mechanism similar to CNI nephrotoxicity.

P0126 **RENAL TRANSPLANT PATIENTS UNDER CALCINEURIN INHIBITOR THERAPY RAPIDLY ACQUIRE AN ABERRANT LYSOSOMAL LESION IN PROXIMAL TUBULAR CELLS**

Benjamin Vervaet[1], Nika Kojc[2], Cynthia Nast[3], Gerd Schreurs[1], Patrick D'Haese[1], Marc De Broe[1]

[1]University of Antwerp, Laboratory of Pathophysiology, Antwerp, Belgium, [2]University of Ljubljana, Institute of Pathology, Faculty of Medicine, Ljubljana, Slovenia and [3]Cedars-Sinai Medical Center, Los Angeles, United States of America

Background and Aims: Calcineurin inhibitor therapy has changed the field of (renal) transplantation by considerably prolonging graft survival. Yet, all immunosuppressive calcineurin inhibitors are nephrotoxic that eventually contribute to complete scarring of the renal allograft. In renal biopsy analysis many histopathological features have been considered indicative of CNI nephrotoxicity, i.e. striped fibrosis, vascular hyalinosis, isometric tubular vacuolization, glomerulosclerosis, cellular infiltration and tubular atrophy, however, all are rather aspecific and can be secondary to many other causes. During the course of evaluating the specificity of a recently discovered proximal epithelial lysosomal lesion (i.e. multiple enlarged (>1,2μm) dysmorphic lysosomes containing dispersed electron dense non-membrane bound aggregates) in patients with Chronic Interstitial Nephropathy in Agricultural Communities (CINAC), we observed it to be present in renal transplant patients treated with cyclosporine or tacrolimus. Here, we test the hypothesis whether this lysosomal lesion is acquired during CNI therapy.

Method: A retrospective transmission electron microscopic analysis was performed to evaluate the presence of the typical lysosomal lesion on the following biopsies from renal transplant patients: 20 deceased donor implantation biopsies; 5 living donor implantation biopsies. For another 10 additional deceased donor renal allograft recipients, we evaluated implantation as well as protocol biopsies taken after 6 and 12 months of CNI treatment that started immediately after transplantation. Also included were 24 indication biopsies of CNI treated renal transplants.

Results: Of the total set of implantation biopsies (n=35), 2 (6%) were positive for the aberrant lysosomal phenotype on EM, whereas in the protocol and indication biopsies prevalence of the lesion was considerably higher ranging between 56% (protocol) and 80% (indication) of cases.

Conclusion: CNI therapy is associated with the fairly rapid appearance of a particular proximal tubular lysosomal phenotype observable on EM, that was not (or rarely) present at implantation. Whether this lesion is related to CNI toxicity and indicative for the outcome for the graft and/or patient survival after renal transplantation has to be investigated in a prospective trial.

P0127

ROUTINE USE OF COMBINATION CD3/PAS STAIN IN EVALUATING RENAL ALLOGRAFT BIOPSIES FOR REJECTION RESULTS IN MORE ACCURATE BANFF SCORES FOR TUBULITIS

Mandolin Ziadie[1,2], Lauren Abrahams[1], Katherine Freeman-Costin[3], Cecilia Obregon[1], Neil Abrahams[1,4]

[1]Memorial Healthcare System, Department of Pathology, Division of Renal Pathology, Hollywood, United States of America, [2]Memorial Healthcare System, Division of Pediatric Pathology, Hollywood, United States of America, [3]Florida Atlantic University, Charles E. Schmidt College of Medicine Biostatistics Core, Boca Raton, United States of America and [4]Florida Atlantic University, Charles E. Schmidt College of Medicine, Boca Raton, United States of America

Background and Aims: The BANFF Classification of renal allograft rejection consists of scores for cellular rejection which rely primarily on the evaluation of lymphocytic infiltration into tubules (t), non-atrophic interstitial inflammation (i), total inflammation (ti), and endotheliatis (v.) CD3/PAS is a combination stain that highlights T lymphocytes (CD3) and basement membrane (PAS). The original BANFF scoring was developed using a hematoxylin and eosin (H&E) stain only. This study compares scores for (t) using H&E versus CD3/PAS.

Method: 50 consecutive renal allograft biopsies were retrieved and on each case H&E and CD3/PAS combination stains (Ventana/Roche tissue Diagnostics Clone 2GV6 for CD3) were performed. One blinded group of matching CD3/PAS and H&E slides were evaluated and reviewed independently by two renal pathologists (Reviewer 1 and 2). Each case was graded in an identical manner following criteria designated for (t) as previously described in the Banff Classification for Renal Allograft Biopsies. Briefly (t)=0 no lymphocytes in 10 tubule cross section (tcx), (t)=1 between 1-4 lymphocytes per tcx, (t)=2 5-10 lymphocytes per tcx and (t)=3 greater than 10 lymphocytes per tcx. Cases were not graded for (v) as there were too few cases with endotheliatis to allow for statistical evaluation. The difference between CD3/PAS versus H&E scores were tested for significance using the Wilcoxon Signed Rank test. All p values were two-tailed and values of <0.05 were considered statistically significant.

Results: Mean age was 44 years with a range of 9 -75 years. Standard deviation (SD) for age was 18 years. Gender distribution was 20% female and 80% male. 28 cases were graded as (t) = 0 in H&E versus 18 in the CD3/PAS group (59% versus 36%). 17 cases were graded as (t)=1 in H&E group versus 19 in the CD3/PAS group (36% versus 38% respectively). 2 cases were graded (t)=>2 in H&E versus 12 cases in CD3/PAS groups (4% versus 24% respectively). In all categories of (t) there was a higher (t) score when using a CD3/PAS with 42% showing a one digit score increase and 8% showing a 2 digit increase. The difference in scoring for (t) between the H&E set versus the CD3/PAS set for both Reviewers 1 and 2 were statistically significant ($p<0.0001$).

Conclusion: This study showed statistically significant higher tubulitis scores when using a CD3/PAS combination stain to grade allograft biopsies. Since (t) scores directly affect the diagnosis of cellular rejection, we propose routine use of CD3/PAS in addition to H&E when reviewing renal allograft biopsies. Compared with H&E, CD3/PAS makes recognition and quantification of lymphocytes crossing the tubular basement membrane easier to detect and therefore more accurate.

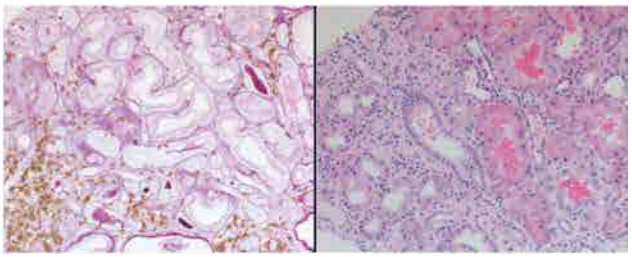


Figure: Comparison photograph of renal allograft biopsy with CD3/PAS versus H&E stain.

P0128

COMPARISON OF ULTRASTRUCTURE FEATURES BETWEEN PATIENTS WITH MERCURY-ASSOCIATED MEMBRANOUS NEPHROPATHY AND IDIOPATHIC MEMBRANOUS NEPHROPATHY

Aibo Qin[1], Zishan Lin[1], Fude Zhou[1], Minghui Zhao[1], Suxia Wang[2], Zhao Cui[1]

[1]Renal Division, Department of Medicine, Peking University First Hospital, Beijing, P.R. China and [2]Electron Microscopy, Electron Microscopy Laboratory, Peking University First Hospital, Beijing, P.R. China

Background and Aims: Prolonged exposure to mercury can cause membranous nephropathy. The routine clinicopathological features of mercury-associated membranous nephropathy (M-MN) and idiopathic membranous nephropathy (I-MN) are similar. The difference in ultrastructure between them was observed clinically. The current study retrospectively compared the ultrastructure features, clinical and pathological data, treatment and prognosis of patients with M-MN and I-MN.

Method: Thirteen patients with M-MN and 13 patients with I-MN were enrolled. The clinical and pathological data were retrospectively collected. Electron micrographs of glomerular capillaries were taken and the foot process width (FPW) and the number of foot processes per 10 μm glomerular basement membrane (GBM) were measured. The presence and location of electron-dense deposits in mesangium and subendothelial region were recorded.

Results: Patients with M-MN were younger (38.7±8.5 versus 45.8±5.7 years, *P*=0.020), with a shorter duration of complete remission (9.0±6.1 versus 20.3±9.8 months, *P*=0.004) and lower relapse rate (0% versus 45.5%, *P*=0.014) than patients with I-MN. As to ultrastructure, patients with M-MN had lower levels of FPW [974.3nm (range 791.2∼1504.4) versus 2370.6nm (range 2219.4∼2559.1), *P*=0.001, **Figure 1**], more foot processes per 10 μm GBM [8.1 (range 5.2∼10.0) versus 3.3 (range 3.1∼3.5), *P*=0.001], and higher ratio of mesangial electron-dense deposits (41.7% versus 0, *P*=0.015, **Figure 2**) than those with I-MN. Multivariate analysis showed that type of disease (M-MN or I-MN) and stage of MN (stageIor stageIIand above) were the two only determinants of FPW. FPW over 1645 nm differentiated M-MN from I-MN with high sensitivity (92.3%) and specificity (83.3%).

Conclusion: The quantitative analysis of foot processes may offer a potential tool to distinguish M-MN from I-MN. Better prognosis in patients with M-MN may be related to minor podocyte damage.

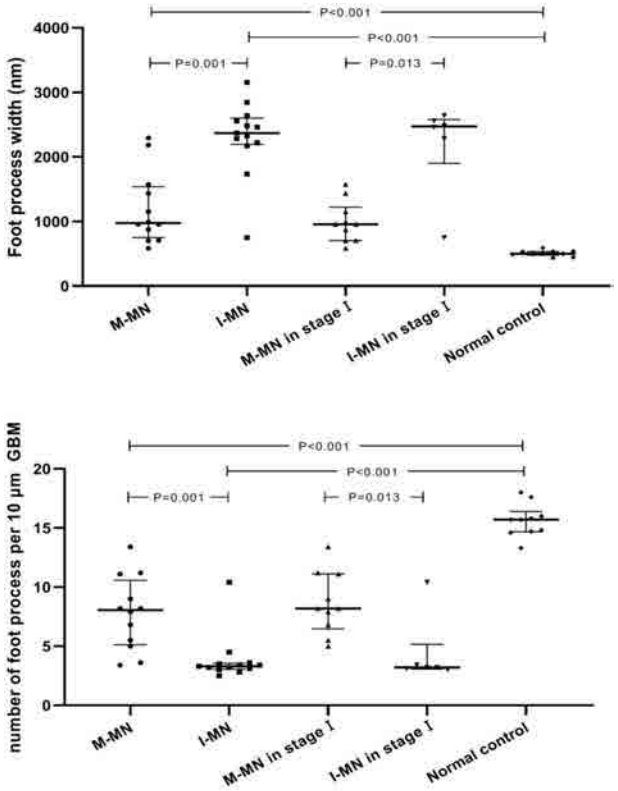


Figure 1. Foot process width of patients with M-MN, I-MN, M-MN in stage I, I-MN in stage I and normal control. Data expressed as median with range [interquartile range (IQR)].

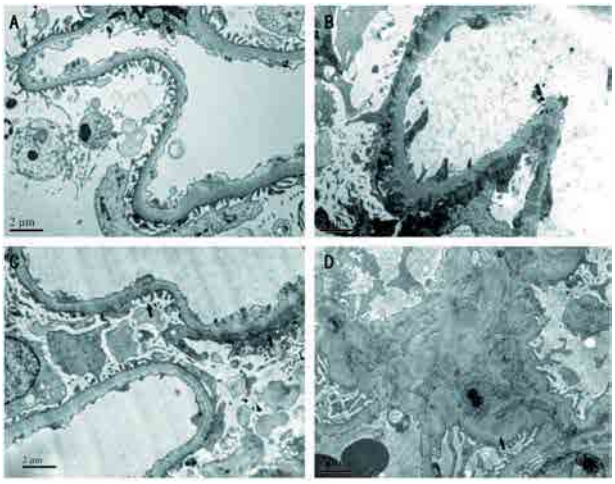


Figure 2. Electron microscopy (original magnification ×10000). (A) Normal control. The foot processes were separate. (B) Example of M-MN. Extensive effacement of foot processes with a large amount of electron-dense deposits diffusely located in the subepithelial region. (C) Example of M-MN. Partial effacement of foot process and partially location of electron-dense deposits. The arrow on the left indicate the separate foot processes and there was no electron-dense deposits. The arrow on the right indicate the extensive effacement of foot processes and electron-dense deposits located in the subepithelial region. (D) Example of M-MN. A small amount of electron-dense deposits in the mesangial region (arrow). M-MN: mercury-associated membranous nephropathy

P0129 DIET INDUCED ACCELERATION OF RENAL INJURY IN THE BTBROB/OB MOUSE MODEL OF DIABETIC KIDNEY DISEASE

Lena William-Olsson[1], Pernilla Tonelius[1], Tajana Tesan Tomic[2], Magnus Söderberg[3], Anna Björnson Granqvist[1]

[1]Early Cardiovascular, Renal and Metabolism, R&D Biopharmaceuticals, AstraZeneca, Bioscience Renal, Gothenburg, Sweden, [2]Early Cardiovascular, Renal and Metabolism, R&D Biopharmaceuticals, AstraZeneca, Bioscience Cardiovascular, Gothenburg, Sweden and [3]R&D Pharmaceuticals, AstraZeneca, Clinical Pharmacology and Safety Sciences, Gothenburg, Sweden

Background and Aims: There is a need of disease relevant models for efficient evaluation of new drug targets in the renal field. The obese diabetic BTBR*ob/ob* mouse model have features resembling important aspects of human diabetic kidney disease and is extensively used in pharmacological studies. Since diet composition plays a role in diabetic- and renal disease it is important to have detailed control of nutritional intake in our pre-clinical models, especially since many studies use in-diet drug administration. In this study we compared disease progression in obese diabetic mice on non-defined chow diet (R3) with the defined control diet D12450B (Research Diets).

Method: BTBR*ob/ob* mice were fed either regular laboratory rodent chow (R3) or the defined control diet D12450B containing 35% sucrose from 6 weeks of age. The animals were studied for 14 to 20 weeks of age and both physical parameters, urine and blood parameters, histology and gene expression was examined. (R3 group n=14, D12450B group n=8).

Results: Mice on the defined D12450B diet displayed increased calorie- and water intake, but gained less weight compared to R3 group. Blood glucose and HbA1c was higher at all timepoints, and urinary albumin-to-creatinine ratio was highly elevated compared to mice on R3 diet. Mice fed D12450B also displayed lower levels of plasma insulin and increased plasma b-hydroxybutyrate levels. Histopathological evaluation revealed that the defined D12450B diet increased induction both of mesangial injury score and gene expression of tubular injury markers NGAL and Kim-1.

Conclusion: : In summary, the choice of diet composition will have a huge impact on the disease progression in diabetic leptin-deficient overeating mouse models. These finding underline the importance of describing the diet composition in detail and take precaution on diet selection for preclinical studies.

P0130 THE MORPHOMETRIC ANALYSIS OF GLOMERULI IN OBESE AND NON-OBESE PATIENTS WITH GLOMERULAR DISEASES

Elena Jordanova[1], Radmila Jankovic[2], Radomir Naumovic[3], Dejan Celic[4], Bojana Ljubicic[4], Igor Pantic[5], Sanja Simic-Ogrizovic[6], Gordana Jovanovic-Basta[7]

[1]Belgrade, Department of Nephrology, Clinic for Internal Medicine, Clinical Hospital Center Zemun, Belgrade, Serbia, [2]Faculty of Medicine, Institute of Patology, University of Belgrade, Belgrade, Serbia, [3]Clinical Hospital Center Zvezdara, Department of Nephrology, Belgrade, Serbia, [4]Clinical Center of Vojvodina, Clinic of Nephrology and Clinical Immunology, Novi Sad, Serbia, [5]Faculty of Medicine, Institute of Medical Physiology, University of Belgrade, Belgrade, Serbia, [6]Medigroup Hospital, Belgrade, Serbia and [7]Faculty of Medicne, Institute of Patology, University of Belgrade, Belgrade, Serbia

Background and Aims: The aim of the study was to evaluate glomerular morphometry in obese and non-obese patients with glomerular diseases: FSGS, IgA nephropathy, membranous glomerulonephritis (MGN) and membranoproliferative glomerulonephritis (MPGN).

Method: The study included 125 patients with glomerular diseases (77 males, mean age 46± 15.2 years): obese (BMI> 27kg/m^2- 63 patients) and non-obese (BMI< 27kg/m^2- 62 patients). The serum concentration of creatinine, proteins, albumin, cholesterol, trygliceride, daily proteinuria were measured at the time of kidney biopsy. Formula Cockcroft-Gault#(Cockcroft-Gault: non-obese) and Cockcroft-$Gault_{LBW}$: obese) was calculated. Glomerular radius (GR), glomerular volume (GV) and glomerular density (GD) were compared morphometrically between two groups.

Results: At the time of kidney biopsy the obese had significantly lower eGFR, significantly higher creatinine, trygliceride, daily proteinuria compared to non-obese. Obese FSGS patients had significantly higher GR (109.44±6.03 μm vs 98.53±14.38 μm) and GV (3.13±0.49 x10^6 μm?vs 2.26±0.83 x10^6 μm?, only midly lower GD (1.91±0.39/ mm^2 vs 1.95±0.61/mm^2) compared to non-obese. Obese IgA nephropathy patients had higher GR (110.69± 15.24 μm vs 107.77±14.53 μm), significantly higher GV(3.34±1.78 x10^6 μm?vs 2.31± 1.51 x10^6 μm? and significantly lower GD (1.21±0.29/mm^2 vs 2.14±0.54/mm^2) in comparation with non-obese. Significant positive association between GV and BMI (r=0.439; p<0.01) in FSGS patients was found. Significant positive correlation between GV and BMI (r=0.683; p< 0.01), but significant negative correlation between GD and BMI (r=-0.710; p< 0.01) in IgA nephropathy patients were found. Obese MGN patients had lower GR (112.82± 13.65 μm vs 118.39± 14.52 μm), GV (3.57± 1.19 x10^6 μm?vs 4.07± 1.28 x10^6 μm? and GD (1.89± 0.17/ mm^2 vs 1.91± 0.92/mm^2) but without significance compared to non-obese. Obese MPGN patients had higher GR(105.89± 12.24 μm vs 92.73± 30.01 μm), GV (2.94± 0.91 x10^6 μm?vs 2.31± 1.27 x10^6 μm? and GD (2.32± 0.63/ mm^2 vs 2.03± 0.73/ mm^2) but without significance in comparation with non-obese. Significant negative association between GD and daily proteinuria (r=-0.417; p<0.01) in MGN patients was found.

Conclusion: Obese FSGS patients had significantly higher GV, lower GD compared to non-obese. Obese IgA nephropathy patients had significantly higher GV and significantly lower GD. Obese MGN patients had lower and obese MPGN patients had higher morphometric parameters of glomeruli compared to non-obese. Significant positive correlation between GV and BMI in FSGS and IgA nephropathy patients were found.

P0131

HIGH-DOSE URIC ACID ALTERS CELLULAR PROTEOME, INCREASES INTRACELLULAR ATP, ENHANCES TISSUE REPAIR CAPABILITY AND INCREASES CALCIUM OXALATE CRYSTAL-BINDING CAPABILITY OF RENAL TUBULAR CELLS: IMPLICATIONS TO HYPERURICOSURIA-INDUCED KIDNEY STONE DISEASE

Suchitra Sutthimethakorn[1], Visith Thongboonkerd[1]

[1]*Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background and Aims: Hyperuricosuria is well documented to get involved in the pathogenesis of kidney stone disease, especially uric acid (UA) and calcium oxalate (CaOx) types. Nevertheless, hyperuricosuria-induced alterations in renal tubular cells and cascade mechanisms that subsequently trigger kidney stone formation remained largely unknown. This study aimed to examine changes in cellular proteome and function in renal tubular cells after treatment with high-dose UA.

Method: MDCK cells were incubated with 3.5 mM uric acid for 48-h. Cellular proteins were extracted and subjected to quantitative proteomics analysis using 2-D PAGE followed by nanoLC-ESI-ETD MS/MS. The proteome data were confirmed by Western blotting, whereas functional analyses were performed using various assays.

Results: Quantitative proteomics analysis revealed significant changes in levels of 22 proteins in the UA-treated cells that were related to ATPase activity, mitochondrial transport, cell adhesion and molecule binding, cell projection organization and maintenance of location network, metabolic process, response to unfold proteins, and vesicle-mediated transport. Western blotting confirmed changes in levels of cellular proteins identified by quantitative proteomics. Functional assays revealed an increase in intracellular ATP level and enhancement of tissue repair capability in the UA-treated cells. Interestingly, isolation/purification of apical membranes followed by Western blotting showed the increased levels of HSP70 and HSP90 (the known receptors for CaOx crystals) on apical membranes of the UA-treated cells. CaOx crystal-cell adhesion assay revealed significant increase in CaOx-binding capability of the UA-treated cells, whereas neutralization of the surface HSP70 and HSP90 using their specific monoclonal antibodies caused significant reduction in such binding capability (even below the basal level).

Conclusion: These findings highlighted changes in renal tubular cells in response to high-dose UA that might be related to the pathogenic mechanisms of kidney stone disease associated with hyperuricosuria.

P0132 DIAGNOSIS OF HYPEROXALURIA FROM RENAL BIOPSY

Marwa Omrane[1], Raja Aoudia[1], Mondher Ounissi[1], Nada Sellami[1], Mouna Jerbi[2], Hanene Gaied[2], Hayet Kaaroud[1], Amel Harzallah[1], Taieb Ben Abdallah[1], Rim Goucha[2]

[1]Charles Nicole Hospital, Internal medicine A, Tunis, Tunisia and [2]Mongi Slim Hospital, Nephrology, La Marsa, Tunisia

Background and Aims: Crystal-induced kidney disease refers to kidney injury caused by intratubular crystal deposition. The most common forms of crystalline nephropathy encountered in renal pathology are nephrocalcinosis and oxalate nephropathy. The purpose of our study is to determine the epidemiological and clinical characteristics of hyperoxaluria diagnosed from renal biopsy.

Method: We retrospectively reviewed all kidney biopsy specimens evaluated at renal pathology laboratory, from 1976 to 2019. The biopsy specimens were received from multiple medical department and medical centers. We studied 8900 biopsy specimens and we were focused on patients whose diagnosis of hyperoxaluria was made from renal biopsy

Results: We identified 25 cases (15 children and 10 adults) with a sex ratio H / F of 0.9. Mean age at diagnosis was 17.2 years old [4 months-73 years old]. Most patients were offspring of consanguineous mating (14 of 25) with intermarriage of first-degree cousins being the most common pattern. A family history of chronic kidney disease was found in 13 patients: indeterminated nephropathy (n = 6) and renal stone (n = 5) and primary hyperoxaluria (n=2). Among our patients, five had a history of urolithiasis. One patient had a history of chronic diarrhea related to Crohn's disease and one patient had a history of cephalic pancreatectomy and ileal resection. Initial symptoms and signs were dominated by renal failure (n = 25) with mean creatinine of 789.5 µmol / l [306-1832µmol / l], associated with proteinuria in 10 patients and hematuria in 11 patients. Arterial hypertension was present in 4 patients. Oligo anuria was reported in 4 patients without dilation of the urinary excretory pathways. In our patients, the diagnosis of crystalin nephropathy was revealed by renal biopsy. In one case, the diagnosis was made after renal transplant. In 4 cases the diagnosis was made by postmortem kidney biopsy. In all cases, the kidney biopsy specimen showed extensive intratubular crystal deposition and tubulointerstitial mononuclear cell infiltration with features of tubular injury and interstitial fibrosis. Examination of histologic slides showed colorless refractile crystals of polygonal appearance. Multicolored birefringence under polarized light identified these crystals as calcium oxalate. After different investigations (genetic and biological analysis), the diagnosis of hyperoxaluria was confirmed. Hyperoxaluria was primary in 23 patients and secondary in 2 patients.

Conclusion: Hyperoxaluria is a rare condition, often serious, involving renal prognosis and sometimes life-threatening, especially in early-onset forms. Early diagnosis and treatment should be done as soon as possible to slow the progression to end-stage renal failure. In patients with renal insufficiency, the diagnosis of hyperoxaluria is difficult. Renal biopsy can help when clinical and radiological data are not sufficient.

P0133

INCREASED INTRA-ABDOMINAL PRESSURE DURING LAPARASCOPIC PNEUMOPERITONEUM ENHANCES ALBUMINURIA VIA RENAL VENOUS CONGESTION, ILLUSTRATING PATHOPHYSIOLOGICAL ASPECTS OF HIGH OUTPUT PREECLAMPSIA.

Melanie Schoutteten[1,2,3], Dreesen Pauline[1,2], Nele Vande Velde[1], Line Heylen[1,4], Iris Kaminski[1], Bart De Moor[1,5], Manu Malbrain[6], Wilfried Gyselaers[1,7]

[1]UHasselt, Faculty of Medicine and Life Sciences, Hasselt, Belgium, [2]Ziekenhuis Oost-Limburg, Future Health, Genk, Belgium, [3]Catharina Ziekenhuis Eindhoven, Nephrology, Eindhoven, Netherlands, [4]Ziekenhuis Oost-Limburg, Nephrology, Genk, Belgium, [5]Jessa Ziekenhuis, Nephrology, Hasselt, Belgium, [6]Universitair Ziekenhuis Brussel, Intensive care unit, Brussel, Belgium and [7]Ziekenhuis Oost-Limburg, Gynaecology, Genk, Belgium

Background and Aims: Intra-abdominal hypertension (IAH) causes severe organ dysfunction. Our aim is to evaluate the effect of increased intra-abdominal pressure (IAP) on renal function, hypothesizing that venous congestion may increase proteinuria and fluid retention without endothelial dysfunction.

Method: Three urine samples were collected from 32 non-pregnant women undergoing laparoscopic assisted vaginal hysterectomy (LAVH) and from 10 controls placed in Trendelenburg position for 60 minutes. Urine sampling was done before (PRE), during or immediately after (PER), and two hours after (POST) the procedure. Urinary albumin, protein and creatinine concentrations were measured in each sample, ratios were calculated and compared within and between groups.

Results: During LAVH, the albumin/creatinine ratio (ACR) increased and persisted POST-procedure, which was not observed in controls. A positive correlation existed between the LAVH duration and the relative change in both ACR and protein/creatinine ratio (PCR) PER- and POST-procedure.

Conclusion: Iatrogenic IAH increases urinary ACR and PCR in non-pregnant women via a process of venous congestion. This mechanism might explain the presentation of one specific subtype of late-onset preeclampsia, where no drop of maternal cardiac output is observed.

P0134 PROTEINURIA IS NOT ALWAYS ASSOCIATED WITH PROGNOSIS IN IGA NEPHROPATHY.

Byoung-Soo Cho[1], Hyaejin Yun[2], Sungmin Jung[3], Hyun-soon Lee[4]

[1]Dr. Cho's Kidney center, Pediatric, Seoul, Korea, Rep. of South, [2]NUR hospital, Internal medicine, Seoul, Korea, Rep. of South, [3]Dr. Cho's Kidney center, Internal medicine, Seoul, Korea, Rep. of South and [4]Korea pathology lab, Pathology, Seoul, Korea, Rep. of South

Background and Aims: To date the most widely well studied risk factor for progression to ESRD in patients with IgA nephropathy is proteinuria. Recent report suggests proteinuria reduction as a surrogate end point in trial of IgA nephropathy(2019,CJASN). Sensitivity of most biomarkers such as blood and urine gd-IgA1 level, IgG/IgA autoantibody, sCD89, sCD71, NGAL, KIM-1, Cystatin-C etc were compared with the amount of proteinuria. Most nephrologists do not performing kidney biopsy in patients without proteinuria or proteinuria less than than 500mg/day even though IgA nephropathy is suspected. However we recently experienced severe IgA nephropathy (HSD Lee, grade IV) in patients with normal urinalysis, and more than half the patients showed stationary or aggravated renal pathology at the follow up renal biopsy although urinalysis findings were normalized after methylprednisolone pulse therapy.

Method: In our center we performed 892 renal biopsies during last 6 years, we experienced 253 IgA nephropathy, of which 152 cases were done follow up renal biopsies to see the pathologic changes who showed normalized urinalysis findings after methylprednisolone pulse therapy.

Results: Of the 253 patients 241 patients showed initial abnormal urinalysis like hematuria and or proteinuria. However eleven patients showed normal urinalysis at the time of renal biopsy, of which 5 cases were diagnosed as essential hypertension and 6 cases were normal urinalysis associated with lowered GFR. Of the 152 follow up renal biopsies we evaluated 99 cases who showed normalized urinalysis findings after therapy, of which 65 cases(65.7%) showed stationary or aggravated renal pathology.

Conclusion: In conclusion further long term studies are needed, proteinuria could not be a surrogate marker for prognosis of the IgA nephropathy, Regardless of proteinuria if associated with hypertension and or lowered GFR, renal biopsy should be done. Follow up renal biopsy might be needed to confirm the healing of IgA nephropathy regardless of urinary findings to see the disappearance of IgA deposition, decreasing mesangial and endocapillary hypercellularity, disappearance of crescent formation, decreasing sclerosis, etc.

P0135 **EFFECT OF LYSOPHOSPHATIDIC ACID REGULATION ON THE AGING KIDNEY**

YONGJIE JIN[1], Eun Nim Kim[1], Ji Hee Lim[1], Hyung Duk Kim[1], Yaeni Kim[1], Tae Hyun Ban[1], Cheol Whee Park[1], Bum Soon Choi[1]

[1]Division of Nephrology, Internal medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South

Background and Aims: Lysophosphatidic Acid (LPA) is a bioactive lysophospholipid that is present in all tissues. It has been reviewed that LPA could induce oxidative stress and inflammation. Oxidative stress is a major characteristic of aging which is a critical risk factor of renal dysfunction. Nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that regulates the expression of antioxidants, which could improve cell viability by reducing oxidative stress, is found to be decreased in the aging kidney. Also, LPA regulates the expression of Nrf2 has been reported. In this study, we evaluate the effect of LPA in the aging kidney by elucidating the potential LPA-Nrf2 signaling pathway.

Method: Male 2- and 24-month-old C57/BL6 mice were used in this study. We measured histological change, oxidative stress, and aging-related protein expression in the kidneys.

Results: 24-month-old mice displayed increased albuminuria. Creatinine clearance decreased with aging. There were increases in mesangial volume and tubulointerstitial fibrosis in 24-month-old mice. There were also increases in autotaxin, LPAR1, PI3K, Akt, GSK3β expression with aging and Nrf2, NQO1, HO1, SOD1, SOD2 were decreased in 24-month-old mice.

Conclusion: LPA signaling decreased antioxidants expression via down-regulating Nrf2. Targeting the LPA-Nrf2 pathway provides new evidence to decrease aging-related disease in the kidney.

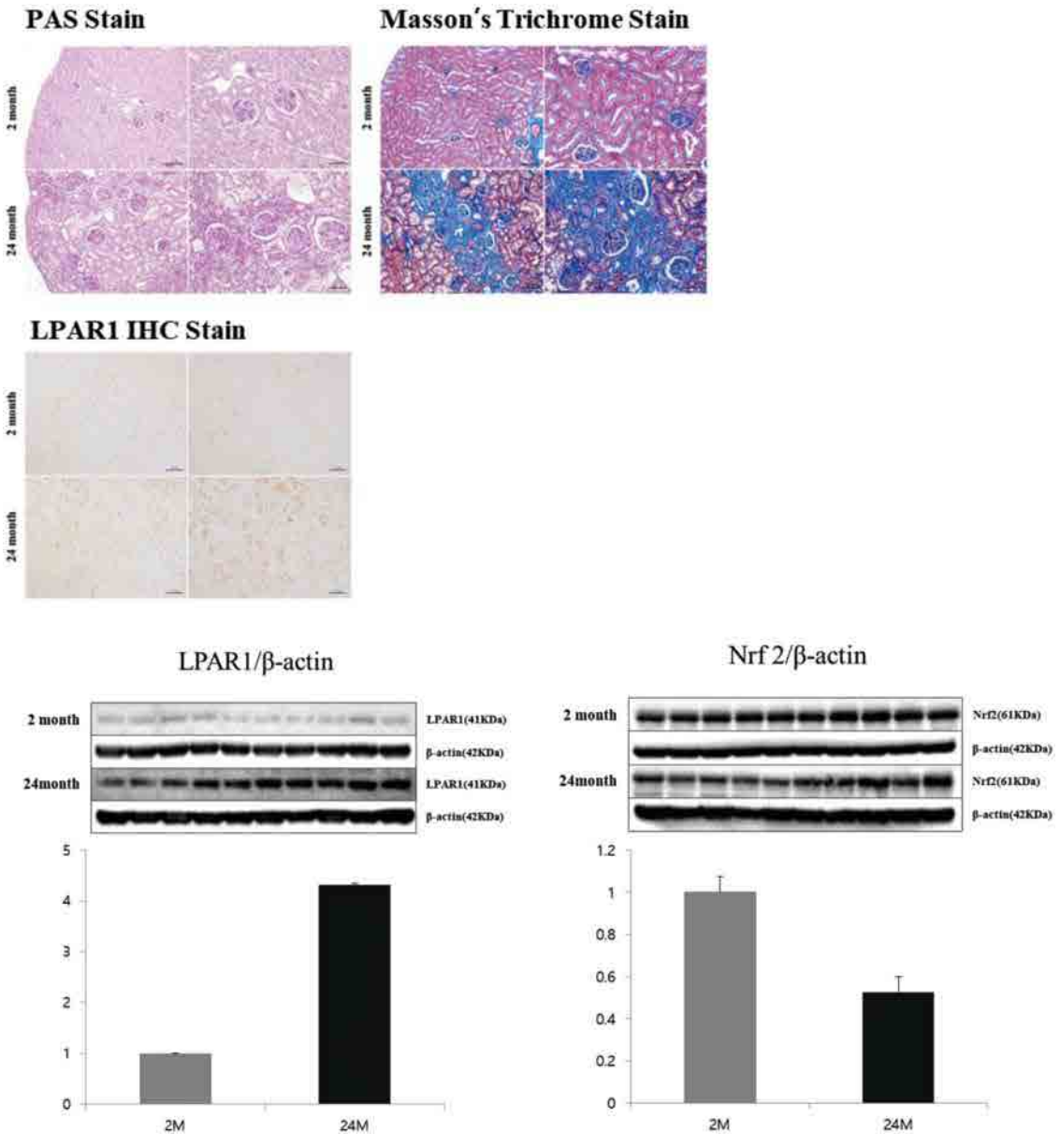


Figure:

P0136

COMPARISON OF SECONDARY IGA NEPHROPATHY OF ANKYLOSING SPONDYLITIS AND PRIMARY IGA NEPHROPATHY IN CLINICAL AND PATHOLOGICAL FEATURES

Qin Xue[1], Guang Li Zhang[1,2], Zebo Tian[3]

[1] Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Department of Nephrology, Shanghai, P.R. China, [2]Southern medical university affiliated Shenzhen Baoan Hospital, Department of Rheumatology and Immunology, Shenzhen, P.R. China and [3]Xishui People's Hospital, Department of Nephrology, Huanggang City, Hubei Province, P.R. China

Background and Aims: Renal involvement is one of the most common extra-articular complications caused by ankylosing spondylitis (AS). The main pathological manifestation is secondary IgA nephropathy(SIgAN) in Chinese AS patients. The difference between SIgAN and primary IgAN (PIgAN) remains unclear due to the lack of cases. Therefore, the aim of this retrospective study was to compare the clinical and pathological features of SIgAN of AS (SIgAN-AS) and PIgAN, to detect the pathogenesis of SIgAN

Method: Clinical characteristics and pathological data were collected in patients who were diagnosed with IgAN by renal biopsy in our hospital from Jan 2008 to Oct 2018. Patients with SIgAN-AS were recruited by the ratio 1:5 of patients with primary IgAN as the control group in the study. Fifteen patients with SIgAN-AS and Seventy-five patients with PIgAN were enrolled in this retrospective study.

Results: There were 15 cases in AS group, including 13 male and 2 female. The cohort of 75 patients with PIgAN included 34 male and 41 female. There were more males in AS group 13/15 (86.7%) vs 37/75(49.3%) ,$P < 0.05$. Compared with PIgAN patients, SIgAN-AS patients had higher incidences of hematuria(13/15(86.7%)vs 44/75 (58.7%) , $P < 0.05$), lower levels of 24-hour urinary protein(0.85 ± 0.68 vs 1.57 ± 1.54g, $P < 0.05$), but higher levels of eGFR (CKD-MDRD formula) (117.60 ± 37.33 vs 85.35 ± 31.36, $P < 0.05$),eGFR (CKD-EPI formula) (128.01 ± 41.58 vs 92.75 ± 36.09, $P < 0.05$), Albumin (44.67 ± 3.48 vs 41.09 ± 7.07 g/L, $P < 0.05$) ESR (43.20 ± 33.94 vs 18.79 ± 16.26mm/h, $P < 0.001$) , and CRP (21.19 ± 30.61 vs 2.11 ± 4.58mg/L, $P < 0.001$) . From the perspective of renal pathology of PIgAN, SIgA-AS patients had fewer incidences of renal tubular atrophy / interstitial fibrosis of nephropathy ($P < 0.05$). The immunohistostaining analysis showed higher incidences of dominant deposits of single IgA in mesangial cell area ($P < 0.05$).

Conclusion: Patients with SIgAN-AS is more common in male and display a milder progression than those with primary IgAN. Majority of the SIgAN-AS can be improved with early intervention.

P0137 **FIRST RUSSIAN BOSIMILAR OF ECULIZUMAB IN THE TREATMENT OF AN ADULT PATIENT WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME**

Yulia Lavrishcheva[1], Alexander Jakovenko[2], Dmitriy Kudlay[3]

[1]AlmazovNational Medical Research Centre, Saint Petersburg, Russian Federation., Saint-Petersburg, Russia, [2]Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation., Saint Petersburg, Russia and [3], NRC Institute of Immunology FMBA of Russia, Moscow, Russian Federation., Moscow, Russia

Background and Aims: The disease diagnostics results and the efficacy of pathogenetic treatment when transferring from the original drug to the biosimilar were evaluated during clinical observation of an adult patient with aHUS.

Method: A 46-year-old patient has a history of hypertension since 2012 and maximum ABP of 230/130 mmHg. In 2016, newly diagnosed azotemia was identified (blood creatinine — 140 μmol/L, GFR by EPI — 54 mL/min/1.73m2). In 2018, the patient suffered an acute cerebrovascular accident in the vertebrobasilar area. On admission to Almazov National Medical Research Centre, blood test showed: creatinine – 260 μmol/L (GFR by EPI — 28 mL/min/1.73m^2), urea – 11.52 mmol/L, LDH – 130 U/L, complement system C3 – 1.32 g/L, C4 – 0.37 g/L, hemoglobin – 144 g/L, platelets – 302*10^9/L; urinalysis showed: daily protein loss – 2.6 g/day, RBC – 0–1 per field. Taking into account the kidney damage, the renal fine-needle aspiration biopsy was performed, revealing histopathological findings typical of chronic thrombotic microangiopathy of extreme severity, arteriolar arteriosclerosis with total or subtotal luminal occlusion, extensive secondary perihilar segmental glomerulosclerosis (27%); and global glomerulosclerosis (55%). According to the study results, the secondary genesis of TMA was ruled out, as well as STEC-HUS and thrombotic thrombocytopenic purpura (TTP), systemic diseases (systemic lupus erythematosus, antiphospholipid syndrome (APS), scleroderma), malignancies, HIV infection, sepsis, malignant arterial hypertension, adverse drug events, or disseminated intravascular coagulation (DIC). Plasma ADAMTS-13 levels were also assessed. Its activity was 64% (normal range 93–113%) of ADAMTS-13 activity in the control plasma, thus the diagnosis of thrombocytopenic purpura was ruled out. Due to the absence of anti-CFH-antibodies the antibody origin of aHUS was also ruled out. To assess the contribution of additional factors promoting the development of TMA, the polymorphism of hemostasis genes was studied to reveal homozygous genotypes of platelet collagen receptors (ITGA2: 807 C/E), heterozygous genotypes of fibrinogen genes (FGB: 455 G/A), folate cycle enzymes (methylenetetrahydrofolate reductase (MTHFR: 677 C/T), methionine synthase (MTR: 2756 A/G (D919G)), responsible for a pronounced tendency towards hyperhomocysteinemia. In the clinical case the diagnosis of aHUS was obvious, which was supported by the classical symptom cluster of TMA and histopathological verification in the absence of data suggestive of other pathological conditions. The peculiarity of this clinical case is the late diagnosis, long-standing course, and severity (complications such as an acute cerebrovascular accident in the vertebrobasilar area, target lesions, kidneys in particular).

Results: Taking into account the primary diagnosis, treatment with a standard dose of eculizumab was initiated. After three months of treatment the patient was transferred to therapy with Russian biosimilar of eculizumab. After the switch from the original drug, the therapy with eculizumab biosimilar continued to be associated with a positive trend including a gradual decline in azotemia level (blood creatinine – 115 μmol/L (GFR by EPI – 52 mL/min/1.73m^2), blood urea – 7.10 mmol/L), proteinuria (daily protein loss – 0.6 g/day). The comprehensive treatment including antihypertensive therapy also led to the normalisation of ABP values. No adverse events associated with the therapy were noted.

Conclusion: The obtained results demonstrate high efficacy and safety of eculizumab biosimilar in the treatment of the adult patient with aHUS.

P0138 THE ROLE OF TREFOIL FACTOR 3 IN THE EVALUATION OF RENAL ALTERATION IN PATIENTS WITH ANKILOSING SPONDYLITIS

Lidia Plenkina[1], Olga Simonova[1]

[1]*Kirov State Medical University*

Background and Aims: Kidney damage in ankylosing spondylitis (AS) has one of the leading positions. The diagnostic value of traditional markers of renal damage is not high, which often leads to delayed diagnosis. Therefore, an active research for alternative methods is conducted. The Aim was to evaluate urinary excretion of Trefoil factor-3 (TFF-3) in patients with AS.

Method: Urine samples of 50 patients (male/female =37/13) were evaluated. The requrentments for patients providing samples were: confirmed diagnosis of AS, age 18 and over and and absence of intercurrent diseases. Median age of patients was 39 [34; 56] years, duration of articular syndrome was 10 [7;18] years, glomerular filtration rate (GFR) - 105 [83;119] ml/min/1.73 m? Patients received nonsteroidal anti-inflammatory drugs (NSAIDs) and tumor necrosis factor alpha inhibitors (TNFα inhibitors). TFF-3 level was measured by enzyme-linked immunosorbent assay. Urinary excretion was expressed as nanograms per millimol of urinary creatinine. The results were compared with the results of the control group.

Results: The level of TFF-3 in patients without chronic kidney disease (CKD) was higher than in the control group: 53.4 [20.8;105.7] and 23.3[1.9;62.9] ng/mmol respectively, ($p=0.02$). A correlation with disease activity was found for BASDAI ($rs=0.3$, $p<0.05$) and ASDAS ($rs=0.3$, $p<0,05$). Marker values in patients receiving NSAIDs were higher compared with TNFα inhibitors: 89,5 [39.8;118.9] and 32,6 [13.5; 88.2] ng/mmol respectively, ($p=0.04$). The level of TFF-3 did not depend on sex, age and AS duration. It did not correlate with GFR and albuminuria.

Conclusion: TFF-3 urinary excretion is higher in patients with AS compared with healthy individuals, as well as in patients receiving NSAIDs compared with TNFα inhibitors. Thus, the marker may be of interest for diagnosis in patients with pre-clinical tubulointerstitial damage, including those associated with the NSAIDs toxicity.

P0139

RETROSPECTIVE ANALYSIS OF RENAL PATHOLOGY AND CYTOGENETIC EXAMINATION IN PATIENTS WITH MULTIPLE MYELOMA WITH RENAL IMPAIRMENT

Ying Chen[1], Jia Lyu[2]

[1]The First Affiliated Hospital of Xi'an Jiaotong University, Hematology, Xi'an, P.R. China and [2]The First Affiliated Hospital of Xi'an Jiaotong University, Nephrology, Xi'an, P.R. China

Background and Aims: Renal impairment is one of the common implications in multiple myeloma. But the relationships between the renal pathology and cytogenetic features are not fully understood. To explore the renal pathology and cytogenetic features in patients of multiple myeloma with renal impairment.

Method: Retrospective of our hospital from January 2009 to January 2019, newly diagnosed multiple myeloma patients with renal impairment. The relationship between the results of Fluorescence in situ hybridization (FISH) and renal pathological findings was analyzed. Statistical analysis was performed using SPSS 20.0.

Results: A total of 20 patients underwent renal biopsy, included 12 males and 8 females. FISH result showed that there were 7 cases of interstitial nephritis, 3 of them were negative for FISH, and the remaining that IgH rearrangement, 1q21 amplification, RB1 deletion, D13S319 deletion, and P53 deletion detection rates were 42.86%, 28.57%, 28.57%, 28.57% and 14.29%. The incidence was lower, which was statistically significant (P<0.01). There were 6 cases of cast nephropathy, IgH rearrangement, 1q21 amplification, RB1 deletion, D13S319 deletion, and P53 deletion detection rates were 66.67%, 50%, 66.67%, 50% and 0%. Compared with the total probe positive rate, there was no statistical significance (P>0.05). There were 4 cases of acute tubular necrosis, IgH rearrangement, 1q21 amplification, RB1 deletion, D13S319 deletion, and P53 deletion detection rates were 100%, 50%, 50%, 25% and 25%, respectively. Compared with the total probe positive rate, there was no statistical significance (P>0.05). There are 1 of amyloidosis and 1 of tubular nephropathy with amyloidosis were positive for 5 probes. One case of light chain deposition disease was positive for RB1 gene deletion + D13S319 gene deletion.

Conclusion: FISH in patients with different renal pathological changes is characterized by heterogeneity, which can be used to predict the risk of renal damage and speculate on possible renal pathological types to guide prognosis.

RI in MM (biopsy proven)	n (%)
Total	20 (100)
Sex	12 (60)
Male	8 (40)
Female	
Age (median(range))	61 (50-76)
Male	58 (31-73)
Female	
Ig isotype	15 (3: 12) (75)
Light chain (Kappa: Lambda)	2 (10)
IgG	3 (15)
Non-secretory	
DS staging	3 (15)
II	17 (85)
III	
ISS staging	20 (100)
III	
Creatinine at baseline (median(range))(umol/L)	426.5 (83-1125)
Serum M protein (median(range))(%)	3.8 (0-50.5)
Percentage of plasma cells in bone marrow (median(range))(%)	38 (6.5-86)

Figure 1: The clinical and laboratory characteristics of RI patients proved by renal biopsy.

Table 1. The correlation between renal pathology and FISH results in RI in MM

Result of Renal Pathlolgy	N(%)	FISH Result (Probe positive rate %)					F-test
		IgH	RB1	1q21	D13S319	P53	
Acute and Chronic interstitial nephritis	7(35)	42.86	28.57	28.57	28.57	14.29	$P<0.01^*$
Myeloma cast nephropathy	6(30)	66.67	66.67	50	50	0	$P>0.05$
Acute tubular necrosis	4(20)	100	50	50	25	25	$P>0.05$
Amyloidosis	1(5)	100	100	100	100	100	
Light chain deposition disease	1(5)	0	100	0	100	0	
Myeloma cast nephropathy + Amyloidosis	1(5)	100	100	100	100	100	
Total	20	65	55	45	45	20	-

*$P<0.01$,compared with probe positive group.

**case less than three: Do not do statistical analysis.

P0140 **RENAL PATHOLOGICAL CHANGES AFTER SUCCESSFUL TREATMENT OF LCDD USING CYCLOPHOSPHAMIDE, THALIDOMIDE AND DEXAMETHASONE: A CASE REPORT**

Yan Wang[1], Di Wang[2,3], Shiren Sun[4]

[1]Xijing Hospital, Fourth Military Medical University,, Department of Nephrology,, Xi'an, P.R. China, [2]Xijing Hospital, Fourth Military Medical University,, Department of Nephrology,, Xi, , [3]Department of Nephrology,, Xijing Hospital, Fourth Military Medical University,, Xi'an, P.R. China and [4]Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China., Department of Nephrology,, Xi'an, P.R. China

Background and Aims: The combined of cyclophosphamide, thalidomide and dexamethasone (CTD) haven't reported in treatment of LCDD, and how the renal pathologic injury changes after treatment is still unknown.

Method: Here we descript a LCDD patients who undergone repeated renal biopsy after treatment.

Results: We report a 56-year-old woman presented with nephrotic syndrome, impaired renal function, and serum M-protein of IgG lambda. First renal biopsy showed severe nodular glomerulosclerosis with single lambda light chain linear deposit along GBM. The patient treated with 14 cycles CTD regimen, and reached the complete hematologic response and renal response. At the 29 months of follow up, the repeated biopsy showed the glomerular nodular sclerosis attenuated significantly, only trace granular electron-dense deposits along inner side of GBM.(Details in figure 1: The pathological findings of the first (A-D) and second (E-H) renal biopsy.)

Conclusion: This case highlights the hematologic response not only can improve the renal function, but also alleviate the renal nodular sclerosis. And the low-cost regimen, CTD, maybe a good choice.

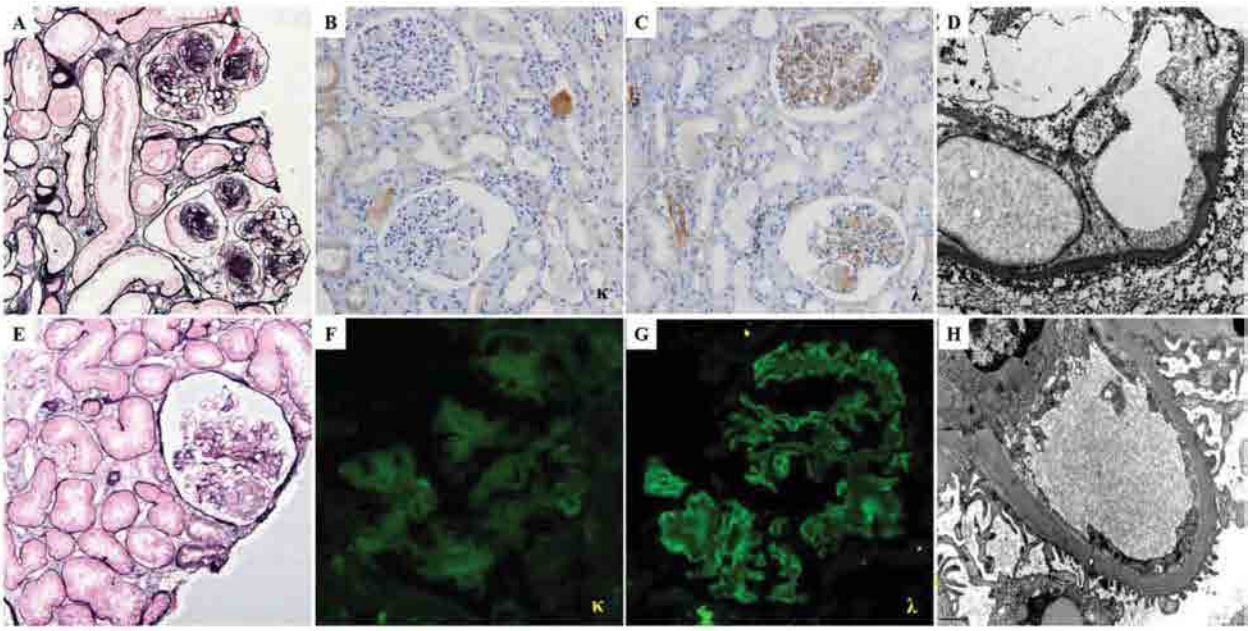


Figure 1:

P0141 **KIDNEY BIOPSY INDICATIONS AND OUTCOMES: SEVEN YEARS EXPERIENCE OF A SINGLE CENTRE IN SRI LANKA**

Dilukshi Pilapitiya[1], Nayomi Wadduwage[1], Chanaka Aberathna[1], Chinthana Galahitiyawa[1], Chula Herath[1], Sonali Rodrigo[2]

[1]Sri Jayewardenepura General Hospital, Department of Nephrology, Dialysis and Transplantation, Nugegoda, Sri Lanka and [2]Sri Jayewardenepura General Hospital, Department of Histopathology, Nugegoda, Sri Lanka

Background and Aims: Histopathological analysis of renal biopsy is the cornerstone of diagnosis in renal disease and guides treatment and prognosis. The prevalence of various renal diseases varies according to the geographical area, socioeconomic condition, race, age, demography and indication of renal biopsy.

Method: A retrospective study of all native and transplant kidney biopsies performed at the renal unit of Sri Jayewardenepura General Hospital, Sri Lanka, between 1st October 2012 and 30th September 2019. Samples were processed for light microscopy in all cases, with immunofluorescence in most cases.

Results: 771 biopsies were analyzed. Majority of biopsies 514 (67%) were male patients. Most biopsies (n= 345, 45%) were in 40 – 59yr age group, followed by 267 (35%) 20–39yr, 117 (15%) 60–69yr, 12 (1%) >70yrs, 30 (4%) 12–19yr age groups. Maximum age was 84 years. In 35 cases, tissue were inadequate.

547 (71%) were native biopsies and 224 (29%) were graft biopsies. Among transplants, majority was for an indication (n=146, 66%) followed by time-zeroes (n=59, 26%) and protocols (n=19, 9%). Rising creatinine (81%) was the strongest reason for transplant biopsies, next proteinuria (10%) and delayed graft function (7%). Time zeroes: majority were normal, few ATN, 1 chronic tubulointerstitial nephritis, and 1 hypertensive glomerulosclerosis. Grafts revealed, acute antibody-mediated rejection 41 (18%) with acute cell-mediated rejection 27 (12%), (total rejections n=68, 30%) followed by normal histology 48 (21%), acute tubular necrosis 43 (19%), chronic allograft nephropathy 23 (10%), BKV nephropathy 5 (2%), and 18% other etiologies: CNI-toxicity (n=4), hypertensive glomerulosclerosis (n=3), diabetic nephropathy (n=2), thrombotic microangiopathy (n=2), FSGS (n=2), MPGN (n=1), vasculitis (n=2), PTLD (n=1), cast nephropathy (n=1), and granulomatous interstitial nephritis (n=1).

The most common indication for native biopsy was nephrotic syndrome 209 (38%), followed by non-proteinuric CKD 105 (19%), unexplained renal failure 77 (14%), subnephrotic proteinuria 102 (18%), nephritic syndrome 54 (9%). Primary glomerulonephritis (GN) was the commonest 291 (53%). Commonest lesion amidst primary GN was IgA nephropathy 90 (16%), followed by FSGS 63 (12%), CGN 27 (4%), minimal change 36 (6%), MPGN 32 (5%), membranous 6 (1%), DPGN 22 (4%), mesangiocapillary GN 3 (0.5%) and post-streptococcal GN 11 (2%). In the secondary forms of GN, SLE was the commonest 39 (7%), next diabetic nephropathy 29 (5%), amyloidosis 2 (0.3%). Chronic tubulointerstitial nephritis 92 (16%) was the second common, with 42 (7%) CINAC – chronic interstitial nephritis in agricultural communities. Other etiologies: acute tubulointerstitial nephritis 14 (2.5%), hypertensive glomerulosclerosis 12 (2%), thrombotic microangiopathy 6 (1%), ischemic nephropathy 9 (1%), end stage disease 6 (1%), inconclusive 13 (2%). 5 cast nephropathy due to multiple myeloma, 1 monoclonal deposition disease due to lambda chain deposition, 1 sarcoidosis, 1 cholesterol embolism.

Conclusion: Female: male ratio 1:2 with commonest age group being 40 – 59yrs. Strongest indication for transplant biopsy was rising creatinine. Acute rejection was the most frequent finding in grafts, with normal histology being the next, probably due to high number of time zeroes and protocols performed in our centre. Biopsy proven BKV nephropathy was 2% (n=5).

Nephrotic range proteinuria was the commonest native biopsy indication, with non-proteinuric CKD being the second. Primary GN was the commonest finding with IgA nephropathy scoring the highest. This does not coincide with global data, which shows FSGS to be the leading cause. The second common histology was FSGS, and primary CTIN was third. The prevalence of biopsy-proven GN varies due to a wide array of factors and different studies have shown different leading patterns.

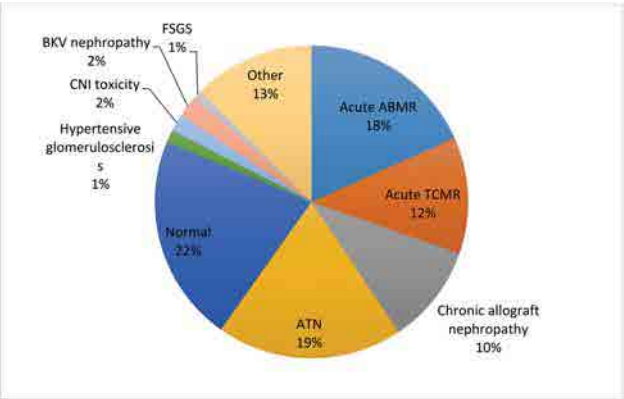


Figure 1: Transplant histology

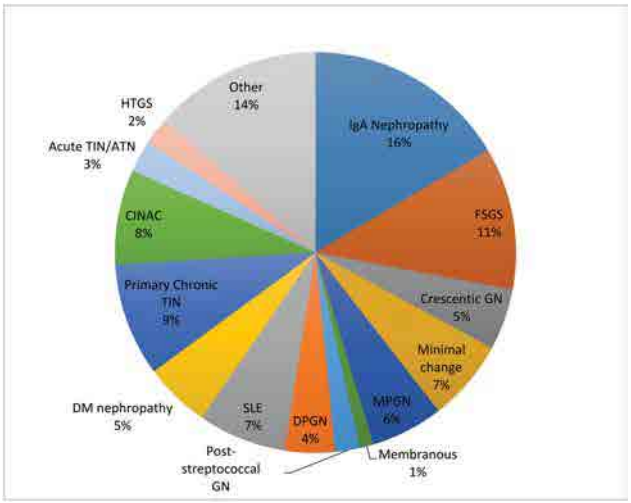


Figure 2: Native biopsy histology

P0142 CONTRAST INDUCED NEPHROPATHY AFTER CORONARY ANGIOGRAPHY

Durdona Saipova[1], Shavkat Muminov[1], Baxodir Nigmanov[1], Kamila Olimxanova[1]
[1]*Tashkent Medical Pediatric Institute, Internal disease, Tashkent, Uzbekistan*

Background and Aims: Determination of markers of kidney damage in patients with coronary artery disease after coronary angiography. HYPERLINK "https://www.healthline.com/health/coronary-angiography"

Method: The study included 303 patients with coronary artery disease who were planned coronary angiography. The initial examination of patients included an assessment of the structural and functional state of the kidneys, metabolic profile and the functional state of the cardiovascular system. Renal filtration function was assessed by the clearance of creatinine and cystatin C with the calculation of glomerular filtration rate (eGFRcr and eGFRcis) All coronary artery disease patients included in the study underwent coronary angiography using a contrast drug unigexole. If there is necessity, stenting of the coronary arteries was performed. On the 2nd day after coronary angiography, a serum creatinine concentration was determined to isolate patients in whom coronary angiography was complicated by CIN. Contrast induced nephropathy was defined as an increase in serum creatinine concentration by 25% 24 hours after coronarography. According to the study, patients were divided into 2 groups - 67.99% of patients with an uncomplicated postoperative period of caranoroangiography; CIN (-) group and CIN (+) group 32.01% of patients who developed contrast-induced nephropathy. Subsequently, the CIN + and CIN- groups were retrospectively compared according to the initial hemodynamic parameters, structural and functional state of the kidneys, and metabolic characteristics.

Results: The results of the study showed that eGFRcr did not significantly differ in the CIN(+) and CIN(-) groups, although it turned out to be lower in both groups. ($p < 0.05$). While eGFRcis in the CIN(+) group was significantly lower than in patients with uncomplicated coronary angiography. Correlation analysis showed a reliable positive average relationship between the values of eGFRcr and eGFRcis in the CIN(+) group ($r = 0.32$, $p < 0.001$). Correlation revealed a reliable average negative relationship between eGFRcis and the relative density of urine ($r = -0.46$, $p < 0.001$), indicating a combined violation of the glomerular and canalicular function of the kidneys, which indicates that in these patients, despite the preserved eGFRcr, pathogenetic markers of impaired renal function are detected. The Resistance Index (RI), which characterizes the resistance of the microvasculature of the kidneys in all patients with coronary artery disease significantly exceeded the control values. The selected groups according to the value of RI were arranged as follows: the minimum value of RI is in the CIN(–) without diabetes mellites group, and the maximum value is in patients with CIN(+) and diabetes mellitus.

Conclusion: In patients with coronary artery disease undergoing endovascular procedures, eGFRcis is a more accurate indicator of latent impaired renal filtration function than eGFRcr. Decrease in eGFRcis below 89ml / min in patients with coronary artery disease at risk of developing contrast-induced nephropathy during caranoroangiography. An increase in RI of segmental arteries of the kidneys is associated with a decrease in the filtration function of the kidneys and patients with maximum RI have the greatest risk of developing glomerular dysfunction under conditions of exposure to contrast.

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HYPERTENSION. EXPERIMENTAL

P0143 OPPOSING EFFECTS OF P38 MAPK IN PODOCYTES ON ALDOSTERONE-INDUCED GLOMERULAR INJURY IN POD-GC-A CKO MICE

SAYAKA SUGIOKA[1], Yukiko Kato[1], Akira Ishii[1], Keita Mori[1], Keisuke Osaki[1], Takeshi Tokudome[2], Taiji Matsusaka[3], Motoko Yanagita[1], Hideki Yokoi[1]

[1] Graduate School of Medicine, Kyoto University, Kyoto, Japan, Department of Nephrology, Kyoto, Japan, [2]National Cerebral and Cardiovascular Research Institute, Department of Biochemistry, Osaka, Japan and [3]Tokai University School of Medicine, Isehara, Department of Basic Sciences, Japan

Background and Aims: Previously, we demonstrated that uninephrectomized aldosterone-infused, high salt-fed podocyte-specific guanylyl cyclase-A (natriuretic peptide receptor 1) conditional KO (pod-GC-A cKO) mice exhibited glomerular injury and that pharmacological inhibition of p38 MAPK ameliorates podocyte damage. However, the effects of genetic deletion of p38 MAPK in podocytes of pod-GC-A cKO mice have been unclarified.

Method: We generated p38 MAPK(fl/fl);Nephrin-Cre (pod-p38 MAPK cKO) mice and p38 MAPK(fl/fl);GC-A(fl/fl);Nephrin-Cre (pod-p38MAPK/GC-A DKO) mice. For induction of glomerular injury, we treated them with aldosterone and high salt at 2 months of age for 3 weeks without nephrectomy (B-ALDO). In vitro, we examined the effect of p38 MAPK inhibitor in cultured human podocytes transfected with GC-A siRNA.

Results: B-ALDO-treated pod-p38 MAPK/GC-A DKO mice resulted in significant elevation of serum Cr (0.29 ± 0.04 mg/dl), massive albuminuria (42,660 ± 20,200 μg/mgCr) and severe foot process effacement in addition to intracapillary fibrin thrombi which indicated endothelial damage. Vehicle-treated DKO mice, B-ALDO-treated pod-GC-A cKO mice, and B-ALDO-treated pod-p38 MAPK cKO showed normal serum Cr levels (0.14 ± 0.01, 0.18 ± 0.02, 0.20 ± 0.01 mg/dl, respectively), mild increase of albuminuria (223 ± 6.5, 1,496 ± 592, 649 ± 303 μg/mgCr, respectively) and only segmental foot process effacement. Blood pressure was not elevated in either mutant mice compared with that of B-ALDO control mice. Furthermore, glomerular mRNA expressions of MCP-1, PAI-1, and FN were upregulated and that of VEGF-A was downregulated in DKO mice. *In vitro*, suppression of GC-A mRNA by siRNA in combination with p38 MAPK inhibitor downregulated VEGF mRNA in human cultured podocytes. Our previous works showed that pharmacological inhibition of p38 MAPK in the whole body ameliorated podocyte damage, whereas our current result showed that genetic deletion of p38 MAPK in podocytes aggravated renal injury. In order to explain the discrepancy in these results, we added an analysis of podocyte specific GC-A fl/fl p38 fl/+ cKO mice. Pod GC-A fl/fl p38 fl/+ cKO mice exhibited considerably milder renal damage than pod GC-A fl/fl p38 fl/fl double cKO mice.

Conclusion: Genetic complete p38 MAPK deletion in GC-A-nul podocytes exacerbated aldosterone-induced glomerular endothelial cell injury as well as podocytes, and resulted in renal dysfunction, probably through VEGF downregulation, whereas partial p38 MAPK inhibition in podocytes ameliorated aldosterone-induced glomerular injury in pod-GC-A cKO mice. These results suggest a certain level of p38 MAPK in podocytes is necessary to protect endothelial and epithelial cells from aldosterone-induced renal injury.

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P0144

LOW-ENERGY SHOCKWAVE TREATMENT PROMOTES ENDOTHELIAL PROGENITOR CELL HOMING TO THE STENOTIC PIG KIDNEY

Yu Zhao[1], Xiao liang Zhang[1], Bicheng Liu[1], Lilach Lerman[2]

[1]Institute of Nephrology, Zhong Da Hospital, Southeast University, School of Medicine, Nanjing, P.R. China and [2]Mayo Clinic, Rochester, MN, United States, Division of Nephrology and Hypertension, rochester, United States of America

Background and Aims: Endothelial progenitor cells (EPCs) patrol the circulation and contribute to endothelial cell regeneration and tissue revascularization. Atherosclerotic renal artery stenosis (ARAS) induces microvascular loss in the stenotic kidney. A regimen of low–energy shockwave therapy (SW) induces angiogenesis and reduces chronic ischemia, but the mechanism remains unclear. This study tested the hypothesis that SW increases EPCs homing to the stenotic kidney and increases renal capillary regeneration in a unilateral ARAS swine model.

Method: Domestic pigs were randomized to normal control or unilateral ARAS (induced by a local irritant coil in the renal artery and a high-fat diet). ARAS pigs were treated with low-energy SW (0.1 mJ/mm2) or sham (n=6 each group), bi-weekly for 3 consecutive weeks, starting after 3 weeks of ARAS. Blood samples for EPCs (CD34+ and KDR+ by flow cytometry) and the homing factor SDF-1 were collected 4 weeks after completion of SW treatment from the inferior vena cava (IVC) and the stenotic kidney (STK) vein and artery. Urine was collected from the urinary bladder. Kidneys were studied ex vivo for morphology and expression of an endothelial cell marker (CD31) and the pro- angiogenic growth factor angiopoietin (Ang)-1.

Results: In ARAS, tubulointerstitial fibrosis, tubular score, urinary protein, serum creatinine and mean arterial pressure were significantly increased and capillary count (Fig. 1A) decreased ($P<0.05$ vs. control), but all markedly improved in ARAS+SW ($P<0.05$ vs. ARAS). EPC number was decreased in the IVC and renal artery of ARAS pigs (Fig. 1B), but improved in ARAS+SW. SDF-1 levels in the IVC, STK vein and artery, and Ang-1 expression in the kidney of ARAS+SW, were all increased ($P<0.05$ vs. ARAS).

Conclusion: Low-energy shockwave improves ischemic kidney capillary density, which is associated with and may be at least in part mediated by promoting EPC mobilization and homing to the stenotic kidney.

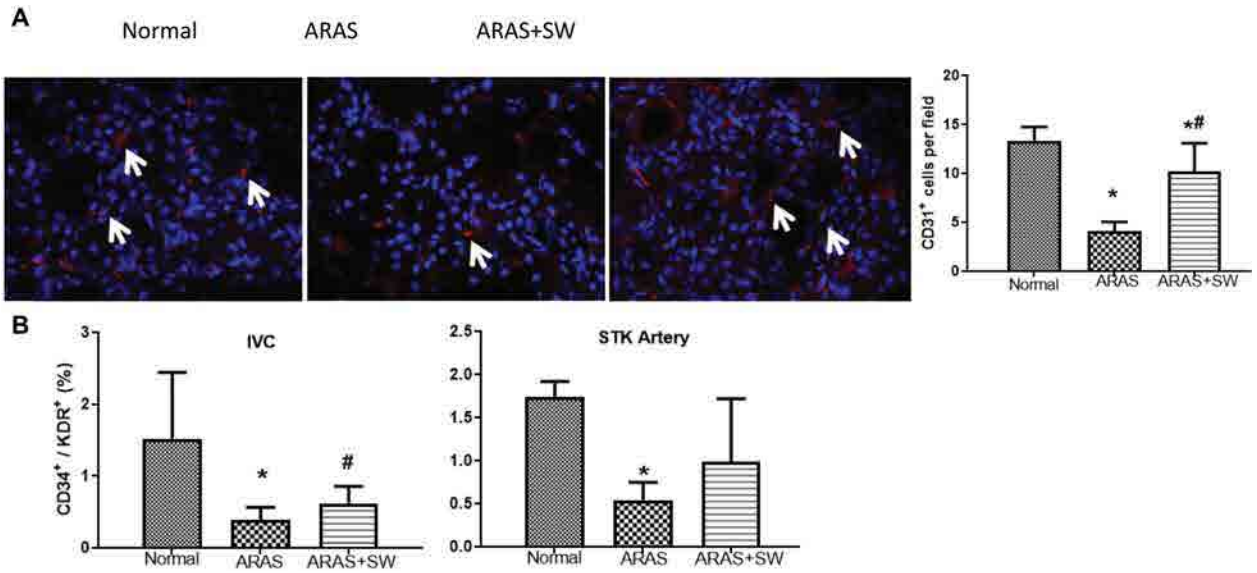


Fig. 1 The effect of SW on CD31+ capillary density in the kidney and EPC recruitment in blood samples of ARAS pigs.
A: CD31+ capillaries observed by immunolabeling and confocal microscopy imaging in pig kidneys (white arrows) (×400; bars=50μm). B: EPCs (CD34+/KDR+) counted by flow cytometry in the IVC and artery. Data are expressed as mean±SD (n=6 per group). *$P<0.05$ vs. Normal; #$P<0.05$ vs. ARAS.

P0145 **MESENCHYMAL STEM CELLS PROTECT RENAL TUBULAR CELLS VIA TSG-6 REGULATED MACROPHAGE FUNCTION AND PHENOTYPE SWITCHING**

Yu Zhao[1], Xiao liang Zhang[1], Bicheng Liu[1], Lilach Lerman[2]

[1]Institute of Nephrology, Zhong Da Hospital, Southeast University, School of Medicine, Nanjing, P.R. China and [2]Mayo Clinic, Rochester, MN, United States, Division of Nephrology and Hypertension, rochester, United States of America

Background and Aims: Tumor necrosis factor-α-induced gene/protein (TSG)-6 is a key factor influencing mesenchymal stem cells (MSCs) immunomodulatory properties, but its renoprotective efficacy is unknown. Using a novel swine model of renal artery stenosis (RAS) complicated by metabolic syndrome (Mets), we assessed the therapeutic effects of adipose tissue-derived MSCs-produced TSG-6 and mechanisms underlying the immunomodulatory properties of MSCs.

Method: Five groups of pigs (n=6 each) were studied after 16 weeks of diet-induced Mets and unilateral RAS (Mets+RAS), either untreated or treated 4 weeks earlier with a single intra-renal delivery of autologous posrcine adipose tissue-derived MSCs (pMSC). Lean, Mets, and RAS shams served as controls. We studied renal function in vivo (using CT imaging) and kidney histopathology and macrophage phenotype ex vivo. In vitro, TSG-6 levels were measured in conditioned media of human MSCs (hMSCs) incubated with or without TNF-α. Additionally, levels of the tubular injury marker LDH were measured in conditioned media after co-culturing macrophages with injured HK-2 cells (achieved by TNF-α and antimycin-A, AMA) with or without addition of TSG-6. The effects of TSG-6 on macrophage phenotype (M1/M2), adhesion, and migration capability were determined.

Results: Mets+RAS pigs showed increased renal M1 macrophages and renal vein TNF-α levels. After p-MSCs delivery, renal vein TSG-6 increased and TNF-α decreased, M1 macrophage switched to M2 (Fig. A)„ renal function improved, and fibrosis alleviated. In vitro, TNF-α increased TSG-6 secretion by h-MSCs. TSG-6 decreased LDH release from injured HK-2, induced a macrophage phenotypic switch from M1 to M2 (Fig. B), and reduced M1 macrophage adhesion and migration (Fig. C).

Conclusion: TNF-α-induced TSG-6 release from MSCs in vivo and in vitro may decrease renal tubular cells injury, which is associated with and may be at least in part mediated by regulating macrophage function and phenotype.

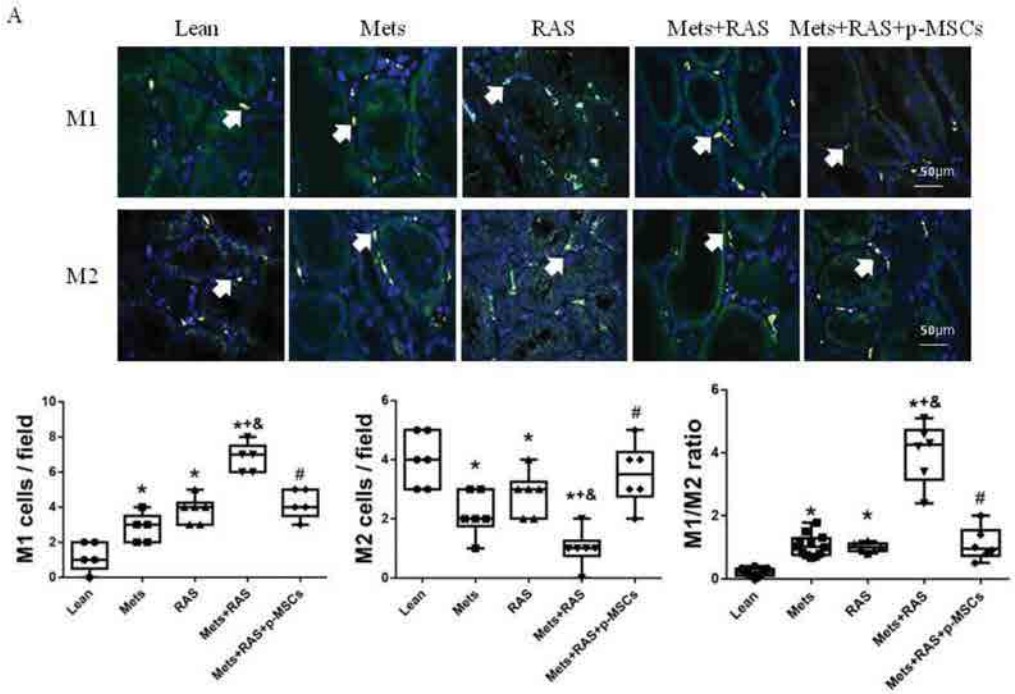


Figure. TSG-6 attenuates M1/M2 macrophage phenotype, adhesion and migration.
A. p-MSCs induce a shift in renal pathology and macrophage phenotype. Representative merged images (x40) of immunofluorescence staining for stenotic kidney M1 [CD68 (red)/ inducible nitric oxide synthase (green)] and M2 [CD68/arginase-1 (green)] macrophages (double staining yellow). Quantification of stenotic-kidney M1 and M2 macrophages and M1/M2 ratio. B. TSG-6 decreases protein expression of the M1 marker iNOS (inducible nitric oxide synthase), and increases the M2 markers MR (mannose receptor) and Arg-1 (arginase-1) in macrophages (M0) (GAPDH loading control). C. TSG-6 decreases M1 macrophage adhesion and migration in transwell. Data are mean ± SD (n=3 per group). *P<0.05 vs M0; #P<0.05 vs M1.

P0146 **MESENCHYMAL STEM CELLS AND THEIR EXTRACELLULAR VESICLES PROGENY DECREASE RENAL INJURY IN EXPERIMENTAL SWINE RENAL ARTERY STENOSIS THROUGH DIFFERENT MECHANISMS**

Yu Zhao[1], Xiao liang Zhang[2], Bicheng Liu[2], Lilach Lerman[3]

[1]Institute of Nephrology, Zhong Da Hospital, Southeast University, School of Medicine, Nephrology, Nanjing, P.R. China, [2]Institute of Nephrology, Zhong Da Hospital, Southeast University, School of Medicine, Nanjing, P.R. China and [3]Mayo Clinic, Rochester, MN, United States., Division of Nephrology and Hypertension, rochester, United States of America

Background and Aims: Novel therapies are needed to address the increasing prevalence of chronic kidney disease. Mesenchymal stem cells (MSCs) and MSC-derived extracellular vesicles (EVs) augment tissue repair. EVs have practical benefits, but their efficacy relative to MSCs is incompletely understood. We tested the hypothesis that EVs are as effective as MSCs in protecting the stenotic kidney but target different injury pathways.

Representative images of pig kidney from Lean, RAS, Mets+RAS, Mets+RAS+MSC, Mets+RAS+EV obtained by micro-CT (A) or blood-oxygen-level-dependent magnetic-resonance imaging (B). C: Endothelial cell (PL-VAP) staining. D-F: Quantifications of images. The spatial density of renal cortical microvessels was lower than normal in Mets+RAS, increased in Mets+RAS+MSC, but not in Mets+RAS+EV. Medullary hypoxic regions (red) were increased in Mets+RAS, but similarly decreased by MSC and EV. Similarly, PL-VAP expression was decreased in Mets+RAS, but similarly increased by MSC and EV. *P<0.05 vs. Lean; &P <0.05 vs. RAS; #P<0.05 vs. Mets+RAS.

Method: Pigs were studied after 16 weeks of renal injury achieved by diet-induced metabolic syndrome (Mets) and renal artery stenosis (RAS). Pigs were untreated or treated four weeks earlier with a single intrarenal delivery of autologous adipose tissue-derived MSCs (1×10^7) or EVs (1×10^{10}). Lean pigs and sham RAS served as controls (n=6 each). Stenotic kidney function was studied in-vivo using CT. Histopathology and expression of necroptosis markers (RIPK-1 and RIPK-3), inflammatory and growth factors (angiopoeitin-1 and VEGF) was studied ex-vivo.

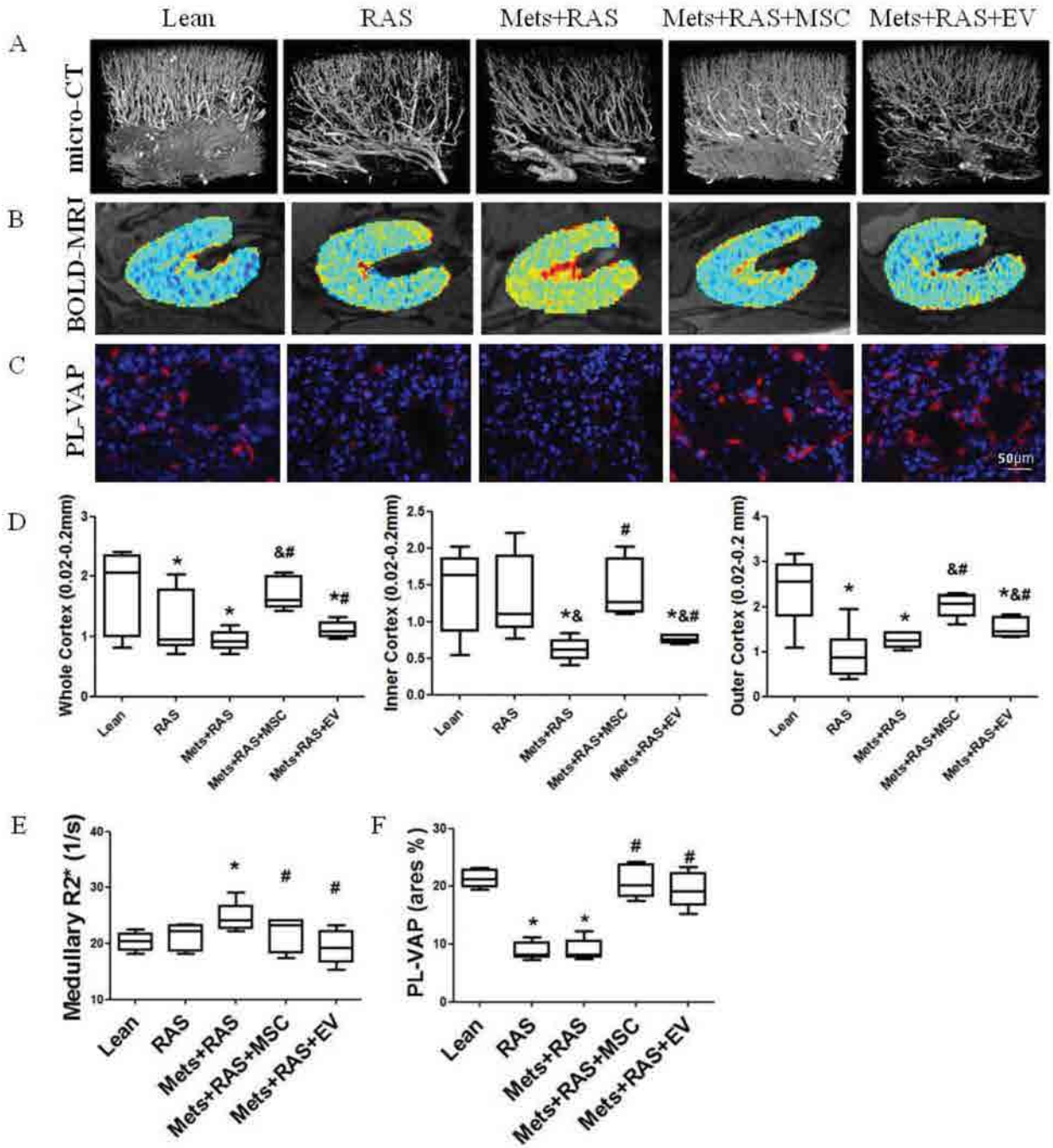


Figure. Both MSC and EV improved renal microcirculation and hypoxia.

Results: Stenotic-kidney glomerular filtration rate and blood flow in Mets+RAS were both lower than Mets, increased in Mets+RAS+MSCs, and further improved in Mets+RAS+EV. Both MSCs and EVs improved renal function, hypoxia, and decreased renal fibrosis and apoptosis. MSC were slightly more effective in preserving microvascular density (0.02-0.2mm in diameter), and prominently attenuated renal inflammation. However, EVs more significantly upregulated growth-factor expression and decreased necropotosis.

Conclusion: Adipose tissue-derived MSCs and their EVs both improve stenotic kidney function and decrease tissue injury in Mets+RAS. MSCs more effectively preserve the microcirculation, while EVs bestow better preservation of renal cellular integrity. These findings encourage further exploration of this novel approach to attenuate renal injury.

P0147 THE EFFECT OF HIGH SODIUM CHLORIDE CONTENT IN THE DIET ON THE CARDIOVASCULAR SYSTEM OF MACACUS FASCICULARIS

Sergey Orlov[1], Olga Beresneva[2], Aleksander Kulikov[3], Marina Parastaeva[3], Anatoly Kucher[3], Galina Ivanova[4], Mokhamad Khasun[3], Dzhina Karal-ogly[5], Ivan Kayukov,[3], Alexei Smirnov[3]

[1]Institute of Medical Primatology, St. Petersburg, Russia, [2]Pavlov First St. Petersburg State Medical University, Institute of Nephrology, St. Petersburg, Russia, [3]Pavlov First St. Petersburg State Medical University, Institute of Nephrology, St. Petersburg, Russia, [4]Pavlov Institute of Physiology Russian Academy of Sciences, Laboratory of Physiology of Cardiovascular and Lymphatic systems, St. Petersburg, Russia and [5]Institute of Medical Primatology, Sochi, Russia

Background and Aims: It is traditionally believed that high consumption of sodium chloride leads to the development of arterial hypertension, which, in turn, will cause heart remodeling. However, more and more evidence is accumulating that a high sodium chloride content in the diet can cause heart damage without increasing blood pressure (BP). This is confirmed in experiments on rats. In addition, in animals of this species, supplementing a high-salt diet with soy proteins can prevent cardiovascular damage. Whether such mechanisms operate in primates remains unclear.

Method: The study was performed on male Macacus fascicularis. Monkeys were included in the experiment at the age of 4.6 -7.0 years and had a body weight of 5,5-7,5kg. Animals were divided into 3 groups. The first (control) included 5 animals, received standard ration; the second – 5 animals, received diet with high sodium chloride content (8 g NaCl/1 kg of the feed); the third – 6 animals, who were on a diet with high salt contents supplemented by soya isolated proteins (200 g/kg of the feed). In anesthetized animals measured blood pressure and performed an echocardiographic investigation. Follow up period lasted four month.

Results: Initially, in all groups of animals, blood pressure levels ($Mean_{(SEM)}$) and echocardiographic parameters did not significantly differ. During the observation period, the studied parameters did not change much. For example, in the first group, an ejection fraction (EF) increased from $61.7_{(1.67)}$ to $71.6_{(4.74)}$, %; P=0.045. In the same group, a tendency toward a decrease in the left ventricle end-systolic dimension ($1.50_{(0.056)}$ *vs* $1.29_{(0.118)}$, mm; P=0.079) was noted. Whereas the level of systolic and diastolic blood pressures in this group (for example, systolic BP: $115.4_{(3.95)}$ *vs* $126.0_{(5.39),}$ mm Hg; P=0.134) as well as in other groups of monkeys did not change significantly. Nevertheless, after four months of observation, the level of systolic blood pressure in the second group ($126.0_{(5.39)}$ mm Hg) of animals was significantly higher than in the first ($103.0_{(5.54)}$, P=0.0118) and nonsignificantly - in the third ($104.0_{(8.39)}$, mm Hg; P=0.065). EF in the end of follow up period in second group ($71.6_{(4.74\%)}$ was significantly higher than in control ($58.1_{(2.72)}$,%; P=0.039) but not in the third group ($60.9_{(5.03)}$,%; P=0.162). Tricuspid annular plane systolic excursion in second group ($1.02_{(0.08)}$, mm) had an insignificant tendency to increase in comparison to the first ($0.782_{(0.096)}$, mm; P=0.094) or third ($0.818_{(0.049)}$, mm; P=0.052) groups.

Conclusion: Our data do not exclude the possibility that a high salt content in the food of lower primates can contribute to an increase in blood pressure and a change in heart function. However, to resolve the issues of the relationship between changes in heart function and the level of blood pressure and the presence of the cardioprotective effect of soy proteins under these conditions, longer observations are needed.

P0148

BLOOD PRESSURE CONTROL IS ASSOCIATED WITH HEALTHIER THIOL/DISULPHIDE DYNAMICS IN PRIMARY HYPERTENSION

Özant Helvacı[1], Burcak Helvaci[2], Gamze Dam[2], Salim Neselioglu[3], Ozcan Erel[3], Ülver Derici[4]

[1]Yildirim Beyazit University, Nephrology, Turkey, [2]Yildirim Beyazit University, Internal Medicine, Turkey, [3]Yildirim Beyazit University, Biochemistry, Turkey and [4]Gazi University, Nephrology, Turkey

Background and Aims: Hypertension is the most common chronic disease that leads to death. Oxidative stress plays a not yet fully understood role in the pathogenesis. OS is the result of excessive reactive oxygen species (ROS) and insufficient anti-oxidant mechanisms.

Thiol/disulphide ratio measurement is founded on the fact that ROS frequently target thiol groups of sulphur-containing amino acids on proteins. The more OS there is in the environment, there is less native or total thiols and more disulphides. Newly diagnosed hypertensive patients and those with masked hypertension have this dynamic altered towards disulphide.

In this study, we aimed to further evaluate this relation in terms of medication choice and blood pressure (BP) control in select cases with primary hypertension.

Method: This cross-sectional, multi-centre study was conducted in two tertiary referral centres between January 2018 and January 2019. Patients with diabetes, coronary artery disease, heart failure, atrial fibrillation, cerebrovascular disease, rheumatoid disease, active infection, GFR lower than 60 ml/min and microalbuminuria or proteinuria were excluded. Active smokers were also excluded.

Drug classes allowed were chosen as ACE inhibitors, ARB's, dihydropyridine calcium channel blockers (CCB) and thiazides and their combinations. Patients on other antihypertensives were excluded from the study.

Two hundred eighty-nine patients were recruited. Demographical and clinical data were recorded. Laboratory parameters were creatinine, CKD-EPI eGFR, uric acid and cholesterol levels. Patients' home and office BP recordings were analysed. Those with mean BP higher than 140/90 mmHg were accepted as uncontrolled.

Native thiol (NT), total thiol (TT) and disulphide (D) levels were obtained with an automated colourimetric measurement method developed by two of the authors.

Results: The study included 289 (183 female and 106 male) patients. Mean age was 56±9 (19-84). Mean duration of hypertension was 9±7 (1-38) years. Mean BMI was 29±4 (20-48). Four per cent had hypertensive retinopathy. Mean blood pressures were systolic 128±14 and diastolic 80±7 mmHg respectively.

There were nine drug schemes, including monotherapy. The most common form was ARB+thiaz (33.6% of cases) and the least common was ACE inhibitor+thiaz+CCB (1.4%). ANOVA between nine groups did not reveal any statistically significant differences in NT, TT or D levels. The analysis was repeated after combining patients on ACE inhibitors and ARB, thereby reducing the number of groups to five. Yet, the results did not change.

Forty-seven patients (16%) had uncontrolled BP. They had similar demographical data with their counterparts. Duration of hypertension, BMI and laboratory data were also identical. Patients with uncontrolled BP had lower native thiol, total thiol but higher disulphide levels ($p < 0{,}001$, Table1).

Conclusion: Patients with primary hypertension have increased oxidative stress evident by altered thiol/disulphide homeostasis. BP control but not drug regimen is associated with better dynamics. Causality remains to be elucidated with prospective trials.

Table1: Comparison of patients with controlled and uncontrolled BP

Parameter	Uncontrolled	Controlled	P value
Number (%)	47 (16%)	252 (84%)	-
Age	57±8	56±8	,478
Male/female ratio	18/29	88/154	,800
Ht duration (years)	8±6	9±7	,560
BMI	29±4	29±4	,246
Systolic BP	151±11	123±9	**<0,001**
Diastolic BP	90±4	77±5	**<0,001**
Creatinine (mg/dL)	0,73±0,14	0,76±0,15	,224
eGFR	96±11	94±12	,325
Uric acid (mg/dL)	5,2±1,2	5,29±1,1	,607
Albumin (g/dL)	4,3±0,3	4,4±0,3	,457
Native thiol (μmol/L)	342,7±72,0	413,2±61	**<0,001**
Total thiol (μmol/L)	389,6±74	452±63,2	**<0,001**
Disulphide (μmol/L)	18,9±8,3	13,5±10,9	**<0,001**
D/TT ratio (%)	3,4±2,9	4,5±2,2	**,007**
D/NT ratio (%)	4,2±4,5	4,3±1,9	,966
NT/TT ratio (%)	87,7±3,7	91,6±6,1	**<0,001**

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HYPERTENSION. CLINICAL

P0150 EFFECT OF SEROTONIN REUPTAKE INHIBITORS (SSRIS) AND SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIS) ON BLOOD PRESSURE VARIABILITY USING 24 HOURS AMBULATORY BLOOD PRESSURE MONITORING

Nabeel Aslam[1], Sobia Memon[1], Hani Wadei[2], Shehzad Niazi[3]

[1]Mayo Clinic, Medicine, Nephrology and Hypertension, Jacksonville, United States of America, [2]Mayo Clinic, Medicine, Nephrology and Hypertension; Transplantation, Jacksonville, United States of America and [3]Mayo Clnic, Psychiatry, Jacksonville, United States of America

Background and Aims: Hypertension (HTN) and psychiatric disorders frequently co-exist in general population. Serotonin re-uptake inhibitors (SSRIs) and serotonin-norepinephrine re-uptake inhibitors (SNRIs) affect serotonin and norepinephrine and may lead to variation in blood pressure (BP). There is paucity of data on blood pressure variations using 24 hours ambulatory blood pressure monitoring (ABPM) with the use of SSRIs/NSRIs.

Method: Subjects who underwent psychiatric evaluation and ABPM within six month of each other between 1/1/2012 to 12/31/2016 at Mayo Clinic Florida were identified using billing data. Demographics, co-morbidities, medications, ABPM, and laboratory results were retrospectively collected from medical records. Subjects were divided into groups – subjects with no psychiatric diagnosis and no psychiatric medicine (Group 1) and subjects with psychiatric diagnosis and on SSRIs/NSRIs (Group 2). BP systolic and diastolic levels (day time, night time) were compared between groups controlling for age, sex, race, presence or absence of HTN, diabetes mellitus (DM) and smoking. Single and multivariable linear regression models were used to analyze group differences.

Results: Total of 367 subjects met inclusion criteria – Group 1=135; Group 2=232. The subjects in group 2 were older (median age 57 yrs vs 47 yrs $p<0.001$), white (69.8 vs 60% $p=0.002$), smokers (15.9 vs 3.0% $p<0.001$), history of HTN (62.5 vs 9.6%), and DM (21.1% vs 0%). ABPM showed that subjects in group 2 had higher median daytime systolic BP (131 vs 124), higher median night time systolic BP (120 vs 110), and higher median night time diastolic BP (68 vs 63). Multivariable linear regression controlling for age, sex, race, presence or absence of HTN, DM, and smoking showed that use of SSRIs/NSRIs (group 2) was significantly associated with higher night time systolic BP (8.36 mm; 95% CI 4.2, 12.5; $p<0.0001$) and higher night time diastolic BP (4.6 mm, 95% CI 1.9, 7.29, $p=0.001$). On subgroup analysis comparing subjects with use of SSRIs vs NSRIs, there was no statistically significant difference in the daytime or night time systolic or diastolic BP.

Conclusion: Use of SSRIs and NSRIs are associated with higher nocturnal systolic and diastolic BP, which can potentially increase the risk of adverse cardiovascular outcome in this population. Higher nocturnal BP may be due to ongoing sympathetic activation during sleep with serotonin and norepinephrine with the use of SRRIs and NSRI. Further well designed prospective studies using ABPM are needed to determine the risk of nocturnal hypertension with the use of SSRIs/NSRIs that could have potential adverse cardiovascular outcome.

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P0150A **PREECLAMPSIA ABOUT 252 PATIENTS**

Boubchir Akli[1], Boubchir Akli[2], Brahim Kichou[3,4], MADIOU ALI[5]

[1]medical, medecine, BEJAIA, Algeria, [2]hospital, Nephrologia, BEJAIA, Algeria, [3]UNIVERSITE, medecine, TIZI OUZOU, Algeria, [4]hospital, nephrologie, TIZI OUZOU, Algeria and [5]Biomédical, néphrologia, TIZI OUZOU, Algeria

Background and Aims: The main objective was to estimate the prevalence of pre-eclampsia (PE) in pregnant women in Tizi-ouzou (Algeria). Secondary objectives were to estimate the frequency of PE risk factors, and the incidence of maternal and fetal complications.

Methods: Our study was observational, prospective and descriptive, including all pregnant women at the prenatal appointment in the 2 maternity units of Tizi-ouzou, between January 2012 and June 2013. PE was diagnosed if gestational hypertension was associated with proteinuria > 300mg/24h, after 20 weeks of gestation.

Results: We had 252 cases of PE on 3225 pregnant women. The prevalence of PE was 7.8% (CI 95%: 6.9%–8.7%). The most frequent PE risk factors were nulliparity (56%), age >40 years (27%), obesity (26%) and PE in any previous pregnancy (21%). The incidence of maternal adverse events was 28.7% (CI 95%: 23.1%–34.3%), including 5 deaths. The rates of prematurity, small for gestational age infant and fetal death were 58.2%, 49.7% and 6.7%, respectively.

Conclusion: The prevalence of PE in pregnant women in Tizi-ouzou is around 8%. The incidence of maternal and fetal adverse outcomes remains high. Only earlier diagnosis and closer monitoring could improve the prognosis of our patients, since the treatment of PE remains currently childbirth.

P0151 **SEXUAL DIMORPHISM IN HYPERTENSION ACCORDING TO THE CHANGE OF URINE SODIUM AND VOLUME EXCRETION BY SEX OR MENOPAUSE**

Yang-Gyun Kim[1], MI JI KIM[1], WON HEE CHO[1], Ju-Young Moon[1], Kyung Hwan Jeong[1], Hyeon Seok Hwang[1], Jin Sug Kim[1], Sang-Ho Lee[1], Jin Ho Hwang[2], Sejoong Kim[3], HO JUN CHIN[3], Dong Ki Kim[4], Suhnggwon Kim[4], Jung Hwan Park[5], Sung Joon Shin[6], Bum Soon Choi[7], Chun Soo Lim[8]

[1]KyunHee University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of South, [2]Chung-Ang University Hospital, Internal Medicine, Seoul, Korea, Rep. of South, [3]Seoul National University Bundang Hospital, Internal Medicine, Seoul, Korea, Rep. of South, [4]Seoul National University Hospital, Internal Medicine, Seoul, Korea, Rep. of South, [5]Konkuk University School of Medicine, Internal Medicine, Seoul, Korea, Rep. of South, [6]Dongguk Universkty Ilsan Hospital, Internal Medicine, Goyang, Korea, Rep. of South, [7]Seoul St. Mary's Hospital, Internal Medicine, Seoul, Korea, Rep. of South and [8]Seoul National University Boramae Medical Center, Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: A recent study demonstrated female rats more rapidly excreted urine sodium and water under saline bolus infusion than male rats, and suggested sexual dimorphisms in renal transporters. However, the sexual differences in renal salt and water excretion was not yet investigated with human data. We purposed to clarify whether the sexual difference of natriuretic and diuretic ability exists, and it contributes to decreasing blood pressure (BP) in nondiabetic chronic kidney disease (CKD) patients.

Method: This is a secondary analysis of an open-label, randomized, controlled study determining the effect of intensive low-salt diet education on BP and albuminuria in nondiabetic CKD patients. A total of 235 patients had stopped all renin-angiotensin blocking agents or diuretics during a run-in period for eight weeks (0w). After the run-in period, they received olmesartan (40mg daily) for eight weeks (8w), and then maintained the same medicine with low-salt diet education for an additional eight weeks (16w).

Results: Mean age of premenopausal women (n=50), same-aged young men (n=76), postmenopausal women (n=68), and same-aged older men (n=41) was 40.7, 40.2, 59.0, and 69.9 years old, respectively. Their MDRD eGFR was 76.2, 71.6, 59.8, and 58.8 mL/min/1.73m^2, respectively. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was lower in premenopausal women (129/79 mmHg) than in young men (134/83 mmHg). Daily salt intake decreased in 16w in premenopausal women (1839 → 1288mg, p=0.008) and young men (2494 → 1552mg, p=0.001) compared with them in 0w, while there was no significant change in postmenopausal women (2443 → 2171mg, p=0.610) and older men (2870 → 2366mg, p=0.458). Except for the premenopausal women (136 (0w) → 133 (16w) mEq/day, p=0.749), urine sodium excretion for 24 hours significantly decreased in 16w compared with that in 0w or 8w (young men: 154 (8w) → 137 (16w)mEq/day p=0.042, postmenopausal women: 152 (0w) → 128m (16w)Eq/day p=0.016, older men: 181 (0w) → 145 (16w)mEq/day p=0.019). Also, urine volume was significantly larger in the premenopausal women than in young men in 8w and 16w (8w: 1009 vs. 980mL p=0.002, 16w: 1004 vs. 978mL, p=0.006), while it was not different between postmenopausal women and older men (8w: 1002 vs. 990 p=0.347, 16w: 1003 vs. 1001 p=0.895). The urine volume was positively correlated with BP in the premenopausal women, while it was negatively associated with BP in young men in 16w.

Conclusion: Although sodium intake was similarly decreased in premenopausal women and young men, urine sodium excretion did not fall, and urine volume increased in premenopausal women. This phenomenon disappeared in postmenopausal women. Augmented natriuretic and diuretic potency might contribute to lower BP in premenopausal women with nondiabetic CKD.

P0152

EFFECT OF LOSARTAN ON AMBULATORY SHORT-TERM BLOOD PRESSURE VARIABILITY AND CARDIOVASCULAR REMODELING IN HYPERTENSIVE PATIENTS ON HEMODIALYSIS

Koichi Azuma[1]

[1]*asamizo jin clinic, head doctor, sagamihara, Japan*

Background and Aims: Previous studies have shown increases in ambulatory short-term blood pressure (BP) variability to be related to cardiovascular disease. In this study, we examined whether an angiotensin II type 1 receptor blocker losartan would improve ambulatory short-term BP variability in hypertensive patients on hemodialysis.

Method: 40 hypertensive patients on hemodialysis therapy were randomly assigned to the losartan treatment group (n=20) or the control treatment group (n=20). At baseline and 6 and 12 months after the treatment, 24-h ambulatory BP monitoring was performed. Echocardiography and measurements of brachial-ankle pulse wave velocity (baPWV) and biochemical parameters were also performed before and after therapy.

Results: After 6- and 12-months of treatment, nighttime short-term BP variability, assessed on the basis of the coefficient of variation of ambulatory BP, was significantly decreased in the losartan group, but remained unchanged in the control group. Compared with the control group, losartan significantly decreased left ventricular mass index (LVMI), baPWV, and the plasma levels of brain natriuretic peptide and advanced glycation end products (AGE). Furthermore, multiple regression analysis showed significant correlations between changes in LVMI and changes in nighttime short-term BP variability, as well as between changes in LVMI and changes in the plasma levels of AGE.

Conclusion: These results suggest that losartan is beneficial for the suppression of pathological cardiovascular remodeling though its inhibitory effect on ambulatory short-term BP variability during nighttime.

P0153

IS THERE ANY VALUE FOR HOSPITALIZATION FOR CHECKING MEDICATION ADHERENCE DUE TO RESISTANT AND REFRACTORY HYPERTENSION SUSPICIOUS? IMPLICATIONS FOR MID-TERM FOR BLOOD PRESSURE CONTROL.

Andrea Pio de Abreu[1], Fernanda Trani[1], Giovanio Vieira[1], Luiz Aparecido Bortolotto[2], Luciano Ferreira Drager[1,2]

[1], Hypertension Unit, Renal Division, Department of Internal Medicine, University of São Paulo, Brazil and [2]Hypertension Unit, Cardiology Division, Heart Institute (InCor), Department of Internal Medicine, University of São Paulo

Background and Aims: Resistant hypertension (RH) and refractory hypertension (RefH, an extreme phenotype of RH) are associated with increased cardiovascular events and target-organ damage. However, appropriate RH and RefH diagnosis require good drug adherence. In this context, the "gold standard" method for assessing adherence is supervised medication intake. However, it is not clear the real utility of supervised medication intake during a hospital stay. Therefore, this study was aimed to evaluate whether hospitalization for confirming antihypertensive adherence in patients with RH and RefH may impact blood pressure (BP) values and BP control after hospital discharge in patients with RH or RefH suspicious at a tertiary outpatient clinic.

Method: From June 2015 to June 2017, we recruited consecutive patients with RH or RefH suspicious admitted to the Hospital for confirming treatment adherence and the respective diagnosis. We excluded patients with secondary forms of hypertension. RH was defined as uncontrolled office BP ($\geq$140 and/or $\geq$90mmHg) despite using $\geq$3 classes at optimal doses (one of them being diuretic) or controlled BP using $\geq$4 classes. RefH was defined as no BP control despite using $\geq$5 antihypertensive drugs. During hospitalization, all patients used low sodium diet ($\sim$3grs of salt/day) and had supervised taking of prescribed drugs by the medical team aiming BP control. We defined not only the rate of adherence and RH/RefH status but also BP and number of antihypertensive drugs at hospital discharge and in the two first outpatients visits returns.

Results: We studied a total of 83 patients with suspected RH/RefH (age 53$\pm$14 years; 76% female gender; body mass index 28.8$\pm$6.2 Kg/m2; pre-hospitalization systolic 177$\pm$28mmHg and diastolic BP 106$\pm$21mmHg). Of these, 68.7% (57 patients) had suspected RefH in the outpatient clinic. The average number of antihypertensive drugs on admission was 5.3$\pm$1.3 classes. After hospitalization, the overall frequency of RH fell to 80% (66 patients). The average number of antihypertensive drugs at hospital discharge as well as systolic and diastolic BP was 4.5$\pm$1.3 classes, 131$\pm$17mmHg and 80$\pm$12mmHg, respectively ($p<0.001$ vs. pre-hospitalization for all comparisons). Among the RH types, RefH was confirmed in only 27 patients (32.5%). As compared to pre-hospitalization data, we noticed consistent lower number of antihypertensive drugs and lower levels of systolic and diastolic BP both at first outpatient visit post-discharge (mean returned time 2.1$\pm$1.7 months) and second outpatient visit post-discharge (mean returned time 7.1$\pm$2.6 months): First visit: 4.3$\pm$1.2 classes, systolic BP: 152$\pm$24 mmHg, diastolic BP: 89$\pm$17 mmHg; second visit: 4.5$\pm$1.3 classes, systolic BP: 150$\pm$26 mmHg, diastolic BP: 89$\pm$15 mmHg; ($p<0.001$ vs. pre-hospitalization for all comparisons). As a consequence, the rate of patients that reached at least 140x90mmHg increased from 0% to 35% (first visit post-discharge) and 38.5% (second visit post-discharge).

Conclusion: Supervised medication intake with controlled salt diet during hospitalization may help not only to define the RH and RefH status in uncontrolled hypertensive outpatients but also to have impact on the number of antihypertensive drugs and lower BP values in the mid-term follow-up.

P0154 **BLOOD PRESSURE CONTROL IN ELDERLY PATIENTS WITH HEART FAILURE AND MORTALITY RISK: A POPULATION-BASED PROSPECTIVE COHORT STUDY**

Antonios Douros[1], Alice Schneider[2], Dörte Huscher[2], Natalie Ebert[2], Nina Mielke[2], Markus Van der Giet[2], Elke Schaeffner[2]

[1]McGill, Medicine, Canada and [2]Charite, Germany

Background and Aims: Current guidelines on the management of heart failure (HF) recommend control of blood pressure (BP) in elderly patients. However, the exact treatment goals in this vulnerable population are unclear. Thus, our population-based prospective cohort study aimed to assess whether BP values <140/90 mmHg are associated with a decreased risk of cardiovascular (CV) death and all-cause mortality in HF patients ≥70 years.

Method: The study included participants of the Berlin Initiative Study (BIS), all ≥70 years, who were treated with antihypertensive drugs and had a diagnosis of HF (ICD-10 codes: I11.0, I13.0, I13.2, I50.x) at baseline. The study period was from 2009 to 2017. Demographics, lifestyle factors, medications, and comorbidities were assessed in face-to-face interviews and from linked administrative healthcare data. Outcomes were adjudicated using death certificates and hospital discharge notes. Cox proportional hazards models yielded crude and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) of CV death and all-cause mortality associated with normalized BP (systolic BP <140 mmHg and diastolic BP <90 mmHg) compared with non-normalized BP (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg) in patients with HF. In sensitivity analyses we restricted to high-risk HF patients (≥80 years or with previous CV events). We also repeated the analyses in patients without HF to assess a potential effect modification.

Results: Among 1623 BIS participants treated with antihypertensive drugs at baseline, 544 (33.5%) had a diagnosis of HF. Of those, 255 (46.9%) showed normalized BP and 289 (53.1%) had non-normalized values. Mean age (standard deviation [SD]) was 82.8 (6.8) years (45.4% female). Selected patient characteristics are shown in the Table. Median (interquartile range) duration of follow-up was 6.7 (4.1-7.3) years. Compared with non-normalized BP, normalized BP was associated with a numerically increased risk of CV death (HR, 1.40; 95% CI, 0.90-2.17) and all-cause mortality (HR, 1.28; 95% CI, 0.96-1.71) in patients with HF. The associations were more pronounced or reached statistical significance when restricting to HF patients ≥80 years (CV death: HR, 1.54; 95% CI, 0.94-2.53 / all-cause mortality: HR, 1.56; 95% CI, 1.11-2.18) or HF patients with previous CV events (CV death: HR, 1.65; 95% CI, 0.83-3.29 / all-cause mortality: HR, 1.33; 95% CI, 0.85-2.07) (Figure). The effect estimates in patients without HF were comparable to those with HF (CV death: HR, 1.18; 95% CI, 0.78-1.78; p for interaction, 0.695 / all-cause mortality: HR, 1.20; 95% CI, 0.93-1.54; p for interaction, 0.604).

Table. Ba seline characteristics of elderly patients with HF

Selected characteristics	Normalized BP (n = 255)	Non-normalized BP (n = 289)
Age in years, mean (SD)	83.0 (6.6)	82.7 (6.9)
Female sex	111 (43.5)	136 (47.1)
Body mass index in kg/m^2, mean (SD)	28.5 (4.7)	28.5 (4.5)
Smoking status		
Ever	154 (60.4)	155 (53.6)
Never	101 (39.6)	134 (46.4)
Physical exercise		
Once weekly	89 (34.9)	100 (34.6)
One to five times weekly	114 (44.7)	124 (42.9)
More than five times weekly	52 (20.4)	65 (22.5)
$eGFR_{BIS2}$ in ml/min per 1.73m^2		
≥60	68 (26.8)	94 (32.5)
<60	186 (73.2)	195 (67.5)
Albuminuria	180 (70.9)	153 (53.3)
Diabetes mellitus	76 (29.9)	104 (36.0)
Prior myocardial infarction	83 (32.9)	70 (24.7)
Prior stroke	47 (18.7)	39 (13.8)
Cancer	60 (23.5)	69 (23.9)
Duration of treated hypertension in years, mean (SD)	15.1 (11.6)	15.8 (11.9)

Values are numbers (percentages) unless stated otherwise.
Abbreviations: eGFR, estimated glomerular filtration rate.

Conclusion: Our study suggests that normalized BP does not decrease the risk of CV death or all-cause mortality in elderly patients with HF and it could even increase the risk especially in high-risk subgroups. Thus, individualized benefit-risk assessment is required for the pharmacotherapy of HF in this vulnerable population.

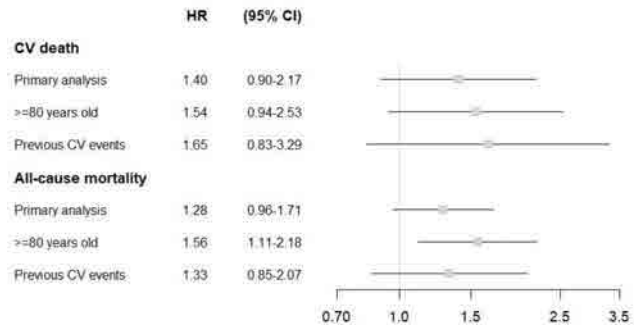


Figure. Forest plot with primary analysis and sensitivity analyses

P0155 CHARACTERISTICS OF HYPERTENSIVE NEPHROSCLEROSIS DIAGNOSED BY RENAL BIOPSY BASED ON 40-YEAR EXPERIENCE

Hea Eun Kim[1], HO JUN CHIN[1,2]

[1]Seoul National University Bundang Hospital, INTERNAL MEDICINE, Seongnam-si, Korea, Rep. of South and [2]SEOUL NATIONAL UNIVERSITY COLLEGE OF MEDICINE, INTERNAL MEDICINE, Seoul, Korea, Rep. of South

Background and Aims: Hypertensive nephrosclerosis (HT-N) is known as the second common cause of end stage renal disease (ESRD) in Korea as well as in other countries. However, the HT-N is assumed by clinical findings which are not well correlated to the pathologic findings. Therefore, we report the clinical characteristics of HT-N diagnosed by renal biopsy and compare the prognosis between patients with HT-N and hypertensive patients with focal segmental nephrosclerosis (FSGS) without pathologic HT-N.

Method: We enrolled 21,617 patients having native kidney biopsy for diagnosis of nephritis between 1979 and 2018, retrospectively. Among them, we selected 267 adult hypertensive patients with only HT-N and 984 hypertensive patients with FSGS without HT-N or other diagnoses (FSGS-HT). The estimated glomerular filtration rate (GFR) was calculated by original MDRD equation. The final outcomes were incidences of end stage renal disease (ESRD) and death. We matched blood pressures and GFR between two groups and analyzed the difference of outcomes within the matched cohort (mHT-N and mFSGS-HTN), also.

Results: The age of patients with HT-N was 49.5 $\pm$ 15.3 years at renal biopsy. There were 175 (65.5 %) men. Systolic blood pressure (SBP) was 139.1 $\pm$ 24.0 mmHg and diastolic blood pressure (DBP) was 83.7 $\pm$ 15.6 mmHg at renal biopsy. Levels of serum creatinine, GFR, and urine protein to creatinine ratio were 3.17 $\pm$ 3.05 mg/dl, 40.7 $\pm$ 32.5 ml/min/1.73 m^2, and 2.277 $\pm$ 2.803 g/g cr, respectively. During follow-up period of 64.1 months (median), there were 52 (22.7%) patients progressed to ESRD and 8 (3.1%) patients were dead. Age, SBP, and hemoglobin were risk factors to mortality by Cox's hazard proportional model adjusted with related factors to mortality. With increase of 10 mmHg in the level of SBP at renal biopsy, hazard ratio(HR) of mortality was increase by 1.645 folds (95% CI: 1.192-2.270, P=0.002). Presence of diabetes mellitus, serum albumin, and GFR were risk factors to incident ESRD. Compared to patients with FSGS-HT, patients with HT-N showed higher levels of SBP, DBP, and serum creatinine and lower levels of GFR, serum albumin, hemoglobin, and UPCR (all p-values <0.05), however, the risk of incident ESRD and mortality was not different. Therefore, we matched BP and GFR between groups and selected 235 patients in each group. The matched groups were not different in the values of age, SBP, DBP, and GFR. The risk of mortality was not different between groups (p-value =0.502), however, HR of incident ESRD was 1.558-fold higher (95% CI: 1.004-2.419, P=0.048) in mFSGS-HT compared to mHT-N by Cox's hazard proportional model adjusted by factors related to ESRD.

Conclusion: Hypertensive nephrosclerosis was diagnosed in more advanced stage of CKD compared to hypertensive FSGS. Considering levels of GFR and SBP as risk factors to hard outcomes, we should consider early pathologic diagnosis for proteinuric and/or azotemic hypertensive patients and control blood pressures and renal dysfunction in more aggressive manners.

P0156 **SHORT-TERM BLOOD PRESSURE VARIABILITY IN DIABETIC AND NON-DIABETIC PATIENTS WITH CKD STAGE 2, 3A, 3B AND 4**

Maria Schoina[1], Charalampos Loutradis[1], Ioanna Minopoulou[1], Marieta Theodorakopoulou[1], Theodoros Dimitroulas[2], Michael Doumas[3], Alexandros Garyfallos[2], Asterios Karagiannis[3], Aikaterini Papagianni[1], Panteleimon Sarafidis[1]

[1]Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece, [2]Aristotle University of Thessaloniki, Fourth Department of Internal Medicine, Thessaloniki, Greece and [3]Aristotle University of Thessaloniki, Second Propedeutic Department of Internal Medicine, Hippokration Hospital, Thessaloniki, Greece

Background and Aims: Blood pressure variability (BPV) is an important risk factor for cardiovascular events and mortality in patients with chronic kidney disease (CKD). Previous evidence suggests that BPV is gradually increasing across CKD stages. Whether type 2 diabetes mellitus (DM) is an additional risk factor for increased BPV has never been studied. The aim of this study is to examine in comparison BPV in diabetic and non-diabetic patients with CKD.

Method: We included 48 diabetic and 48 non-diabetic adult patients (>18 years) with CKD (eGFR: <90 και ≥15mL/min/1.73m^2), matched in a 1:1 ratio for age, sex and eGFR within each CKD stage (2, 3a, 3b and 4). All patients underwent 24-hour ambulatory blood pressure (BP) measurement with the Mobil-O-Graph device. Brachial BP variability was calculated with validated formulas. We calculated standard deviation (SD), weighted SD (wSD), coefficient of variation (CV), and average real variability (ARV) of BP during the 24-hour, day- and night-time periods with validated formulas.

Results: In total population, ambulatory systolic BP (SBP) levels were significantly higher in diabetics compared to non-diabetic counterparts in all studied periods. No significant differences were evidence for ambulatory diastolic BP (DBP) in total or across CKD stages. In total, 24-hour SBP SD (15.43±4.34 vs 13.38±3.35, p=0.011), wSD (14.41±4.11 vs 12.53±3.19, p=0.014) and ARV (10.94±2.75 vs 9.46±2.10, p=0.004) were higher in patients with DM compared to those without DM. In addition, 24hour DBP SD (11.04±2.39 vs 9.80±2.28, p=0.010), wSD (10.30±2.52vs 9.05±1.99, p=0.008), CV (14.77±3.05 vs 13.14±2.96, p=0.009) and ARV (8.23±2.10 vs 7.10±1.33, p=0.002) were again different between groups. Across CKD stages 2 and 3a, BPV indices were insignificantly higher in patients with DM. In CKD Stage 3b, 24-hour SBP-SD (16.30±4.52 vs 11.35±2.62, p=0.003), wSD (15.42±4.54 vs 10.77±2.30, p=0.004), ARV (12.46±3.19 vs 8.34±2.07, p=0.001) and 24-hour DBP-CV (14.84±3.63 vs 12.18±1.91, p=0.035) were higher in diabetic compared to non-diabetic patients. In contrast, no difference between groups existed in CKD Stage 4.

Conclusion: Patients with DM present increased BPV in CKD Stages 2, 3a and 3b (moderately impaired renal function). This difference is not apparent in patients with advanced CKD at Stage 4.

P0157 **GENETICALLY DETERMINED HYPOALBUMINEMIA AND THE RISK OF HYPERTENSION: GWAS-BASED INSTRUMENTAL VARIABLE ANALYSIS**

Sang-Woong Han[1], Mi-yeon Yu[1], Jong Wook Choi[2], Joo-Hark Yi[1], Chang Hwa Lee[1], Joon-Sung Park[1]

[1]Hanyang University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of South and [2]Konkuk University School of Medicine, Research Institute of Medical Science, Chungcheongbuk-do, Korea, Rep. of South

Background and Aims: Hypoalbuminemia is a clinical indicator of vascular endothelial dysfunction. However, the genetic association of hypoalbuminemia with hypertension has not yet been clarified. We investigated whether genetic variation(s) associated with decreased serum albumin level is deeply related with increased risk of hypertension.

Method: Mild hypoalbuminemia was defined as a serum albumin concentration of less than 4.0 g/dL. We performed GWAS-based instrumental variable analysis using the population-based cohort data collected from KoGES. Eligible as cases were all native Koreans without significant medical illness and a total 4326 participants were divided in into control (n = 3157) and hypoalbuminemic (n = 1168) according to their serum albumin level.

Results: Our GWAS revealed that 71 susceptibility loci were associated with mild hypoalbuminemia and subsequent two-stage least squares estimation analysis showed that both genetic variations at rs2894536 in *LOC107986598* gene and rs10972486 in the *ATP8B5P* gene were related with systolic blood pressure. In subsequent Cox-proportional hazards model, we found that not only low serum albumin (HR = 0.654, 95% CI = 0.521-0.820), but also polymorphisms of rs2894536 (HR = 1.176, 95% CI = 1.015-1.361) and rs10972486 (HR = 1.152, 95% CI = 1.009-1.316) were significant predictor of hypertension. Our two-stage residual inclusion analysis indicated that candidate genetic variation attenuated the association between serum albumin and hypertension, showing hazard ratios of hypoalbuminemia on development of hypertension were 0.762 (0.659-0.882) for rs2894536 and 0.759 (0.656-0.878) for rs10972486.

Conclusion: These findings support a causal relationship between hypoalbuminemia-associated genetic variation, hypoalbuminemia and development of hypertension.

P0158

RENAL DENERVATION VERSUS SPIRONOLACTONE IN THE TREATMENT OF RESISTANT HYPERTENSION: A META-ANALYSIS

Sherida Edding[1], Brian Michael Cabral[1], Monica Therese Cating-Cabral[1]

[1]*St. Luke's Medical Center - Global City, Taguig, Philippines, The*

Background and Aims: Resistant hypertension (RH) is defined as blood pressure that remains above guideline-directed goal despite the concurrent use of at least three antihypertensive agents of different classes, one of which is a diuretic. Treatment of RH is focused on the addition of fourth-line therapy. Several studies revealed impressive blood pressure reductions when spironolactone was added to the therapeutic regimen. In the recent years, there has been a growing perception that controlling blood pressure in resistant hypertension is beyond the reach of existing drug therapies, leading to the emergence of device-based therapies, such as renal denervation. Our aim is to do a systematic review of randomized controlled trials that compares the use of Spironolactone and Renal Denervation in patients with RH.

Method: A comprehensive literature search from the PubMed, Embase, Cochrane Library, and Ovid was performed with the following search terms: Resistant Hypertension, Spironolactone, Renal Denervation. The search was limited to randomized-controlled trials that compared Spironolactone to Renal Denervation in patients with Resistant Hypertension. Three prospective clinical trials were selected and analyzed using Cochrane Revman v5.3. Primary outcome were mean changes in 24-hour Ambulatory Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP). Secondary outcomes include mean changes in Office SBP and DBP. Safety was assessed by changes in eGFR and potassium levels.

Results: Two trials comprising 130 patients were selected - 63 patients treated with RDN and 67 patients with Spironolactone. Pooled analysis of the 2 trials for 24H SBP and DBP showed an adjusted standardized mean difference of 0.55 mmHg (CI -0.72, 1.82; P = 0.39) and 0.32 mmHg (CI -0.72, 1.35; P = 0.55) with significant heterogeneity. No significant differences were also noted in terms of decline in eGFR (p = 0.07) and changes in serum potassium (p = 0.29) from baseline to 6 months.

Conclusion: Based on our results, RD appears to be safe and effective treatment for RH. However, additional larger studies should be done including a cost-benefit analysis to explore that possibility of RD as treatment alternative for those intolerant of spironolactone or as a possible 5th line of treatment for those already taking spironolactone.

P0159

PROTEINURIC PHENOTYPE OF CHRONIC KIDNEY DISEASE IS ASSOCIATED WITH WORSE PROFILE OF 24-H CENTRAL BP AND HIGHER ARTERIAL STIFFNESS IN HYPERTENSIVE PATIENTS WITH TYPE 2 DIABETES MELLITUS

Viktoria Chernomorets[1], Elena Troitskaya[1], Zhanna Kobalava[1]

[1]*Peoples' Friendship University of Russia (RUDN University), Department of Internal Medicine with the subspecialty of cardiology and functional diagnostics named after V.S. Moiseev, Moscow, Russia*

Background and Aims: 24-h blood pressure (BP) may be superior to office BP in the prediction of cardiovascular mortality and also central aortic BP may better predict outcomes than brachial one. Hypertensive patients with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) have higher risk and poorer BP control than patients with normal glycemic state and renal function. 24-h profile of central BP and arterial stiffness according to CKD phenotypes are not well described in this population. The aim of the study was to evaluate the associations of kidney function and proteinuria with 24-h central BP and parameters of arterial stiffness in hypertensive patients with T2DM and CKD.

Method: 90 patients with hypertension (HTN), T2DM and CKD (eGFR 30-60 ml/min/1.73 m^2 and morning spot urine albumin–creatinine ratio (UACR) <300 mg/g) were included. 66% of them were females, median age was 60 years, 69% were smokers, 53% obese, 77% with dyslipidemia. Median duration of T2DM and HTN was 7.5 years and 18 years, respectively. All received antihypertensive drugs (77% – combinations of 2 or 3 drugs) and glucose lowering therapy (insulin in 58%). The analysis was performed according to CKD phenotype: proteinuric (UACR 30-300 mg/g) and non-proteinuric (UACR <30 mg/g) and according to CKD stage assessed by GFR (G3a and G3b, KDIGO (2012)). Office brachial BP was measured with a validated oscillometric device. Office aortic BP and arterial stiffness were assessed with applanation tonometry (SphygmoCor AtCor). 24-hour ABPM of brachial and aortic BP was performed with BPLab Vasotens. All results are presented as median values. $P<0.05$ was considered significant.

Results: Median brachial BP was 156/83 mmHg, aortic BP 139/90 mmHg. Median eGFR was 53 ml/min/1.73 m^2, UACR – 62.2 mg/g. Phenotypes of CKD were as follows: proteinuric in 78% (GFR 50 ml/min/1.73 m^2, UACR 62 mg/g) and non-proteinuric in 22 % (GFR 54 ml/min/1.73 m^2, med UACR 5 mg/g, $p<0.01$ for trend compared non-proteinuric). Patients with proteinuric phenotype compared to non-proteinuric were characterized by higher rate of dyslipidemia (85% vs 45%, $p<0.001$), longer duration of HTN and DM (19.5 vs 7.5 years and 8 vs 3 years, respectively, $p<0.01$ for trend) and lower HDL-C (1.2 vs 1.9, p=0.02). Both groups had similar office brachial SBP (156 vs 157 mmHg; p=0.48), but patients with proteinuric phenotype had higher office central SBP (147 vs 137 mmHg, p=0.007) and worse 24-h profile of central SBP (daytime 147 vs 138 mmHg, p=0.008; night-time 143 vs 130 mmHg, p=0.04). Proteinuric phenotype significantly correlated with office aortic SBP (r=0.28; p=0.01) and daytime and night-time aortic SBP (r=0.28 and 0.21 respectively, $p<0.05$ for trend).

The eGFR phenotypes were as follows: G3a in 82.2% (GFR 54 ml/min/1.73 m^2, UACR 20 mg/g) and G3b in 17.8% (GFR 38 ml/min/1.73 m^2, med UACR 46 mg/g, $p<0.01$ for trend compared to G3a). Patients with worse kidney function had longer duration of HTN and DM (16 vs 11 years and 10 vs 6 years, respectively, $p<0.01$ for trend), higher median brachial and aortic BP levels (158/90 vs 146/82 mmHg and 150/95 vs 138/80 mmHg, respectively, $p<0.01$ for trend), worse 24-h profile of central SBP (daytime 148 vs 138 mmHg, p=0.008; night-time 146 vs 130 mmHg, p=0.006), higher central pulse pressure (56 vs 49 mmHg, p=0.007), augmentation index (33 vs 14%, p=0.007).

Conclusion: Hypertensive patients with T2DM and CKD G3b and proteinuria were characterized by worse 24-profile of central BP and higher arterial stiffness.

P0160 HOW TO MANAGE INTRADIALYTIC HYPERTENSION?

Ramia BENHAMOU[1], Hajar ELASSAS[1], Meriem Chettati[1], Wafaa Fadili[1], Inass Laouad[1]

[1]*Mohammed VI University Hospital Center of Marrakesh, Cadi Ayyad University, Nephrology, Marrakesh, Morocco*

Background and Aims: Hypertension in subjects on long term dialysis is frequent. Intradialytic hypertension affects up to 20% of hemodialysis patients and occurs more frequently in patients who are older, have lower dry weights, are prescribed more antihypertensive medications. Elevated BP detected by home or ambulatory BP monitoring is clearly associated with shorter survival.

Method: We realized a cross sectional study in two hemodialysis center patients during october 2019. We compared two groups of patients: group 1 with HTA (HTA+) and the second without (HTA-). Prevalence of hypertension intra dialysis (increase in systolic BP $>$ 15mmHg during dialysis) was determined by blood pressure recordings every thirty minutes during hemodialysis. We collect information about prescription patients (bolus dose of IV nicardipine or administration of captopril orally) after HTA inicident. We collected and analyzed datas of 1476 hemodialysis sessions for 123 patients.

Results: The mean age of your patients was 46 $\pm$ 26,3 years with a female predominance.

The mean duration of hemodialysis was 9,8 years. The initial nephropathy was hypertensive in 14,6%. 44,7% (n=55) patients used at least one antihypertensive treatment (HTA+ group), in 72,7% calcic inhibitor. Hypertension crisis in HTA+ group was higher than HTA- group, respectively 37,9% and 4,7% (p=0,0002).

Concerning HTA+ group, in 9,35% of cases patients receveid IV bolus of nicardipine, 7,9% captopril and 17,9% of cases have not receveid any antihypertensive medication. In HTA- group they receveid IV nicardipine on only 2,5% cases and no drugs in half of all cases.

Patients who were older and receive erythropoietin-stimulating agents were more likely to exhibit an increase in SPB despite similar amounts of ultrafiltration in each groups.

It appears HTA- group had better control of hypertension crisis in 77,5% versus 65,5% in HTA+ group, at 20minutes of crisis (p= 0,004). Administration of captopril in the both group allowed better control of hypertension 90% (HTA+ group) and 84,2%(HTA- group). Hypertension crisis was more controlled in group with high ultrafiltration rate with administration of captopril .

Conclusion: Use of ACE inhibitors during dialysis to manage hypertension crisis appears a great solution and confirm hypothesis of activation of the renin–angiotensin–aldosterone system. Treatment of intradialytic hypertension may include careful attention to dry weight, avoidance of dialyzable antihypertensive medications, limiting the use of high calcium dialysate, achieving adequate sodium solute removal during hemodialysis, and using medications which inhibit the rennin-angiotensin-aldosterone system or which lower endothelin 1.

P0161 TO EVALUATE THE TH PROFILE (TH1/TH2/TH17) AMONG GESTATIONAL DIABETES AND NORMAL PREGNANCY

Anupma Kaul[1], Amita Pandey[2], Vikas Aggrwal[3]

[1]Sanjay Gandhi Post graduate institute of Medical sciences, Nephrology, Lucknow, India, [2]King george medical college, Obstrtrtics and gyneocology, Lucknow, India and [3]Sanjay Gandhi Post graduate institute of Medical sciences, Immunology, Lucknow, India

Background and Aims: Gestational diabetes mellitus (GDM) is a common pregnancy complication, characterized by insulin resistance and low-grade systemic inflammation with a pro-inflammatory immune system response. Our objective was to study the peripheral Th1, Th2, Th17 and Treg response in GDM compared to normal pregnancy.

Method: Th1, Th2, Th17 and Treg subsets was determined by flow cytometry based on staining for specific intracellular cytokines levels and their CRP levels were also assessed.. The health status of all offspring was also assessed 6 months post-delivery.

Results: A total of 32 adult pregnant women were enrolled into a GDM (n=18) and Control (n=14) group. At the third trimester of pregnancy, the GDM group had a higher proportion of Th2, Th17 and Treg cells compared to control. Contrary to the control group, the GDM group exhibited no significant change in the Th1/Th2/Th17/Treg profile postpartum. A higher circulating CRP were noted in the GDM group compared to controls. At the 6-month post-delivery assessment, 23.6% of the offspring from the GDM group were found to have developed atopic dermatitis or food allergy compared to none from the control group.

Conclusion: Compared to an uncomplicated pregnancy, GDM exhibits a significantly different peripheral T-cell profile at the third pregnancy trimester characterized by higher proportion of Th2, Th17 and Treg cells which persist six months post-delivery, while the increased high sensitivity CRP (hsCRP) levels stressed the low-grade inflammatory profile of this disease

P0162

HEMODIALYSIS AND PERITONEAL DIALYSIS PATIENTS HAVE SEVERELY IMPAIRED ENDOTHELIAL POST-OCCLUSIVE FOREARM VASODILATORY RESPONSE ASSESSED WITH LASER SPECKLE CONTRAST IMAGING

Maria Eleni Alexandrou[1,2], Eugenia Gkaliagkousi[3], Charalampos Loutradis[1], Chrysostomos Dimitriadis[1], Eustathios Mitsopoulos[2], Antonios Lazaridis[3], Varvara Nikolaidou[3], Panagiotis Dolgiras[3], Dorothea Papadopoulou[2], Stella Douma[3], Aikaterini Papagianni[1], Panteleimon Sarafidis[1]

[1]Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece, [2] Papageorgiou General Hospital of Thessaloniki, Department of Nephrology, Greece and [3]Aristotle University of Thessaloniki, 3rd Department of Internal Medicine, Papageorgiou General Hospital of Thessaloniki, Greece

Background and Aims: Endothelial dysfunction is associated with cardiovascular events and mortality in various disease states, including end-stage-renal-disease (ESRD). Novel technological approaches have emerged for real-time assessment of endothelial reactivity. This study examined forearm skin microcirculation using Laser Speckle Contrast Imaging (LSCi) before and after arterial occlusion in ESRD patients undergoing hemodialysis (HD) or peritoneal dialysis (PD)

Method: 38 patients undergoing HD were matched in a 1:1 ratio with 38 PD patients (for age, sex and dialysis vintage) and 38 controls (for age and sex). Skin microvascular reactivity parameters assessed with LSCI included baseline perfusion, occlusion perfusion, and peak perfusion during post-occlusive reactive hyperemia (PORH); time to peak perfusion; proportional change from baseline to peak perfusion; baseline and peak cutaneous vascular conductance (CVC); proportional change from baseline to peak CVC; and the amplitude of the PORH response (calculated as the difference between peak and baseline CVC).

Results: Baseline perfusion [HD: 46.97±14.6; PD: 49.32±18.07; controls: 42.02±11.94 Laser-Specle-Perfusion-Units (LSPU), p=0.097] and peak post-occlusion perfusion (104.77±28.68 vs 109.04±40.77 vs 116.96±30.96 LSPU, p=0.238) did not differ between groups. However, the post-occlusive vascular response was completely different, since time to peak response (HD: 7.24±6.99; PD: 10.68±9.45; controls: 11.11±5.1 sec, p=0.003) and the (%) increase from baseline to peak perfusion (HD: 133%±66; PD: 149%±125; controls: 187%±61, p=0.001) was significantly lower in ESRD patients. ESRD patients had also lower levels of peak CVC, indicating the maximum capillary recruitment (HD: 1.05±0.3; PD: 1.07±0.44; controls: 1.57±0.52 LSPU/mmHg, p<0.001), lower % increase of CVC at peak (p=0.001), and lower amplitude of the PORH response (p=0.001) (a measure of the difference between baseline and maximum capillary recruitment).

Conclusion: Using this novel non-invasive technology endothelial post-occlusive skin vasodilatory response was found to be similar between HD and PD patients and significantly impaired compared to controls. Future studies are needed to assess the prognostic implications of this microcirculatory functional defect.

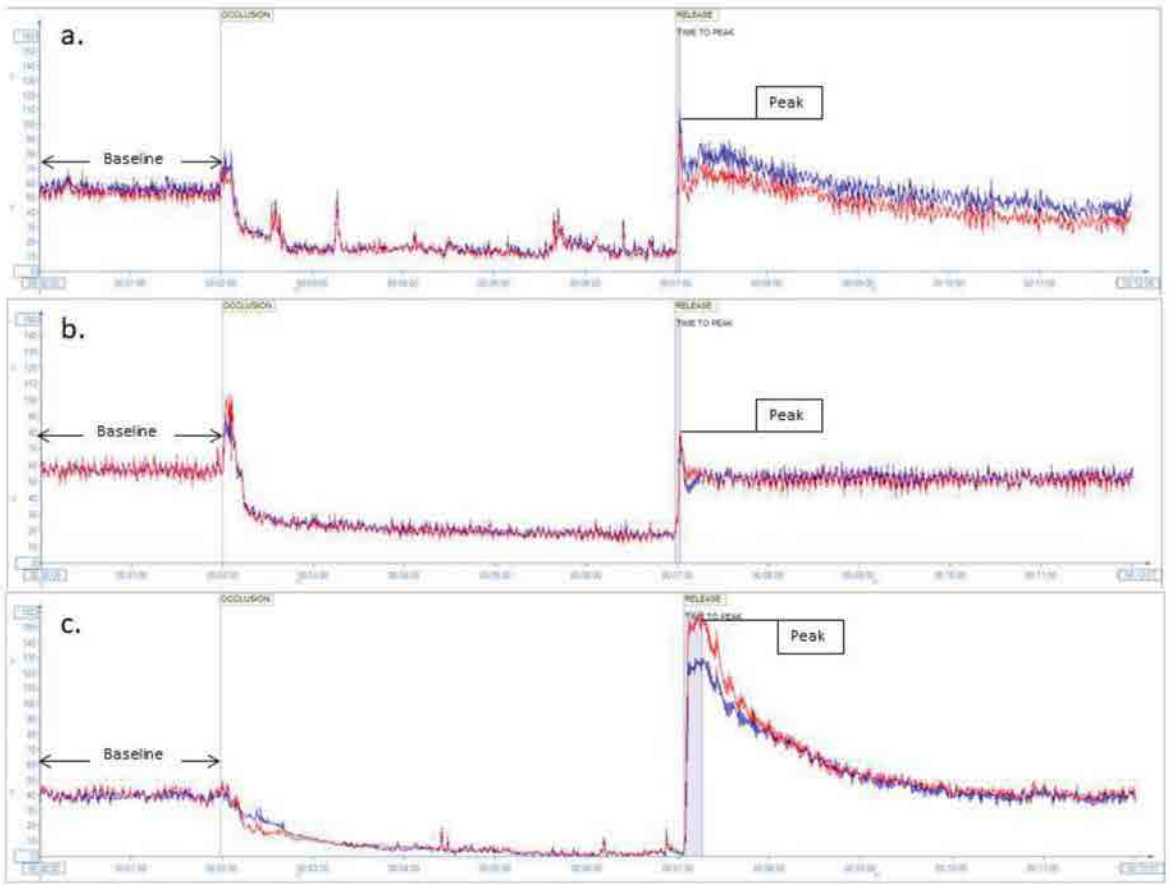


Figure:

P0163 EPIDEMIOLOGY OF FMD: A REVIEW OF THE SALFORD EXPERIENCE

Aine De Bhailis[1], Tina Chrysochou[1]

[1]*Salford Royal Foundation Trust, Nephrology, SALFORD, United Kingdom*

Background and Aims: Fibromuscular dysplasia (FMD) is a non-atherosclerotic, non-inflammatory disease of medium arteries that has been described in multiple vascular beds from cranial to pelvic with a wide variety of manifestations such as beading, stenosis, occlusion, aneurysm or dissection.

Both the United States and European Registries for FMD have made significant contributions to our understanding of FMD however many questions remain. To date those with a diagnosis of FMD within the UK have not been captured within any such registry. The RaDaR (National registry of rate kidney diseases) FMD group in Salford Royal NHS Foundation Trust aims to recruit UK based patients to a national registry, which will align with the European registry to facilitate collaboration and future research.

Salford Royal Trust is unique as it has the only dedicated FMD clinic in the UK. This clinic aims to effectively diagnose screen and treat those with suspected FMD. Here we describe the experience of a dedicated clinic for those with FMD, the first of its type in the United Kingdom.

Method: Screening of all electronic patient records from January 2010 to October 2019 was undertaken for diagnosis of fibromuscular dysplasia, coronary artery dissection, middle aortic syndrome along with the acronyms "SCAD" and "FMD". This search yielded 36 patients with a possible relevant diagnosis. Incidence, clinical characteristics, risk factors and treatment modalities were reviewed.

The diagnosis had to be confirmed in the vascular bed by angiography, either computed tomographic angiography (CTA) or magnetic resonance angiography reviewed by experienced radiologist. FMD was diagnosed as non-atherosclerotic arterial stenosis affecting the trunk or branch of medium sized vessels, in the absence of aortic wall thickening, inflammation and known syndromic arterial disease

The diagnosis of SCAD was made based on coronary angiographic characterised by a tear in the arterial wall that is nontraumatic and non-iatrogenic with no secondary aetiology of the dissection

Clinical data collected included:

- Clinical presentations leading to diagnosis (i)Renal ie accelerated phase hypertension, poorly controlled hypertension or incidentally noted renal artery disease on imaging (ii) Cerebral/Neck ie migraine, cerebrovascular events or tinnitus and (iii) Cardiac ie acute coronary syndrome without evidence of atherosclerotic disease
- Patient characteristics such as sex, age, positive family history, smoking history and number of anti-hypertensive agents
- Use of secondary prevention agents ie statins and aspirin
- Requirement for intervention
- Formal screening of other vascular beds

Results: From January 2010 to September 2019 36 patients were identified using the pre-specified search terms. 9 patients were excluded leaving 27 patients with a diagnosis of FMD, SCAD or middle aortic syndrome.

The median age was 50 with a 2:1 ratio for females to males.

The majority of patients with FMD (17/20) presented with a renal manifestation i.e. hypertension.

Renal artery FMD was confirmed by CTA/MRA in 20 patients. Of these 60% had extra-renal screening. 11 patients had cerebral screening (8 CTA and 6 MRAs). 7 patients had aortic imaging (4 CTAs, 4 MRAs). Only 6 of the 12 had head to toe screening.

In terms of secondary prevention 50% of those with an FMD diagnosis were on a statin and 45% were on an anti-platelet agent.

In relation to those with an initial diagnosis of SCAD (5), 3 patients had screening in terms of CTA/MRA and 1 patient was found to have cerebral vessel manifestations consistent with FMD.

Conclusion: A dedicated clinic for FMD allows for prompt diagnosis and appropriate screening for possible involvement of other vascular beds. It also allows appropriate treatment with secondary prevention agents such a to those who are most likely to benefit. Although in its infancy there is great potential for this bespoke clinic to continue to expand to become a national centre of excellence.

P0164 **AMBULATORY BLOOD PRESSURE MONITORING AND CLINICAL SIGNIFICANCE IN PATIENTS WITH GASTROESOPHAGIAL REFLUX DISEASE**

Sule Ozdemir Arabaci[1], Ilhan Kurultak[2], Ahmet Tezel[3], Sedat Üstündağ[2]

[1]Trakya University, Faculty of Medicine, Internal Medicine, Edirne, Turkey, [2]Trakya University, Faculty of Medicine, Nephrology, Edirne, Turkey and [3]Trakya University, Faculty of Medicine, Gastroenterology, Edirne, Turkey

Background and Aims: The patients with gastro-esophageal reflux disease (GERD) have distortion of sympathetic and parasympathetic components of the autonomic nervous system. The increase in sympathetic activity results in hyperkinetic circulation with peripheral vasoconstrictor and tachycardia and also regulates blood pressure with increase of renin in kidneys. We aimed to elucidate the patterns of pulse pressure in GERD patients, and also to investigate possible relationship between patterns of pulse pressure and laboratory/urinary parameters in adults

Method: The ambulatory blood pressure measuring was performed in all cases. Fifty patients in the reflux group and fifty individuals in the control group were included. Blood and urine specimens were examined. The individuals with cardiovascular disease, hypertension, malignancy, asthma disease, gastric peptic ulcer, hepatitis disease, tuberculosis, gastrointestinal disease excluding reflux, cerebrovascular disease, vasculitic disease, chronic alcohol usage, drugs with affect on autonomic system usage were excluded from study.

Results: We found lower diastolic blood pressure and increased pulse pressure values in reflux group and these were significant statistically. When patients were evaluated separately as men and women, this situation was found to be more pronounced in women. The decrease in serum potassium, chloride levels and the increase in serum LDL cholesterol, triglyceride levels in reflux group considered as statistically significant. Urinary parameters were similar in both groups. Non-dipper pattern found more common in reflux group, but considered as insignificant. The results were summarized in Table 1 and Table 2.

Conclusion: This study supports the hypothesis that increased vascular risk may be present in patients with GERD. Thus, perhaps a new population at risk for cardiovascular disease will be identified and mortality rates will able to decrease with early clinical evaluation.

Blood Parameters		**Control (n=57)**		**GERD (n=50)**		**p****
		Mean	**SD**	**Mean**	**SD**	
MCV	*(fL)*	86,19	4,64	83,98	4,71	**0,021**
Lymphocyte Count	*(10^3/uL)*	2,28	0,73	2,59	0,78	**0,040**
Trygliseride	*mg/dL*	106,92	66,35	144,17	89,43	**0,023**
Cholesterol	*mg/dL*	185,37	40,42	207,33	46,21	**0,024**
LDL	*mg/dL*	115,31	31,21	134,46	30,83	**0,003**
K	*mmol/L*	4,45	0,3	4,32	0,31	**0,036**
Cl	*mmol/L*	104,94	1,95	103,89	1,75	**0,007**
UrinaryParameters						
Total Protein / Creatinine	*gr/gr*	0,0056	0,0035	0,0054	0,0043	0,805
Na /Creatinine	*mmol/mg*	1,2745	0,7378	1,2169	0,7898	0,707
Uric Acid/ Creatinine	*gr/gr*	0,4051	0,2039	0,365	0,1683	0,287
Microalbümin / Creatinine	*gr/gr*	0,0846	0,0967	0,0635	0,0333	0,148

Table 1: The demographic and hemodynamic characteristics of Control and GERD patients

Parameters		Control (n=50)		GERH (n=50)		p*
Sex	Female	48% (n=24)		42% (n=21)		0,546
	Male	52% (n=26)		58% (n=29)		
Age, *year*		36,68	8,02	34,2	7,96	0,124
Waist Circumference, *cm*		81,04	11,67	83,48	13,02	0,326
Weight, *kg*		71,04	11,99	74,68	14,52	0,175
Lenght, *cm*		169,54	8,56	170,58	9,93	0,576
Body Mass Index		24,64	3,37	25,57	4,01	0,212
Systolic Blood	Whole day	112,1	10,05	111,46	9,55	0,745
Pressure, *mm Hg*	Day time	115,26	10,64	114,22	10,08	0,617
	Night time	105,94	10,07	106,64	11,1	0,742
Diastolic Blood	Whole day	74,86	2,78	69,38	6,38	0,001
Pressure, *mm Hg*	Day time	73,64	7,61	71,82	7,8	0,240
	Night time	65,5	7,34	64,44	8,74	0,513
Pulse Pressure,	Whole day	37,24	9,22	42,08	6,92	0,004
mm Hg	Day time	41,62	6,12	42,4	5,57	0,507
	Night time	40,44	5,74	42,2	6,31	0,148
Pulse Pressure,	Whole day	32,17	6,75	40,67	7,44	<0,001
mm Hg Female	Day time	39,46	3,83	41,38	4,94	0,150
	Night time	38,46	3,88	40,81	4,66	0,072
Male	Whole day	41,92	8,79	43,1	6,46	0,570
	Day time	43,62	7,17	43,14	5,95	0,789
	Night time	42,27	6,6	43,21	7,19	0,618
Reverse Dipper (<0%)		8% (n=4)		8% (n=4)		0,601
Non-dipper (0-10%)		52% (n=26)		64% (n=32)		
Dipper (10-20%)		36% (n=18)		24% (n=12)		
Extreme Dipper (>20%)		4% (n=2)		4% (n=2)		

*Chi square test, p<0.05

P0165 HYPERTENSION IN OVERWEIGHT AND OBESE CHILDREN: IMPACT ASSESMENT OF ABPM PARAMETERS

Diletta Apuzzo[1], Luigi Annicchiarico Petruzzelli[1], Serena Ascione[1], Adele Corcione[1], Deianira Pedoto[1], Giuseppina Barra[1], Maria Chiara Rocco[1], Carmine Pecoraro[1], Gabriele Malgieri[1]

[1]*Santobono Childrens Hospital, Pediatric Nephrology, Napoli, Italy*

Background and Aims: We describe the relationship between overweight and obesity and Hypertension on ABPM.

Method: We conducted a cross-sectional study using a database of patients aged 6-16 years, who had undergone 24h ABPM from December 2002 through December 2016. ABPM were performed using the validated device Spacelab 90217. Were evaluated the 24h MAP, daytime MAP, nocturnal MAP, systolic and diastolic load, MAP Systolic and Diastolic. Subjects were grouped by BMI Z-score into overweight (>1<2), obese (BMI Z-score >2<3) and severe obese (BMI Z-score >3). A total of 1016 patients were enrolled and recorded n.1210 ABPMs. Obese pts were 202 (19.8%); 126 M;76F;median age 10,2 y. Overweight childrens were 97 (11.9%);52 M;45F;median age 8,4y.

Results: Among overweight childrens (BMI Z-Score >1<2): 12 (12.3%) had hypertension, 22 (22.6%) pre-hypertension, 15 (15.4%) MH; non dipping pattern was recorded in 26 (52%). 48 were normotensive. Among obese childrens, 122 had hypertension (60.3%): 24 pts had Masked Hypertension (19.6%); 72 (59.0%) had severe ambulatory hypertension with BMI z-score >3 (mean 3.8) ,and in this category all pts were both systolic and diastolic non dipping. 32 (64%) obese with BMI z-score >2, <3 were non-dipping. Diastolic load was significantly higher (p>0,0001) in severe obese. 28 pts had ambulatory prehypertension (13.8%), 11 pts had White Coat Hypertension (4.9%).41 pts had normotension (20.2%).

Conclusion: The severity of ambulatory hypertension increased with increased BMI Z-score. The non-dipping status is associated, not only with higher BMI Z-score, but was present in overweight and obese with BMI z-score >2<3 also. ABPM is an effective tool that should become routine in all obese patient, but also in overweight childrens, which may lead to better treatments and prevention methods.

P0166 ADDITIVE INTERACTION OF HIGH SODIUM INTAKE AND INCREASED SERUM TRIGLYCERIDE ON HYPERTENSION

Joo-Hark Yi[1], Mi-yeon Yu[1], Jong Wook Choi[2], Sang-Woong Han[1], Chang Hwa Lee[1], Joon-Sung Park[1]

[1]Hanyang University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of South and [2]Konkuk University School of Medicine, Research Institute of Medical Science, Chungcheongbuk-do,

Background and Aims: Both high salt diet and abnormal lipid metabolism are critical risks of vascular endothelial dysfunction. This study investigated the interactive effects of increased sodium intake and elevated serum triglyceride (TG) on elevated blood pressure (BP).

Method: We conducted nation-wide, population-based interaction analysis using Kawasaki method for estimating 24-h urinary sodium excretion ($e24hUNaE_{Kawasaki}$) as a candidate indicator of dietary sodium intake. Eligible as cases were all native Koreans aged 20 years or older without significant medical illness.

Results: A total of 16936 participants were divided into quintiles according to their $e24hUNaE_{Kawasaki}$ results. Participants in the highest quintile were more obese and hypertensive and had increased white blood cell count, decreased hemoglobin, greater glycemic exposure, and poor lipid profiles as compared to lower quintiles. Linear regression showed that $e24UNaE_{Kawasaki}$ was closely related with dietary sodium intake, systolic BP, diastolic BP, and TG. Multiple logistic regression, adjusted for dietary sodium intake and various conventional risk factors of hypertension**, demonstrated that both $e24UNaE_{Kawasaki}$ and TG were significant predictors of hypertension. Our interaction analysis revealed that high sodium intake had a bigger effect on the *risk of* hypertension in participants with elevated TG than those without (adjusted RERI = 0.022, 95% *CI* = 0.017-0.027; adjusted AP = 0.017, 95% *CI* = 0.006-0.028; adjusted SI = 1.010, 95% *CI* = 1.007-1.014).**

Conclusion: Our findings indicate that the interaction of high salt diet and abnormal lipid metabolism may exert synergistic biologic effect on the increased arterial BP.

P0167 HYPERTENSION IN PATIENTS WITH LUPUS NEPHRITIS

Marwa Omrane[1], Raja Aoudia[1], Mondher Ounissi[1], Mariem Najar[1], Mouna Jerbi[2], Hanene Gaied[2], Samia Barbouche[1], Imen Gorsane[1], Taieb Ben Abdallah[1], Rim Goucha[2]

[1]Charles Nicole Hospital, Internal medicine A, Tunis, Tunisia and [2]Mongi Slim Hospital, Nephrology, La Marsa, Tunisia

Background and Aims: Hypertension is a common manifestation during systemic lupus erythematosus (SLE). Its mechanism is multifactorial and microthromboses of renal arterioles seem to be the most important mechanism. The objective of our study is to identify the histological and evolutionary characteristics of patients with lupus nephritis (LN) presenting with hypertension.

Method: A retrospective study of 85 patients followed for LES with lupus nephritis documented by a renal biopsy collected in 17 years and presenting with hypertension.

Results: Among 174 patients with LN, eighty-five (48.58%) are hypertensive. A sex ratio F / H of 6.08. The mean age of LN diagnosis was 36.4 years old [13 -75 years old]. The average time to onset of hypertension was 25.8 months [0-204 months]. Malignant hypertension was present in 12% of patients. Antiphospholipid Antibody Syndrome (APLS) was found in 35.3% of cases. Renal biopsy showed LN class II in 2 cases, class III in 8 cases, class IV in 43 cases, class V isolated in 8 cases and class VI in 3 cases. Vascular lesions were arteriolosclerosis in 40% of cases and thrombotic microangiopathy (TMA) lesions in 17.6% of cases. The treatment was essentially based on blockers of the renin angiotensin system, either as monotherapy or in combination with calcium channel blockers, beta blockers or central antihypertensives. The evolution was marked by the occurrence of cerebrovascular accidents associated in 7 cases with APLS and coronary artery disease in 2 cases. Renal evolution was marked by total and durable remission in 27.5%, chronic renal disease in 31.7%, and end-stage renal failure in 40.8% of cases. Blood pressure was balanced in 40,5 % of cases and unbalanced in 59,5% of cases.

Conclusion: In our lupus patients, hypertension was common, associated with severe glomerular and vascular lesions and a rather severe renal prognosis.

NEPHROLITHIASIS AND URIC ACID

P0169 DYSFUNCTION OF ABCG2, URATE TRANSPORTER, IS RELATED WITH UROLITHIASIS.

Yuki Ohashi[1], Satoshi Yamaguchi[2], Hirotaka Matsuo[3], Makoto Hosoyamada[4], Kimiyoshi Ichida[1]

[1]Tokyo University of Pharmacy and Life Sciences, Hachioji, Japan, [2]Kitasaito Hospital, Asahikawa, Japan, [3]National Defense Medical College, Tokorozawa, Japan and [4]Teikyo University Itabashi Campus, Itabashi City, Japan

Background and Aims: Urolithiasis is one of the rapidly increasing diseases in developed countries. It has been reported that urolithiasis is related with lifestyles, diet, obesity, climate and chronic diseases including hyperuricemia, diabetes mellitus, metabolic syndrome, chronic kidney disease et cetera. Among them, hyperuricemia is the leading cause of urolithiasis. ATP–binding cassette subfamily G member 2 (ABCG2), urate transporter, excretes uric acid in the kidney and the intestinal tract and ABCG2 dysfunction increases a risk of hyperuricemia. In this study, we investigated the estimated ABCG2 function by common two dysfunctional variants, Q126X (rs72552713) and Q141K (rs2231142), in patients with urolithiasis, and we evaluated the relation between urolithiasis and ABCG2 dysfunction.

Method: One hundred and ninety-seven urolithiasis patients without gout (150 males and 47 females) were enrolled. Q126X totally abolishes ABCG2 function, while Q141K reduces its function by about 50%. Since these two SNPs do not link each other and two SNPs do not exist on same chromosome, these two are regarded as independent risks. Namely, based on the genotype of Q126X and Q141K, it can be divided into three categories: a full functional group, a 75% functional group and a ≦50% functional group. Serum uric acid levels and amount of urinary uric acid were measured. Renal uric acid handling of the patients was classified into renal uric acid underexcretion type or renal uric acid overload type based on uric acid clearance and amount of urinary uric acid. Stone composition was analysed, if it had been possible.

Results: ABCG2 function of the patients was evaluated as follows: 82 patients, ABCG2 full function (41.6%); 78 patients, 75% function (39.6%); 37 patients, ≦50% function (18.8%). 155 patients were classified into renal uric acid underexcretion type, 13 patients were classified into renal uric acid overload type and 2 patients were classified into normal type (27 patients have not had 24-hour urine biochemical test). Stone composition analysis was performed for 136 patients; calcium oxalate stone was identified in 107 patients and uric acid stone in 29 patients. In this study, 58.4 % of the patients with urolithiasis had some ABCG2 dysfunction as against 49.8 % of the healthy individuals previously reported ($p=0.0246$). In addition, the ratio of subjects with urolithiasis having 50% or less of ABCG2 function was higher than healthy individuals significantly (OR=1.773, $p=0.007$). The high ratio of ABCG2 dysfunctional patients with urolithiasis suggested that ABCG2 dysfunction is a risk factor for urolithiasis. In the patients with urolithiasis, renal uric acid underexcretion type accounted for about 90% of the patients. This means that this type accelerated urolithiasis as well as hyperuricosuria.

Conclusion: ABCG2 dysfunction and renal uric acid underexcretion type were suggested to be a risk factor for urolithiasis.

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P0170

ETHANOL EXTRACT OF LIRIODENDRON CHINENSE(HEMSL.) SARG BARKS ALLEVIATES HYPERURICEMIC NEPHROPATHY VIA MEDIATING RENAL FIBROSIS AND INFLAMMATION

Jing Pan[1], Liang Ma[1], Ping Fu[1]

[1]*West China Hospital of Sichuan University, Division of Nephrology, Chengdu, P.R. China*

Background and Aims: The barks of *Liriodendron Chinense (Hemsl.) Sarg* is used in folk for expelling "wind and dampness", alleviating rheumatic arthralgia in traditional Chinese medicine. The aim of the study was to evaluate the protective effect of ethanol extract of the barks of *Liriodendron Chinense (Hemsl.) Sarg* (EELC) in a mouse model of hyperuricemic nephropathy (HN) and the mechanisms involved.

Method: EELC at a respective dose of 250 mg/kg/d or 500 mg/kg/d were orally administered to HN mice induced by a mixture of adenine (160 mg/kg/d)/potassium oxonate (2.4 g/kg/d) for 21 days. At the end of the treatment, serum uric acid, kidney functions (serum creatinine, BUN and urine microalbumin), 24-h urine uric acid excretion, as well as kidney pathological changes were investigated by biochemical assay, histopathological score, immunofluorescence and histochemistry, RT-PCR, and western blotting analysis.

Results: Oral administration of EELC to HN mice lowered serum uric acid, improved renal functions and attenuated renal fibrosis, especially the high-dose of EELC. EELC treatment also inhibited the activation of NF-κB, ASK1/JNK/c-Jun, JAK2/STAT3 signaling pathways and reduced the release of pro-inflammatory cytokine TNF-α in the kidneys of HN mice. Furthermore, EELC remarkably increased urine uric acid excretion of HN mice, which may be achieved by the upregulation of organic anion transporter 1 (OAT1), OAT3 and ATP-binding cassette subfamily G member 2 (ABCG2) proteins.

Conclusion: EELC alleviated the progression of HN by suppressing the activation of NF-κB, ASK1/JNK/c-Jun and JAK2/STAT3 signaling pathway, reducing the infiltration of inflammatory factors and uric acid accumulation in the kidney.

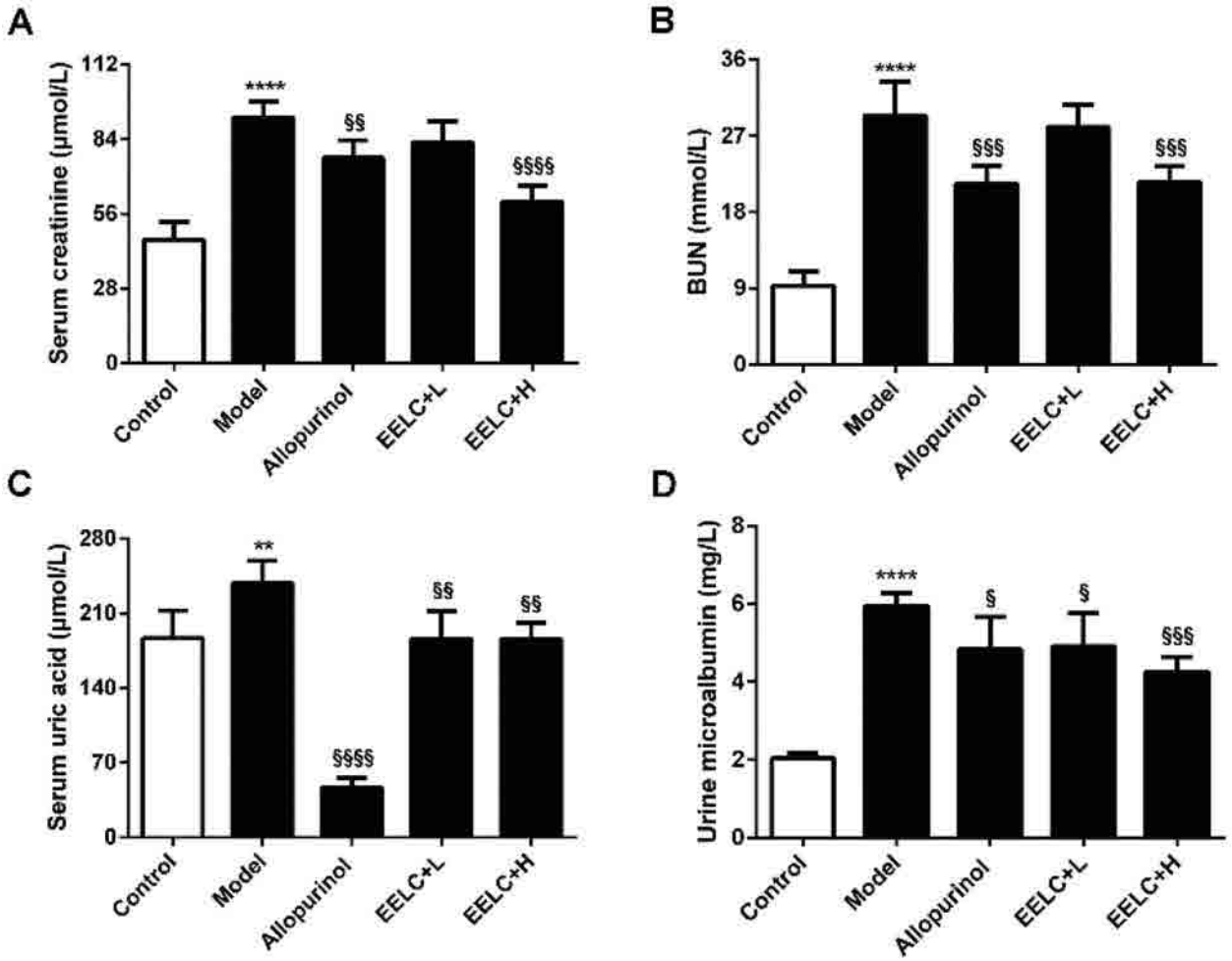


Fig.1 Effects of EELC on serum creatinine, serum UA, BUN, and urine microalbumin in hyperuricemic nephropathy. (A) Serum creatinine. (B) Serum uric acid. (C) BUN. (D) Urine microalbumin.

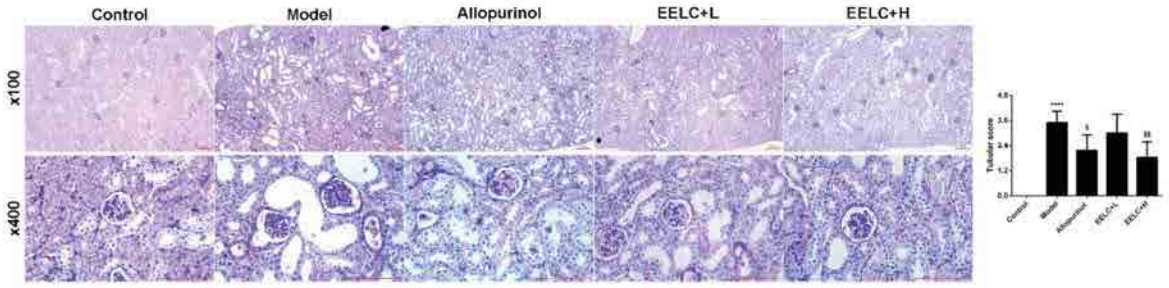


Fig.2 Effects of EELC on kidney histopathological changes in the mice of hyperuricemic nephropathy. (A) PAS staining of kidney sections were compared between different groups. (B) Tubular injury score.

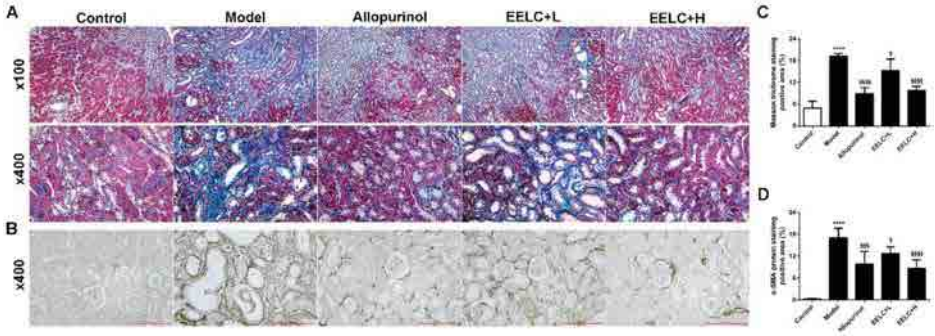


Fig.3 Effects of EELC on renal fibrosis in the mice of hyperuricemic nephropathy. (A) Photomicrographs illustrated MASSON staining of the kidney tissues. (B) Immunohistochemistry staining for α-SMA in kidneys. (C) The graph showed the degree and extent of collagen positive area (blue) relative to the whole area. (D) Quantitative data of α-SMA staining in different groups of mice.

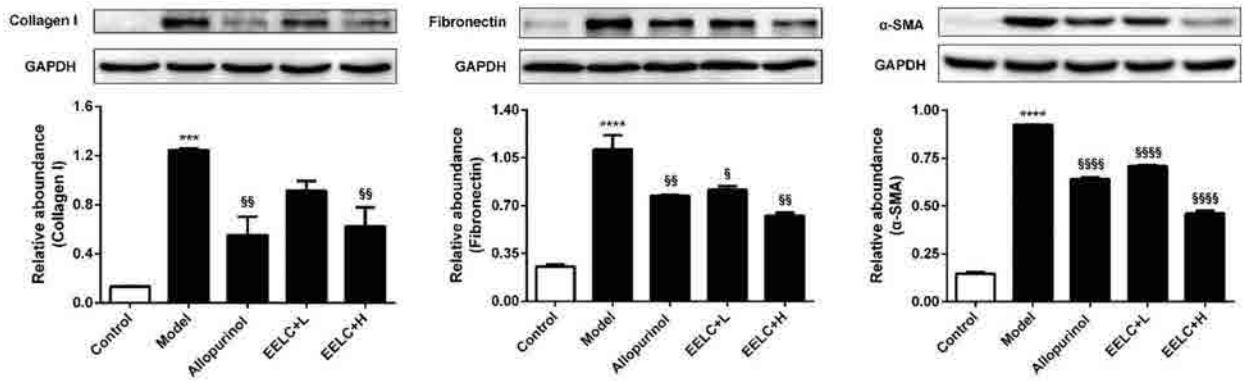


Fig.4 Effects of EELC on extracellular matrix deposition in the kidneys of hyperuricemic nephropathy mice. The protein expressions of collagen I, fibronectin and α-SMA in kidneys were quantified by densitometry and normalized to GAPDH.

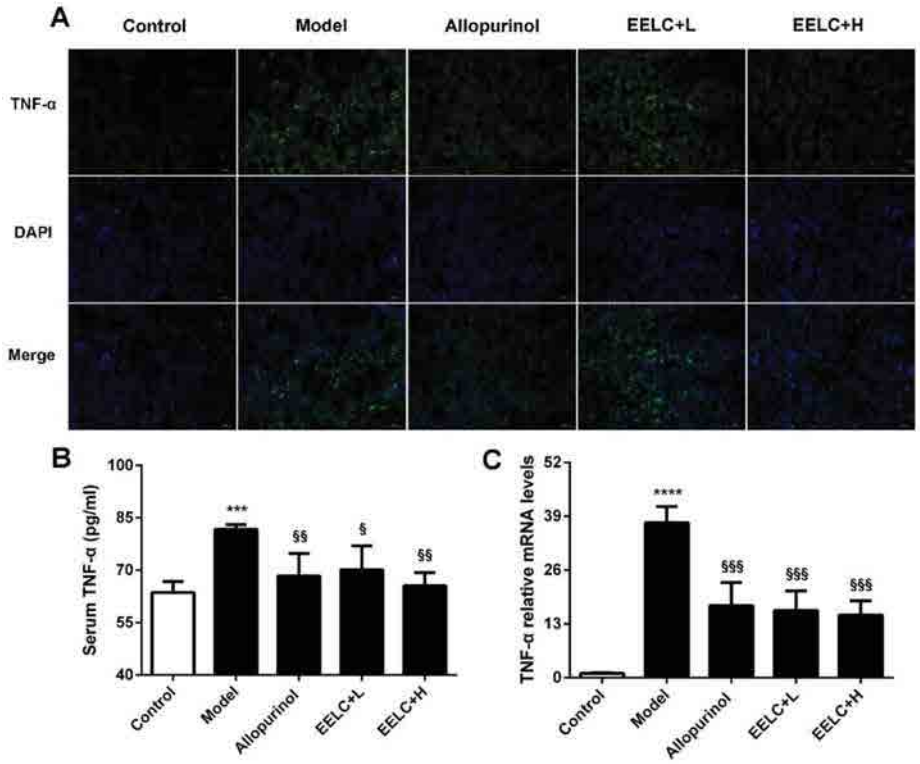


Fig.5 Effects of EELC on serum and renal TNF-α levels of hyperuricemic nephropathy mice. (A) Immunofluorescence staining of TNF-α in kidneys. (B) Serum TNF-α level. (C) Renal TNF-α relative mRNA level.

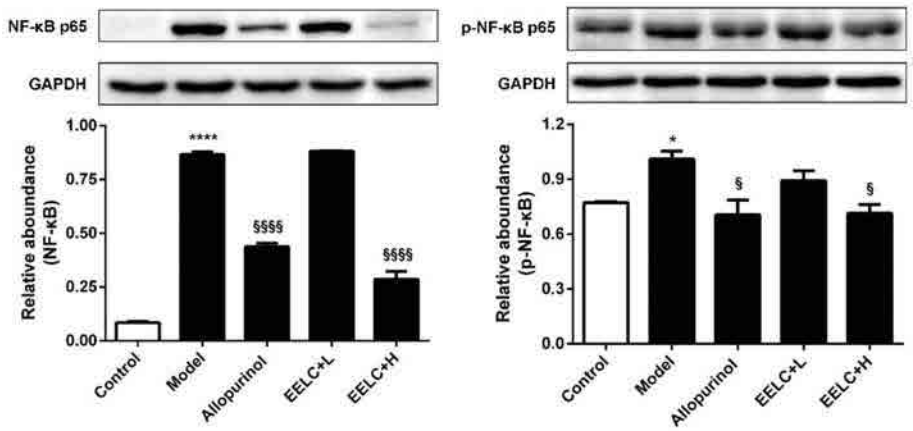


Fig.6 Effects of EELC on p-p65 and p65 protein levels in kidneys of hyperuricemic nephropathy mice.

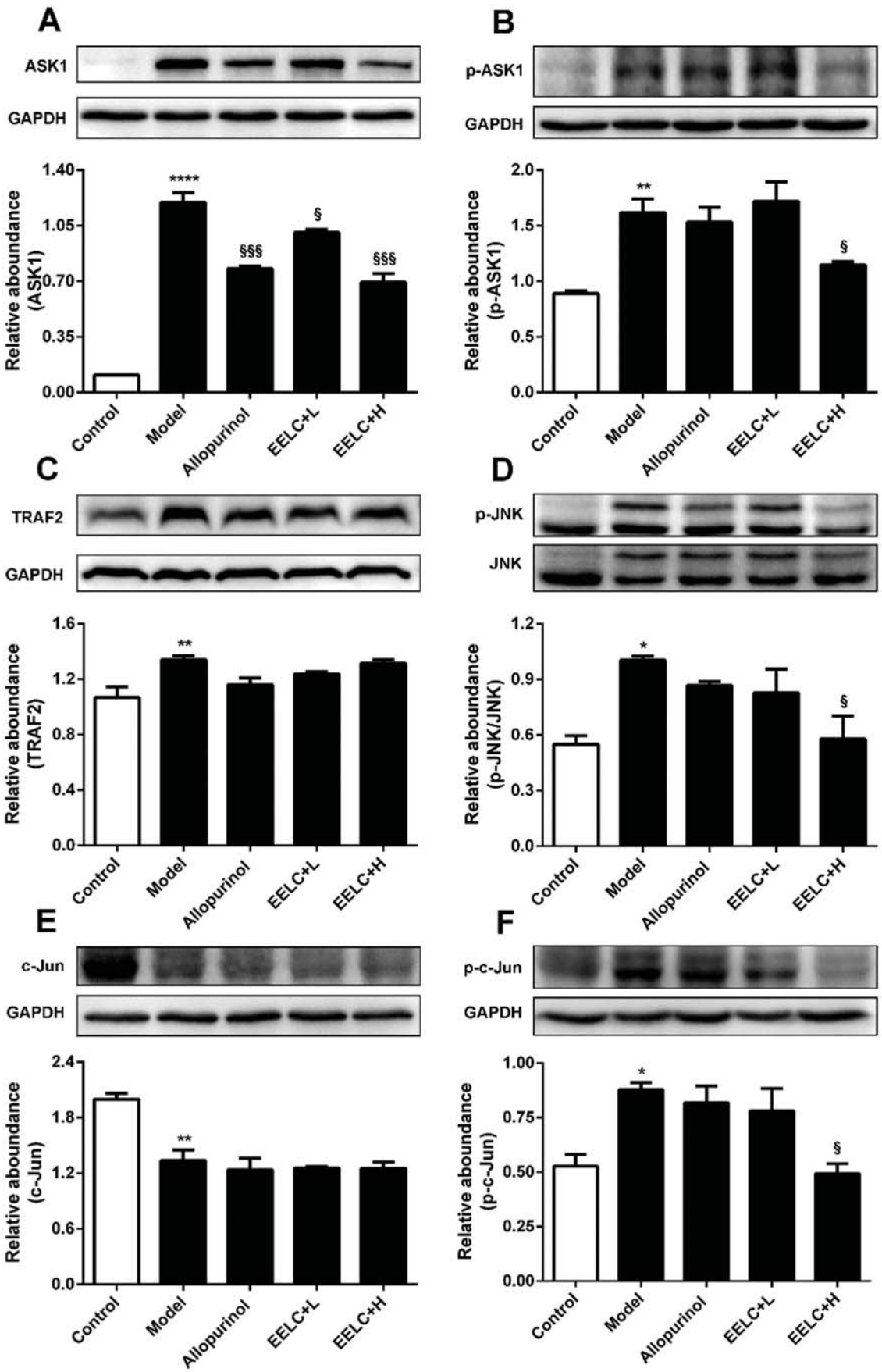


Fig.7 Effects of EELC on ASK1/JNK/c-Jun signaling in the kidney of hyperuricemic nephropathy mice. Renal protein levels of ASK1 (A), p-ASK1 (B), TRAF2 (C), c-Jun (E), p-c-Jun (F) were normalized to GAPDH. The relative protein levels of p-JNK was normalized to JNK (D).

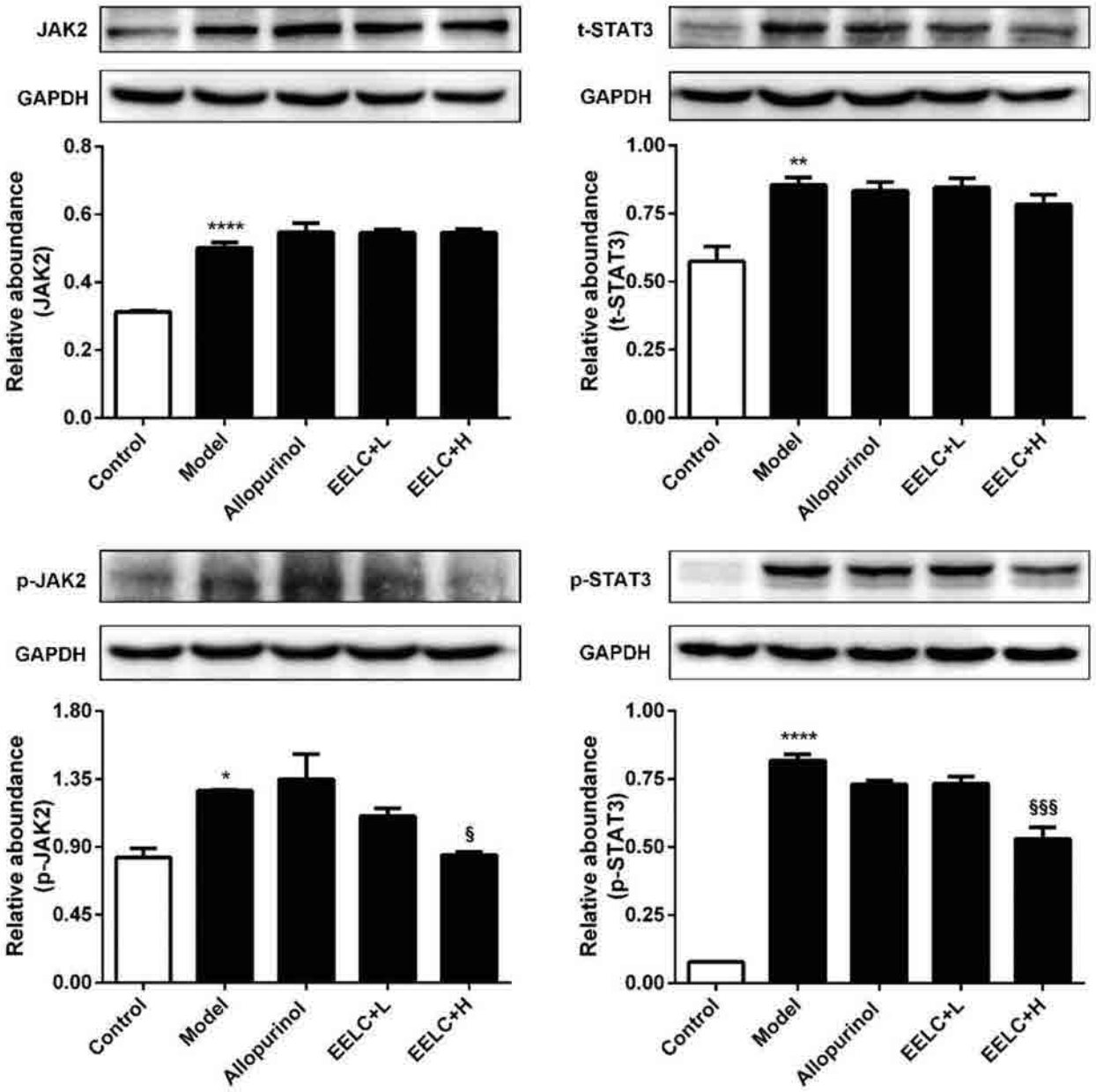


Fig.8 Effects of EELC on JAK2/STAT3 signaling in the kidney of hyperuricemic nephropathy mice. The relative protein levels of JAK2, p-JAK2, t-STAT3, p-STAT3 were normalized to GAPDH.

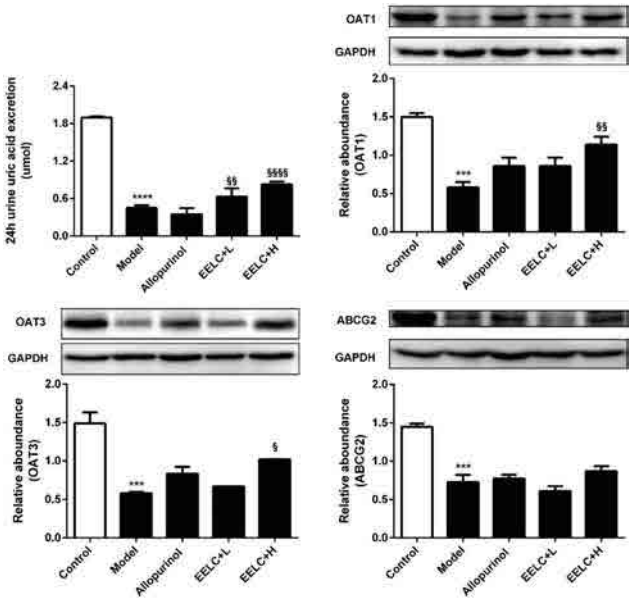


Fig.9 Effects of EELC on 24-h urine uric acid excretion and renal urate transport-related proteins in the mice of hyperuricemic nephropathy.

Figure: Date are represented as the mean ± SD. *p<0.05,**p<0.01,***p<0.001, ****p<0.0001 *vs.* control, §p <0.05, §§p<0.01, §§§p<0.001,§§§§p<0.0001 *vs.* model.

P0171

NON COMPLIANCE AND ACUTE DEHYDRATION ARE MAIN REASON FOR ACUTE KIDNEY FAILURE IN NON-INFANTILE PRIMARY HYPEROXALURIA TYPE I (PH I)

Bernd Hoppe[1], Cristina Martin Higueras[2], Bodo B. Beck[3]

[1]German Hyperoxaluria Center, Bonn, Germany, [2]University de la Laguna, Tenerife, Spain and [3]Human Genetics, Cologne, Germany

Background and Aims: Patients with primary hyperoxaluria type 1 have an increased risk of acute or chronic kidney failure (AKF/CKF). There are two risk groups: first the infantile oxalosis patients with an unremarkable family history and second, the adult patients with only an oligosymptomatic course (minor stone events), who get into end-stage renal disease (ESRD) due to oxalate-induced chronic inflammatory processes in the kidney. We were interested in the prevalence of acute kidney failure in the PH1 patients seen in our Hyperoxaluria Center over the last 10 years.

Method: We retrospectively analyzed the database of the German Hyperoxaluria Center for those patients being routinely seen in our outpatient clinic for AKF and its specific reason. AKF was defined as patients with a sudden onset of kidney failure and the necessity of dialysis installment, but a documented stable kidney function (no worse than stage 2-3 CKD) prior to onset of AKF.

Results: Currently, we routinely follow (3-4 times a year) 49 of 117 patients with genetically proven PH1. For the patients not routinely seen, we act as the reference center and primary lab. Out of the 117 PH1 patients, 6 had infantile oxalosis and thus early ESRD; 8 patients are currently on dialysis; and 6 patients have died, 2 patients each either post liver or liver/kidney transplantation (LTx, LKTx), under dialysis or as sudden death, the latter two due to systemic oxalosis. Transplantations were performed in 35 patients with PH1 (LKTx in 28 patients, LTx in 4 patients and 3 had an isolated kidney transplantation). Out of the 49 PH1 patients we routinely follow, AKF was diagnosed in 8 patients aged 11-56 years (one pediatric patient, 3 patients 18-19 years old, and 4 patients 29-56 years old), which has led to CKF and hence, maintenance hemodialyis in 7/8 and even death in one patient. Non-compliance regarding either medication or recommended fluid intake was the reason for AKF in 6 of the 8 patients, the 11 year-old girl, 2 adult patients and the 3 young adults being on the edge of leaving pediatric care. Acute massive diarrhea without adequate fluid substitution led to AKF in 2 middle aged male patients.

Conclusion: AKF is not uncommon in patients with PH1 and is frequently related to either non-compliance or to situations of severe fluid losses with inadequate fluid substitution. In the situations described, AKF is not based on already extremely altered renal function. Therefore, interruption of medication or lack of fluid intake, even for short periods of time, can lead to severe clinical consequences in these patients.

P0172

ARE FREQUENT STONE REMOVAL PROCEDURES IN PATIENTS WITH PRIMARY HYPEROXALURIA TYPE 3 (PH 3) RELATED TO DECLINE IN KIDNEY FUNCTION?

Bernd Hoppe[1], Cristina Martin Higueras[2], Bodo B. Beck[3], Marcin Zaniew[4], Przemyslaw Sikora[5]

[1]German hyperoxaluria Center, Bonn, Germany, [2]Universita de la Laguna, Tenerife, Spain, [3]Human Genetics, Cologne, Germany, [4]Kierownik Katedry Pediatrii, Zielona Gora, Poland and [5]Medical University of Lublin, Lublin, Poland

Background and Aims: PHIII is seen as the less problematic type of autosomal recessive inherited PH. This group of disorders in glyoxylate metabolism is clinically characterized by recurrent urolithiasis and/or progressive nephrocalcinosis, and, in type I and II, end-stage renal failure. The cause of PHIII was identified only in 2010 and unlike in PHI/II a remarkable low prevalence of symptomatic adults was observed, hence long-term clinical data are scarce. This phenomenon is commonly attributed to reduced penetrance of causative hydroxy-oxo-glutarate aldolase 1 gene (*HOGA1)* variants and a still unexplained tendency for clinical remission with age. Most PHIII patients present in early childhood with recurrent urolithiasis and undergo (repeated) stone removal procedures. We now hypothesized that repeated stone removal procedures may be associated with decline in kidney function.

Method: We retrospectively analyzed clinical and laboratory data of 41 genetically confirmed PHIII patients (0.5-29.3 years of age, with (20 different) biallelic mutations in the *HOGA1* gene). Period of follow-up ranged from just diagnosed to 22 years.

Results: Recurrent urolithiasis was most prominently found in the first 3 years of life (>25% of patients). Not all patients experienced clinical remission, 3/6 patients > 20 years of age have ongoing kidney stone development. In addition, patients presented with nephrocalcinosis and/or urolithiasis. A high amount of stone removal procedures during the first years, but also later in life was observed. Urinary oxalate excretion is significantly elevated, and within the range of PHI/II. A decline in kidney function was observed, which is related to a decreased clearance of oxalate (figure). Two patients each post multiple stone removal procedures had CKD stages 2 or 3. Seven further patients had CKD stage 2, which was not related to stone removal.

Conclusion: PHIII is said to be the most favorable PH type, but early diagnosis is mandatory to treat the patients adequately and to avoid repeated stone removal procedures, which may have an influence on decline in kidney function. This decline may also be related to hyperoxaluria per se, as reported for PHI and II.

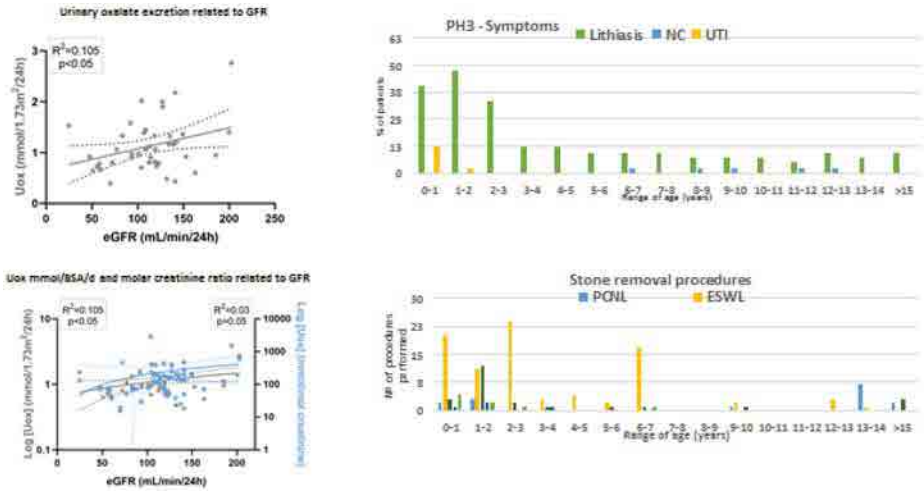


Figure:

P0173 CHRONIC KIDNEY DISEASE IN PATIENTS WITH PRIMARY HYPEROXALURIA TYPE 3 (PH 3) - A LITERATURE META-ANALYSIS

Bernd Hoppe[1], Cristina Martin Higueras[2]

[1]German Hyperoxaluria Center, Bonn, and [2]Universidad de La Laguna, Dept. Ciencias Médicas Básicas, Fac. Medicina, Tenerife, Spain

Background and Aims: Primary Hyperoxaluria type 3 (PH3) is considered the most benign phenotype of all forms of primary hyperoxaluria. Being it typical that patients with PH type 1 and 2 develop chronic kidney disease (CKD) or end-stage renal disease (ESRD), it appears to be more or less uncommon that patients with PH3 are on risk of CKD and even do not develop ESRD. We now aimed to determine the number of PH3 patients reported to have any kind of CKD.

Method: We performed a literature meta-analysis, searching in PubMed with the following keywords: primary hyperoxaluria, PH, primary hyperoxaluria type III, PH III or PH3.

Results: We found 154 patients in 18 relevant papers published between 2010-2019. The number of patients reported per paper ranged from 1-2 up to 38 patients. Age of diagnosis/disease onset ranged from 1 month to 48 years of life. Most of the patients suffered recurrent urolithiasis, most often during the first years of life, but recurrent kidney stone episodes were also found later in life. In 77 patients no adequate information was provided with regard to renal function. In 14 patients it was only mentioned that they did not have renal failure at time of reporting. Five patients were said to be in stable kidney function without providing eGFR or serum creatinine levels. In 62 patients we were able to assess kidney function at time of paper and only in 41 patients (27%) eGFR values were available (18-232 ml/min/1.73m^2). Only one patient in ESRD was reported, however the clear reason for ESRD is not provided in the reference. One patient with CKD stage 4-5 was found with an eGFR of 18 ml/min/ 1.73m^2, after hemi-nephrectomy was performed due to renal carcinoma. He was diagnosed at age 78 but has had recurrent kidney stones over a period of 30 years. Other three patients had stage 2-3 kidney disease (eGFR 53-61.8 ml/min/1.73m^2). CKD stages 1-2 were found in 17 patients (eGFR from 77-104 ml/min/1.73m^2). In six patients follow-up measures were available, as their data were included in two papers (4 years apart from each other). Here, in one patient eGFR significantly declined from 134 to 68.1 ml/min/1.73m^2, while in the other 5 it remained stable over time.

Conclusion: Based on this non-comprehensive dataset, the majority of PH3 patients remain in stable kidney function over time. However, there is a massive bias in the data published, as data on kidney function is mostly not adequately reported. Nevertheless, CKD was observed in 13.7% of PH3 patients, and even one patient with ESRD was described. Also, one PH3 patient had died at age 4 months, but because of respiratory failure and not because of PH. Thus, as true long-term follow-up data is still missing, we nevertheless suspect PH3 not being as benign as currently being reported.

P0174

NEPHROPROTECTIVE ACTIVITY OF GOSSYPETIN THROUGH INHIBITORY EFFECT ON XANTHINE OXIDASE, NUCLEAR FACTOR KAPPA B (NF-KB) AND SOLUBLE EPOXIDE HYDROLASE (SEH): IN-VITRO AND IN-SILICO EXPERIMENT.

Dinesh Kumar Patel[1], Kanika Patel[1]

[1]*Shalom Institute of Health and Allied Sciences, Faculty of Health Sciences, Department of Department of Pharmaceutical Sciences, Payagraj, India*

Background and Aims: Oxidative stress and inflammation is the major contributor of kidney injury and the drugs which have antioxidant and anti-inflammatory activity could protect kidney against renal damage. Mechanisms involved in renal failure include oxidative stress, inflammation and apoptosis which lead myoglobinemia, myoglobinuria and cast formation. Inflammatory mediators such as IL-1, ICAM-1 and TNFα also play important role in renal failure. Excess production of uric acid can cause serious consequence in hyperuricemia and xanthine oxidase (XO) catalyzes the oxidation of xanthine to uric acid. Protective effects of gossypetin in the management of kidney injury and related disorders have been investigated in the present work through inhibitory potential of gossypetin on nuclear factor kappa B (NF-κB), soluble epoxide hydrolase (sEH) and XO.

Method: Present work described the medicinal importance of gossypetin with their beneficial effect on kidney disorder. In-silico molecular docking and dynamic experiments were carried out with gossypetin against nuclear factor kappa B (NF-κB) and soluble epoxide hydrolase (sEH). Further docking was also performed to investigate how gossypetin and the active site of XO fit together.

Results: From the analysis of the available data's in the present work, it was found that gossypetin have protective effect against nephrotoxicity. Gossypetin also showed potent anti-inflammatory activity in kidney mesangial cells which further support application of natural compounds on nephritis treatment. Importance of gossypetin for preventing renal damage has been also emphasized due to its antioxidants potential. In-silico studies showed that, gossypetin exhibited a higher docking score against NF-κB and sEH. Docking studies revealed gossypetin surrounds the active sites of XO and reduces conversion of xanthine to uric acid.

Conclusion: Study revealed their antioxidant, anti-mutagenic, anti-atherosclerotic, anti-microbial and cytoprotective properties. The protective effect of gossypetin in kidney could be due to its antioxidant and anti-inflammatory activity through inhibition of NF-κB and sEH upregulation.

P0175 DETERMINANTS OF RENAL PAPILLARY APPEARANCE IN RENAL STONE FORMERS: AN IN-DEPTH EXAMINATION

Matteo Bargagli[1], Rossella De Leonardis[1], Mauro Ragonese[2], Angelo Totaro[2], Francesco Pinto[2], Salvatore Recupero[3], PierFrancesco Bassi[1,2], Giovanni Gambaro[4], Pietro Manuel Ferraro[1,5]

[1]Università Cattolica del Sacro Cuore, Roma, Italy, [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Clinica Urologica, Roma, Italy, [3]Ospedale Fatebenefratelli, U.O.C. Urologia, Roma, Italy, [4]University-Hospital of Verona, Renal Unit, Department of Medicine, Verona, Italy and [5]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Nefrologia, Roma, Italy

Background and Aims: Nephrolithiasis is a medical condition characterized by high prevalence among the general population both in Europe and in the U.S. and it is responsible for high costs reaching up to $10 billion per year. It is associated with specific comorbidities such as obesity, arterial hypertension, diabetes mellitus, metabolic syndrome and chronic kidney disease.

Kidney stones development is believed to start either from Randall's plaques or from stone plugs. Both these lesions can be seen on renal papillary surfaces, but what promotes the formation of plaques and plugs is not entirely understood.

The aim of this study is to investigate the association between the urinary metabolic milieu and a published endoscopic papillary evaluation score (PPLA). We also evaluated the correlation of PPLA score with kidney stone recurrence during follow-up.

Method: We prospectively enrolled 31 stone forming patients who undergone retrograde intrarenal surgery procedures. Visual inspection of the accessible renal papillae was performed in order to calculate the PPLA score based on the appearance of ductal plugging, surface pitting, loss of papillary contour and Randall's plaque extension.

Demographic information, blood samples, 24h urine collections and kidney stone events during follow-up were collected. Stone composition was analyzed using infrared-spectroscopy. Relative urinary supersaturations (RSS) for calcium oxalate (CaOx), calcium phosphate (CaPi) and uric acid (UA) were calculated using the Equil2 software. PPLA score > 3 was defined as high.

Results: Median follow-up period was 11 (min/max 5, 34) months. PPLA score was inversely correlated with BMI (rho = -0.39, p = 0.035) and history of recurrent kidney stones (median PPLA 5.0 vs 2.5, p = 0.029), these results were confirmed when PPLA was considered as a categorical variable (median BMI 27 vs 24, recurrent stone disease 12 vs 62%, p= 0.006). Furthermore, high PPLA score was associated with lower odds of new kidney stone events during follow-up (OR 0.154, 95% confidence interval 0.024, 0.998, p = 0.05). No significant correlations were found between PPLA score, stone composition, blood parameters, 24h urine solute excretions and RSS for CaOx, CaPi and UA.

Conclusion: Different papillary abnormalities seem to be linked to specific mechanisms of stone formation. Although data regarding PPLA score are inconsistent, it may be a valid asset for both medical and surgical management of nephrolithiasis. Larger, long-term prospective clinical studies need to be conducted to assess the validity of PPLA score system in evaluating risk of stone recurrence.

P0176 **REGULATION OF OXALATE HOMEOSTASIS BY OXALATE-DEGRADING ACTIVITY IN FECAL MICROBIOTA IN DIALYSIS PATIENTS**

Natalia Stepanova[1], Ganna Tolstanova[2], Iryna Akulenko[2], Lesya Korol[1], Olena Savchenko[1], Lyudmyla Snisar[1], Mykola Kolesnyk[1]

[1]State Institution «Institute of Nephrology of the National Academy of Medical Sciences», Nephrology & Dialysis, Kyiv, Ukraine and [2]Taras Shevchenko National University of Kyiv, Kyiv, Ukraine

Background and Aims: Despite evidence suggesting that a lack of fecal oxalate-degrading bacteria colonization is a risk factor for calcium oxalate stone formation, little is known about the oxalate-degrading activity (ODA) in fecal microbiota in end-stage renal disease (ESRD) patients. In addition, to date, there has been a general lack of research on the effect of fecal ODA on oxalate homeostasis in dialysis patients.

The present pilot cross-sectional study was performed to compare the oxalate homeostasis profiles depending on ODA in fecal microbiota in ESRD patients.

Method: The data of a cross-sectional pilot study examining ODA in fecal microbiota, plasma oxalate concentration (POx) and urinary oxalate excretion (UOx) in 32 ESRD patients were represented in this study. Among the patients, there were 21 hemodialysis (HD) patients and 11 peritoneal dialysis (PD) patients. The average age of the patients was 52.5 [39; 65] years.

The redoximetric titration with KMnO4 was adopted to evaluate total ODA in fecal microbiota. The results were expressed in % oxalate degradation per 0.01 g of feces. POx concentration and UOx excretion were measured spectrophotometrically using a commercially available kit (MAK-315, Sigma, Spain) and an oxalate oxidase/peroxidase reagent (BioSystems, Spain), respectively. Predialysis plasma samples were collected from HD patients.

For further analysis, the patients were allocated to 2 groups according to ODA in feces. Group 1 included the patients with $\geq$ 1 % oxalate degradation per 0.01 g of feces. Group 2 included the patients with negative ODA ($\leq$ 0 % /0.01 g).

For the statistical analysis, we used the nonparametric Kruskal-Wallis test. The median (Me) and interquartile ranges [Q25; Q75] were calculated. The Spearman test was used for the correlation analysis. Univariate logistic regression analysis was used for predicting hyperoxalemia. All statistical analyses were performed using MedCalc.

Results: ODA in fecal microbiota ranged from -23 to 24 %/0.01 g of feces in ESRD patients and was statistically higher in HD patients compared with PD patients (3.2 [-0.5; 16] vs -4 [-6.5; 6.2], p=0.05). Negative ODA in fecal microbiota ($\leq$ 0 % /0.01 g) was observed in 5/21 (23.8%) HD patients and 7/11 (63.6%) PD patients (χ^2=3.9, p=0.04). Consequently, it might be associated with the negative effects of peritoneal dialysis solution.

High POx concentration and low UOx excretion were diagnosed in patients with negative ODA in fecal microbiota (Group 2): 30.7 [25.5; 41.5] vs 50 [43.3; 75.5] µmol/L, p=0.01 and 60.9 [51; 65] vs 34.2 [24.4; 39] mg/d, p=0.0002, respectively (Fig. 1). Fecal ODA was directly associated with daily UOx excretion (r=0.85; p<0.0001) (Fig. 2) and had an inverse correlation with POx concentration (r=-0.36; p=0.04) (Fig. 3). In univariate logistic regression analysis, negative fecal ODA was determined as an independent risk factor for high POx concentration (OR: 40; 95% CI: 4.8-331, p<0.0001).

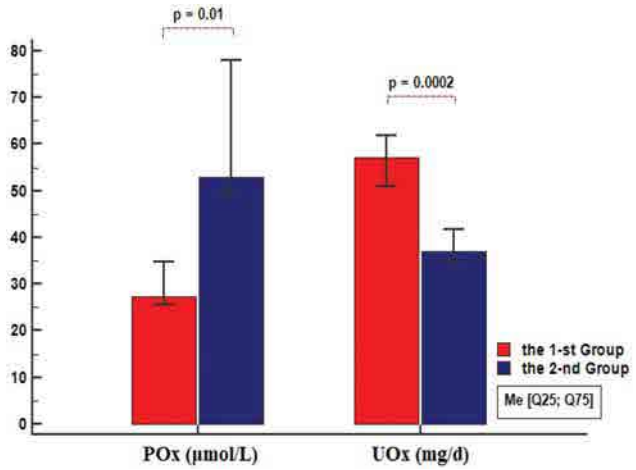


Figure 1: The concentration of plasma and urinary oxalate depending on ODA in ESD patients.

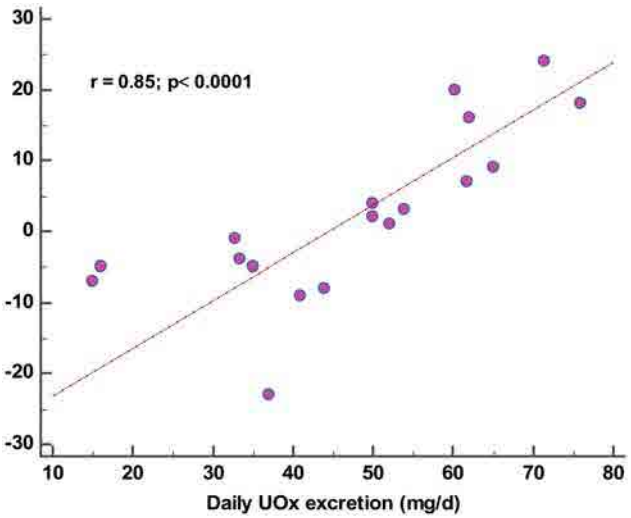


Figure 2: The association between ODA and daily UOx excretion in ESRD patients.

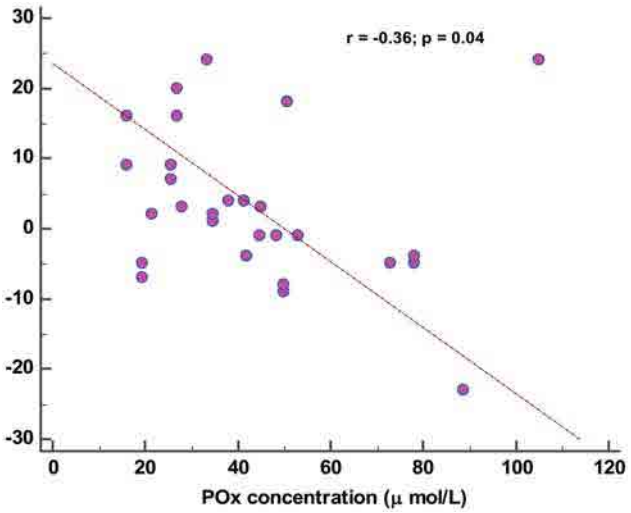


Figure 3: The association between ODA and POx concentration in ESRD patients.

Conclusion: Our pilot cross-sectional study firstly demonstrated a close association between ODA in fecal microbiota and oxalate homeostasis in ESRD patients: less ODA in fecal microbiota was, higher POx concentration and lower UOx excretion occurred. We suppose that the potential significance of our findings provides preliminary information on the feasibility and necessity of further research in this area.

P0177 **PREVALENCE AND RISK FACTORS OF HYPERURICEMIA IN THE BAI ETHNIC GROUP IN SOUTHWESTERN CHINA**

Chenni GAO[1], Yuhua DUAN[2], Liangqin JIA[2], Wen ZHANG[1], Hong REN[1], Jingyuan XIE[1], Xiaonong CHEN[1]

[1]Ruijin Hospital, Shanghai Jiaotong University, School of Medicine, Nephrology department, Shanghai, P.R. China and [2]The people's hospital of Jianchuan County, The medical examination center, Jianchuan, P.R. China

Background and Aims: The Bai ethnic group is one of the officially recognized minorities in the People's Republic of China, with a total population of 1.93 million. More than 80% of the Bai ethnic group live in Dali Bai Autonomous Prefecture in Yunnan Province. Because of their dietary habit and chronic exposure to high altitude, hyperuricemia is not rare among the Bai ethnic group. Hyperuricemia is not only related to the presence of hypertension, obesity and dyslipidemia, but also increases the risks of stroke, heart disease and chronic kidney disease. But the prevalence of hyperuricemia in the Bai ethnic group remains unclear.

Method: We collected the demographic information as well as laboratory test results of 1393 Bai ethnic people undergoing medical examination during Jan 2019 to Dec 2019 in the People's Hospital of Jianchuan County, Yunnan Province (average altitude 2300m). Written informed consent was obtained from all the participants. Hyperuricemia is defined as serum uric acid level superior to 360 μmol/L for female and 420 μmol/L for male. We investigated the prevalence of hyperuricemia and its risk factors in the Bai ethnic group in southwestern China.

Results: Of the 1393 participants enrolled in the study, the prevalence of hyperuricemia was 24.8%, and the prevalence was significantly higher in male gender (33.2% in men vs. 11.0% in women, P<0.001). The prevalence of hyperuricemia increased from 19.2% among participants aged 30-40 years to 30.1% among participants aged 50 years and older (Fig 1). Also, the prevalence of hyperuricemia elevated from 17.2% among participants with normal body mass index (BMI) to 35.5% among those who were overweighed or obese (Fig 2). Interestingly, we found a positive correlation between hemoglobin level and serum uric acid (β=2.19, *P*<0.01). Logistic regression analysis revealed main risk factors for hyperuricemia in the Bai ethnic group included age, sex, BMI, systolic blood pressure (SBP) and hemoglobin level.

Conclusion: Hyperuricemia is common in the Bai ethnic group. Its prevalence differs in different sex, age and BMI groups. Furthermore, polycythemia secondary to chronic exposure to high altitude may also contribute to the hyperuricemia.

Tab 1. Logistic regression analysis of risk factors for hyperuricemia in the Bai ethic group

Parameter	regression coefficient β	Wald value	OR (95% CI)	*P* value
Sex	-1.059	25.64	0.347 (0.230-0.522)	<0.01
Age	-0.013	4.23	0.987 (0.975-0.999)	0.040
BMI	0.155	53.93	1.167 (1.120-1.216)	<0.01
SBP	0.014	7.37	1.014 (1.004-1.024)	0.027
Hemoglobin	0.010	4.91	1.011 (1.001-1.020)	<0.01

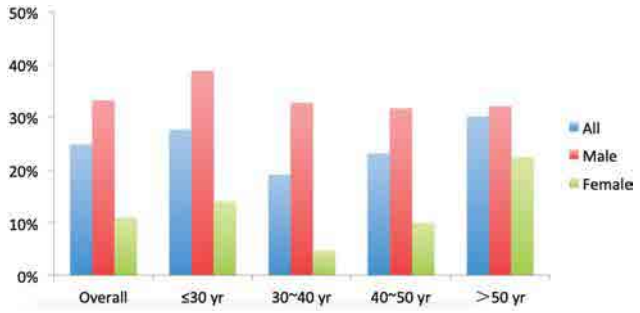


Fig 1. Prevalence of hyperuricemia in different age group

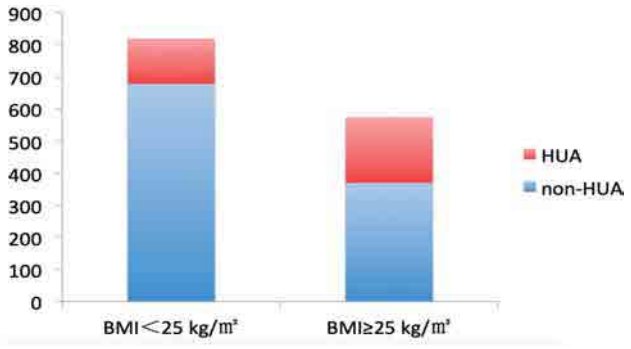


Fig 2. Prevalence of hyperuricemia in different BMI group

CLINICAL NEPHROLOGY

P0180 U-SHAPED RELATIONSHIP BETWEEN SERUM URIC ACID LEVEL AND THE RISK OF END STAGE RENAL DISEASE AND ALL-CAUSE MORTALITY IN MEN

Su-Ryeong Go[1], Hajeong Lee,[2], Nam Ju Heo[3], HO JUN CHIN[1,4], Ki Young Na[1,4]

[1]Seoul National University Bundang Hospital, INTERNAL MEDICINE, Seongnam-si, Korea, Rep. of South, [2]Seoul National University Hospital, INTERNAL MEDICINE, SEOUL, Korea, Rep. of South, [3]SNUH HEALTHCARE GANGNAM CENTER, INTERNAL MEDICINE, SEOUL, Korea, Rep. of South and [4]SEOUL NATIONAL UNIVERSITY COLLEGE OF MEDICINE, INTERNAL MEDICINE, Seoul, Korea, Rep. of South

Background and Aims: High uric acid level was known as a risk factor to incident chronic kidney disease, mortality, or cardiovascular mortality. However, it is obscure which level of uric acid (UA) is safe to prevent end stage renal disease (ESRD) and mortality. We searched the optimal range of UA level to escape the incident ESRD and death in a large cohort of general population.

Method: We enrolled 143,762 adult subjects participated in voluntary health check-up program from three referral hospitals in Korea between 1995 and 2009. We defined 48,147 control subjects (CONTROL) without risk factors of high UA level, to calculate 5, 20, 80, and 95 percentiles of UA level and allocated whole participants into five groups (G1, G2, G3, G4, G5) according to the criteria in each gender. We merged the incident data of ESRD from the Korean ESRD registry by December 2017 and the mortality data from the Ministry of the Interior and Safety by May 2018 based on the identifier of Koreans. This project was approved by institutional review boards of the three hospitals.

Results: The UA levels of 5, 20, 80, 95 percentiles in CONTROL were 2.9 mg/dL, 3.5 mg/dL, 4.9 mg/dL, and 5.7 mg/dL in females, and 4.1 mg/dL, 5.0 mg/dL, 6.8 mg/dL, and 7.8 mg/dL in males. There were 76,784 (53.4%) males and 66,978 (46.6%) females. The age was 50.5 $\pm$ 12.2 years and the level of GFR by CKD-EPI equation was 94.3 $\pm$ 15.2 ml/min/1.73 m^2 at enrollment. Among females, ESRD was developed in 110 subjects (0.2%) and 1,922 subjects (2.9%) were dead during more than 12 years. The level of UA and groups of UA were not independent risk factors to mortality or incident ESRD in females. Among males, there were 162 subjects with ESRD (0.2%) and 4293 subjects (5.6%) were dead. Compared to G3 group (5.0 mg/dL $\leq$ UA$<$6.8 mg/dL), other groups showed higher risk of incident ESRD adjusted with related factors by Cox's hazard proportional model in males (p=0.016). The Hazard ratios (HRs) for incident ESRD in G1 group ($<$4.1 mg/dL), G4 group (6.8 mg/dL $\leq$ UA$<$ 7.8 mg/dL), and G5 group (7.8 mg/dL $\leq$ UA) were 2.409 (95% CI, 1.312-4.423, P=0.005), 1.710 (95% CI, 1.080-2.707, P=0.022), and 1.742 (95% CI, 1.098-2.762, P=0.018), respectively. The HRs for all-cause mortality in G1, G4, and G5 group were 1.203 (95% CI, 1.017-1.346, P=0.001), 1.099 (95% CI, 1.006-1.201, P=0.037), and 1.137 (95% CI, 1.015-1.272, P=0.026), respectively. We found there were 591 subjects died from cardiovascular disease (CVD) among 3,352 deaths with valid cause of death. G1 and G5 group showed higher risk for CVD-mortality compared to G3 group in men ($p<0.001$).

Conclusion: Serum uric acid level showed U-shaped pattern of HRs for incident ESRD and all-cause mortality in men, only. The appropriate uric acid level might be 4.1-6.7 mg/dL in men.

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P0181 PERSISTENT C3 HYPOCOMPLEMENTEMIA AND MODERATE TUBULOINTERSTITIAL SCARRING AS EARLY PREDICTORS OF END-STAGE RENAL DISEASE IN LUPUS NEPHRITIS

Giovanni Maria Rossi[1], Francesco Peyronel[1], Marco Delsante[1], Avi Z Rosenberg[2], Paride Fenaroli[1], Giuseppe Daniele Benigno[1], Maria Letizia Urban[1], Michael Davis[3], Zerai Manna[3], Augusto Vaglio[4], Enrico Fiaccadori[1], Sarfaraz Hasni[3], Lucio Manenti[1]

[1]Parma, Nephrology Unit, Parma University Medical School, Parma, Italy, Parma, Italy, [2]Johns Hopkins University, Renal Pathology, Baltimore, United States of America, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, United States of America and [4]University Hospital Meyer, Firenze, Italy

Background and Aims: The prognosis of lupus nephritis (LN) has become progressively more favorable thanks to the introduction of cyclophosphamide and mycophenolate as the mainstay of induction of remission treatment regimens. However, 10-15% of patients still progress to end-stage renal disease (ESRD). Early predictors of ESRD, i.e. in the first six months between kidney biopsy and the completion of induction, are currently limited to few histological and clinical features: $\geq$ 25% interstitial fibrosis and tubular atrophy (IFTA), fibrinoid necrosis, fibrous crescents, and thrombotic microangiopathy (TMA) [Rijnink EC et al *CJASN* 2017; Song D *Arthritis Res Ther* 2013]; lack of decrease in proteinuria $<$ 0.5 g/24-h at 3 and 6 months from kidney biopsy [Tamirou F *Ann Rheum Dis* 2016], baseline GFR $\leq$ 90 ml/min/1.73 m2, lack of decrease in urinary protein-to-creatinine ratio (UPCR) $<$ 1 and anti-dsDNA positivity at the end of induction [Dall'Era M *Lupus Sci Med* 2015]. In this study we sought to identify further clinical and histological predictors of ESRD in LN.

Methods: Adult patients diagnosed with LN between 1995 and 2018 in two centers (NIAMS, Bethesda, Maryland, USA, and Nefrologia, AOU di Parma, Italy) were retrospectively identified. Patients with available serum C3 and C4 levels at the time of biopsy and 6 months thereafter, and a follow-up of at least 6 months, were included. Baseline and follow-up data (until March 2019) including age, sex, ethnicity, clinical, histological and laboratory findings were collected. Histology slides were reviewed by an experienced renal pathologist and biopsies re-scored using the ISN/RPS classification and NIH activity and chronicity indices. Distinct histological features were assessed individually (e.g. TMA). Persistent C3 hypocomplementemia was defined as decreased serum C3 levels at the time of biopsy and after 6 months (i.e. after the completion of induction), with concurrent normal serum C4 levels at 6 months. Early renal recovery was defined as either an increase in eGFR above 60 in those with a baseline eGFR $<$ 60 ml/min/1.73 m^2, or a 50% decrease in proteinuria in those with a baseline eGFR $\geq$ 60 ml/min/1.73 m^2 and $\geq$ 0.5 g/24-h or g/g UPCR at the time of biopsy.

Variables were tested for their predictive power of death-censored ESRD in univariate and multivariate Cox regression models.

Results: 74 patients (NIAMS n = 36; Parma n = 38) met our criteria. Median follow-up duration was 64 months (range 6-230). On univariate analysis, the following parameters predicted ESRD: Hispanic ethnicity; age at biopsy; persistent C3 hypocomplementemia; normalization of both C3 and C4; renal recovery after induction; NIH activity index; presence of TMA; $\geq$ 25% IFTA. Multivariate Cox regression models for ESRD were created considering statistically significant variables ($p < 0.05$). In a model including Hispanic ethnicity, age at biopsy, and persistent C3 hypocomplementemia, the latter predicted ESRD with an HR of 5.22 (95% CI [1.33, 20.58] p = 0.018) when adjusting for renal recovery after induction. Upon including histological features in the model, persistent C3 hypocomplementemia, TMA, and the NIH activity index lost significance, while $\geq$ 25% IFTA predicted ESRD with an HR of 27.26 (95% CI [2.12, 350.54], p = 0.011).

Conclusion: In patients with LN, $\geq$ 25% IFTA at baseline biopsy is a predictor of ESRD, allowing for early risk stratification with the potential of informing treatment strategies. Where percent IFTA is unavailable or its assessment unreliable (e.g. inadequate biopsy specimen for tubulointerstitial assessment), persistent C3 hypocomplementemia represents a reliable and reproducible early predictor of ESRD, irrespective of early renal recovery after induction.

P0182

SAFETY AND EFFICACY OF INTRA-RENAL ARTERIAL AUTOLOGOUS CD34+ CELL TRANSFUSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A RANDOMIZED, OPEN-LABEL, CONTROLLED PHASE II CLINICAL TRIAL

Chihchao Yang[1], Yi-Chen Li[2], Honkan Yip[2]

[1]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Division of Nephrology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C. and [2]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Division of Cardiology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C.

Background and Aims: This was a randomized, open-label, controlled phase II clinical trial to investigate the safety, efficacy and the outcomes of intra-renal artery (RA) infusion of autologous peripheral-blood-derived CD34+ cells for chronic kidney disease (CKD) (i.e., stage III or IV) patients.

Method: Between December 2016 and November 2018, 52 consecutive patients with CKD at stage III or IV were randomly allocated into treatment group (TG) (2.5×107 cells for each RA; n=26) and control group (CG) (standardized pharmacotherapy only; n=26). The primary endpoints included safety and change of creatinine level/creatinine clearance (Ccr). The secondary endpoints were 12-month combined unfavorable clinical outcomes (defined as dialysis or death), improvement in proteinuria, and CD34+cell-related adverse events.

Results: All patients were uneventfully discharged after CD34+ cell therapy. Flow cytometric analysis showed increases in circulating EPC (i.e., CD34+KDR+CD45dim/CD34+CD133+ CD45dim/CD31+CD133+CD45dim/CD34+CD133+KDR+/CD133+) and hematopoietic stem cell (HSC) (CD34+) populations after G-CSF treatment. Besides, Matrigel assay of angiogenesis was also significantly enhanced (all $p<0.001$). Renal vein blood samplings (i.e., at 0/5/10/30 min after CD34+ cell infusion) demonstrated significant progressive increases in EPC level (p for trend<0.001) among the TG patients. The baseline EPC populations did not differ between TG and CG ($p>0.5$). One-year combined unfavorable clinical outcomes were significantly lower in TG than those in CG [0% (0) vs. 13.3% (4), p=0.038](Figure). By 12-month after CD34+ cell therapy, circulating creatinine level, ratio of urine protein to urine creatinine, and creatinine clearance did not differ between TG and CG (all $p>0.1$).

Conclusion: CD34+ cell therapy was safe and improved one-year outcome.

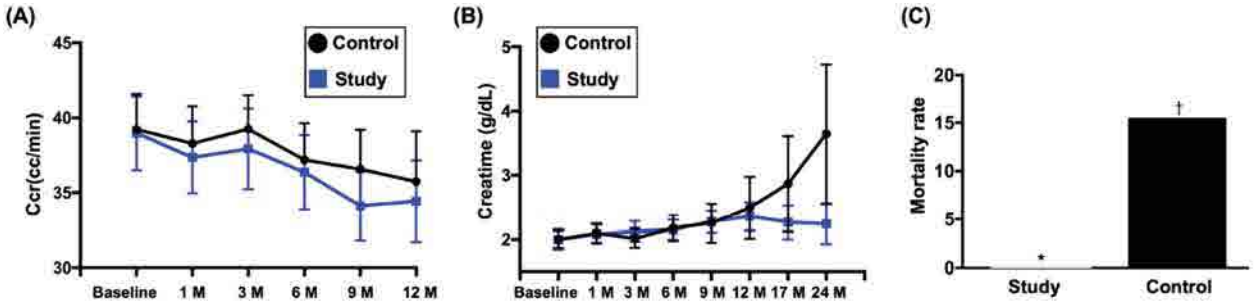


Figure:

P0183 THE USE OF PCSK9 INHIBITORS COULD REDUCE PROTEINURIA IN CHRONIC KIDNEY DISEASE PATIENTS

Patricia Muñoz Ramos[1], Leydy Yohana Gil Giraldo[1], Javier Reque[2], Borja Quiroga[1], Vicente Alvarez Chiva[1]

[1]Hospital de La Princesa, Nephrology, Madrid, Spain and [2]Parking Hospital General de Castellón, Nephrology, Castelló de la Plana, Spain

Background and Aims: . Chronic kidney disease (CKD) is a cardiovascular risk factor *per sé* and enhances the risk of cardiovascular events. Dyslipidemia is one of the most studied risk factors and current guidelines recommend the universal treatment in CKD patients (not in dialysis) irrespective of low density lipoprotein (LDL) cholesterol level. However, the latest European Cardiology guidelines recommend monitoring LDL cholesterol to achieve levels lower than 70 mg/dl in CKD stage 3 and lower than 55 mg/dl in stages 4 and 5. Proprotein convertase subtilisin-kexin type 9 inhibitors (PCSK9i) have opened a new era leading greater reduction of LDL cholesterol and subsequently cardiovascular events but real-life data is not available in CKD patients. The aim of the present study is analysing the evolution of renal function and proteinuria in a cohort of patients with PCSK9i.

Method: This is a retrospective study that included all the patients treated with PCSK9i in our centre. Inclusion criteria were the presence of CKD and dyslipidemia with indication of the use of PCSK9i (not reaching LDL target with maximum tolerated statin dose or intolerance for the use of statins). At baseline, epidemiological data and comorbidities were collected, as well as renal function using glomerular filtration rate (GFR) estimation with CKD-EPI equation, proteinuria (mg/g of creatinine) and lipid profile. During a one-year follow up, renal function, proteinuria, lipid profile and adverse events were collected and analysed.

Results: . Forty-one patients were included with a mean age of 70±10 years and 26 men (62%). Thirty-four patients (83%) had hypertension, 11 (27%) were diabetic, 19 (44%) had coronary disease, 8 (20%) history of heart failure, 3 (7%) peripheral vascular disease and 6 (15%) history of stroke. Regarding renal function, at baseline mean of creatinine was 1.3±0.5 mg/dl, GFR 54±19 ml/min/1.73m^2 and proteinuria 456±215 mg/g. Lipid profile at baseline demonstrated an LDL cholesterol value of 163±58 mg/dl, triglycerides of 255±389 mg/dl and high density lipoprotein (HDL) of 53±14mg/dl.

During follow up, total cholesterol, LDL-cholesterol and triglycerides improved significantly ($p<0.001$ for all in comparison to baseline values). GFR remained stable during the first year of follow up (CKD-EPI at 1 year 52±20 ml/min/1.73m^2). Proteinuria improved at first month (235±71 mg/g), achieving stability at 3 months (124±44 mg/g), 6 months (176±94 mg/g) and 1 year (163±83 mg/g) (p for trend 0.02) (figure 1). No adverse events were registered during follow up, and two patients required hospitalization due to cardiovascular events.

Conclusion: The treatment of dyslipidemia with PCSK9i could decrease proteinuria in CKD patients via controlling lipoid nephrotoxicity. Clinical trials are needed to further investigate this effect.

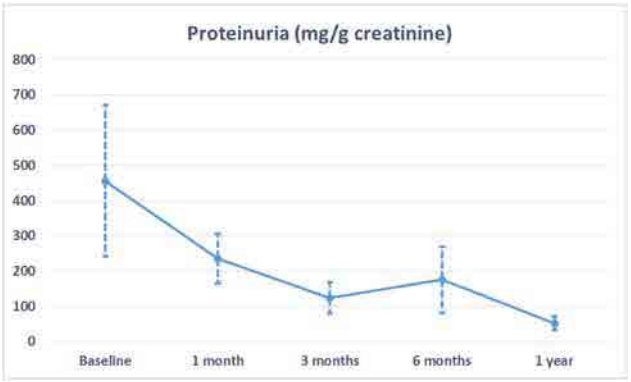


Figure 1. Evolution of proteinuria after PCSK9i.

P0184 **RISK PREDICTION FOR DEATH AND END-STAGE RENAL DISEASE DOES NOT PARALLEL REAL-LIFE TRAJECTORY OF OLDER PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE - A ROMANIAN CENTER EXPERIENCE**

Andra Nastasa[1,2], Mugurel Apetrii[1], Mihai Onofriescu[1], Ionut Nistor[1], Hani Hussien[1,2], Cristina Popa[2], Irina Apascaritei[2], Adrian Covic[1,2]

[1]GRIGORE T. POPA UNIVERSITY OF MEDICINE AND PHARMACY, Iași, Romania and [2]Hospital Doctor C.I. Parhon, Iași, Romania

Background and Aims: In Europe, the share of the elderly (≥65 years of age) in the total population is estimated to increase from 19.2% in 2016 to 29.1% by 2080. In 2016, European Renal Best Practice (ERBP) group published a clinical practice guideline on management of older patients with CKD stage3b or higher (eGFR<45ml/min/1.73 m^2). Two risk stratifications scores were emphasized: Bansal score for prognosticating risk of death in medium term, and Kidney Failure Risk Equation (KFRE) for estimating progression of CKD stage 3b or 4 to ESRD. Our group, as part of the ERBP team, aimed to evaluate and apply the framework proposed by the guideline, consisting of risk prediction for both mortality and progression to ESRD in a cohort of elderly patients with advanced CKD. After dividing the population in groups of risk, we described their real-life trajectory in terms of either reaching ESRD/death.

Method: In this retrospective cohort study we included patients aged ≥65 years with CKD stage 3b-4, evaluated at the Outpatient Nephrology Department of Dr. C. I. Parhon Hospital from Iași, Romania, between October 2016 – October 2018.

Individual risk for mortality was predicted using Bansal score, a nine-variable equation model. A total score of 7 (associated with a mortality risk of 53.82%) was established as cut-off value to differentiate between 2 groups: high risk of mortality (Bansal ≥ 7) and low risk of mortality (Bansal < 7), given the fact that the ERBP guidelines don't define a threshold for high risk in respect to mortality outcome.

According to the algorithm proposed by the guideline, individual risk for progression to ESRD at 5 years was calculated in the low mortality risk group, using the 4-variable Kidney Failure Risk Equation (KFRE).

Results: The final cohort included 958 patients, with a mean age of 74 years (SD: 7), and with similar gender distribution (50.6% female vs. 49.4% male).

Predicted trajectory in terms of reaching ESRD / death:

When we applied Bansal score for mortality, the total study population (N=958) was divided in two groups: N1 with high risk of mortality, which comprised more than half of the cohort (548 patients, 57.2%) and N2 with low risk of mortality (410 patients, 42.8%).

Individual risk of progression to ESRD was then estimated in N2 group, using 4-variable KFRE. Nearly ¾ of this group (75.4%, 309 subjects) presented a low-risk of progression and ¼ (24.6%, 101 subjects) had high-risk.

Real-life trajectory in terms of reaching ESRD / death:

From the entire cohort, 31 patients started renal replacement therapy (RRT) and 164 patients died as their first clinical event. The RRT initiation rate was 3.6% of N1 group (20 subjects) versus 2.7% of N2 group (11 subjects). The mortality rate was 15.5% of N1 group (85 deaths) versus 19.3% of N2 group (79 deaths). Figure 1 depicts the real-life trajectory of the population groups in terms of reaching ESRD / death.

Conclusion: In a large population from Eastern Europe, the application of the algorithm from the Clinical Practice Guideline on management of older patients with advanced CKD showed that risk prediction for death and end-stage renal disease does not parallel the real-life trajectory of the population. More than half of the subjects had a high risk of mortality, however we found similar death rates in the 2 groups (high versus low risk of mortality). Also, the RRT initiation rates were similar, irrespective of predicted mortality risk or kidney failure risk, suggesting that implementing the guideline in real-life settings is still a challenge.

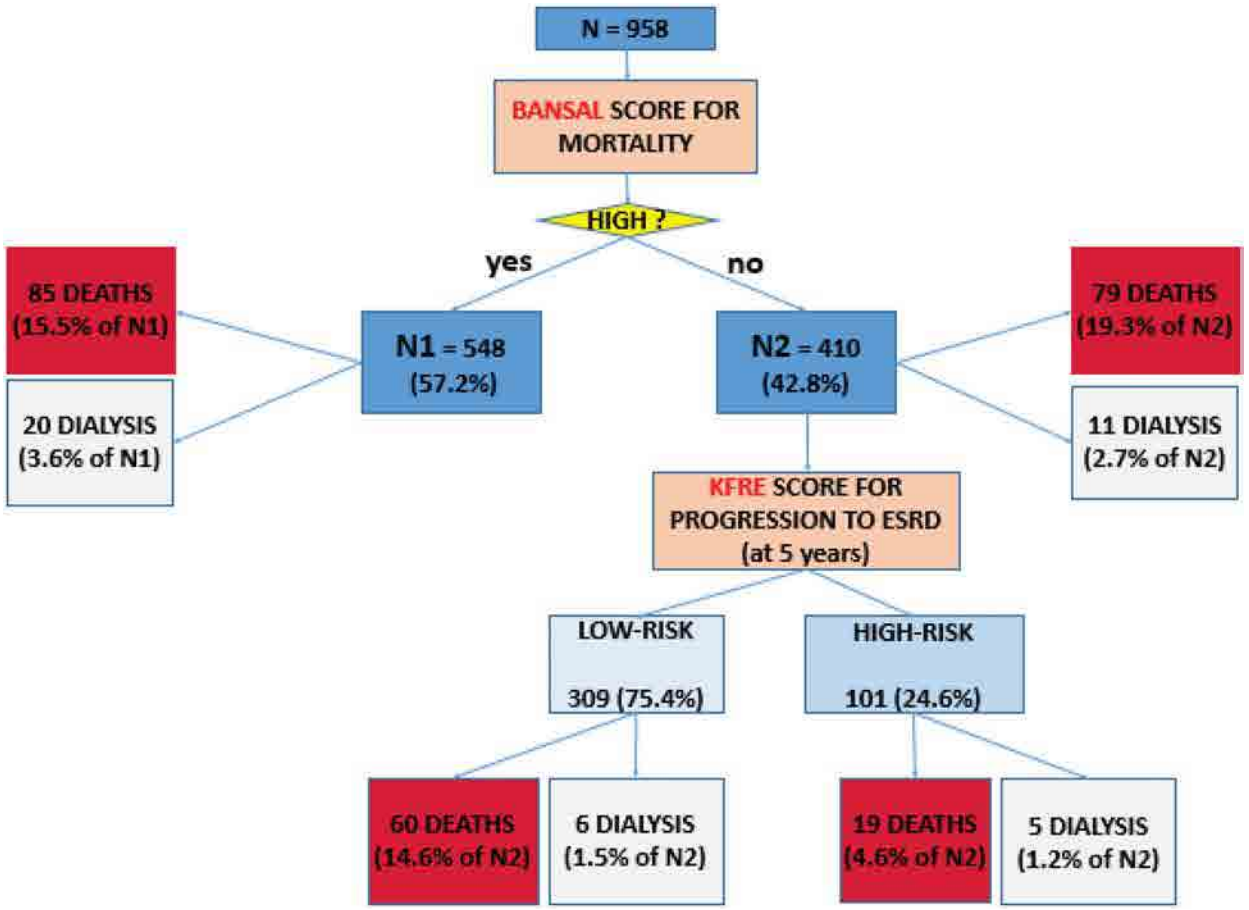


Figure 1:

P0185 ROLE OF THE COMPLEMENT SYSTEM IN PROLIFERATIVE LUPUS NEPHRITIS

Andres Ribas[1], Isabel Galcerán[1], Sara Outón[1], Tarek Salman[2], Javier Gimeno[3], Adriana S. Ochoa[1], Clara Barrios[1], Ana Belén Latzke[1], Julio Pascual[1], Eva Rodriguez[1]

[1]Hospital del Mar, Nephrology, Barcelona, Spain, [2]Hospital del Mar, Reumathology, Barcelona, Spain and [3]Hospital del Mar, Pathology, Barcelona, Spain

Background and Aims: Lupus Nephritis (LN) is a serious complication in patients with Systemic Lupus Erythematosus (SLE) which confers a worse prognosis in patients that develop this condition. It is well known that histological lesions correlate poorly with the prognosis of the disease, but little is known about the role of complement proteins deposition in kidney tissue. The aim of this study was to evaluate the effect on renal manifestations of the deposition in renal tissue of C3, as a marker of alternative pathway, C4 as a marker of the classical pathway and C1q representing the lectin pathway.

Method: A retrospective observational study was performed, including native kidney biopsies with a diagnosis of lupus proliferative nephritis (class III/IV) *(ISN/RPS 2003)*. Direct immunofluorescence microscopy was performed in -80°C frozen sections to evaluate IgA, IgG, IgM, C4d, C1q and C3, and LES activity and chronicity scores were calculated according to NIH disease activity scoring system. The intensity of staining was graded as 0 (no staining), +1 (stainvisible at 40X magnification), +2 (at 20X), +3 (at X10), and +4 (at 2-4X). For statistical purpose we considered weak staining: 0, +1, +2 and strong staining: +3, +4. Patient́s files were retrospectively reviewed and clinical and analytical data were collected using a standardized form.

Results: 64 native kidney biopsies from 56 patients with a diagnosis of lupus proliferative nephritis were included, basal characteristics are described in attached Table. Activity index was significantly higher in biopsies showing strong intensity C3 staining compared to biopsies showing weak intensity C3 staining [(n=25) 10±1 vs (n=13) 5±1; p=0.002 respectively], alb/creat was significantly higher in patients in whom biopsy showed strong intensity C3 staining, compared to biopsies showing weak intensity C3 staining [(n=10) 1964.4±585.2 mg/gr vs (n=6) 823.6±58 mg/gr; p<0.001, respectively], prot/creat was significantly higher in biopsies that showed strong C3 staining intensity [(n=27) 2302.5±325 mg/gr vs (n=12) 1287.7±235 mg/gr, p<0.005, respectively], haematuria at NL diagnosis was more frequently in patients whose biopsy showed strong intensity C3 staining (n=21, 80.8%), compared to biopsies showing weak intensity C3 staining (n=5, 19.5%, p<0.001); most of the patients without haematuria at diagnosis showed a weak intensity C3 staining or not C3 staining (n=13, 62%). Endocapillary proliferation was significantly higher in biopsies showing strong intensity C3 staining (90.9% vs 9.1%, p<0.001).Time to proteinuria response is higher in patients showing strong intensity C4d stainingcompared with biopsies showing weak intensity C4d staining (15.2±2.4 vs 6.4±1.8 months; p=0.001), time to haematuria response is higher inbiopsies showing strong intensity C4d staining (19.5±5.5 vs 7.5±2.3 months, p=0.003). Time to proteinuria response is higher in patients showing strong intensity C1q stainingcompared to biopsies showing weak intensity C1q staining (14.0±9 vs 3.3±2.6 months, p <0.001).

Conclusion: Our results suggest that complement system is activated in kidney tissue of proliferative LN patients; C3 staining is associated with clinical, analytical and histological data related to acute lupus activity, whereas C4d and C1q staining are related with long-term outcomes like treatment response. Further studies are needed to elucidate the role of complement system in LN.

Age (years)	39,75 ± 13 years
Gender	52 (81,2%) Women
	12 (18,7%) Men
Stages of LN	
• Class III	43 (67%)
• Class IV	21 (33%)
Creat diagnosis (mg/dl)	1,16 ±0,74
Alb/creat diagnosis (mg/gr)	1406±1400
Prot/creat diagnosis (mg/gr)	1941±1604
Haematuria diagnosis (n;%)	42 (65,6%)
Renal response (n; %)	
• Complete	32 (50%)
• Partial	22 (34,3%)
• No response	6 (9%)
Time to response	40,68±68,3 weeks
Follow-up time	56 ± 75 weeks

P0186 SERUM CYSTATIN C, INFLAMMATION AND AUTONOMIC DYSFUNCTION : A HIDDEN "MÉNAGE À TROIS"?

Alicia PELAEZ[1], Miriana Dinic[1], Barthelemy Jean-Claude[1], Frederic Roche[1], Eric Alamartine[1], Etienne Cavalier[2], Pierre Delanaye[2], Nicolas Maillard[1], Christophe Mariat[1]

[1]Saint-Étienne, Saint-Étienne, France and [2]Liège, Liège, Belgium

Background and Aims: While being a GFR biomarker with comparable performance than serum creatinine (SCr), Serum cystatin C (ScysC) is a better predictor of morbi-mortalilty in the general as well as the CKD population. The mechanisms underlying the prognostic dimension of ScysC are unclear. Unlike SCr, ScysC is known to strongly and positively correlate to C Reactive Protein (CRP) and thereby could reflect autonomic nervous system (ANS) dysfunction. Transversal studies have underlined the association between the decline in autonomic nervous system (ANS) activity and all-cause mortality. ANS is thought to reflexively regulate the inflammatory response (« inflammatory reflex ») and autonomic dysfunction has been shown to be associated with deleterious sustained inflammatory stress.

The Proof study is a prospective observational cohort of 1011 individuals, all aged 65 years at baseline (i.e. 2001), that was designed to assess the prognostic values of the ASN activity and its decline for the cardiovascular morbidity and mortality. We took advantage of the Proof cohort to explore the relationship between ScysC and ANS activity.

Method: The PROOF Cohort Study (PROgnostic indicator OF cardiovascular and cerebrovascular events) is constituted of elderly subjects aged 65 years in 2001 recruited from the electoral list of Saint-Etienne, France. Three initial 2-year examination were scheduled (2001–2007) along with late events monitoring which is still ongoing. At each examination, ANS activity was evaluated (baroreflex sensitivity by TILT testing) along with clinical and biological cardiovascular risk factors. Individuals with diagnosed CKD, history of myocardial infarction or stroke, heart failure, insulin-dependent diabetes mellitus, and a severe disease that limited life expectancy to 5 years or less could not be included in the Proof cohort.

SCr and ScysC were measured from sera drawn at baseline and stored at -80°C, using IDMS-traceable enzymatic method and immunoturbidimetry calibrated method, respectively.

Relationhip between SCysC and baroreflex sensitivity was analysed by univariate linear and multivariate logistic regressions.

Results: SCr and ScysC were measured in 803 patients of the Proof Cohort (71% of men) follow up to December 2019. Mean (+/- SD) SCr was 77 (+/- 15) micromol/l. ScysC was significantly associated to 18 years - all cause mortality (OR=4.1, p=0.01) and baseline CRP (p= 0.002). In univariate analysis, ScysC was the covariate most strongly associated to impaired BRS (coeff=-1.62, p=0.02), followed by diabetes (coeff=-0.73, p=0;04), gender (coeff=-0.59, p=0.001), hypertension (coeff=-0;48, p=0.009), active smoking (-0.47, p=0.01), CRP (-0.03, p=0;04) and SCr (-0.01, p= 0;02). Dyslipidemia and age were not significantly associated to BRS. In multivariate analysis, ScysC and gender (male) were the 2 covariates that independently and significantly associated with BRS.

Conclusion: By reporting for the first time an association between ScysC and BRS, our data suggest a new mechanism by which ScysC could predict excess risk of morbi-mortality beyond its sole ability to predict GFR. ScysC could be an easy-to-monitor marker of the "inflammatory reflex".

P0187 **COMPARING OPAL-HK DATA TO REAL-WORLD DATA FROM THE UNITED KINGDOM: HOW EFFECTIVE IS PATIROMER AT ACHIEVING NORMOKALAEMIA?**

Ibrahim Ali[1], Georgiana Cornea[2], Michele Intorcia[3], Philip A. Kalra[1]

[1]Salford Royal NHS Foundation Trust, Salford, United Kingdom, [2]Vifor Fresenius Medical Care Renal Pharma Ltd., St. Gallen, Switzerland and [3]Vifor Pharma, Meyrin, Switzerland

Background and Aims: The first phase of the published OPAL-HK study showed that Patiromer, an oral potassium binder, was effective at reducing serum potassium levels in patients with chronic kidney disease (CKD) stages 3 to 4. This phase was a 4-week, single-group treatment phase. Given the lack of a control arm, the aim of our study was to use real-world data from a large CKD cohort to provide a control comparison to evaluate the efficacy of Patiromer in normalising serum potassium.

Method: The initial phase of OPAL-HK comprised 243 patients with CKD G3-4 with a baseline serum potassium of 5.1 to <6.5mmol/L. To acquire a comparative matched cohort, patients were selected from the Salford Kidney Study (SKS), a prospective observational cohort study in the United Kingdom that has been recruiting patients aged ≥18 years old with CKD G3-5 since 2002. A 3-step process was applied to generate a propensity matched cohort. First, patients were chosen if they had an outpatient potassium level at any point after recruitment into SKS between 5.1mmol/L to <6.5mmol/L and whose next outpatient potassium level was checked 24 to 42 days (3.5 to 6 weeks) later (n=755). Second, all key OPAL-HK inclusion and exclusion criteria were applied. This left 162 patients who were then accurately matched in a 1:1 fashion to the 243 OPAL-HK patients using propensity score matching based on 6 baseline variables: age, gender, eGFR, diabetes mellitus, heart failure and potassium level. This produced a cohort of 87 SKS patients matched to their 87 OPAL-HK partner patients. We compared the two patient groups for the following OPAL-HK study endpoints: the mean change in serum potassium from baseline to follow-up at week 4, and the proportion of patients with a serum potassium of 3.8 to <5.1mmol/L at week 4.

Results: The groups were extremely well matched: between SKS vs. OPAL-HK, the mean (±SD) age was 63.9±13.3 vs. 63.7±9.5years (p=0.93); mean eGFR was 30.9±11.6 vs. 31.2±11.7ml/min/1.73m^2 (p=0.85); 45 vs. 46 patients were diabetics (p=0.88); 29 vs. 24 had heart failure (p=0.41) and the mean potassium was 5.5±0.3mmol/L in both groups (p=0.68). The follow-up in the SKS cohort was 31±5 days.

At the end of follow-up, the mean potassium level remained 5.5±0.3mmol/L in SKS patients but had reduced to 4.5±0.5mmol/L in the OPAL-HK group (p<0.001), a mean (±SE) change of -1.00±0.06mmol/L. For the secondary endpoint, 74% of patients in OPAL-HK reached the target potassium range of 3.8 to <5.1mmol/L at week 4 compared with 0% from the comparator SKS cohort (see Figure).

Conclusion: Using real-world data as a tightly-matched control arm for the first phase of the OPAL-HK study, Patiromer is shown to be effective at reducing potassium levels in patients with CKD G3-4.

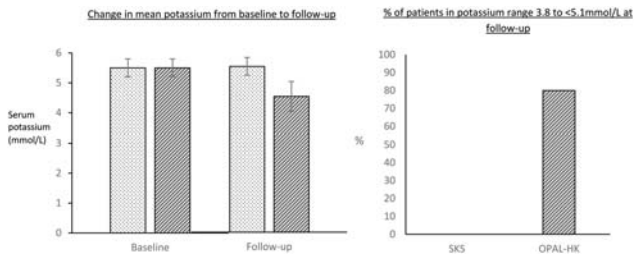


Figure: Comparison of primary and secondary endpoints between the matched cohorts

SKS: Salford Kidney Study

P0188

TOTAL CHOLESTEROL EXCESS DOESN'T AFFECT CORONARY ARTERY CALCIFICATION INDEPENDENTLY OF RENAL FUNCTION

Olexandr Kuryata[1], Viktor Shatailo[2], Alina Nikolaichyk[1], Viktor Semenov[1]

[1]Dnipropetrovsk Medical Academy, Internal Medicine 2 and Phtisiology, Dnipro, Ukraine and [2]Dnipropetrovsk Mechnikov Regional Hospital, Radiology Department, Dnipro, Ukraine

Background and Aims: Coronary artery calcium score (CACS) allows to improve significantly predictive value of traditional tools for cardiovascular risk estimation. Reduced renal function is associated with increase of rates of cardiovascular events. Dyslipidemia is an important factor of cardiovascular system injury in chronic kidney disease. The Aim. To investigate association between glomerular filtration rate (GFR), total cholesterol and CACS.

Method: We performed the study on 170 patients (77 males and 93 females, aged 56 [52;63] years) who underwent CACS at Dnipropetrovsk Mechnikov Regional Hospital, Dnipro, Ukraine, from December 2017 till March 2019. Patients in the study were free of known cardiovascular disease and required reclassification of cardiovascular risk. Patients were subdivided by total cholesterol (TC) level (<5.2 mmol/l, n=83; ≥5.2 mmol/l, n=87) and by GFR (≥90 ml/min, n=64; 60-89 ml/min, n=90; 30-59 ml/min, n=16). CACS was presented in Agatston units (AU).

Results: Median age in groups by TC was comparable (56 [53;63] vs 56 [51;64] years, p=0.51) and elevated significantly with decline of GFR (54 [49;59], 57 [53;65] and 70 [59;77] years for patients with GFR≥90, 60-89 and 30-59 ml/min respectively, p for trend <0.001). We didn't observe any statistically significant differences of CACS after patients subdivision, though it was higher in TC≥5.2 mmol/l group.

Conclusion: We didn't find convincing data supporting significant impact of TC excess on coronary artery calcification.

Figure: Table 1. CACS in groups by GFR and TC.

	TC<5.2 mmol/l	TC≥5.2 mmol/l	p
GFR≥90 ml/min	30[0.5;112.5]	37[0;87]	0.81
GFR 60-89 ml/min	25[0;320.8]	12[0;74]	0.31
GFR 30-59 ml/min	66[8.2;146.2]	165[100;315.8]	0.10

P0189

SODIUM ZIRCONIUM CYCLOSILICATE CORRECTS HYPERKALAEMIA WITHIN 72 HOURS AMONG OUTPATIENTS WITH SEVERE HYPERKALAEMIA (BASELINE SERUM POTASSIUM ≥6 MMOL/L) REGARDLESS OF RENAL FUNCTION LEVEL OR RAASI USE: POST HOC SUBGROUP ANALYSIS OF A PHASE 3 TRIAL

David Packham[1,2], Philip Lavin[3], Pablo Pergola[4], Mikhail Kosiborod[5,6,7], Edgar Lerma[8], June Zhao[9], Bhupinder Singh[10,11], Julian Martins[12], Steven Fishbane[13], Bruce Spinowitz[14], S Roger[15]

[1]Melbourne Renal Research Group, Reservoir Private Hospital, Reservoir, Australia, [2]University of Melbourne, Department of Medicine, Melbourne, Australia, [3]Boston Biostatistics Research Foundation, Framingham, United States of America, [4]Renal Associates PA, San Antonio, United States of America, [5]Saint Luke's Mid America Heart Institute, Department of Cardiology, Kansas City, United States of America, [6]University of Missouri–Kansas City, Department of Medicine, Kansas City, United States of America, [7]The George Institute for Global Health, Sydney, Australia, [8]Advocate Christ Medical Center, University of Illinois at Chicago, Section of Nephrology, Oak Lawn, United States of America, [9]AstraZeneca, Gaithersburg, United States of America, [10]ZS Pharma, Inc. (part of AstraZeneca), San Mateo, United States of America, [11]University of California, Irvine, School of Medicine, Irvine, United States of America, [12]inScience Communications, Springer Healthcare, Paris, France, [13]Zucker School of Medicine at Hofstra/Northwell, Department of Medicine, Great Neck, United States of America, [14]New York-Presbyterian Queens, Division of Nephrology, Department of Medicine, New York, United States of America and [15]Renal Research, Gosford, Australia

Background and Aims: Most patients with severe hyperkalaemia are treated in hospital settings and are often receiving renin–angiotensin–aldosterone system inhibitors (RAASi) and/or have chronic kidney disease. Sodium zirconium cyclosilicate (SZC; formerly ZS-9) is an orally-administered, non-absorbable, inorganic, selective potassium (K^+) binder for the treatment of adults with hyperkalaemia. SZC entraps K^+ throughout the gastrointestinal tract in exchange for hydrogen and sodium ions and significantly reduces serum K^+ within one hour of administration. We report time to achievement of normokalaemia by baseline RAASi use and estimated glomerular filtration (eGFR) level from a 12-month Phase 3 sub-study among outpatients with baseline serum K^+ ≥6 mmol/L undergoing acute treatment up to 72 hours.

Method: This international, multicentre, open-label, single-arm trial among adults with point-of-care (i-STAT) K^+ ≥5.1 mmol/L included prespecified efficacy analyses by baseline serum K^+ ≥6 mmol/L. During the acute phase (AP), patients received SZC 10 g three times a day from 24 up to 72 hours until normokalaemia (i-STAT K^+ 3.5–5 mmol/L) was achieved, whereupon they entered maintenance treatment. In this analysis of the AP only, we report time to achievement of normokalemia (serum K^+ 3.5–5 mmol/L) using the Kaplan-Meier (KM) method, mean change in serum K^+ from baseline at 24 hours and distribution of change during the entire AP, and adverse events (AEs) by baseline RAASi use and eGFR level (<30 vs ≥30 mL/min/1.73m^2).

Results: Of 749 patients in the intention-to-treat AP population of the main study, 126 (16.8%) had baseline serum K^+ ≥6 mmol/L, and the vast majority of these patients had achieved normokalaemia by 72 hours (KM estimated proportions 98.6% and 96.1% in the serum K^+ <6 and ≥6 mmol/L groups, respectively).

Among patients with baseline serum K^+ ≥6 mmol/L not on RAASi with an eGFR ≥30 mL/min/173m^2 (no RAASi/eGFR ≥30), KM estimated median time to normokalemia was fastest, 22.5 hours (95% Confidence Interval [CI]: 22.0, 68.3), followed by patients on RAASi with an eGFR ≥30 mL/min/173m^2 (RAASi/eGFR ≥30), 23.5 hours (95% CI: 22.6, 46.1), followed by patients not on RAASi with an eGFR <30 mL/min/173m^2 (no RAASi/eGFR <30), 45.2 hours (95% CI: 22.6, 46.6), and slowest among patients on RAASi with an eGFR <30 mL/min/173m^2 (RAASi/eGFR <30), 46.6 hours (95% CI: 45.7, 47.4). KM estimated proportions achieving normokalaemia at 24, 48 and 72 hours, respectively, were 57.1%, 69.4%, and 89.8% with no RAASi/eGFR ≥30; 54.9%, 73.0%, and 86.5% with RAASi/eGFR ≥30; 41.3%, 80.4%, and 100% with no RAASi/eGFR <30; and 25.4%, 75.8% and 100% with RAASi/eGFR <30.

Median/range/mean change serum K^+ values at 24 hours were 4.9/4.3-6/−1.22, 5.1/3.8-6.2/−1.26, 5.3/4.7-6/−1.02, and 5.3/4-6.6/−1.00 mmol/L in the no RAASi/eGFR ≥30, RAASi/eGFR ≥30, no RAASi/eGFR <30, and RAASi/eGFR <30 groups, respectively. No patients with baseline serum K^+ ≥6 mmol/L experienced an increase in serum K^+ or hypokalaemia.

No AEs occurred in the no RAASi/eGFR ≥30 group. AEs occurred in 10.3% of patients in the RAASi/eGFR ≥30 group (n=1 each of myopia, nausea, urinary incontinence, and hypertension), 23.1% of patients in the no RAASi/eGFR <30 group (n=1 each of diarrhoea, urinary tract infection, and muscle spasms), and 8.7% of patients in the RAASi/eGFR <30 group (n=1 each of constipation, peripheral oedema, sinusitis, urinary tract infection, back pain, and skin ulcer). No AEs were serious or led to discontinuation.

Conclusion: Outpatient treatment with SZC rapidly normalized serum K^+ among patients with baseline serum K^+ ≥6 mmol/L with few adverse events. Although patients on RAASis and with an eGFR <30 mL/min/1.73m^2 normalized at a slower rate, these patients nevertheless achieved normokalaemia by 72 hours. Neither concomitant RAASi therapy nor eGFR level appear to limit achievement of normokalemia with SZC among this population of outpatients with high baseline serum K^+ ≥6 mmol/L.

P0190

POINT-OF-CARE ULTRASONOGRAPHY FOR VOLUME ASSESSMENT IS EASY TO LEARN AND HAS GOOD REPRODUCIBILITY IN NEW USERS

Lee Ying Clara Ngoh[1,2], Hazel Teng[1], Yan Ting Chua[1], Weng Kin Wong[1,2]

[1]National University Hospital, Division of Nephrology, University Medical Cluster, Singapore, Singapore and [2]National University of Singapore, Department of Medicine, Yong Loo Lin School of Medicine, Singapore, Singapore

Background and Aims: In recent years, point-of-care ultrasonography (POCUS) with lung ultrasonography (LUS) and inferior vena cava diameter (IVCD) measurements have attracted growing attention due to their capacity to estimate volume status in end-stage kidney disease (ESKD). There have been concerns about inter-operator reproducibility in POCUS, particularly the new user's ability to distinguish varying lung pathologies on LUS accurately. For instance, lung diseases with thickening of subpleural structures, such as pulmonary fibrosis, can mimic LUS B-lines. B-lines are artefacts produced by extravascular lung water, which is summated into a B-line score (BLS). This study aims to investigate the ease of learning, and the inter-operator reproducibility of LUS and IVCD in an Asian haemodialysis (HD) cohort, in users with no prior ultrasound experience.

Method: A subgroup of 14 HD patients from the observational study by Teng et al comparing LUS and IVCD with other fluid assessment methods in a HD cohort, underwent LUS and IVCD pre- and post-HD with 2 operators in separate settings. LUS was performed via a 28-point protocol, while IVCD was measured in both inspiration (IVCDmin) and expiration (IVCDmax). IVCDi was calculated by indexing IVCD to body surface area. Study details are available elsewhere.

One operator was a Nephrologist experienced in ultrasonography who had done 150 previous studies, whilst the second operator was a Resident who had no prior exposure to POCUS. The Resident underwent 4 hours of instructional teaching including theory sessions, simulation and image interpretation. Images acquired by the Resident during the study were audited for interpretative accuracy, such as the ability to diagnose lung pathology accurately. The Resident was required to review the clinical presentations of all patients before making ultrasound diagnoses.

Results: 392 lung images and 56 IVC images were acquired for 14 HD patients. 100% of patients' clinical notes were reviewed prior to making ultrasound diagnosis. >98% of the diagnoses were correctly made, and only in 1 patient (7 lung images; case of bronchiectasis), was the ultrasonographic diagnosis incorrectly made of B-lines, although B-lines were seen in other lung fields in the same patient.

There was excellent inter-operator variability for BLS ($r = 0.983$, $p < 0.001$). There was moderate agreement between both operators in terms of BLS and by BLS categories ($k = 0.586$, $p = 0.015$ and $k = 0.521$, $p = 0.010$). In 14 independent LUS studies, only 1 reading demonstrated interobserver difference exceeding 1.96 standard deviation (SD).

There was also excellent inter-operator variability for IVCDimax ($r = 0.994$, $p < 0.001$) and IVCDimin. In 14 independent IVCDimax readings, 2 readings demonstrated interobserver difference exceeding 1.96 SD.

Conclusion: Point-of-care ultrasonography for volume assessment is able to demonstrate good inter-operator reproducibility and is easy for new users to learn. There is hence potential for more widespread incorporation of these volume assessment tools into community dialysis centres. POCUS has traditionally been performed by medical professionals, but in light of the relative ease of learning curve, it may be possible for allied healthcare professionals to acquire skills in POCUS.

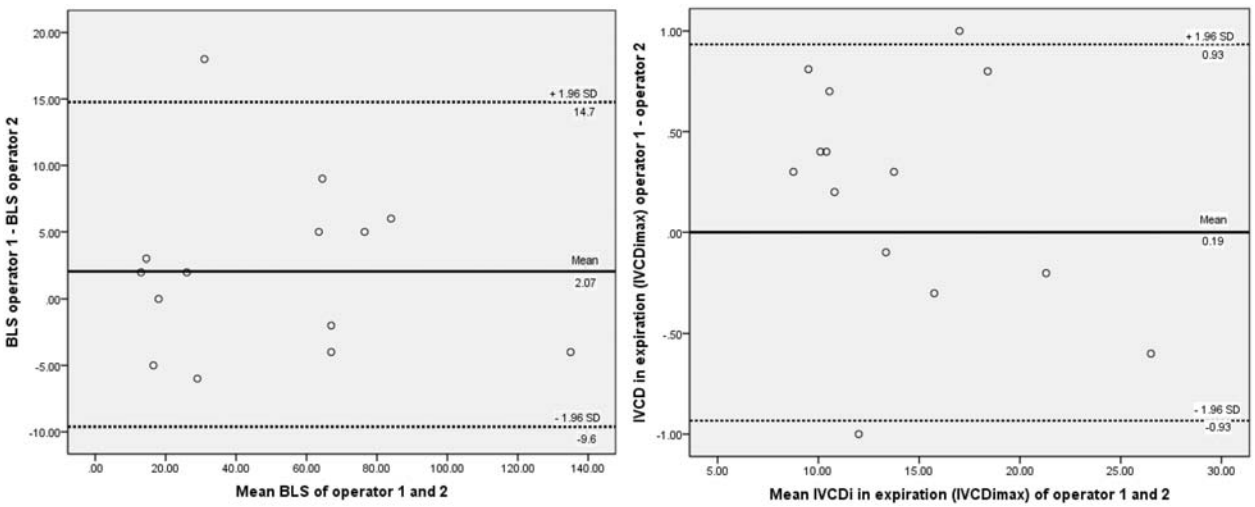


Figure 1. Bland Altman plots of inter-operator reproducibility for (a) BLS; (b) IVCDimax

P0191 USE OF CLINICAL FRAILTY SCALE IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGE 4/5

Wan Shun Wong[1], Amin Manssouri[2], James Robb[2], Zoe Cousland[2], Karen Dingwall[2], Annemarie Brennan[2]

[1]*Queen Elizabeth University Hospital, Renal unit, Glasgow, United Kingdom and* [2]*University Hospital Monklands, Renal Unit, Airdrie, United Kingdom*

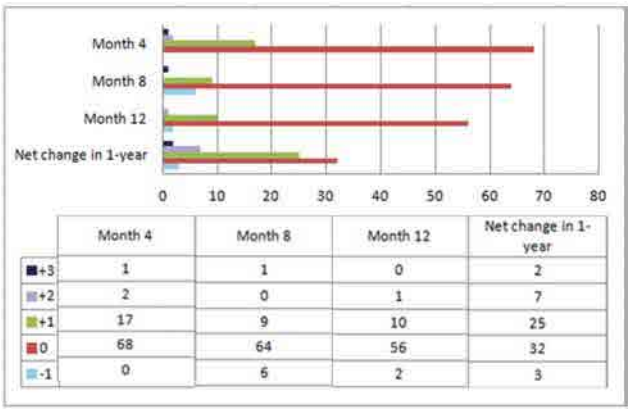
Background and Aims: Frailty and comorbidity have been shown to predict mortality in end stage renal failure patients. This knowledge can help inform patients and clinicians when undertaking the joint decision-making process regarding the management of advanced renal disease. This project sets out to record the serial and net frailty scores of patients with stage 4 and 5 kidney disease and study the change of frailty score in association with mortality and patient's preferred modality of renal replacement therapy (RRT).

Method: All patients followed up in Low Clearance Clinic with eGFR <30ml/min/1.73m^2 were identified from West of Scotland Electronic Renal Patient Record (SERPR). Biochemical data, patient's preferred modality of RRT, clinic/admission records were extracted from SERPR and Clinical Portal. Rockwood Clinical Frailty Scale (CFS) was used to determine patients' degree of frailty (1 being fittest and 9 being frailest). Patient's CFS was reviewed by our Low Clearance Nurse Specialists at 4-monthly interval over a 12-month period. Frailty score was not repeated once patient commenced RRT.

Results: 125 patients with CKD stage 4 and 5 had a baseline CFS in April 2018. 54.4% were female and median age was 66 years old. 40.8% patients had a diagnosis of diabetes. Table 1 shows the demographics for patients with baseline CFS 1-3 (not frail), 4-5 (mild frailty) and 6-9 (moderate – severe frailty) respectively.

RRT was planned for 82.8% of patients with CFS1-3 (63.3% HD, 36.7 PD), 52.1% of patients with CFS 4-5 (96.0% HD, 4.0% PD) and 36.8% patients with CFS 6-9 (100% HD, 0% PD). 29.2% of patients with CFS 4-5 and 47.4% of patients with CFS 6-9 were for conservative care. 1-year mortality for patients with CFS 1-3, 4-5 and 6-9 was 1.7%, 18.8% and 26.3% respectively.

A total of 362 CFS were recorded over the 12-month period (125 at month 0, 88 at month 4, 80 at month 8 and 69 at month 12). 49 changes in CFS were noted in 37 patients. 34 patients had a net deterioration of CFS by the end of month 12. Figure 1 shows the changes in patients' CFS at 4-monthly interval and the net changes by the end of 12-month follow up. Four patients changed their RRT planning from dialysis to conservative care and they all had a deterioration of CFS.



	Month 4	Month 8	Month 12	Net change in 1-year
+3	1	1	0	2
+2	2	0	1	7
+1	17	9	10	25
0	68	64	56	32
-1	0	6	2	3

Figure:

Comparing the patients with deterioration of CFS against those without, they had similar number of hospital admissions and clinic appointments and appear to have no association with having the diagnosis of diabetes. However, patients with deterioration of CFS had higher rate of death (14.3% vs 4.7%) and higher likelihood to change their preferred modality of RRT (8.6% vs 4.7%).

Conclusion: Frailty is common among patients with advanced CKD and is associated with significant mortality rate. Serial assessment of frailty score is helpful in monitoring patients' physical and functional status. Consistently high or deteriorating frailty score may correlate with higher mortality and this should trigger a review of their suitability for RRT, and consideration of anticipatory care planning.

	CFS 1-3	CFS 4-5	CFS 6-9
No. of patients	58	48	19
Median Age	62	74	66
Percentage of patients with diabetes	36.2%	39.6%	57.9%

P0192

RELATIONSHIP BETWEEN SERUM HEPCIDIN AND THE PROGRESSION OF CHRONIC KIDNEY DISEASE: KOREAN COHORT STUDY FOR OUTCOME IN PATIENTS WITH CHRONIC KIDNEY DISEASE (KNOW-CKD)

Su Ah Sung[1], Kum Hyun Han[2], Jien Lee[3], Taehee Lee[4]

[1]Nowon Eulji Medical Center, Eulji University, Internal Medicine, Seoul, Korea, Rep. of South, [2]Inje University Ilsan Paik Hospital,, Internal Medicine, Goyang-si, Korea, Rep. of South, [3]Wonkwang University Sanbon Hospital, Internal Medicine, Gyeonggi-do, Korea, Rep. of South and [4]Woori Yonsei Clinic, Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Hepcidin plays a central role in iron metabolism. However, few studies have evaluated the relationship between serum hepcidin and the progression of chronic kidney disease (CKD). This study aimed to determine the relationship between serum hepcidin levels and the progression of renal diseases in patients with CKD.

Method: We reviewed data of 2,016 patients from a large-scale multicenter, prospective study enrolled between 2011 and 2016, who had data regarding the serum hepcidin level, hemoglobin level, iron indices, usage of erythopoiesis-stimulating agents (ESA) or iron, and follow-up of renal events. Renal events were defined as a >50% decrease in kidney function from the baseline values, doubling of the serum creatinine level, or initiation of renal-replacement treatment.

Results: During a mean 3.6 years, 556 patients developed renal events (27.6%). In multivariate Cox proportional hazard regression analysis adjusted for confounders including kidney function, the hemoglobin level, conventional iron indices, usage of ESA or iron, and other chronic diseases, the hazard of serum hepcidin for renal events was evident in the comparison between only the first and fourth quartiles (hazard ratio 1.603, 95% confidence interval, 1.187-2.163, $P = 0.002$). In the multivariate penalized spline curve analysis, the relationship between serum hepcidin and renal events was J-shaped, and the renal hazard was particularly evident at a serum hepcidin level $\geq$60 ng/ml.

Conclusion: Increased serum hepcidin levels independently predict the progression of CKD in non-dialysis patients with CKD. The potential direct renal hazard of serum hepcidin needs to be confirmed in future randomized controlled trials.

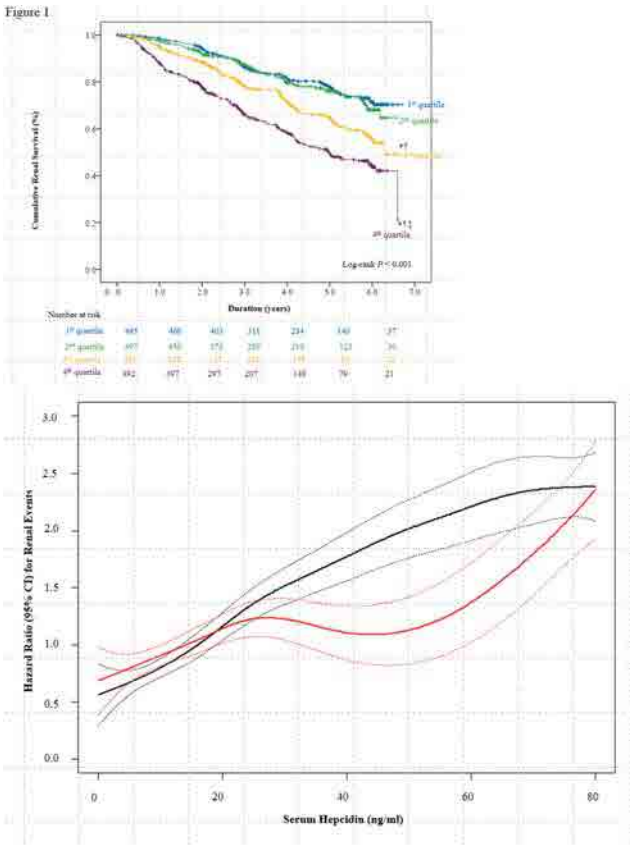


Figure:

P0193

MEASUREMENTS OF SERUM CREATININE AND EGFR IN PATIENTS WITH CHRONIC CARDIORENAL SYNDROME TYPE 2 ARE INSUFFICIENT TO ASSESS RENAL RESPONSES TO RESYNCHRONIZATION THERAPY DURING A TREE-MONTH FOLLOW-UP

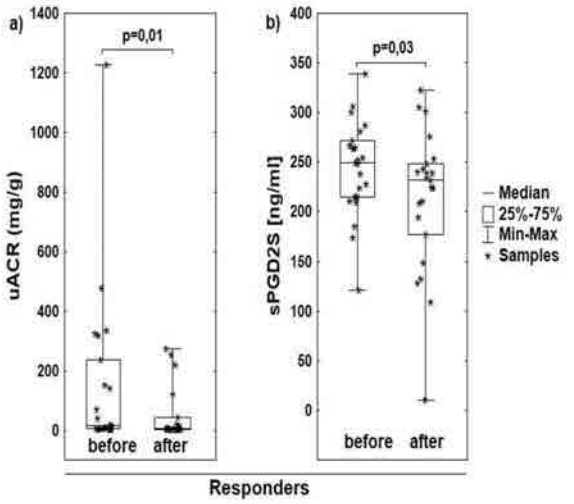
Agnieszka Gala-Błądzińska[1,2], Tomasz Kubrak[3], Joanna Czech[3], Krzysztof Gargasz[3], Danuta Mazur[4], Andrzej Przybylski[1,4]

[1]Medical College of Rzeszów, Institute of Medical Sciences, Rzeszow, Poland, [2]St Queen Jadwiga Clinical District Hospital No2 in Rzeszów, Department of Internal Medicine, Nephrology and Endocrinology, Rzeszów, Poland, [3]Medical College of Rzeszow University, Institute of Medical Sciences, Rzeszów, Poland and [4]St Queen Jadwiga Clinical District Hospital No2 in Rzeszów, Department of Cardiology, Rzeszów, Poland

Background and Aims: Chronic cardiorenal sydrome type 2 (CRS-T2) has a complex pathophysiology. Treatment and evaluation of the clinical effects of CRS-T2 therapy is difficult in clinical practice. The study's aim was to non-invasively assess renal function using biomarkers associated with nephron injury sites in patients with CRS-T2 following cardiac resynchronization therapy (CRT).

Method: The study included patients with CRS-T2 and heart failure in NYHA classes II-IV, in whom CRT devices had been implanted. Before cardiac resynchronization therapy and after 3 months, patients' renal function was assessed using biomarkers measured in single urine and blood samples. Test results were correlated with cardiovascular fitness assessments.

Results: CRT was implanted in 56 (n = 17; 30.4% ♀) patients with a mean age of 66 ± 10 years with CRS-T2 in the course of coronary artery disease (n = 38) or dilated cardiomyopathy (n = 18) with eGFRCKD-EPI = 68.55 ± 20.34 ml / min / 1.73m2. The three-month follow-up was continued in 33 (61.11%) patients. Three months after implantation CRT, the responders group cardiovascular endurance improved by at least on NYHA class; showed a significant decrease in NT-pro BNP (n = 24; 72.72%; p = 0.004), a significant ($p < 0.05$) decrease in serum prostaglandin D2 synthase (sPGD2S) and albuminuria (uACR) concentrations (Figure 1 a), and increases in hematocrit (HCT), erythrocyte count (RBC) and hemoglobin (Hb). The urine samples of the non-responders group following CRT, showed significant ($p < 0.05$) increases in lipocalin concentrations associated with neutrophil gelatinase (uNGAL), and a decrease in cystatin C (uCysC) concentrations (Figure 1 b). There were no significant changes in the concentration of serum creatinine (sCr), eGFRCKD-EPI, serum cystatin C or uromodulin in urine and serum; and urinary kidney injury molecule-1 (uKIM-1) was found in the urine of both responding and nonresponding groups ($p > 0.05$).



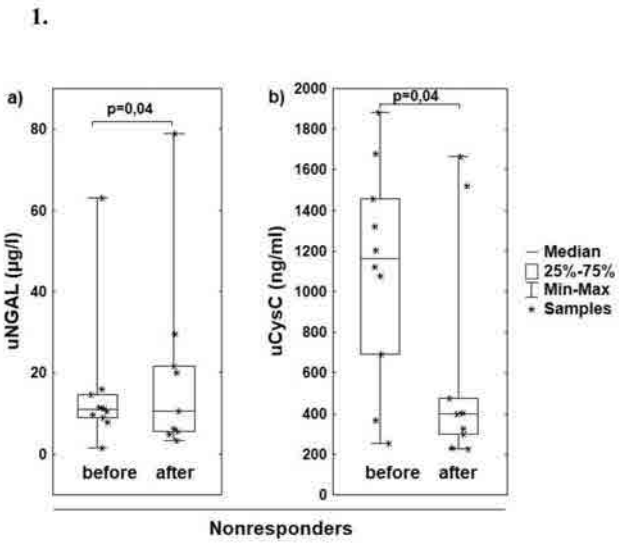


Figure 1: Graph showing statistically significant changes before and 3 months after cardiac resynchronization therapy in:

1) albuminuria (a) and sPGD2S (b) in those patients with cardiovascular improvement

2) uNGAL (a) and uCysC (b) in those patients without improving myocardial function

Conclusion: The sCR and eGFR CKD-EPI assessment should not be used to assess renal function in patients with type 2 chronic cardiac renal syndrome who have undergone CRT implantation. Renal function biomarkers that account for the pathophysiology of nephron injury and correlated with myocardial function: sPGD2S, uACR, uCysC, uNGAL. Also, increased HCT, RBC, and Hb are characteristic in responders.

P0194 **UNRAVELING FATIGUE IN HAEMODIALYSIS PATIENTS: A PLEA FOR THE USE OF MOBILE HEALTH EXPERIENCE SAMPLING METHODOLOGY**

Astrid Brys[1,2], Frank Stifft[3], Caroline Van Heugten[4], Maurizio Bossola[5], Giovanni Gambaro[6], Bert Lenaert[7]

[1]Università Cattolica del Sacro Cuore, Roma, Italia, Divisione di nefrologia, Rome, Italy, [2]Maastricht University, Department of Neuropsychology and psychopharmacology, Maastricht, Netherlands, [3]Zuyderland Medical Centre, Internal Medicine - Nephrology, Sittard-Geleen, Netherlands, [4]Maastricht University, Department of Neuropsychology and Psychopharmacology, Maastricht, Netherlands, [5]Università Cattolica del Sacro Cuore, Roma, Italia, Haemodialysis Unit, Rome, Italy, [6]University hospital of Verona, Division of Nephrology, Verona, Italy and [7]Maastricht University, department of Neuropsychology and psychopharmacology, Maastricht, Netherlands

Background and Aims: Fatigue is one of the most prioritized outcomes among haemodialyis (HD) patients with great impact on health-related quality of life. However, evidence-based therapies are lacking. A better understanding of fatigue symptoms and related behavioral, social and psychological factors in HD patients is of primary importance. Conventionally used fatigue measurement instruments, such as the Fatigue Severity Scale (FSS), only provide a general picture of fatigue severity and are prone to memory bias due to their retrospective nature. However, they cannot provide detailed insight in diurnal variations in fatigue and related factors in daily life. The Experience Sampling Methodology (ESM) overcomes these limitations by repeated "real-time" assessments in patients' natural environments using digital questionnaires. The aims of this study were (i) to gain in-depth understanding of HD patients' diurnal fatigue patterns and related variables using a mobile Health (*mHealth*) ESM application, (ii) to better understand the nature of their interrelationships, and (iii) to explore the relationship between real-time experience of fatigue and its retrospective assessment.

Method: Forty chronic HD patients used the *mHealth* ESM application for seven consecutive days to assess momentary fatigue and potentially related variables, including daily activities, self-reported physical activity, social company, location and mood patterns. In addition, patients retrospectively evaluated their fatigue experience over the preceding day and week by means of end-of-day, and end-of-week questionnaires and the FSS.

Results: Multilevel regression analyses of momentary observations (N=1778) revealed that fatigue varied between and within individuals (Fig.1). Fatigue was significantly related to type of daily activity and mood. Time-lagged analyses showed that HD treatment predicted higher fatigue scores at a later time point, $\beta = 0.22$, $p = 0.013$. Interestingly, higher momentary fatigue also significantly predicted more depressed feelings at a later time point, $\beta = 0.05$, $p = 0.019$, but not the other way around. Retrospective evaluation of fatigue experience over the preceding week was significantly higher than the average of momentary fatigue scores, $t(38) = 3.54$, $p = 0.001$. The FSS correlated moderately with the average of momentary fatigue scores, $r = 0.63$.

Conclusion: This study demonstrates diurnal variability of fatigue in chronic HD patients. It also corroborates a previous result from our research group showing that fatigue increases as a response to HD treatment (i.e. post-dialysis fatigue) and should, at least partially, be distinguished from a more general fatigue experience. Furthermore, our findings may suggest that depressed mood is secondary to fatigue in HD patients given their temporal relationship. Finally, retrospective fatigue assessment led to overestimation of the real-time fatigue experience. ESM offers novel insights in fatigue in HD patients by capturing informative symptom variability in the flow of daily life, which is not provided by conventional fatigue measures. Moreover, ESM provides personalized information about fatigue symptoms and their relationship with other variables in daily life, paving the way towards personalized interventions for HD patients.

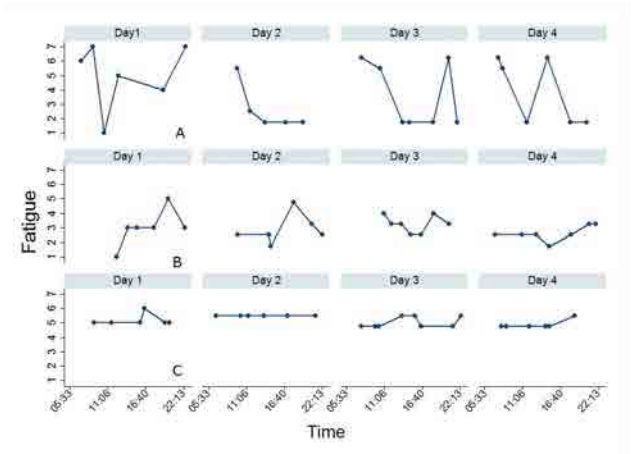


Figure 1: Diurnal patterns of momentary fatigue of three different HD patients (subjects A, B, and C) during four consecutive study days illustrating variability in fatigue between as well as within individuals.

P0195 **THE RELATIONSHIP BETWEEN CALCIFICATION INHIBITOR LEVELS IN CHRONIC KIDNEY DISEASE AND THE DEVELOPMENT OF ATHEROSCLEROSIS**

Can Sevinc[1], Gulay Yilmaz[2], Sedat Ustundag[3]

[1]Ataturk University Faculty Of Medicine, Nephrology, Erzurum, Turkey, [2]Acibadem International Hospital, Nephrology, Istanbul, Turkey and [3]Trakya University Faculty Of Medicine, Edirne, Turkey

Background and Aims: Atherosclerosis and its associated cardiovascular diseases starting from the early stages of chronic kidney disease (CKD) are the most important cause of increased morbi-mortality in the CKD process. In studies performed in patients with end-stage renal disease (ESRD), it is observed that the calcification occured in the vascular structures was an important component of the atero-arteriolosclerosis process.

Table-1: Comparison of demographic, clinical and laboratory data of healthy control group and chronic kidney disease group according to stages.

	Healthy control group (n=32)	Stage 2 (n=26)	Stage 3 (n=34)	Stage 4 (n=23)	Stage 5 (n=8)
Age (years)	46.2±10.4	46.1±11.4	47.4±11.5	46.2±8.1	47.4±7.2
BMI (kg/m^2)	25.9±4.0	25.6±3	26.1±3.6	26.5±4.2	26.3±3.7
CIMT (mm)	0.520±0.052	0.752±0.170* **	0.778±0.154* **	0.794±0.148* **	0.911±0.249* **
CRP (mg/dl)	0.31±0.22	0.4±0.3	0.6±0.9*	0.9±1.4**	0.9±0.8***
Fetuin-A (ng/ml)	95.4±16	99.1±7.3	82.1±24.4*	85.3±22.6	77.7±20.2*
OPG (ng/ml)	12.9±8.6	18.3±10.3*	17.9±10.2*	18.2±13.2	22.4±7.3*
MGP (ng/ml)	3.0±2.8	2±2.4*	1.4±1.5**	1.3±0.9**	1.1±1*

BMI: Body mass index, C-IMT: Carotid intima media thickness, CRP: C-reactive protein, OPG:Osteoprotegerin, MGP:Matriks Gla Protein

*In the comparison of healthy control group and CKD groups * = p <0.05, ** p = 0 <0.005, *** = p <0.0005, in the comparison of Stage 2, Stage 3, Stage 4 and Stage 5, δ = p <0.05, in the comparison of Stage 3 and Stage 4 and Stage 5 patients γ = p <0.05, in the comparison of Stage 4 and Stage 5 patients 5 = ψ <0.05.*

Figure:

The number of studies investigating the relationship between vascular calcification and the development of atherosclerosis and increased morbi-mortality in the process of CKD are quite small and limited to patients undergoing hemodialysis (HD) treatment for ESRD. We aimed to investigate the factors affecting the development of atherosclerosis and the role of calcification inhibitors fetuin-A, matrix-Gla protein (MGP), osteoprotegerin (OPG) in atherosclerosis progress.

Method: Our study was planned to investigate the relationship of serum OPG, MGP and fetuin-A levels with the development of atherosclerosis in the stage 2-3-4-5 chronic kidney patients who did not require dialysis treatment. Thirty-two (17 female, 15 male) healthy individuals and 92 (49 females, 43 males) CKD cases were included. The healthy control group did not have a history of regular use of medication for any reason, known acute or chronic disease. Chronic kidney disease group, with no acute disease, no history of known malignancy and cerebrovascular disease. The patients' GFR was also calculated with CKD-EPI Formula. The mean carotid artery intima media thickness was calculated by dividing the sum of right and left carotid artery intima media thickness. Statistical analysis was performed with IBM SPSS Statistics 20.0.0.

Results: The laboratory data of the healthy control group, stage 2 CKD group, stage 3 CKD group, stage 4 CKD group and stage 5 CKD groups were statistically compared with the healthy control group, between themselves and the whole CKD group, the results were given in Table-1. Chronic kidney disease group divided into two groups; carotid artery intima media thickness less than 0.750 millimeters (without subclinical atherosclerosis) and those above 0.750 millimeters (with subclinical atherosclerosis). The mean C-IMT, CRP, FETUIN-A, OPG and MGP of the two groups were compared statistically and the results are shown in Table-2. In chronic kidney patients, age ($r = 0.493$, $p < 0.001$), BMI ($r = 0.337$, $p = 0.001$), CRP ($r = 0.301$, $p = 0.004$), TG ($r = 0.245$, $p = 0.019$), urea ($r = 0.228$, $p = 0.029$), SBP ($r = 0.212$, $p = 0.043$), fasting blood sugar ($r = 0.212$, $p = 0.043$) have positive linear relationship, fetuin-A ($r = -0.409$, $P = 0.001$), OPG ($r = -0.235$, $p = 0.024$), GFR ($r = -0.209$, $p = 0.046$) have a negative linear relationship with CIMT. The multiple relationships between CIMT and other variables are given in Table-3. The mean CIMT ($r = -0.417$, $p = 0.001$), right CIMT ($r = -0.412$, $p = 0.001$), left CIMT ($r = -0.410$, $p = 0.001$), urea ($r = -353$, $p = 0.007$), CRP ($r = -0.322$, $p = 0.014$), UPE ($r = -0.301$, $p = 0.022$), creatinine ($r = -0.277$, $p = 0.035$), age ($r = -0.262$, $p = 0.047$) show a negative linear relationship with Fetuin-A. Multiple relationships between fetuin-A and other variables are given in Table-4.

Conclusion: Our study shows that; In particular, fetuin-A levels, which is a vascular calcification inhibitor, begin to decline from the early stages of CKD and is significantly lower in patients with atherosclerosis. This suggests that fetuin-A may be used as an early marker in CKD with increased cardiovascular mortality. On the other hand, contradictions related to the levels of OPG and MGP in CKD and its role in the development of atherosclerosis continue. The results in our study also support this situation. Reducing mortality and morbidity in CKD primarily depends on reducing the risk of cardiovascular events. Pre-recognition of these risks is important, so large-scale studies on vascular calcification inhibitors are needed.

P0196 **ACUTE TUBULOINTERSTITIAL NEPHRITIS (ATIN) INDUCED BY CHECKPOINT INHIBITORS (ICI) VERSUS CLASSICAL ATIN. ARE THEY THE SAME DISEASE?**

Laura Martinez Valenzuela[1], Juliana Draibe[1], Clara Garcia Carro[2], Irene Agraz[2], Xavier Fulladosa[1], Monica Bolufer[2], Ariel Tango[1], Joan Torras[1], María José Soler[2]

[1]Bellvitge University Hospital, Nephrology, L'Hospitalet de Llobregat, Spain and [2]Vall d'Hebron University Hospital, Nephrology, Barcelona, Spain

Background and Aims: The incidence of acute tubulointerstitial nephritis (ATIN) related to drugs has dramatically increased during the past years. A new subtype of ATIN apparently different from classical drug related ATIN has emerged, which has been related to the administration of immune check point inhibitors (ICI). We herein investigated these differences between ICI related ATIN and non-ICI related ATIN, in terms of clinical features, response to treatment with steroids, and the kidney function evolution.

Method: A total of 47 patients diagnosed with acute tubulointerstitial nephritis (ATIN) from two centers were recruited. Of these, 13 patients presented with ATIN during the treatment with ICI, and 34 patients were diagnosed with ATIN attributed to other drugs. The main demographical, clinical and analytical variables such as gender, age, and current medication were recorded. The type of malignancy, oncological treatment, dose of ICI, and presence of extra-renal immune-related adverse-events were also reviewed. Renal biopsy diagnostic, time to drug withdrawal and ATIN specific treatment, as well as laboratory data during the follow-up were also studied.

Results: Patients diagnosed with ICI related ATIN presented with lower creatinine (ICI ATIN 3.8±1.03mg/dl vs. classical ATIN 5.98±4.15, p=0.007) at diagnostic and higher urinary leukocyte count (ICI ATIN 263.2±418.04 vs. classical ATIN 133.55±284.62, p=0.048) as compared to patients with non-ICI related ATIN. Time elapsed from the initiation of the culprit drug to the ATIN diagnostic was longer in ICI ATIN compared to classical ATIN (197.07±184.99 vs 114.4±352.16 days, p=0.006). In addition, during follow-up, the slope of decreasing creatinine over time was lower in ICI related ATIN compared to non-ICI related patients.

Conclusion: In this study we analyzed the differences between ICI ATIN and the classical ATIN. We found that ICI ATIN patients presented a larger latency period after offending drug initiation, milder acute kidney injury, and slower creatinine amelioration as compared to the classical ATIN. These results may be in part ascribed to potential differences in the pathological mechanisms in ATIN development, suggesting that ICI ATIN and the classical ATIN may be different disease with similar renal histology.

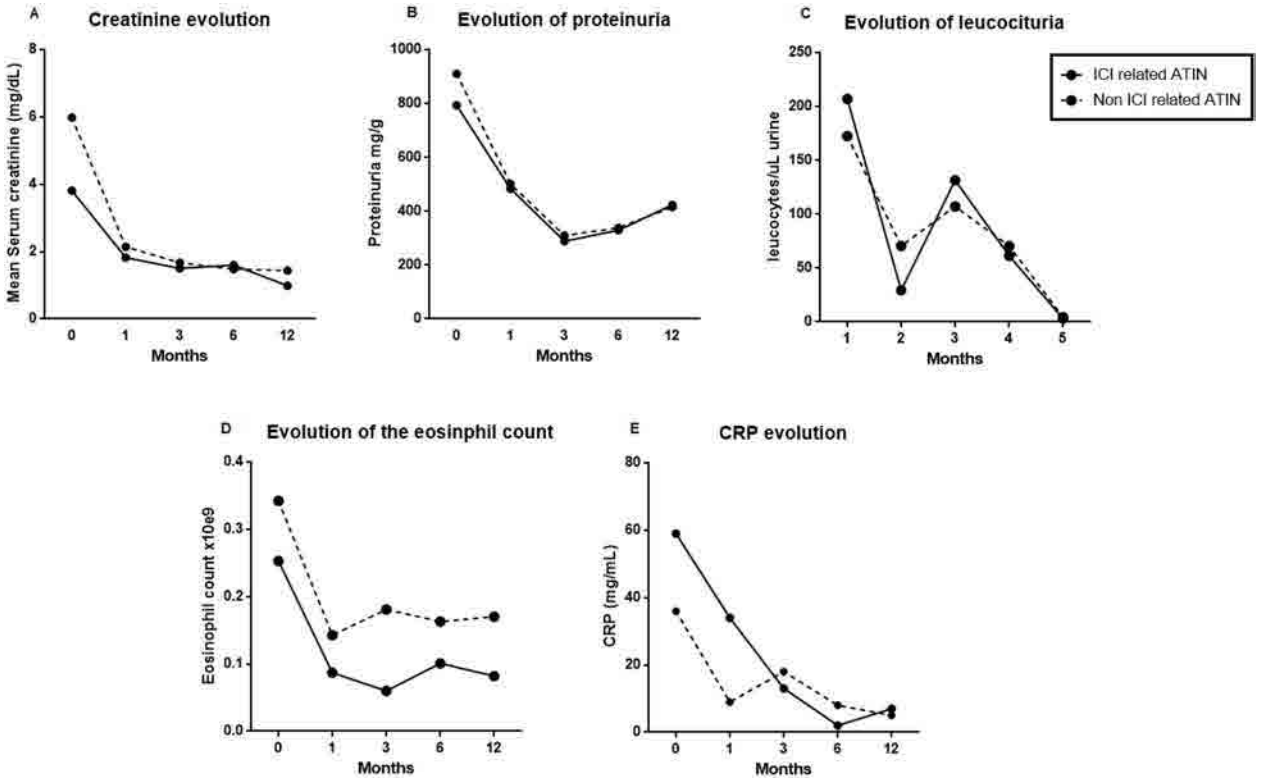


Figure:

P0197 CLINICAL FRAILTY SCORING IN PATIENTS WITH END STAGE RENAL DISEASE: A PREDICTOR OF DECLINING HEALTH?

Lucy Hetherington[1], Joanna Prentice[1], Mark Findlay[2], Tara Collidge[2]

[1]Beatson West of Scotland Cancer Centre, Palliative Medicine, Glasgow, United Kingdom and [2]Queen Elizabeth University Hospital, Nephrology, Glasgow, United Kingdom

Background and Aims: The incidence of frailty increases as GFR decreases. In the end stage renal disease (ESRD) population frailty is associated with early mortality, increased hospitalisations, and significant symptom burden. We examined the use of formal frailty scoring and its role in identifying deteriorating patients with advanced renal disease.

Method: The Rockwood Clinical Frailty Scale (CFS) has high inter-rater reliability and correlates well with objective measures of frailty. We introduced routine recording of the CFS from January 2018 in the renal electronic record for patients on hospital haemodialysis therapy and those undergoing renal replacement therapy (RRT) planning. Based on CFS scoring patients were divided into 'frail' (CFS$\geq$6) or 'robust' based (CFS$<$6) and patient demographics are described. The association of being 'frail' or a decline in score with mortality at seven months were described using adjusted logistic regression analyses.

Results: A total of 1663 scores were recorded in 800 patients. 57.3% of patients were male. The median age at entry date was 66 (IQR 55,75) years. The median CFS score was 4 (IQR 3,5). At follow-up 74 (9.3%) had died. The median score prior to death was 5.5. 182 (22.8%) were 'frail'. During the study period 469 patients had more than one score documented. Death at follow-up was more common in those who were 'frail', 20.9 vs 5.8%, $p<0.001$. Patients who were deceased at follow-up were more likely to have had a deterioration in frailty score, 51.9% vs 24.4%, $p=0.002$. Being 'frail' or having a deteriorating frailty score was associated with death at seven-month follow-up independent of age, sex or diabetic nephropathy status.

Conclusion: The presence of 'frailty' as measured by CFS, or deterioration in CFS is associated with death at follow-up, independent of age, sex or diabetic nephropathy. Routine monitoring of frailty using the CFS provides a simple method to identify patients who are deteriorating and at risk of death. High or deteriorating CFS score should trigger clinical review and anticipatory care planning where appropriate.

P0198

SODIUM ZIRCONIUM CYCLOSILICATE INCREASES SERUM BICARBONATE CONCENTRATIONS AMONG PATIENTS WITH HYPERKALAEMIA: RESULTS FROM THREE RANDOMIZED, MULTI-DOSE, PLACEBO CONTROLLED TRIALS

S Roger[1], Bruce Spinowitz[2], Edgar Lerma[3], Steven Fishbane[4], Stephen Ash[5,6], Julian Martins[7], Carol Moreno Quinn[8], David Packham[9,10]

[1]Renal Research, Gosford, Australia, [2]New York-Presbyterian Queens, Division of Nephrology, Department of Medicine, New York, United States of America, [3]Advocate Christ Medical Center, University of Illinois at Chicago, Section of Nephrology, Oak Lawn, United States of America, [4]Zucker School of Medicine at Hofstra/Northwell, Department of Medicine, Great Neck, United States of America, [5]HemoCleanse Technologies, LLC and Ash Access Technology, Inc., Lafayette, United States of America, [6]Indiana University Health Arnett Hospital, Nephrology, Lafayette, United States of America, [7]inScience Communications, Springer Healthcare, Paris, France, [8]AstraZeneca, Gaithersburg, United States of America, [9]Melbourne Renal Research Group, Reservoir Private Hospital, Reservoir, Australia and [10]University of Melbourne, Department of Medicine, Melbourne, Australia

Background and Aims: Sodium zirconium cyclosilicate (SZC; formerly ZS-9) is an orally-administered, non-absorbable, inorganic, selective potassium (K^+) binder for the treatment of adults with hyperkalaemia. SZC entraps K^+ throughout the gastrointestinal tract in exchange for hydrogen and sodium ions. In addition to serum K^+ reduction, phase 2 clinical trial data have shown an increase in serum bicarbonate and a decrease in serum urea. This may be due to SZC trapping of ammonium ions (which are of a similar size to K^+ ions) in the gastrointestinal tract. Maintaining serum bicarbonate $\geq$22 mmol/L preserves kidney function and reduces metabolic bone disease. Thus, SZC-induced increase in serum bicarbonate may represent an effect of clinical significance. We present a post hoc analysis of central laboratory-measured serum bicarbonate, urea, and urine pH data from three randomized, placebo-controlled, phase 3 studies of SZC among patients with hyperkalaemia (ZS-003, HARMONIZE, and HARMONIZE-Global).

Method: In all studies, patients initially received up to 10 g SZC three times a day (TID) for 48 hours for correction of hyperkalaemia (randomized placebo-controlled in ZS-003, open-label in HARMONIZE and HARMONIZE-Global), followed by randomization to maintenance therapy with SZC up to 15 g once a day (QD) versus placebo for up to 29 days among those who achieved normokalaemia during the correction phase.

Results: The analysis included 753 patients from the initial 48-hour correction phase of ZS-003, and 208 and 214 patients who completed the 29-day maintenance phase of HARMONIZE and HARMONIZE-Global, respectively. Significant dose-dependent increases from baseline in serum bicarbonate of 0.3–1.5 mmol/L occurred within 48 hours of SZC TID in ZS-003 (Figure A), which occurred regardless of chronic kidney disease (CKD) stage (Figure B).

Similar acute increases in HARMONIZE and HARMONIZE-Global were maintained over 29 days with SZC $\geq$10 g (Figure C) and $\geq$5 g QD (Figure D), respectively.

Mixed-model least-squares mean serum bicarbonate increases from baseline versus placebo over 15–29 weeks with SZC were 2.2 mmol/L ($p < 0.001$) and 2.8 mmol/L ($p < 0.001$) in HARMONIZE (SZC 15 g QD) and HARMONIZE-Global (SZC 10 g QD), respectively. In ZS-003, the proportion of patients with serum bicarbonate <22 mmol/L at correction phase baseline, 27.3%, fell to 16.5% ($p = 0.025$) at 48 hours among patients receiving SZC 10 g TID. In HARMONIZE and HARMONIZE-Global, the proportion of patients with serum bicarbonate <22 mmol/L at correction phase baseline, 39.4% and 87.9%, respectively, fell to 4.9% ($p = 0.005$) and 70.1% ($p = 0.006$) at 29 days, respectively, among patients receiving the highest SZC maintenance dose (15 g and 10 g, respectively). Parallel decreases in serum urea and increases in urine pH were also observed with SZC in all three studies. Mixed-model least-squares mean serum urea decreases from baseline versus placebo over 15–29 weeks with SZC were −1.0 mmol/L ($p = 0.029$) and −2.9 mmol/L ($p < 0.001$) in HARMONIZE (SZC 15 g QD) and HARMONIZE-Global (SZC 10 g QD), respectively. Corresponding increases in urine pH were 0.23 ($p = 0.001$) and 0.35 ($p < 0.001$), respectively. Path analysis demonstrated that changes in serum urea (but not changes in serum potassium or urine pH) were associated with the SZC effect on serum bicarbonate.

Conclusion: SZC consistently and dose-dependently increases serum bicarbonate concentrations, reduces the proportions of patients with serum bicarbonate <22 mmol/L, decreases serum urea, and increases urine pH during treatment of hyperkalaemia. These changes in serum bicarbonate occur regardless of CKD stage and are sustained during ongoing maintenance therapy. The increase in serum bicarbonate is associated with change in serum urea rather than with changes in serum K^+ or urine pH, supporting the hypothesis that SZC traps ammonia in the gastrointestinal tract independently to its effect on K^+ binding.

P0199 ASSESMENT OF FILTRATION RATE IN ONCOLOGICAL PATIENTS.

Kamila Klimek[1], FABIOLA ALONSO GARCIA[1], Alfonso Lara Ruiz[1], ANA AGUDO MARTINEZ[2], Marina Almenara Tejederas[1], MERCEDES SALGUIERA LAZO[1]

[1]VIRGEN MACARENA UNIVERSITY HOSPITAL, Nephrology, Seville, Spain and [2]VIRGEN MACARENA UNIVERSITY HOSPITAL, Nuclear Medicine, Seville, Spain

Background and Aims: Accuracy in the estimation of the glomerular filtration rate (GFR) in oncological patients is essential in order to adjust chemotherapy doses accordingly. Finding an appropriate formula for this subgroup of patients is a subject of ongoing debate. The present study introduces a cohort of the aforementioned patients followed in the Onconephrology outpatients clinic, in which different formulas were applied for the calculation of the GFR.

Method: A retrospective study with a cohort of 17 onconephrological patients was conducted. The following variables were evaluated: age, sex, height, weight, body mass index, body surface area and type of tumor. Renal function was estimated with the Cockcroft Gault, the Janowitz-Williams, the CKD-EPI, the adjusted by body surface-CKD-EPI, the MDRD, the adjusted by body surface-MDRD, the CKD-EPI Cystatin C, the adjusted by body surface-CKD-EPI Cystatin C formulas and 24-hour urine creatinine clearance. Every equation was compared with the Cr EDTA clearance which is considered the gold standard. The statistical analysis was carried out by means of the IBM SPSS Statistics software. Concordance between chromatography and the remaining formulas was assessed with the Wilcoxon (null hypothesis of no difference between medians) and Bland-Altman tests.

Results: 6 women and 11 men were included in the study, with a mean age of 64.24 years (SD 9.9), a mean BMI of 28.25kg/m2 (SD 7.98), and a mean Cr EDTA clearance was 37.07ml/min (SD 15.45). 15 patients suffered from solid malignancies, whereas the remaining 2 patients suffered from hematological tumors. The most common solid tumor was lung cancer (n=5), followed by rectal carcinoma (n=2).

The null hypothesis was accepted for the adjusted for body surface-CKD-EPI Cystatin C equation (p-0,089) and 24-hour urine creatinine clearance (p 0.955), when compared to 51Cr EDTA clearance. The Bland-Altman test revealed the smallest differences between the 24-hour urine creatinine clearance and 51Cr EDTA clearance (-0.09867), with 95% concordance limits of -36.14 and 34.17, and a non-significant linear regression coefficient (p 0.915).

Conclusion: This study revealed that the 24-hour urine creatinine clearance is the closest formula to the gold standard for the assessment of the GFR in patients with malignancies. However, the small sample size hinders the generalization of these results. Larger sample size studies are mandatory to confirm these findings.

P0200

KEEP ON (KEEPING RAAS INHIBITION TREATMENT WITH OPTIMAL POTASSIUM CONTROL). DESIGN OF A CLINICAL TRIAL OF USING SODIUM ZIRCONIUM CYCLOSILICATE FOR KEEPING RAAS INHIBITION AND/OR MRAS IN PATIENTS WITH CKD AND CONGESTIVE HEART FAILURE HISTORY.

Maria Jesã°s Puchades Montesa[1], Nayara Panizo Gonzalez[1], Luis D'Marco[1], Miguel Gonzalez-Rico[1], Patricia Tomas[1], Irina Sanchis[1], Ana Isabel Martinez-Diaz[1], Aurora Pérez Ys[1], Elena Gimenez-Civera[1], Elisa Perez-Bernat[1], Jose Luis Gorriz[1]

[1]*University Hospital Clinico. Valencia. INCLIVA. Universidad de Valencia, Nephrology, València, Spain*

Background and Aims: Hyperkalemia (HK) is a potentially life-threatening condition, in patients with chronic kidney disease (CKD) and congestive heart failure (CHF).

The majority of patients affected with CKD or CHF, must be treated with inhibitors of renin angiotensin aldosterone system (RAASi) and mineralocorticoid receptor antagonists (MRAs). However, the treatments previously mentioned, increase the risk of HK episodes, which is the main cause of RAASi and MRAs downtitration or discontinuation, representing an undesirable clinical scenario, given that the patients are at high risk of be deprived of their nephroprotective effect and cardio-renal benefits

The aim of the study is: to analyze if, in patients with HK, CKD and CHF treated with RAASi and/or MRA, serum potassium (sK) reduction by Sodium zirconium cyclosilicate (SZC) treatment is non-inferior to RAASi and/or MRAs discontinuation or downtitration.

Method:

- Design: Randomized, Multicentric, open label, parallel-group, non-inferiority 12 weeks trial, comparing SZC vs discontinuation or downtitration of RAASi and /or MRA as standard of care.
- Key Inclusion Criteria: Patients with hyperkaliemia (defined as sK: 5.5-6.5 mEq/L) and non dyalisis CKD (Stages 2-5) and previous history of CHF (cardiorenal syndrome), receiving RAASi and / or MRAs.
- Primary efficacy end-point: To determine the proportion of patients achieving sK<5 with SZC treatmentversus discontinuation or downtitration of RAASi and/or MRAs at day 90. As
- Main secondary objectives:
- To evaluate Non-inferiority of SZC versus RAASi/MRAs discontinuation or down-titration with respect to achieve sK< 5 m Eq/L or effectively reduces sK > 20 % over the baseline at 7, 30, 60 and 90 days.
- To evaluate the implication of SZS treatment on the reduction of the necessity of additional treatment for hyperkaliemia compared to RAASi and/or MRAs discontinuation.
- To measure the impact of the treatment of SZC on the quality life of HK patients measured by KDQoL questionnaire (Self-Assessment Questionnaire).
- To measure the changes in albuminuria at 90 days from baseline.
- Sample size calculation: Proportion of patients reaching sK of <5 at 90 days with SZC is estimated to be 0.9 while discontinuation of RAASi and/or MRAs 0.80. Considering a non-inferiority margin of 0.1 and type I error rate of 5%, a total of 78 patients (39 per group) are required to achieve a power of 80%.Study conduct: the patients who meet inclusion criteria will be randomized to SZC group or RAAS-I and/or MRAs downtitration or discontinuation. Visits on days: 2,3,7,30, 60 and 90.
  - SZC group: patients will continue treatment with RAAS-I and/or MRAs and they will receive 10 g (sachets) thrice a day. According to sK levels, SZC dosage will be adjusted in each visit (Maintained 10 g thrice a day or reduced up to 5 g once a day or discontinuation if sK<3 mEq/L). If confirmed sK ≥ 6.5 mE/L despite the maximum SZC dose, patient will leave the study and will be counted as treatment failure. Treatment for acute hyperkaliemia will be started following common clinical practice and local protocols.
  - Control group: RAAS-I and/or MRAs will be discontinued or downtitrated at investigator's judgment. If sK ≥ 6.5 mE/L, treatment for acute hyperkaliemia will be started. Patient will leave the study and will be counted as treatment failure.

Results: The study will demonstrate results on serum electrolytes, renal function, albuminuria, KDQoL questionnaire and changes in relative overhydration (multifrequency bioimpedance -BCM Fresenius-)

Conclusion: The KEEP ON study will define the ability of SZC to facilitate the use of RAAS-I and / or MRA in patients with HK and cardiorenal syndrome allowing the maintenance of the medications recommended by international guidelines for the treatment of CHF at different degrees of CKD while maintaining the potential cardio-renal and nephroprotective benefit.

P0201 **ASSOCIATION OF INTRARENAL VEIN FLOW PATTERNS WITH CARDIAC FUNCTION IN OUTPATIENTS WITH CHRONIC KIDNEY DISEASE AND HEART FAILURE**

Ioannis Droulias[1], Aristeidis Stavroulopoulos[2], Efstratios Troganis[3], Helias Katsaounos[4], Dimitrios Chatzigiannakos[1]

[1]"A.Flemig" General Hospital, Nephrology, Athens, Greece, [2]IASIO Hospital - General Clinic of Kallithea, Nephrology, Athens, Greece, [3]"A. Flemig" General Hospital, Cardiology, Athens, Greece and [4]Katsaounos Ultrasuonography, Athens, Greece

Background and Aims: In patients with chronic kidney disease (CKD) and heart failure (HF), renal venous congestion plays a key role in determining renal dysfunction and a worse prognosis. Aim of this ongoing study is to identify Doppler intrarenal venous flow patterns reflecting renal congestion in patients with CKD and HF and to detect possible associations with cardiac function parameters. Prognostic implications will be evaluated at a next stge.

Method: We prospectively enroll outpatients affected by CKD stages 3-4 and HF, in stable clinical conditions and in conventional therapy. All patients undergo clinical evaluation, routine biochemistry, transthoracic echocardiogram and renal echo-Doppler. Pulsed Doppler flow recording is performed at the level of the right interlobular renal veins at the end-expiratory phase. The intrarenal venous flow patterns are divided into five types according to the waveforms of the flow. Type A and B are characterized by a continuous flow and considered normal waveforms. Type C is characterized by a short interruption and/or reversal flow during the end-diastolic or protosystolic phase. Type D and E are characterized by a wide interruption and/or reversal flow, respectively. Types C, D and E are considered abnormal and reflect increasing venous pressure within the kidneys.

Results: Until now, 36 patients (27males / 9 females), 13 (36%) diabetics, aged 69.4±10.6 years old, have been included, and baseline characteristics are presented. Twenty patients (55%) have CKD stage 3, and 16 patients CKD stage 4 (45%). Fifteen (40%) of these patients have HF New York Heart Association (NYHA) class II, 18 (50%) NYHA class III and 3 (10%) NYHA class IV. Mean ejection fraction (EF) is 34.5±7.8%, moderately reduced in 9 (25%) and severely reduced in 27 (75%) of these patients. By analyzing the waveforms, we noticed that 27 patients (75%) had venous patterns of continuous flow (type A 18% and type B 57%) and 9 (25%) had venous patterns with not continuous flows (21% type C and 4% type D). The patients with renal venous patterns A and B had higher EF than those with renal venous patterns C and D (36±8% vs. 30±5%, p=0.045). We have also observed that worsening HF according to NYHA classification was significantly associated to more pathological renal venous patterns (rho=0.402, p=0.034)

Conclusion: In patients with CKD and HF we may observe abnormal intrarenal vein flow patterns, in the context of renal congestion, related to the functional state of the heart. Further studies will indicate the clinical and prognostic significance of these measurements to better characterize patients with cardio-renal syndrome.

P0202

FIRST REAL-LIFE DATA OF PATIENTS TREATED FOR THROMBOTIC THROMBOCYTOPENIC PURPURA FROM THE FRENCH THROMBOTIC MICROANGIOPATHIES NETWORK.

Mehdi Maanaoui[1], Eric Maury[2], AUGUSTO Jean François[3], Jean Michel Halimi[4], Christelle Barbet[4], Sandrine Malot[5], Marie Haeck[6], Paul Coppo[5]

[1]CHU Lille, Nephrologie, Lille, France, [2]CHU Saint Antoine, Réanimation médicale, Paris, France, [3]CHU Angers, Néphrologie, Angers, France, [4]Hôpital universitaire de Tours, Néphrologie, Tours, France, [5]CHU Saint Antoine, Hématologie clinique, Paris, France and [6]CH Valenciennes, Néphrologie, Valenciennes, France

Background and Aims: Caplacizumab, a bivalent Nanobody, targets the A1 domain of von Willebrand Factor, inhibiting the interaction between ultra-large vWF and platelets in the treament of Acquired Thrombotic Thrombocytopenic Purpura (aTTP). Results of the Phase 3 HERCULES study confirm that treatment with caplacizumab reduces the time to platelet count response, resulting in faster resolution of aTTP. Treatment with caplacizumab also resulted in a highly clinically meaningful reduction in aTTP-related death, recurrence of aTTP, or a major thromboembolic event during study drug treatment. Data from clinical practice confirming the clinical trial data is still scarce. We report here the first real world evidence collected in the French thrombotic microangiopathies network.

Method: Patients with an acute episode of aTTP were included in an observational prospective multicentric study. The diagnosis of aTTP was done according to the French score (platelet count < 30 g/l and serum creatinine< 200µmol/l) or ADAMTS13 activity if available. Adult patients were proposed to be treated with daily plasma exchange (PE) in addition to corticosteroid and frontline rituximab plus early initiation of caplacizumab. PE was stopped after 2 days of platelet count normalization.

Results: Fifty patients (36 females, median age of 46 years old) were treated for aTTP. 30 patients (60%) had cerebral involvement and 13 (26%) had cardiac involvement. Cardiac troponin I was above upper normal value for 61% of patients. Before treatment, median platelet count was 16 g/l and median serum creatinine was 86 µmol/l. Three initial clinical suspicions of aTTP were finally diagnosed as HUS (2 patients) or vitamin deficiency (1 patient) resulting in the stop of treatment. A median number of 6 plasma exchanges was administered (min:3 - max:16). 375mg/m² rituximab injections (3 to 4 for 35/43 patients with reported data) were mostly initiated within 3 days after the first plasma exchange. Caplacizumab treatment was initiated early (37/42 patients with reported data within 2 days after 1st plasma exchange) with a total median duration of treatment of 33 days (min:18 - max:35). The median platelet count normalization was 5 days (min:4 - max:6). 6/41 (14,6%) experienced exacerbations. No deaths and no patients refractory to therapy were reported. Eight adverse events related to caplacizumab therapy were reported, all with good outcomes.

Conclusion: Concomitant start of additional treatments allow to target severe ADAMTS13 deficiency and platelet aggregation which causes early mortality. The clinical French score seems useful in clinical practices.

P0203

EARLY DETECTION OF BREAST ARTERIAL CALCIFICATION IN DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE PATIENTS

Basma Sultan[1], Hamdy Omar[1], Housseini Ahmed[2], Mahmoud Elprince[3], Osama Anter adly[4,5], Gamal Tawfik[1]

[1]faculty of medicine Suez Canal Univesity, Internal Medicine & nephrology, Ismailia, Egypt, [2]faculty of medicine Suez Canal Univesity, Radiology, Ismailia, Egypt, [3]faculty of medicine Suez Canal Univesity, Pulmonolgy, Ismailia, Egypt, [4]faculty of medicine Suez Canal Univesity, plastic surgery, Ismailia, Egypt and [5]faculty of medicine Suez Canal Univesity, dean, faculty of medicine, Ismailia, Egypt

Background and Aims: Vascular calcification (VC) plays a major role in cardiovascular disease (CVD), which is one of the main causes of mortality in patients with chronic kidney disease (CKD).

The study aims at early detection of breast arterial calcification (BAC) in different stages of CKD (stage 2, 3& 4) patients as an indicator of systemic VC.

Method: A case control study was conducted targeting CKD women, aged 18- 60 years old. The sample was divided into 3 groups; A,B,C (representing stage 2, 3 & 4 of CKD) from women who attended nephrology and Internal medicine clinics and admitted in inpatient ward in Suez Canal University Hospital. A 4th group (D) was formed as a control group and included women with normal kidney functions (each group (A, B, C, D) include 22 women). The selected participants were subjected to history taking, mammogram to detect BAC and biochemical assessment of lipid profile, Serum creatinine (Cr), Mg, P, Ca, PTH and FGF23.

Results: Our study detected presence of BAC in about 81.8% of hypertensive stage 4 CKD patients compared with 50% in stage 3 CKD, also in the majority of stage 4 CKD patients who had abnormal lipid profile parameters and electrolyte disturbance. Most of the variables had statistical significance regarding the presence of BAC.

Conclusion: Although it is difficult to determine the definite stage at which the risk of VC begins **but in our study**, it began late in stage 2 CKD, gradually increased prevalence through stage 3 and became significantly higher in stage 4. These results suggest that preventive strategies may need to begin as early as stage 2 CKD.

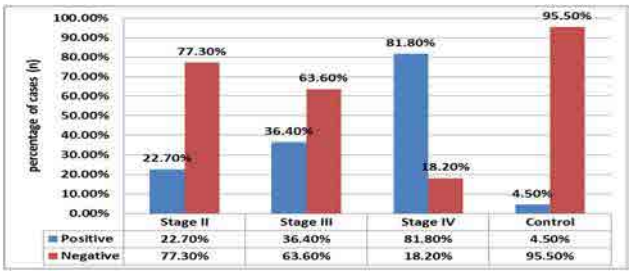


FIGURE 1: Frequency of breast arterial calcification among study population

TABLE 1: Demographic and Clinical Data of The Study Population

Demographic properties of study population						
Group		**Stage II**	**Stage III**	**Stage IV**	**Control**	**p-value**
Variables	**Attributes**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Hypertension	**No**	3 (13.6)	6 (27.3)	0 (0)	10 (45.5)	**<0.05***
		19 (21.6%)				
		Yes	19 (86.4)	16 (72.7)	22 (100)	12 (54.5)
	69 (78.4%)					
Dyslipidemia	**No**	15 (68.2)	11 (50)	4 (18.2)	15 (68.2)	**<0.05***
		45 (51.1%)				
		Yes	7 (31.8)	11 (50)	18 (81.8)	7 (31.8)
	43 (48.9)					
Age	**Mean± SD**	41.81±9.53	36.50±11.52	47.86±9.54	33.77±7.01	**<0.05***
		39.98 + 10.82				
	Range	41(60-19)				

Table 2: Relationship between hypertension, dyslipidemia and use of anticoagulants and BAC among all study population stratified by each of the CKD stages from 2 to 4 and the control group:

			Positive BAC per stage			p-value
Stage		Control	Stage 2	Stage 3	Stage 4	
Variables	Attributes	N (%)	N (%)	N (%)	N (%)	
HTN	Yes	1(8.3%)	4(21.1%)	8(50%)	18(81.8%)	**<0.05***
	No	0(0%)	1(33.3%)	0(0%)	0(0%)	0.06
Dyslipidemia	Yes	1 (14.3%)	4 (57.1%)	8 (72.7%)	18 (100 %)	**<0.05***
	No	0 (0%)	1 (6.7%)	0 (0%)	0 (0%)	0.563

Table 3: Multivariate logistic regression model :

		B	**S.E.**	**Wald**	**Df**	**p-value**	**OR**	**95% CI of OR**
Model A	**cholesterol**	0.066	0.017	15.507	1.000	**<0.05***	1.068	(1.034 - 1.104)
	creatinine	-2.640	1.219	4.690	1.000	**<0.05***	0.071	(0.007 - 0.778)
	eGFR	-0.065	0.030	4.601	1.000	**<0.05***	0.937	(0.883 - 0.994)
	calcium	-2.492	1.126	4.900	1.000	**<0.05***	0.083	(0.009 - 0.752)
	Constant	14.472	11.085	1.704	1.000	0.192	1927691.224	(1.034 - 1.104)

S.E. = Standard error, df = degrees of freedom, OR = Odds ratio, CI = Confidence interval

P0204 PREVALENCE AND PREDICTIVE FACTORS OF BIOPSY-PROVEN NEPHROPATHY RELATED TO MONOCLONAL GAMMOPATHY

Arthur Roux[1], Helene Lazareth[1], Dominique Nochy[2], Anne-Sophie Jannot[3], Camille Nevoret[3], Eric Thervet[1], KARRAS Alexandre[1]

[1]Hôpital Européen Georges-Pompidou, nephrology, Paris, France, [2]Hôpital Européen Georges-Pompidou, renal pathology, Paris, France and [3]Hôpital Européen Georges-Pompidou, Medical Informatics, Biostatistics and Public Health, Paris, France

Background and Aims: The prevalence of monoclonal gammopathy (MG) and kidney disease increases with age. When a patient present with both conditions, it is often necessary to perform a kidney biopsy in order to rule out a Monoclonal Immunoglobulin-Related Nephropathy (MIRN) that may require a specific therapy that targets either an overt hematological malignancy or a MG or Renal Significance (MGRS). The aim of our study was to identify factors that predict the presence of MIRN in this setting.

Method: This retrospective monocentric study included all patients who underwent a kidney biopsy between 2007 and 2018 with concurrent presence of GM, as defined by positive serum immuno-electrophoresis and/or Bence-Jones proteinuria.

Results: 328 patients were included, representing 11.8% of all kidney biopsies performed in our center during this period. Indication of biopsy was renal failure (ï»¿eGFR <60ml/min/1.73m) in 77.4% of cases and/or proteinuria (urine protein-to-creatinine ratio >0.5g/g) in 75.9% of them. Median (IQR) serum creatinine was 155 µmol/L (111-233), eGFR 37.5 (22-56) ml/min/1.73m, serum albumin 29.5 (24-35) g/l. Median age was 67 (57/75), the M/F ratio was 198/130, diabetes mellitus was present in 21.3% of cases, hypertension in 53.1%.

Kidney biopsy revealed that nephropathy was related to MG in 91/328 patients (27.7%). Myeloma cast nephropathy and AL amyloidosis were the most common histopathological subtypes (36 and 34% respectively), followed by monoclonal immunoglobulin deposition disease (15%) and cryoglobulinemic glomerulonephritis (8%). Patients with MIRN had more severe renal function impairment with median (IQR) serum creatinine of 176 (119-307) vs 149 (108-216) µmol/l (p=0.003) and heavier proteinuria, 3.9 (2.2-8.2) vs 2.0 (0.9-5.2) g/g (p< 0.001), when compared to non-MIRN patients.

Hematological malignancy was diagnosed in 83 cases (25,3%) (Multiple Myeloma in 62, non-Hodgkin Lymphoma in 6, Waldenström Macroglobulinemia in 6, Chronic Lymphoid Leukemia in 6, Plasmocytoma in 3). Among them, MIRN was diagnosed in 51 (61%) cases but tumoral lympho-plasmocytic infiltration was observed in 9 (11%) cases. In this subgroup of patients, no laboratory test could predict the presence of a specific nephropathy.

Among patients with no hematological malignancy (n=245), MIRN was diagnosed in 40 cases (16%) to confirm MGRS diagnosis. The markers that were most commonly associated with the presence of MGRS were positive Bence-Jones proteinuria (OR 4.7; 95%CI 2.2-10.3; p< 0.001), abnormal serum Free Light Chain (FLC) ratio (OR 4.2; 95%CI 1.7-10.7; p< 0.001), and serum electrophoresis spike >1.5 g/l (OR 5.9; 95%CI 2.6-13.5; p< 0.001). However, none of those markers had sufficient power to formally predict the result of the biopsy, as positive (PPV) or negative (NPV) predictive values were 36/41/45 % and 89/86/88 % respectively.

Conclusion: Almost one-third of patients with MG and kidney disease referred to our Department have biopsy-proven related nephropathy. Although negativity of Bence-Jones proteinuria and a normal serum FLC ratio are frequently associated with the absence of MGRS, kidney biopsy, beyond its diagnostic and prognostic interest, remains the most discriminating test.

P0205

SYMPTOM BURDEN IN AUSTRALIAN PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE AND END-STAGE KIDNEY DISEASE RECEIVING RENAL SUPPORTIVE CARE: A SINGLE CENTRE COHORT STUDY

Jenny Chen[1,2,3], Narelle Ilic[3], Holly Mitchell[3]

[1]University of New South Wales, School of Medicine, Sydney, Australia, [2]The George Institute, Sydney, Australia and [3]Wollongong Hospital, Renal Department, Wollongong, Australia

Background and Aims: Renal supportive care (RSC) is a novel multidisciplinary patient-centred model of care that focuses on symptom management and quality of life improvement in patients with advanced chronic kidney disease (CKD) and end-stage kidney disease (ESKD), including conservative care. Despite an increased interest in embedding RSC into routine nephrology practice, there is limited literature on the effects of symptom improvement in patients attending RSC services. We aimed to examine symptom improvement and symptom progression in patients receiving renal supportive care.

Method: Using Integrated Palliative care Outcome Scale Renal (IPOS-renal) scores collected during routine RSC clinics, we analysed the changes in individual IPOS-renal items and summative scores for symptoms associated with chronic kidney disease, stratified by time from the initial clinic visit (0-6 months, 6-12 months, and >12 months), in all patients attending our RSC service in a tertiary hospital between November 2015 and July 2019.

Results: Of 245 patients referred to our RSC service, 61 patients completed two or more IPOS-renal surveys. At initial visit, majority of the patients were reviewed at hospital outpatient clinic (n=42, 71%), followed by dialysis (n=8, 13%), home visit (n=6, 10%), and inpatient ward (n=4, 7%). The median (IQR) eGFR was 13 (7-16) ml/min/1.73m^2 and median Karnofsky score was 70 (60-80). Weakness (n=59, 97%) and poor mobility (n=52, 85%) were the most common initial complaints. For all reported symptoms, dyspnea improved the most for all three time periods (summative IPOS score changes of 28, 17, and 8 points for 0-6, 6-12, >12 months, respectively). Poor mobility was the only symptom that continued to deteriorate between 0-6 months despite attending renal supportive care (without a physiotherapist). For asymptomatic patients, more than half of the symptoms remained quiescent after attending RSC service for more than 12 months. Among newly developed symptoms, nausea, dyspnea, and drowsiness were most common between 0-6 months. In contrast, pruritus, dry mouth, and constipation were the most common complaints after 12 months.

Conclusion: RSC interventions provided symptom improvement in patients with advanced CKD and ESKD, but poor mobility remained a concern in this population. Incorporating physiotherapy to RSC may further improve symptom management.

P0206 RITUXIMAB IN ADULT ONSET OF IGA VASCULITIS WITH SEVERE RENAL INVOLVEMENT: A SINGLE CENTER EXPERIENCE

Roberta Fenoglio[1], Martina Cozzi[1], Savino Sciascia[1], Emanuele De Simone[1], Giulio Del Vecchio[1], Michela Ferro[1], Giacomo Quattrocchio[1], Carla Naretto[1], Giorgia Caputo[1], Andrea Careddu[1], Dario Roccatello[1]

[1]CMID-Nephrology and Dialysis Unit (ERK-net Member)-Center of Research of Nephrology, Rheumatology, and Rare Diseases, Interregional Coordinating Center of the Network of Rare Diseases,, G. Bosco Hospital and University of Turin, Italy, Turin, Italy

Background and Aims: IgA-vasculitis (IgAV) is a systemic small vessels vasculitis characterized by deposition of underglycosylated IgA1 immune complexes. Renal involvement indicates severity of illness and chronic kidney disease represents the most serious long-term complication of IgAV. Presently, no treatment is specifically recommended in IgAV Glucocorticoids (GC) have been traditionally thought to be effective in tempering systemic symptoms, but did not show long-term benefits either in reducing flares or progression of kidney disease. The effectiveness of conventional immunosuppressants is controversial. Recently Rituximab (RTX) has been proved to be effective in a few case series of adults with IgAV. However, long term results are lacking. Aim of the study: to evaluate the effectiveness of RTX as first line therapy in induction and maintenance of remission of adults with IgAV with biopsy-proven crescentic glomerulonephritis.

Method: We reviewed the clinical records of patients with adult-onset IgAV treated with RTX at our Center. Patients included 8 males and 4 females, mean age 45 years (range 19-75) with mean follow-up duration of 31 months (range 6-144). Diagnosis was based on the combination of clinical assessment, serological tests and histological analysis according to EULAR criteria. All patients (pts) had a biopsy proven IgAV-severe nephritis. RTX was given for the treatment of relapsing or refractory disease or because of definite contraindications to standard dose CS and/or conventional immunosuppressants. Patients received 4 weekly doses of RTX (375 mg/m^2) given alone (8 pts) or in combination with CS (4 pts). Disease activity was evaluated by Birmingham Vasculitis Activity Score version 3 at the onset and at 1, 6 and 12 months and at the end of follow up. Complete remission (CR) was defined as BVAS of 0

Results: Eleven pts (91.7%) achieved a clinical response at 6 months. Ten pts had a CR while 1 pt had a partial response and was given an additional dose of RTX after 12 months from induction due to persistent proteinuria (1gr/24 hrs), despite systemic remission. He achieved a CR 6 months later. One patient did not respond to RTX and was switched to MMF. Among the 10 pts with CR, 1 patient needed maintenance doses of RTX every 6 months due to relapse of palpable purpura; 1 relapsed after 15 months and received a new induction course showing a CR again.

Significant decrease in 24-hour proteinuria ($P = 0.043$), BVAS ($P = 0.031$),and CRP level from RTX initiation through the last follow-up visit was detected. RTX was generally well tolerated. One patient, who had a CR with RTX alone died after 6 months of follow-up for cardiovascular cause.

Conclusion: This extended experience confirms our initial results supporting the use of RTX in the treatment of IgAV with severe renal involvement. Indeed, RTX proved to be effective and safe for induction and maintenance of long-lasting remission. Present data also suggest that RTX is not only effective for severe and refractory IgAV, but can be also proposed as a first line therapy.

P0207

PLASMA CHEMOKINE CXC MOTIF-LIGAND 16 AS A PREDICTOR OF RENAL PROGNOSIS IN IMMUNOGLOBULIN A NEPHROPATHY

Ran Luo[1], Yi Yang[1], Dan Chang[1], Tingting Liu[1], Yue-Qiang Li[1], Wei Dai[1], Mei-Ying Zuo[1], Yu-lin Xu[1], Chun-Xiu Zhang[1], Gang Xu[1], Shu-wang Ge[1]

[1]Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Department of Nephrology,, Wuhan, P.R. China

Background and Aims: A recognized non-invasive biomarker to improve risk stratification of IgA nephropathy (IgAN) patients is scarce. CXCL16 has been shown to play a key role in inflammatory disease as chemoattractant, adhesion and fibrosis factor. This study assessed the possibility of plasma CXCL16 as a potential biomarker in IgAN patients.

Method: Plasma CXCL16 was measured in 230 patients with renal biopsied IgAN from 2012 to 2014. The patients were followed for 41.3 months with 50% reduction in eGFR or ESRD as end-points.

Results: The plasma CXCL16 levels in IgAN patients were significantly correlated with the uric acid, estimated glomerular filtration rate and tubular atrophy/interstitial fibrosis score in multivariate analysis. In addition, the counts of CD4+ T cells, CD8+ T cells and CD20+ B cells in renal biopsies of IgAN patients were significantly correlated with the plasma CXCL16 levels, but not CD68+ macrophage. Finally, we concluded that patients with higher plasma CXCL16 levels had a higher risk of poor renal outcome compared with those with lower. No association was observed between the CXCL16 polymorphisms and clinical parameters including plasma CXCL16 levels and prognosis.

Conclusion: Plasma CXCL16 levels were associated with clinical parameters, pathological damage, the CD4+ T cells, CD8+ T cells and CD20+ B cells infiltration in renal tissue and renal outcome in IgAN patients. Plasma CXCL16 might be a potential prognosis predictor in Chinese IgAN patients.

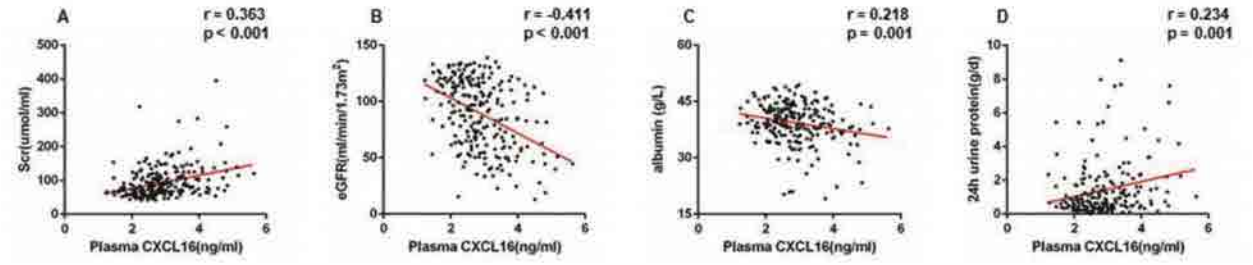


Figure 1

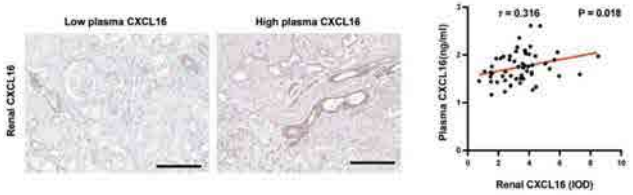


Figure 2

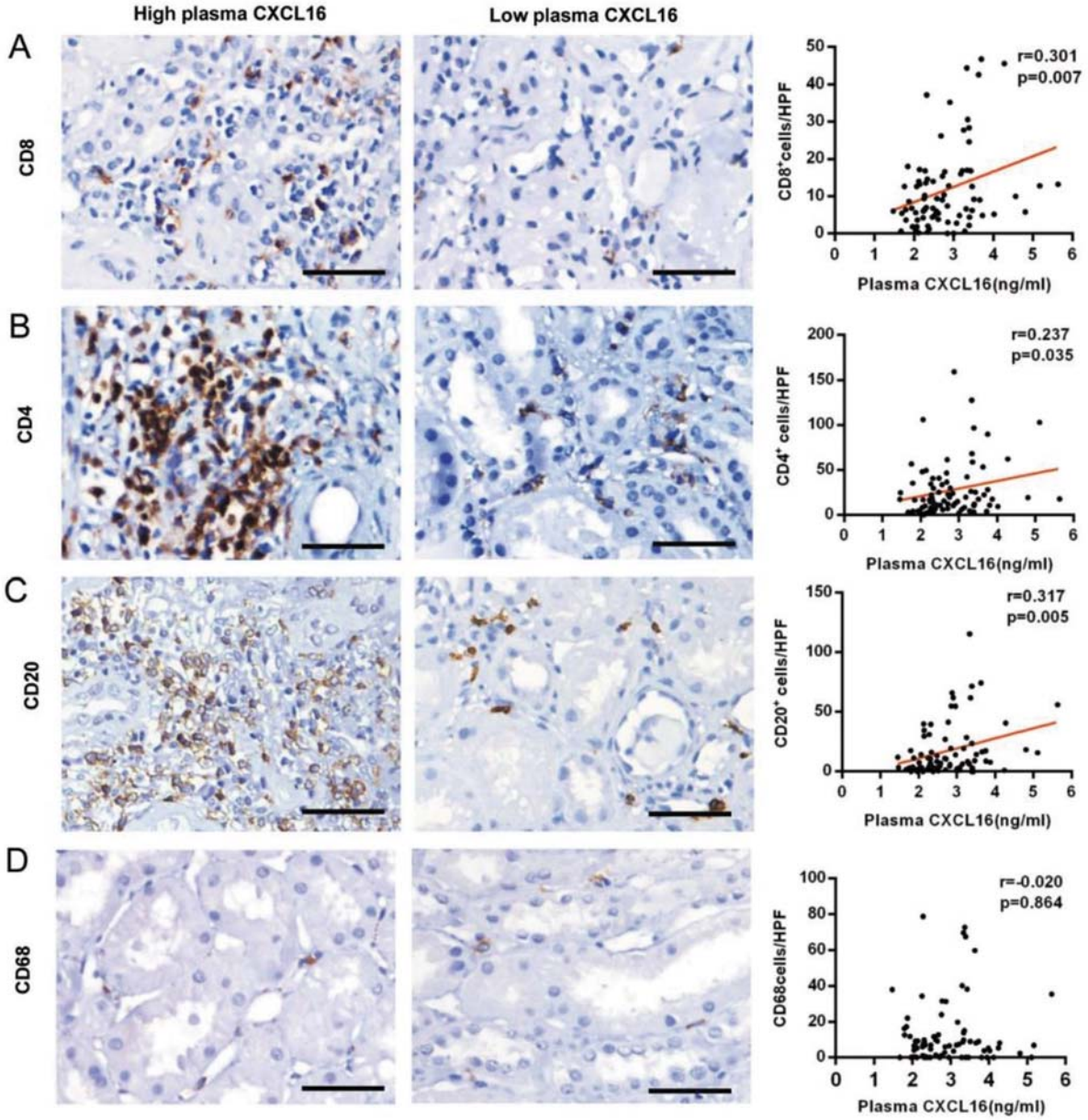


Figure 3

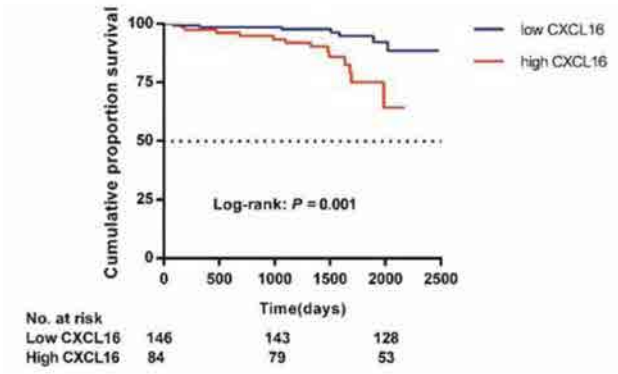


Figure 4

P0208 **DIFFERENTIAL ADAPTATION OF RENAL FUNCTION IN TWO TYPES OF INTENSE PHYSICAL EXERCISE**

Armando Coca[1], Pablo Gonzalez[1], Maria Jesus Rollan[1], Beatriz Toribio[1], Hortensia Marcos[2], Veronica Fidalgo[1], Arturo Lorenzo[1], Melchor Andres[3], Isabel Acosta-Ochoa[1], Alicia Mendiluce[1]

[1]Hospital Clinico Universitario, Nephrology, Valladolid, Spain, [2]Hospital Clinico Universitario, Clinical Analysis, Valladolid, Spain and [3]Centro Regional de Medicina Deportiva, Valladolid, Spain

Background and Aims: Marathon running induces AKI even in adequately prepared and healthy athletes. Heat stress, maintained during more than 2h, has been proposed as one of the leading causes of AKI in marathons runners. Other possible explanations of AKI in this setting could be associated with a reduction of blood supply to the kidneys during the exercise, inadequate hydration or actual structural damage due to microtraumatisms. However, the effect of vigorous exercise of shorter duration on renal function has not been previously described although most risk factors described could also affect kidney function in this type of physical activity.

Method: 40 volunteer healthy athletes were enrolled in this study. Subjects participated in two physical tests (10km running, 1.5km swimming) which were separated by at least two weeks from each other. These tests were chosen because of their similar oxygen consumption rate and metabolic load. Vitals, blood and urine samples were collected immediately before and after each test. Informed consent was obtained from all participants. The project was funded by Consejería de Sanidad, Junta de Castilla y León (GRS1732/A/18).

Results: Athletes ranged from 23 to 53 years old. 35% were female. A comparison of hemodynamic and analytical parameters is summarized in Table 1. Running induced a significantly higher rise of serum creatinine and inflammatory markers compared to swimming. Additionally, running caused an increment of serum phosphorus and uric acid levels. Both types of exercise caused a mild increase of urinary albumin/creatinine ratio.

Conclusion: Compared to swimming, running was associated with a greater rise of serum creatinine, possibly linked to a higher degree of acute inflammation and blood flow redistribution to the muscles. The rise of serum uric acid levels may be associated with increased metabolism and reduced elimination of this molecule while running.

	10km Running	1.5km swimming	P value
N	40	40	
Duration of the test, min	48±6	36±9	<0.001
Δ SBP, mmhg	-15.2±13.1	-7.7±10.6	0.008
Δ DBP, mmHg	-6.9±9.7	-5.5±9.5	0.528
Body temperature (A), °C	35.3 (34.4-35.9)	35.4 (34.6-36)	0.818
Δ Body temperature, °C	-0.5 (-1.1-0.7)	-0.6 (-1.3-0.2)	0.138
Δ Hemoglobin, g/dl	0.1±0.5	0±0.3	0.565
Leukocytes (A), cells/ μl	7260 (6285-8375)	6080 (5360-7045)	0.002
Δ Leukocytes, cells/μl	1085 (460-1685)	360 (-335-858)	<0.001
Serum Creatinine (A), mg/dl	1.14±0.16	1.02±0.15	0.001
Δ Serum Creatinine, mg/dl	0.19±0.09	0.05±0.09	<0.001
Uric Acid (A), mg/dl	5.2±1	5.2±1.2	0.968
Δ Uric Acid, mg/dl	0.65 (0.4-0.8)	0.2 (0-0.5)	0.001
Phosphorus (A), mg/dl	4±0.7	3.5±0.6	0.002
Δ Phosphorus, mg/dl	0.9±0.5	0.5±0.5	0.001
Sodium (A), mEq/l	141 (140-142)	140 (139-141)	0.154
Δ Sodium, mEq/l	1 (-0.2-2)	0 (-1-1)	0.014
Δ Albumin, g/dl	0 (-0.1-0.2)	0.1 (-0.1-0.14)	0.503
CPK (A), U/l	237 (150-460)	232 (131-364)	0.495
Δ CPK, U/l	37 (29-53)	29 (14-53)	0.081
LDH (A), U/l	225 (202-246)	195 (175-233)	0.003
Δ LDH, U/l	26.9±16.3	10.8±16.7	<0.001
Interleukin-6, pg/ml	5.4 (4-7)	5.3 (3.6-7.2)	0.779
Δ Interleukin-6, pg/ml	2 (1.5-3.6)	1.33 (0.3-2.1)	0.001
Urine albumin/ creatinine, mg/g creat.	19 (9-47)	34 (8-98)	0.262
Δ Urine albumin/ creatinine, mg/g creat.	16 (4-36)	42 (5-96)	0.113
Urine sodium (A), mEq/l	69 (44-109)	76 (40-147)	0.75
Δ Urine sodium, mEq/l	-21.2±45	-20.7±40.9	0.959
>5 RBC/HPF, n (%)	1 (2.5)	0 (0)	0.455

A, after the test. CPK, creatine phosphokinase. DBP, diastolic blood pressure. LDH, lactate dehydrogenase. RBC/HPF, red blood cell per high power field. SBP, systolic blood pressure.

P0209 PRESENTATION AND OUTCOMES OF ANCA ASSOCIATED VASCULITIS: THE SCOTTISH EXPERIENCE

Kate Stevens[1], Dana Kidder[2], Michelle Lim[3], Rob Hunter[4], Mike Kelly[5], Nicola Joss[6], Zoe Cousland[7], Jamie Traynor[1], Colin C. Geddes[1], Emily McQuarrie[1], Bruce Mackinnon[1]

[1]Glasgow Renal and Transplant Unit, Glasgow, United Kingdom, [2]Renal Unit, Aberdeen Royal Infirmary, Aberdeen, United Kingdom, [3]Renal Unit, Ninewells Hospital, Dundee, United Kingdom, [4]Renal and Transplant Unit, Edinburgh Royal Infirmary, Edinburgh, United Kingdom, [5]Renal Unit, Dumfries and Galloway Royal Infirmary, Dumfries, United Kingdom, [6]Renal Unit, Raigmore Hospital, Inverness, United Kingdom and [7]Renal Unit, University Hospital Monklands, Airdrie, United Kingdom

Background and Aims: This is a national project undertaken on behalf of the Scottish Renal Biopsy Registry describing the presentation, biopsy appearances, management and outcomes of patients presenting with a new diagnosis of renal biopsy proven ANCA associated vasculitis (AAV) to all units in Scotland.

Method: The Scottish Renal Biopsy Registry collects data annually on all renal biopsies performed across Scotland. From the Registry, all patients with a possible diagnosis of AAV found on renal biopsy performed between1/1/2014 and 31/12/2017 were identified. Individual units searched the electronic patient records of each patient and identified all those with a new diagnosis of AAV. Those undergoing repeat biopsy or who were not felt to have AAV on biopsy were excluded. Demographic data including immunological and outcome data were recorded and statistical analysis was undertaken in SPSS (v22).

Results: 267 patients were identified as having AAV across 8 centres and followed up for an average of 989 (IQR 610-1247) days. In 52% (n= 140) the biopsy indication was acute kidney injury.

38% (n=101) had a diagnosis of granulomatosis with polyangiitis (GPA). 52% (n=140) were female and the mean age at biopsy was 66.6±12.1 years. 38% (n=100) were PR3 positive. The average number of glomeruli on biopsy was 14 (IQR 11-21) with 3 (IQR 2-7 crescents. 28% (IQR 7-51) of viable glomeruli contained crescents. 41% (n=110) had at more than 10% interstitial fibrosis on biopsy. Creatinine at biopsy was 208μmol/L (IQR 141-380 μmol/L) and at 90 days 141 μmol/L (IQR 101-222 μmol/L).

Most patients received standard induction therapy of cyclophosphamide and steroid. 24% (n=65) had plasma exchange at presentation and 11% (n=30) renal replacement therapy (RRT).

15% (n=39) patients relapsed with an average time to relapse of 511 (IQR 223-11127) days. 62% (n=24) of relapses were treated with rituximab. Those with GPA relapsed earlier.

12% (n= 31) developed end stage renal disease (ESRD). 18% (n=49) died with 14 patients (5%) dying within 90 days of biopsy. Average time to death was 246 (IQR 89-321) days. There was a trend towards an increased risk of death with those who developed ESRD. Patients who received PEX or RRT during initial admission were no more likely to relapse or die than those who did not.

Conclusion: This study accurately describes the presentation, management and outcomes of patients with AAV and renal involvement in Scotland. This allows comparison between centres within Scotland and other countries. The cohort will added to and followed to look at longer term outcomes.

P0210

ASSOCIATIONS BETWEEN CHANGES IN RENIN ACTIVITY AND ALDOSTERONE LEVELS AND CHANGES IN KIDNEY FUNCTION AFTER TREATMENT FOR PRIMARY ALDOSTERONISM: A LARGE MULTICENTER COHORT STUDY IN JAPAN

Yusuke Kobayashi[1,2], Yuichiro Yano[3], Tatsuya Haze[2], Yu Hatano[3], Kouichi Tamura[2], Mitsuhide Naruse[4], JPAS/ JRAS study group[5]

[1]Yokohama City University Hospital, YCU Center for Novel and Exploratory Clinical Trials (Y-NEXT), Yokohama, Japan, [2]Yokohama City University Graduate School of Medicine, Department of Medical Science and Cardiorenal Medicine, Yokohama, Japan, [3]Duke University, Department of Community and Family Medicine, North Carolina, United States of America, [4]Kyoto Medical Center, National Hospital Organization, Clinical Research Institute of Endocrinology and Metabolism, Japan and [5]AMED, Japan

Background and Aims: Greater reduction in estimated glomerular filtration rate (eGFR) after treatment for primary aldosteronism (PA) reflects improvement of glomerular hyperfiltration associated with PA and leads to better patient outcomes. However, little is known regarding the mechanisms underlying eGFR reduction after treatment for PA.

Method: We analyzed data from the nationwide PA registry in Japan. Patients were assigned to adrenalectomy (n=419) and mineralocorticoid receptor (MR) antagonist (n=674) groups. We assessed associations between changes in BP, plasma renin activity and aldosterone levels, and eGFR after treatment for both groups.

Results: Reduction in eGFR after treatment was greater in the surgical compared to MR antagonist treatment group (median -11.0; 95% CI, -12.2 to -9.8 ml/min/1.73 m2 vs. -3.5; 95% CI, -4.3 to -2.7 ml/min/1.73 m2; $p < 0.001$). In a multivariable linear regression, the adjusted betas (95% confidence interval) for change in eGFR after treatment for each standard deviation higher level of plasma renin activity and aldosterone were -2.12 (-4.10, -0.14) and 2.41 (1.20, 3.62) ml/min/1.73 m2, respectively, in the adrenalectomy group, and -0.65 (-1.28, -0.02) and –0.64 (-2.04, 0.76) ml/min/1.73 m2, respectively, in the MR antagonist group. Plasma renin activity Change in mean arterial pressure after treatment was not associated with change in eGFR in either group.

Conclusion: Changes in plasma renin activity and aldosterone levels but not BP, after treatment for PA were associated with greater reductions in eGFR. Post-treatment improvements in glomerular hyperfiltration may be attributable to suppressed MR activity within the kidneys, not to reductions in systemic blood pressure. It is important for clinicains not only to treat PA, but also to confirm adequate suppressed MR activity after treatment for correction of glomerular hyperfiltration.

P0211 **GLOMERULAR HYPERFILTRATION AND CANCER: A NATIONWIDE POPULATION-BASED STUDY**

Yaerim Kim[1], Jeongsoo Yoon[2], Jin Hyuk Paek[1], Woo Yeong Park[1], Kyubok Jin[1], Seungyeup Han[1], Kwon Wook Joo[3], Dong Ki Kim[3]

[1]Keimyung University School of Medicine, Department of Internal Medicine, Daegu, Korea, Rep. of South, [2]Yoon's Internal Medicine Clinic, Daegu, Korea, Rep. of South and [3]Seoul National University Hospital, Department of Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Glomerular hyperfiltration is associated with all-cause mortality. Herein, we evaluated the association between glomerular hyperfiltration and the development of malignant disease, the most common cause of death, in an Asian population.

Method: We retrospectively reviewed the National Health Insurance Service database of Korea for people who received national health screenings from 2012 to 2013. Glomerular hyperfiltration was defined as the 95th percentile and greater after adjusting for age and sex. We performed a multivariate Cox regression analysis using glomerular hyperfiltration at the first health screening as the exposure variable and cancer development as the outcome variable to evaluate the impact of glomerular hyperfiltration on the development of malignant disease.

Results: A total of 1,953,123 examinations who followed-up for 4.9 years were included in this study. Among the 8 different site-specific malignant disease categories, digestive organs and female genital organs showed a significant associations between glomerular hyperfiltration and malignancy. The population with glomerular hyperfiltration showed an increased risk for stomach cancer (adjusted hazard ratio [aHR], 1.27), colorectal cancer (aHR, 1.23), and liver or intrahepatic malignancy (aHR, 1.40). In addition, the risk for uterine and ovarian cancer was significantly increased in the population with glomerular hyperfiltration (aHR, 1.36).

Conclusion: Glomerular hyperfiltration was associated with an increased risk for the development of malignant diseases in specific organs, such as the stomach, colorectum, uterus, and ovary. Glomerular hyperfiltration needs to be considered a significant sign of the need to evaluate the possibility of hidden adverse health conditions, including malignancies.

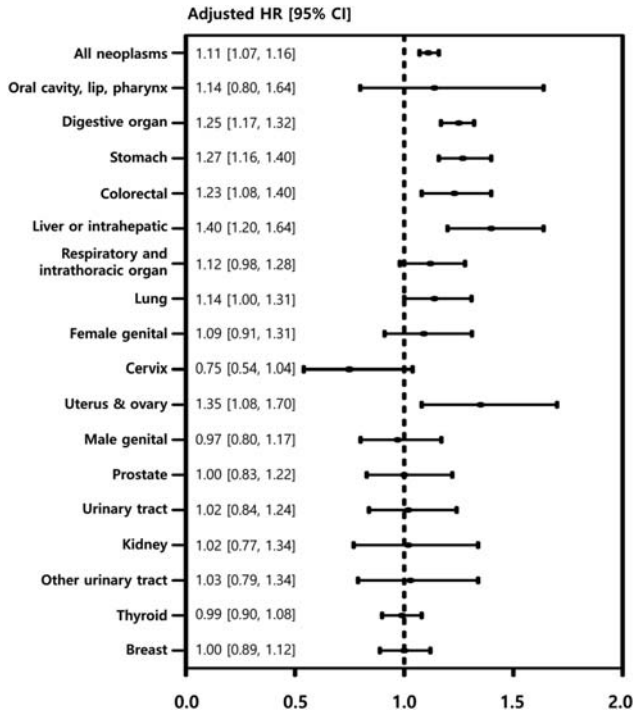


Figure: Adjusted hazard ratio for development of malignancy in the glomerular hyperfiltration group compared to control.

P0212 **IMMUNOSUPPRESSIVE TREATMENT OF PATIENTS WITH ANCA ASSOCIATED VASCULITIS (AAV) IN CHRONIC DIALYSIS PROGRAM**

Ibolya File[1], László Ujhelyi[1], Jozsef Balla[1], László Bidiga[2], Trinn Csilla[1], Csilla Markóth[1], Szűcs Gabriella[3], János Mátyus[1]

[1]University of Debrecen, Institute of Internal Medicine, Nephrology Department, Debrecen, Hungary, [2]University of Debrecen, Institute of Pathology, Debrecen, Hungary and [3]University of Debrecen, Institute of Internal Medicine, Rheumatology Department, Debrecen, Hungary

Background and Aims: There are numerous studies on AAV, however, data describing the use of immunosuppressive treatment in AAV patients (pts) on chronic dialysis are limited. Most studies found that the incidence of infection is much higher than that of relapses (0.05-0.1 pt per year), suggesting that immunosuppression should be stopped after 3 months in pts with end-stage renal failure.

Material, Method: Retrospective analysis of immunosuppressive treatment in pts on chronic dialysis due to AAV. From 1995 to 2019 139 pts were diagnosed with AAV. Among them 38 patients (26 female, 12 male, mean age 58 years) needed chronic dialysis (>90 days) due to severe renal AAV (29), relapsing renal disease (6) or progressive CKD without active vasculitis (3).

Results: Microscopic polyangiitis was diagnosed in 20, granulomatosis with polyangiitis in 14, eosinophilic granulomatosis with polyangiitis in 4 cases. MPO-ANCA was more frequent than PR3-ANCA (23 vs 12), in one case both ANCAs were positive, and in two cases both were negative. The mean dialysis duration was 55 months (4–180 months). 18 pts (47%) had at least one relapse during the observation period. The mean age, the clinical diagnosis, the type of ANCA did not cause any difference, the dialysis time was longer in the relapsed pts group (72+/-38 vs. 40+/-29 months) compared to pts without relapse. High relapse rate was seen in 6 cases. Three patient had continuously high level of PR3-ANCA without relapse or any sign of disease. Relapses were treated mostly with combined therapy of corticosteroids and oral/intravenous cyclophosphamide followed by azathioprin maintenance therapy. Cortocosteroid alone was used in 7 pts, rituximab in five pts as maintenance therapy. Serious infection (needing hospital care) rate during any immunosuppressive treatment was 0.12 per patient-years. There were 12 deaths on dialysis, the median time to death was 61 months (range 3–132). The deaths rate was higher (9/18 vs. 4/20) in relapsed pts, 4 occurring during immunosuppressive treatment. Causes of deaths were cardiovascular (8), sepsis (3), malignancy (2 pts). Seven pts received kidney grafts, 15 pts remained on dialysis, but in three case dialysis could be discontinued after 16, 35 and 36 months.

Conclusion: Our study points to higher relapse rate and lower serious infection rate in AAV pts on chronic dialysis compared to previous studies. It seems reasonable to continue immunosuppression above 3 months in pts remaining on chronic dialysis. This approach may decrease the relapse rate preventing damage of other organs, allowing transplantation and in some pts recovery of renal function could be achieved.

P0213 CHRONIC KIDNEY DISEASE AND ATRIAL FIBRILLATION: RISK OF COMPLICATIONS

Sherzod Abdullaev[1], Rano Igamberdieva[1]

[1]*Tashkent pediatric medical institute, Internal medicine, Tashkent, Uzbekistan*

Background and Aims: The assessment of the thromboembolic risk (TE) and transient ischemic attacks (TIA) in patients with chronic kidney disease (CKD) in combination with atrial fibrillation (AF) and the effect of complex treatment, including rivoraxaban.

Method: The study included 28 patients, 16 men and 12 women, average age - 57.8 ± 6.9 years. Patients with 3rd stage CKD (GFR 30-50 ml/min) associated with various forms of non-valve AF were examined. All patients were at high risk according to the classification of stroke risk stratification. The risk of thromboembolic complications was assessed using the CHA2DS2-VASc scale. Depending on the form of AF, patients with CKD were divided into 2 groups: with paroxysmal AF and CKD (n = 9) and persistent AF and CKD (n = 19). The average age in the 2 groups was 52.7 ± 6.4 and 58.4 ± 7.4 years, respectively. A history of 11 patients (39.3%) had ischemic stroke and TIA. All patients underwent echocardiography and transesophageal echocardiography (TE EchoCG). The peak blood flow velocity was a quantitative reflection of the hemodynamic state of left atrium (LA). Hemoglobin, creatinine, eGFR (CKD-EPI) and coagulogram were also monitored.

Results: According to the results of TE echocardiography, the size of the LA in patients with stage 3 CKD and paroxysmal AF is less than in the group of persistent AF (43.7±2.8 mm and 48.6±5.8 mm, respectively, $p<0.05$). The average value of the peak blood flow velocity was reduced in all patients - 34.88±10.59 cm/sec, in the presence of thrombosis this parameter significantly decreased - 24.3±2.49 cm/sec ($p<0.001$). Atrial thrombi were detected in 10 patients (35.7%). Spontaneous echocardiographic contrast (SEC) was found in 7 people (25%). We found that in patients with a thrombus in the auricle of the LA ejection fraction (EF) was significantly lower than in patients without thrombi. The average score on the CHA2DS2-VASC scale was 5. A higher incidence of a thrombus in the auricle of the LA was revealed in patients with persistent AF than paroxysmal AF (7 and 3, respectively). Only 15 patients (53.6%) received oral anticoagulants (OAC) on an outpatient basis, and 2 (7.1%) took aspirin. In the hospital, everyone was prescribed rivoraxaban in a dose of 15 mg once a day. After 4 weeks of treatment with rivoraxaban, from 7 patients with a revealed SEC during repeated TE echocardiography, the disappearance of SEC was observed in 4 patients (57%). In 6 patients (60%) was revealed thrombus lysis in the LA. In 16 (57.1%) patients was noted an increase in GFR above 50 ml/min. Coagulogram values in all patients throughout the observation were within normal limits.

Conclusion: TE echocardiography allows to distinguish among patients with stage 3 CKD and AF group with a high risk of stroke and TIA. The use of rivoraxaban for 4 weeks allows lysis of blood clots in the auricle of the LA in 60% of patients, and the disappearance of the SEC effect in 57% of cases. This allows us to recommend rivoraxaban for the treatment of patients with AF, especially with a high risk of thromboembolic complications.

P0214 **THE IMPORTANCE OF POINT-OF-CARE ULTRASOUND FOR NEPHROLOGIST IN EMERGENCY ROOM: A MONOCENTRIC STUDY**

Paolo Albrizio[1], Silvano Costa[1], Annalisa Foschi[1], Ivo Angelo Antonio Milani[1], Stefano Rindi[1], Manuela Zucchi[1], Fabio Milanesi[1]

[1]*Voghera Hospital - ASST Pavia, Nephrology and Dialysis Unit, Voghera, Italy*

Background and Aims: ultrasound is progressively expanding beyond Radiology Units getting a key role for the main part of medical and surgical specializations. Nephrology proves how a good mastery in ultrasound is critical for studying many aspects of renal disease such as acute kidney injury (AKI), chronic kidney disease (CKD), secondary causes of hypertension, kidney transplant, hemodialysis vascular accesses, hyperparathyroidism and so on. A place where is important for the Nephrologist to use ultrasound for getting a diagnostic help is hospital emergency room. Here, while having to face frequently with not optimal conditions for outdated ultrasound machines and patients without adequate preparation or compliance, the collection of few critical information with point-of-care ultrasound can make the difference in the diagnostic and therapeutic process.

Method: unprovided of an hospital ward our Unit activity is focused on dialysis, and nephrological examinations for patients hospitalized or not. We evaluated all the advices required to our Unit from the emergency room of our hospital between August 1st, 2016 and July 31th 2019. Then we selected those when Nephrologist decided to evaluate the patient also by point-of-care ultrasound. We collected data about age, sex, diagnostic questions, ultrasound findings, diagnosis and subsequent therapeutic processes.

Results: as shown in figure, among 393 advices, Nephrologists decided to use point-of-care ultrasound in 70 of them (18%, 47 males, 23 females, medium age 75,4±14 years).

More frequent diagnostic questions were related to alterations of biochemical renal function markers (77%) divided between AKI with (30%) or without (47%) a known history of CKD. Less frequent diagnostic questions were focused on clinical anomalies such as oligo-anuria (16%) and lower extremity edema and dyspnea (7%).

During point-of care ultrasound, more common findings were signs of CKD (41%) and urinary retention (48% divided in bladder retention -22%-, monolateral -4%- or bilateral hydronephrosis -22%-). Less frequent findings were normal kidneys (9%), unknown adult polycystic kidney disease (ADPKD) (1%) and suspect kidney myeloma (1%).

Guided by ultrasound, Nephrologist's more frequent diagnosis were: AKI secondary to obstruction by various causes (46%: prostatic hypertrophy, kidney stones, dislodgment of bladder catheter or nephrostomy, solitary kidneys, intrinsic o extrinsic obstruction for subsequently diagnosed gynecological or urological cancers) and dehydration (36%). Less common diagnosis were congestive heart failure (11%) and uremia (7%).

Among all patients, only 17% were discharged: 8.3% entrusted to their general practitioner after intravenous hydration, 50% addressed to a nephrological follow-up, frequently after intravenous hydration, and 41.6% addressed to urological follow-up frequently after urinary catheter placement. The main part of patients (73%) were conservative treated by Nephrologist and hospitalized in various units: Internal Medicine (72,5%), Urology (21,5%, frequently after urinary catheter placement), Cardiology (4% with or without start of intravenous diuretic therapy) and Gynecology (2%). Finally, a significant part of patients (10%) required urgent hemodialysis treatment before being hospitalized.

Conclusion: in evaluated population, more frequent diagnosis formulated during nephrological advices in emergency room by our Unit were CKD and AKI due to obstructive causes. Besides these, point-of-care ultrasound allowed to promptly detect less frequent but not less important conditions such as unknown ADPKD, solitary kidneys or kidney myeloma. These data clarify how point-of-care ultrasound provides an important support for Nephrologist in clinical evaluation of emergency room patients, allowing to direct the subsequent investigations reducing useless examination and focusing the therapeutic process.

Nephrological advices	
With ultrasound	70
Without ultrasound	323
Total	393

Sex	
Males	47
Females	23

Age (mean±SD)
75.4±14

Diagnostic questions	N°	%
AKI	21	30%
AKI in CKD	33	47%
Lower extremity edema and dyspnea	5	7%
Oligo-anuria	11	16%
	70	100%

Ultrasound findings	N°	%
Normal	6	8,57%
Bladder retention	15	21,43%
Bilateral hydronephrosis	15	21,43%
Monolateral hydronephrosis	3	4,29%
CKD	29	41,43%
ADPKD	1	1,43%
Suspect kidney myeloma	1	1,43%
	70	100%

Diagnosis	N°	%
Dehydration	25	36%
Obstruction by kidney stones	5	7%
Obstruction by prostatic hyperplasia	13	19%
Obstruction by other urological condition	12	17%
Obstruction by gynecologycal conditions	2	3%
Congestive heart failure	8	11%
Uremia	5	7%
	70	100%

Subsequent diagnostic process	N°	%
Intravenous hydration and follow-up by general practitioner	1	1,4%
Intravenous hydration and nephrological follow-up	5	7,1%
Nephrological follow-up	1	1,4%
Urological follow-up	1	1,4%
Urinary catheter placement and urological follow-up	4	5,7%
Hospitalization in Cardiology Unit	1	1,4%
Start of intravenous diuretic therapy and hospitalization in Cardiology Unit	1	1,4%
Hospitalization in Gynecology Unit	1	1,4%
Hospitalization in Internal Medicine Unit	6	8,6%
Urinary catheter placement and hospitalization in Internal Medicine Unit	9	12,9%
Start of intravenous diuretic therapy and hospitalization in Medicine Unit	5	7,1%
Intravenous hydration and hospitalization in Internal Medicine Unit	17	24,3%
Hospitalization in Urology Unit	9	12,9%
Urinary catheter placement and hospitalization in Urology Unit	2	2,9%
Urgent hemodialysis treatment and hospitalization in Internal Medicine Unit	5	7,1%
Urgent hemodialysis treatment and hospitalization in Urology Unit	2	2,9%
	70	100%

Figure 1

Figure:

P0215 **EXCESSIVE TISSUE SODIUM STORAGE IN PATIENTS WITH NON-DIALYSIS DEPENDENT CARDIO-RENAL SYNDROME IS COMPARABLE TO HEMODIALYSIS PATIENTS.**

Sandrine Lemoine[1,2], Fabio Salerno[1,2], Alireza Akbari[1,2], Christopher McIntyre[1,2]

[1]London Health Sciences center, Lilibeth Caberto Kidney Clinical research unit, London, Canada and [2]Western University, Medical biophysics, London, Canada

Background and Aims: Both CKD and heart failure (HF) are characterized by a propensity to retain sodium. Renal dysfunction worsens the progression of heart failure and is associated with worse outcomes. This may be a result of synergistic aggravation of sodium retention by the two conditions. We aimed to compare tissue Na storage in skin and muscle between cardiorenal (CR) patients and patients with a range of renal dysfunction, including those requiring hemodialysis (HD).

Method: Proton and ^{23}Na images of the lower limb were acquired on a 3T MRI. We studied 9 CR patients, 7 matched CKD 2-5 patients (without HF) and 31 established HD patients. Regions of interest including skin and soleus were drawn on images to provide a quantitative sodium measurement and these tissue concentrations compared between groups. Blood samples were drawn at each scan in all patients. Spot urine samples were collected for CR patients.

Results: For CR patients, mean age was 66 ± 8 years, 78% of male, mean estimated glomerular filtration rate (eGFR) was 52 ± 18 mL/min/1.73m^2, urea was 11 ± 6 mmol/L. For HD patients, mean age was 66 ± 8.7 years, 68% of male and mean dialysis vintage was 38 ± 37 months for HD patients. Mean age was 63 ± 8, 71 % of male, eGFR 45 ± 29 mL/min/1.73m^2 for CKD patients. CR patients displayed an increased amount of salt in skin (32.5 ± 13 mmol/L) and muscle (26 ±4 mmol/L) with levels significantly higher than that seen in GFR matched controls (without HF) and comparable to HD patients (31 ±12 and 28 ± 6 mmol/L p=0.9 and p=0.3 respectively) without meaningful residual renal function.

Conclusion: The combination of HF and CKD is associated with intense tissue Na storage; resulting in tissue Na accumulation in CR patients (with reasonably well-preserved renal function) similar to CKD patients requiring HD.

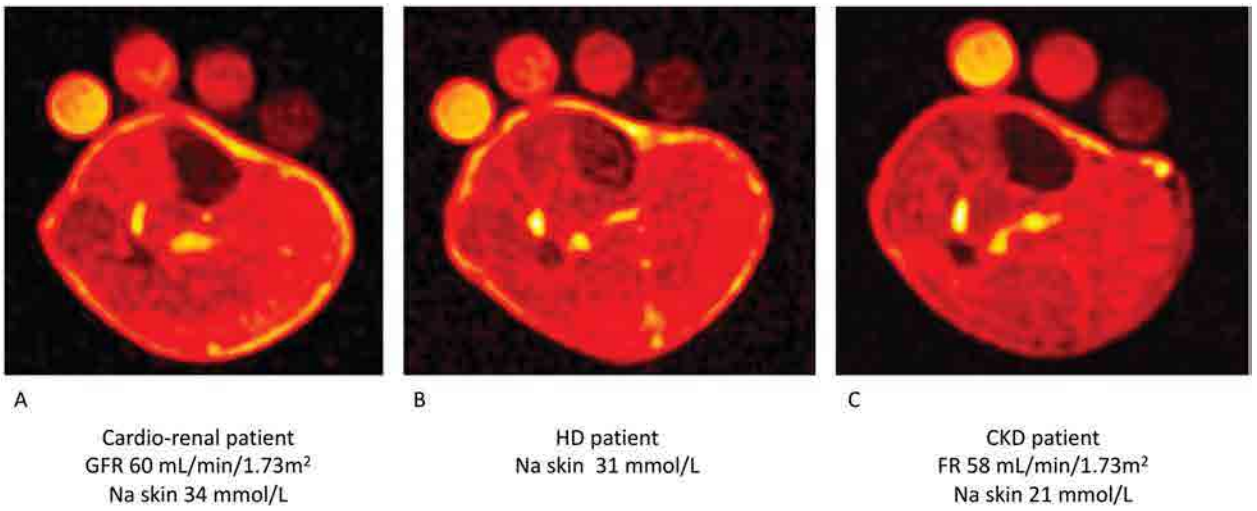


Figure:

P0216 CHECK POINT INHIBITORS AND CANCER. RENAL ADVERSE EVENTS: CASE SERIES.

Selene González Nuez[1], Germán Pérez Suárez[1], Ana Ramírez Puga[2], Delvys Rodríguez Abreu[2], Saulo Jesús Fernández Granados[1], Noemí Esparza Martín[1], César García Cantón[1]

[1]Hospital Insular, Nephrology, Las Palmas de Gran Canaria, Spain and [2]Hospital Insular, Oncology, Las Palmas de Gran Canaria, Spain

Background and Aims: The treatment of cancer with check point inhibitors (CPI) has demonstrated significant benefits. CPI initiate antitumor immunity through negative regulatory components in T cells. However, these agents are associated with adverse events related to the immune system that can affect several organs. Initially, a low incidence of renal adverse events was reported, although recent data suggest an incidence between 9.9% and 29%. The objective of the study was to describe a case series that presented renal dysfunction related to CPI treatment.

Method: 11 patients were studied retrospectively (67% males, mean age 69 ± 13 years), diagnosed with Neoplasms (9 advanced lung cancer, 7 of them metastatic and 2 metastatic melanomas) treated with CPI, who developed renal dysfunction. 5 patients with lung cancer were treated with Pembrolizumab, 3 with Nivolumab and 1 with Pembrolizumab + Ipilimumab combination. Patients with melanoma received Pembrolizumab. In 55% of the cases, immunotherapy was used as first line of antitumor treatment. Demographic and clinical-analytical data were collected, as well as the evolution of renal function.

Results: The median plasma creatinine prior to receiving treatment with CPI was 0.9 mg/dl [0.67-1.5]. The maximum creatinine reached after treatment with CPI was 2.5 mg/dl [1.8-7.5] with Pembrolizumab, 5.4 mg/dl [3-6.7] with Nivolumab and 4.3 mg/dl with the combination Pembrolizumab + Ipilimumab. Renal dysfunction occurred in the fifth cycle of treatment with Pembrolizumab and in the third cycle with Nivolumab and Pembrolizumab + Ipilimumab.

All patients received steroids (1mg/kg) and CPI were permanently discontinued in 3 patients with Pembrolizumab (43%), 1 with Nivolumab (33.3%) and 1 with Pembrolizumab + Ipilimumab (100%). Renal biopsy was performed in 4 patients who initially did not respond to steroids, resulting in acute tubulo-interstitial nephritis (ATIN), 1 of them with granuloma formation and worse renal evolution.

All patients recovered renal function partially or totally, except 1 treated with Pembrolizumab who remained with advanced kidney disease. Tumor progression was observed in 3 patients and 2 died.

Conclusion: CPI have demonstrated significant clinical benefits in the regression and prolonged stabilization of many tumors. The main cause of renal dysfunction after the use of CPI in our patients was the ATIN, with a good initial response to steroids and drug suspension. The presence of granulomas in renal biopsy confers a poor prognosis. It is an increasingly frequent entity in clinical practice, and because of its complicated management, it requires a multidisciplinary approach.

P0217

NEUTROPHIL TO LYMPHOCYTE RATIO AT ADMISSION CAN ESTIMATE VASCULITIS ACTIVITY AND POOR PROGNOSIS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: A RETROSPECTIVE STUDY

Inês Duarte[1], José Agapito Fonseca[1], Joana Gameiro[1], Estela Nogueira[1], Cristina Outerelo[1], Sofia Jorge[1], José António Lopes[1], José Oliveira Guerra[1]

[1]*Centro Hospitalar Universitário Lisboa Norte, Nephrology, Lisboa, Portugal*

Background and Aims: Anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) is a multisystemic disease. Despite the improvement in mortality rate since the introduction of immunosuppression, long-term prognosis is still uncertain not only because of the disease activity but also due to treatment associated adverse effects. The neutrophil-to-lymphocyte ratio (NLR) has been demonstrated as an inflammatory marker in multiple settings. In this study, we aimed to investigate the prognostic ability of the NLR in AAV patients.

Method: We conducted a retrospective analysis of the clinical records of all adult patients with AVV admitted to the Service of Nephrology and Renal Transplantation of Centro Hospitalar Universitário Lisboa Norte from January 2006 to December 2019. NLR was calculated at admission. The outcomes measured were severe infection at 3 months and one-year mortality.

The prognostic ability of the NLR was determined using the receiver operating characteristic (ROC) curve. A cut-off value was defined as that with the highest validity. All variables underwent univariate analysis to determine statistically significant factors that may have outcomes. Only variables which significantly differed were used in the multivariate analysis using the logistic regression method.

Results: We registered 45 cases of AVV. The mean age at diagnosis was 67.5±12.1 years and 23 patients were male. The mean BVAS at presentation was 26.0±10.4. Twenty-nine patients were ANCA-MPO positive, 7 ANCA-PR3 positive and 9 were considered negative ANCA vasculitis. At admission, mean SCr was 6.7 ± 2.9mg/dL, ESR was 76.9 ± 33.8, hemoglobin was 9.5 ± 1.7g/dL, C-reactive protein was 13.2 ± 5.8mg/dL and NLR was 8.5 ± 6.8. Thirty-five patients were treated with cyclophosphamide, eight patients with rituximab for induction therapy.

Twenty patients developed severe infection within the first three months after starting induction immunosuppression. In a multivariate analysis, older age (73.6±10.5 vs 62.6±11.3, p=0.002, adjusted OR 1.08 [95% CI 1.01 – 1.16], p= 0.035) and higher NLR (11.9±7.4 vs 5.9±5.0, p=0.002, adjusted OR 1.14 [95% CI 1.01 – 1.29], p= 0.035) were predictors of severe infection at 3 months. NLR $\geq$ 4.04 predicted severe infection at 3 months with a sensitivity of 95% and specificity of 52% and the AUROC curve was 0.0794 (95% CI 0.647 – 0.900).

Nine patients died within the first year. Severe infection at 3 months was independently associated with mortality within the first year (OR 6.19 [95% CI 1.12 – 34.32], p= 0.037).

Conclusion: NLR at diagnosis was an independent predictor of severe sepsis within the first 3 months after immunosuppression start, and severe sepsis within the first three months was consequently correlated with one-year mortality. NLR is an easily calculated and low-cost laboratory inflammation biomarker and can prove useful in identifying AAV patients at risk of infection and poorer prognosis.

P0218 **SHEAR WAVE ELASTOGRAPHY AS A NON-INVASIVE MARKER OF RENAL FIBROSIS IN NATIVE DIABETIC KIDNEY DISEASE**

Charmaine Sia[1], Emmett Wong Tsz Yeung Wong[1], Christopher Cheang Han Leo[1,2], Weng Kin Wong[1,2], Boon Wee Teo[1,2], Lee Ying Clara Ngoh[1,2]

[1]National University Hospital, Nephrology, Singapore, Singapore and [2]Yong Loo Lin School of Medicine, Medicine, Singapore, Singapore

Background and Aims: Current assessment of diabetic kidney disease (DKD) is limited to estimated glomerular filtration rate (eGFR) and albuminuria. These are inadequate as DKD often has heterogenous clinical phenotypes. There is need for a marker of intra-renal fibrosis. Native kidney biopsy remains the only reference method in clinical practice for this purpose, but is invasive and impractical for repeated evaluations. Recently, two-dimensional ultrasound shear wave elastography (SWE) has emerged as a non-invasive technique to assess renal parenchymal stiffness with renal fibrosis. We aim to investigate SWE-derived estimates of tissue stiffness with different DKD stages in an Asian population.

Method: In this cross-sectional pilot study, 58 patients with DKD were recruited from a single centre ambulatory Nephrology clinic. Laboratory values were taken within 1 week of undergoing SWE, with DKD staging by the Kidney Disease Improving Global Outcomes (KDIGO) guidelines and eGFR calculated using the CKD-EPI equation. 13 patients had histological diagnoses of DKD; 2 (15.3%) Stage G1-2; 5 (38.5%) Stage G3; 5 (38.5%) Stage G4 and 1 (7.7%) Stage G5 subjects, with native kidney biopsies performed within 4 months of study recruitment.

2D SWE was performed with a 2-5 MHz transducer on an Axiplorer© ultrasound system (Supersonic Imagine, Paris) by a single Nephrologist blinded to laboratory results. Using a previously described protocol, 6 SWE measurements were taken from the cortical mid-pole of bilateral kidneys, and renal elasticity estimated as Young's Modulus (YM) in kilopascals (kPa), (Figure 1).

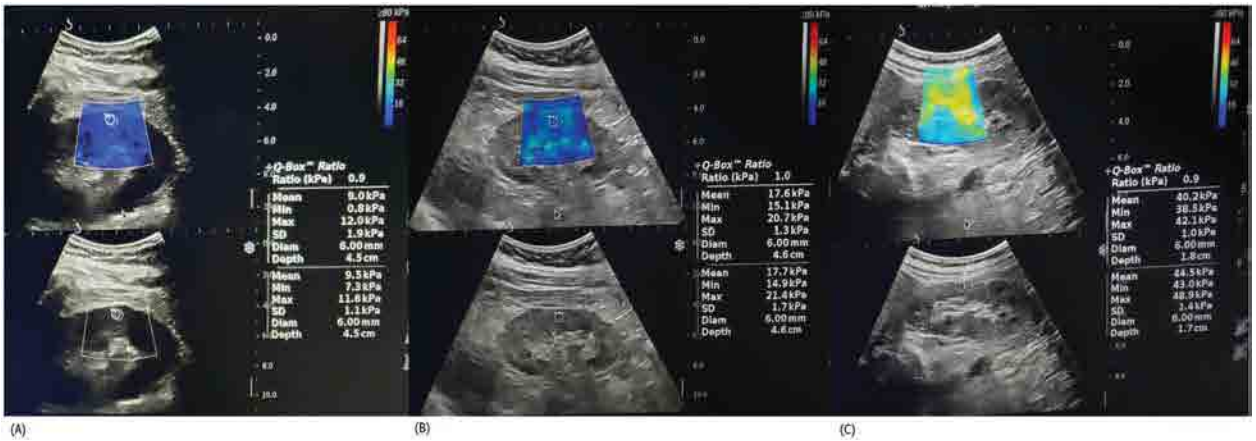


Figure 1: SWE images of various DKD stages

(A) DKD stage 1: eGFR 84, creatinine 80 (μmol/L), mean YM 9

(B) DKD stage 3: eGFR 49, creatinine 130, mean YM 17.6

(C) DKD stage 5: eGFR 8, creatinine 150, mean YM 48.2

Results: Study population were 62.1% male (36/58) and 62.1% ethnic Chinese (36/58), with diabetes duration of 11.7 ± 9.2 years. Median eGFR was 35.0 (40-101) mL/min per 1.73 m^2, with 6 (10.3%) DKD Stage G1-2; 34 (58.6%) Stage G3; 13 (22.4%) Stage G4 and 5 (8.6%) Stage G5 patients.

There were moderate correlations between YM values in bilateral kidneys. Left kidney maximal YM generally increased in accordance with DKD stage (Stage G1-2: 20.6 kPa, Stage G3A: 13.5 kPa, Stage G3B: 22.4 kPa, Stage G4-5: 30.9 kPa, $p < 0.01$). Kidney depth correlated moderately with body mass index (BMI). After controlling kidney depth and BMI, there was a moderately positive correlation between right kidney YM and DKD stage (Maximal YM; $r = 0.4$, $p < 0.01$, Mean YM; $r = 0.31$, $p = 0.02$). eGFR negatively correlated with bilateral kidney maximal YM (right $r = -0.2$, $p = 0.04$, and left $r = -0.3$, $p = 0.03$, respectively). Importantly, there was a strong correlation between right kidney mean YM and histological grading of interstitial fibrosis and tubular atrophy ($r = 0.9$, $p = 0.01$). There is no correlation between kidney elasticity and percentage of sclerosed glomeruli.

Using a cut-off of 13.5 kPa for mean estimated tissue YM, the area under the receiver operator curve was 0.8 to distinguish DKD Stage G1 and G2 from G3A (sensitivity 83.3%, specificity 80.0%).

Conclusion: SWE-derived estimates of renal stiffness appear to increase with DKD stage. The strong correlation with histological markers of fibrosis indicate that observed differences are due to renal parenchymal stiffness. SWE shows promise as a non-invasive marker of renal fibrosis, although large multi-centre studies are required to validate these findings.

P0219

INFLUENCE OF UNDERLYING RENAL DISEASE AND IMMUNOSUPPRESSIVE REGIMEN ON PREMATURE OVARIAN FAILURE IN PREMENOPAUSAL RENAL PATIENTS

Rasała Julia[1], Ciszewska Anna[1], Król Małgorzata[1], Kusztal Mariusz[1], Żabińska Marcelina[1], Kościelska-Kasprzak Katarzyna[1], Kanafa Maciej[1], Augustyniak-Bartosik Hanna[1], Oktawia Mazanowska[1], Krajewska Magdalena[1]

[1]Wroclaw Medical University, Nephrology and Transplantation Medicine, Wrocław, Poland

Background and Aims: Aging, renal pathology (eg SLE, ADPKD), X-ray exposition and pharmacological treatments, especially previous immunosuppressives, may negatively influence the ovarian reserve in childbearing age women. Anti-Müllerian hormone (AMH) is regarded as biomarker for ovarian reserve. The aim was to assess influence of immunosuppressive therapy, X-ray exposition and renal pathology on ovarian in female patients with normal menstrual cycle and chronic kidney disease, including kidney transplant recipients.

Method: Consecutive premenopausal females visiting renal outpatient setting at university hospital who gave informed consent and met exclusion criteria (past ovarian surgical procedure, PCOS, eGFR <30ml/min, diabetes) were enrolled in cross-sectional study. Clinical (renal pathology, smoking, X-rays exposition, eGFR standardized MDRD4, contraceptives) and demographic characteristics, as well as previous and current therapies were recorded. Serum AMH levels were measured by enzyme-linked immunosorbent assay; AMH levels were classified as low or normal/above age-adjusted reference levels (published norms).

Results: In cohort of consecutive 153 premenopausal females (mean age 32,2 y.,range 18-45), 83 (54,2%) were treated recently with antiproliferation immunosuppressive regimen (mycophenolate/azathioprine/methotrexate) and 39 (25,5%) had received cyclophosphamide (CYC) in the past. Median eGFR was 68,5 (IQR 54, 82) ml/min/1.73m2 and renal pathology were as follows glomerulonephritis (n=75), lupus nephritis (n=42), ADPKD (n=6), interstitial (n=5), vasculitis (n=7), other/unknown (n=18). 55 patients were kidney transplant recipients.

Median AMH concentration was 2,9 ng/ml (IQR 1,0 ; 5,2); AMH levels were classified in 45 females as low (median 0,64 IQR 0,05; 1,84) and in 108 as normal/above age-adjusted reference (median 4 IQR 2,1; 5,9). AMH levels did not differ between patients treated with or without antiproliferation immunosuppressives (2.6 IQR 0,9; 5,0 vs. 3.2 IQR 1,1; 5,2 ng/ml, p=0.33) or as well as between being kidney transplant recipients or not (2.72 IQR 0,8; 4,0 vs. 3,0 IQR 1,15; 5,0 ng/ml, p=0.08).

Referring to CYC exposition, AMH levels were lower in females treated with CYC regardless of reason (1.1 ± 1.4 ng/ml vs. 3.2 ± 2 ng/ml, p=0.003). Linking AHA level with renal disease, only lupus patients showed low age-adjusted AMH levels (18/42 – 43%), especially with history of CYC exposition (11 of 18 with low level). Significant negative correlation was found between AMH level and age (r -0,45, p< 0,0001), and very weak with eGFR (r 0,2, p=0,005).

Conclusion: Almost 1/3 of studied childbearing age women with chronic kidney disease (eGFR >30) showed a reduction of the ovarian reserve. It was associated with underlying disease (lupus), cyclophosphamide treatment but not with cumulative X-ray exposition, contraceptives or smoking. Further studies on biomarkers of ovarian reserve in renal patients are still needed for better therapeutic strategy and family planning.

P0220

EFFECTIVENESS OF SODIUM ZIRCONIUM CYCLOSILICATE (SZC) IN HAEMODIALYSIS PATIENTS WITH SEVERE HYPERKALAEMIA IN THE DIALIZE STUDY

Martin Ford[1], Steven Fishbane[2], Bruce Spinowitz[3], Anjay Rastogi[4], Nicolas Guzman[5], Kieran McCafferty[6]

[1]King's College Hospital NHS Trust, London, United Kingdom, [2]Zucker School of Medicine at Hofstra/Northwell, Hempstead, United States of America, [3]New York-Presbyterian Queens, New York, United States of America, [4]David Geffen School of Medicine, Los Angeles, United States of America, [5]AstraZeneca, Gaithersburg, United States of America and [6]Barts Health NHS Trust, London, United Kingdom

Background and Aims: Patients with severe hyperkalaemia require urgent intervention to avoid serious adverse outcomes and mortality. The phase 3b DIALIZE study (NCT03303521) showed that sodium zirconium cyclosilicate (SZC) reduces predialysis serum potassium (sK^+) after the long interdialytic interval and is well tolerated in haemodialysis patients with hyperkalaemia. This *post-hoc* analysis of the DIALIZE data assessed the efficacy of SZC in patients with severe hyperkalaemia (defined as $sK^+ \geq 6.0$ mmol/L) at baseline.

Method: The DIALIZE study randomised 196 patients 1:1 to placebo (n=99) or SZC (n=97). The study consisted of an 8-week treatment period, comprising a 4-week SZC dose titration phase followed by a 4-week evaluation phase. The starting dose of SZC was 5 g orally once daily on non-dialysis days (4 days/week) for the 4-week dose titration phase (titrated in 5 g increments to a maximum of 15 g on non-dialysis days) to achieve predialysis sK^+ 4.0–5.0 mmol/L. Patients maintained a stable dose of SZC for the 4-week evaluation phase (SZC 5, 10 or 15 g). Here, treatment response was defined as achievement of predialysis sK^+ of 4.0–5.5 mmol/L during ≥ 3 of 4 haemodialysis treatments after the long interdialytic interval during the 4-week evaluation phase and not requiring potassium-lowering rescue therapy. Rates of response were compared between those patients with and without baseline severe hyperkalaemia ($sK^+ \geq 6$ mmol/L and <6 mmol/L, respectively). The sK^+ measurement on Visit 1 (Day –7) was used as the baseline value.

Results: At baseline, 88 patients had $sK^+ \geq 6$ mmol/L (SZC n=46, placebo n=42) and 106 patients had $sK^+ < 6$ mmol/L (SZC n=49, placebo n=57); data were missing for two SZC patients. The overall proportion of treatment responders (irrespective of treatment and dose) in patients with baseline $sK^+ \geq 6$ mmol/L and <6 mmol/L was 44.3% and 43.4%, respectively. The proportion of treatment responders was greater with SZC compared with placebo in patients with baseline $sK^+ \geq 6$ mmol/L and $sK^+ < 6$ mmol/L (**Figure**). For patients receiving SZC, the proportion of treatment responders was consistent in those with baseline $sK^+ \geq 6$ mmol/L (67.4%) compared with those with baseline $sK^+ < 6$ mmol/L (71.4%; **Figure**).

Conclusion: Our results suggest that SZC is effective in haemodialysis patients with severe hyperkalaemia.

P0221

SOLUBLE UROKINASE RECEPTOR (SUPAR) IS A PREDICTOR OF DISEASE STATE AND RENAL PROGNOSIS IN PRIMARY NEPHROTIC SYNDROME

Keiji Fujimoto[1], Yu Kagaya[1], Ai Fujii[1], Syo Kumano[1], HIROKI ADACHI[1], Furuichi Kengo[1], Hitoshi Yokoyama[1]

[1]*Kanazawa Medical University, Nephrology, Ishikawa, Japan*

Background and Aims: A hypothesis has been proposed that serum (s-) soluble urokinase receptor (suPAR) activates glomerular podocyte β3 integrin to cause podocyte injury and onset of proteinuria in primary nephrotic syndrome (pNS). However, s-suPAR has been questioned as a disease marker for pNS because it did not correlate with urinary protein (UP). Furthermore, there are a few reports that suggested a correlation between urinary (u-) suPAR and UP by univariate analysis, but the correlation between the two has not been studied by multivariate analysis taking confounding factors into account. In addition, it is unclear how u-suPAR is involved in the pathogenesis of pNS.

Method: In 36 patients with pNS including minimal change (n=18), focal segmental glomerulosclerosis (n=7), membranous nephropathy (n=9) and membranoproliferative glomerulonephritis (n=2), the relationship between u-suPAR (pg/mgCr) and UP (g/gCr) was examined by cross-sectional analysis of baseline values before treatment and longitudinal analysis of changes during the first 2 months of treatment (Δ). In addition, the localization and staining intensity of activated β3 integrin in renal tissue were examined by immuno-histochemistry methods. We also examined whether s-suPAR (pg/ml) or u-suPAR is useful for predicting renal prognosis (1.5-fold increase from baseline in s-Cr) using Cox proportional hazard analysis.

Results: In cross-sectional analysis, u-suPAR was a UP predictor independent of s-suPAR, eGFR and selectivity index (S.I.) [standardized partial regression coefficient (stdβ) = 0.879, $p < 0.00001$]. Also in the longitudinal analysis, Δ u-suPAR was a Δ UP predictor independent of Δ s-suPAR, Δ eGFR and S.I. (stdβ = 0.574, p = 0.003). Furthermore, there were significant correlations between u-suPAR and u-L-FABP (r = 0.522, p = 0.001), and between Δ u-suPAR and Δ u-L-FABP (r = 0.395, p = 0.017). Activated β3 integrin was mainly detected on proximal tubular brush-border (PTBB), but not glomerular capillaries, moderate to strongly positive in pNS. Δ s-suPAR was the only predictor of 1.5-fold increase from baseline in s-Cr (Hazard Ratio: 1.361 per 500 pg/ml increase of s-suPAR, p=0.006).

Conclusion: In pNS, u-suPAR was a proteinuria predictor independent of s-suPAR, suggesting the possibility of the mechanisms of proteinuria through β3 integrin activation in PTBB by u-suPAR. In addition, s-suPAR was useful in predicting renal prognosis.

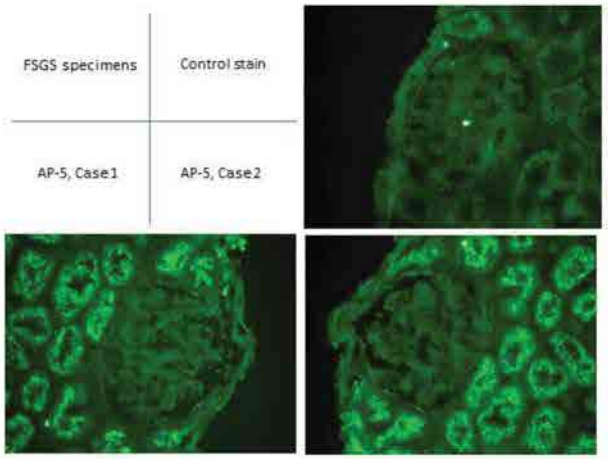


Figure: Activated beta-3 integrin (AP5)-staining in biopsied specimens

P0222 **KIDNEY EFFECTS IN THE MOXIE TRIAL: A STUDY OF OMAVELOXOLONE IN PATIENTS WITH FRIEDRICH'S ATAXIA**

Philippe Zaoui[1], Melanie Chin[2], Martin Delatycki[3], Paola Giunti[4], Angie Goldsberry[2], Colin Meyer[2], Megan O'Grady[2], Susan Perlman[5], S. H. Subramony[6], Theresa Zesiewicz[7], David Lynch[8]

[1]Université Grenoble Alpes, Clinique de Néphrologie CHU Grenoble, La Tronche, France, [2]Reata Pharmaceuticals, Inc., Product Development, Plano, United States of America, [3]Murdoch Children's Research Institute, Parkville, Australia, [4]UCL Queen Square Institute of Neurology, Clinical and Movement Neurosciences, London, United Kingdom, [5]Ronald Reagan UCLA Medical Center, Department Neurology, Los Angeles, United States of America, [6]Norman Fixel Institute for Neurological Diseases, Department of Neurology, Gainesville, United States of America, [7]University Of South Florida, Department of Neurology, Tampa, United States of America and [8]Children's Hospital of Philadelphia, Department Neurology, Philadelphia, United States of America

Background and Aims: Omaveloxolone, an Nrf2 activator, is an investigational drug that targets targets inflammation and mitochondrial dysfunction, metabolic, and bio-energetic pathways. Omaveloxolone is an analog of bardoxolone, methyl which has been shown to improve kidney function in multiple studies of chronic kidney diseases. The MOXIe Part 2 trial investigated omaveloxolone in patients with Friedreich's ataxia (FA), a rare and serious hereditary disease caused by mitochondrial dysfunction that affects multiple organ systems resulting in ataxia, cardiomyopathy, and reduced life-span. The study met its primary efficacy endpoint, and omaveloxolone improved neurological function, as assessed by the modified Friedreich's ataxia rating scale (mFARS). We report the effect of omaveloxolone on kidney function in this patient population.

Method: The MOXIe trial (NCT02255435) was an international, multi-center, double-blind, placebo-controlled, randomized trial that enrolled 103 patients between 16 and 40 years of age with genetically confirmed FA. Patients were randomized 1:1 to receive either omaveloxolone 150 mg or placebo administered once daily for 48 weeks. The trial included 24 patients that were younger than 18 years of age. Baseline eGFR for the overall patient population receiving placebo or omaveloxolone was 109.2 $\pm$ 21.7 and 113.4 $\pm$ 14.7 mL/min/1.73 m2, respectively. Baseline eGFR for the pediatric population receiving placebo or omaveloxolone was 99.1 $\pm$ 33.7 and 106.3 $\pm$ 15.6 mL/min/1.73 m2, respectively. Serum creatinine was collected at baseline, Weeks 4, 12, 18, 24, 36 and 48 on-treatment and 4-weeks off-treatment at Week 52. Glomerular filtration rate was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation for patients $\geq$ 18 years of age. For patients $<$18 years of age, the Bedside Schwartz equation was used to calculate eGFR.

Results: In placebo patients, mean (SD) eGFR decreased by 4.4 $\pm$ 11.0 mL/min/1.73 m2 from baseline whereas patients receiving omaveloxolone had an average increase of +7.0 $\pm$ 10.7 mL/min/1.73 m2 from baseline after 48 weeks, resulting in a difference of 11.4 mL/min/1.73 m2 between treatment groups. At Week 52, mean eGFR was -4.2 $\pm$ 10.9 mL/min/1.73 m2 relative to baseline in placebo patients and remained +0.9 $\pm$ 10.8 mL/min/1.73 m2 above baseline in omaveloxolone patients after 4-weeks off-treatment. In pediatric patients randomized to placebo, at week 48 eGFR decreased by -11.3 $\pm$ 14.3 mL/min/1.73 m2 whereas patients receiving omaveloxolone had an average increase of +5.5 $\pm$ 14.5 mL/min/1.73 m2 from baseline, resulting in a difference of 16.8 mL/min/1.73 m2 between treatment groups.

Conclusion: Patients with FA randomized to placebo in the MOXIe trial had eGFR declines over 48 weeks that were similar to rates of decline observed in the most rapidly progressing forms of chronic kidney disease. The rapid kidney function decline in FA reflects the multi-system nature of the disease whereby mitochondrial dysfunction, and associated chronic inflammation, affects not only the central nervous system but also the heart and possibly the kidney. In contrast to placebo, treatment with omaveloxolone improved eGFR in patients with FA and the effects were sustained through one year of treatment. The durability of eGFR improvements are consistent with those observed with its analog, bardoxolone methyl, in clinical trials for various forms of CKD.

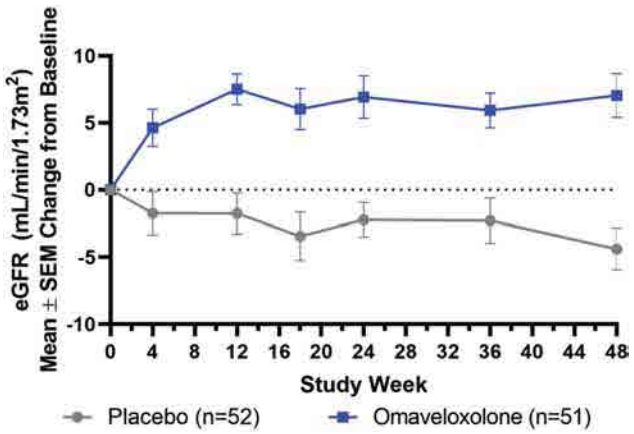


Figure:

P0223

AGING CHANGES OF RENAL FUNCTION AND EVALUATION OF DIFFERENT GLOMERULAR FILTRATION RATE ESTIMATION EQUATIONS IN HEALTH PEOPLE IN BEIJING

Lengnan Xu[1], Yonghui Mao[1], Aiqun Chen[1], Ban Zhao[1]

[1]*Beijing Hospital,National Center of Gerontology;Institute of Geriatric Medicine, Chineses Academy of Medical Sciences, Nephrology, Beijing, P.R. China*

Background and Aims: The kidney is an important organ that removes metabolites and certain wastes and poisons from the body, and retains water and other useful substances through reabsorption. Its aging and function decline have a significant impact on the human health.Rather than simply depending on serum creatinine, glomerular filtration rate (GFR) assessment equation should be given priority in evaluating renal function. Different evaluated GFR (eGFR) equations sometimes have great differences in assessing the true value of GFR, especially for the elderly. The purpose of this study was to analyze the aging changes of renal function in normal people in Beijing and to compare the significance of different eGFR equations in evaluating renal function in Chinese population.

Method: The age, sex and serum creatinine were recorded in the population who underwent routine physical examination in our hospital from January 2012 to December 2014. Kidney function was assessed by CKD-EPI, MDRD, MDRDc, FAS and BIS equations, respectively.

Results: A total of 46 713 persons were enrolled in this study, of whom 27 249 (58.33%) were males. They were followed up for 3 years, ranging in age from 16 to 100 years. Both men and women showed age-related change in serum creatinine: serum creatinine and its standard deviation gradually increases parallel with age, indicating that the range of serum creatinine changes in the elderly was larger. Whether male or female, there were differences in eGFR change between different age groups (male: X^2=141.28, P=0.000; female: X^2=97.55, P=0.000). For male, eGFR decreased more in the elderly, and it was more common for young people to keep the eGFR constant or increase. However, in female, eGFR remained unchanged in most old people, and increased or decreased in the majority of the young. For all age groups, the ICC was very consistent among the equations, 0.849 for males and 0.817 for females. The whole population was divided into three groups according to serum creatinine < 1mg/dL, > 1mg/dL and < 1.5mg/dL, > 1.5mg/dL. The CKD-EPI equation gave higher stages of CKD than other equations. There was no clear age-related change trend in the 3-year average eGFR change rate of all age groups. For the elderly over 70 years of age, the MDRD and MDRDc equations had higher GFR evaluation results than the other three equations. The BIS equation had the lowest results of all equations. The ICC was very consistent among the equations, 0.966 for males and 0.957 for females.

Conclusion: we believed that the annual change of GFR varied from person to person and had little to do with age. GFR needed to be calculated more accurately in order to formulate corresponding medical strategies. Those eGFR equations the above-mentioned can be used to evaluate renal function, but the results were very different for different populations and serum creatinine levels. The use of different eGFR equations may lead to large differences in drug dose adjustment and the risk of serious adverse reactions. For the elderly in China, which equation was more suitable was inconclusive and further research was urgently needed.

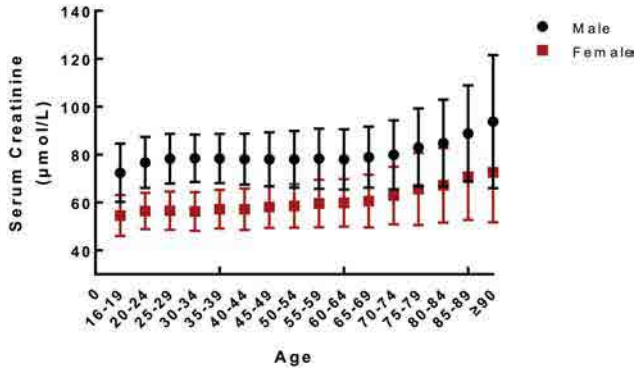


Fig 1. Aging changes in serum creatinine in normal people

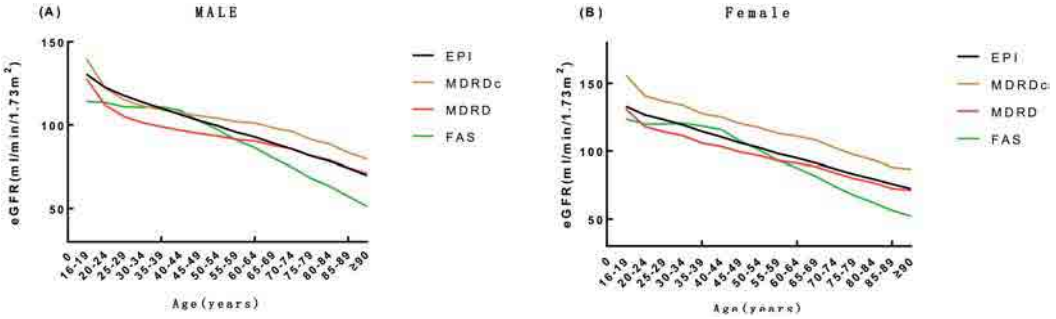


Fig 5. Comparison of eGFR equations for different serum creatinine levels. (A) male. (B) female.

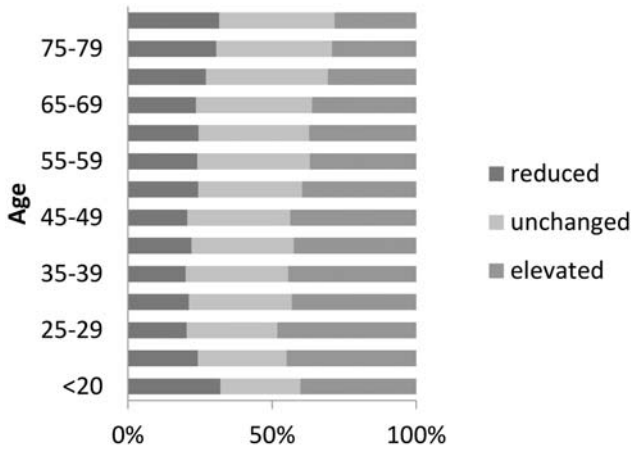


Fig 2. The change of eGFR in male. (A) male. (B) female.

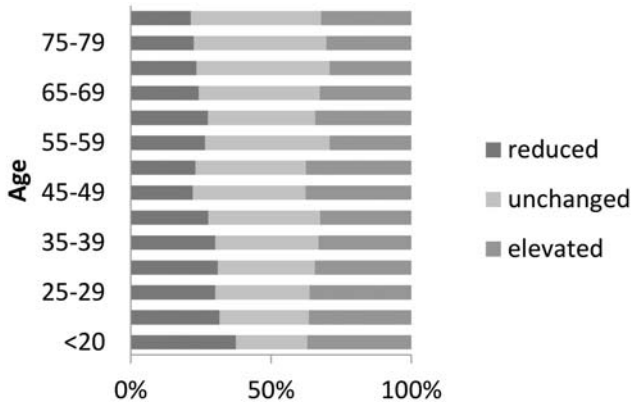


Fig3. Comparison of different eGFR equations in all age groups. (A) male. (B) female.

P0224

THE POSSIBLE LINK BETWEEN UNDETERMINED CHRONIC KIDNEY DISEASE (CKDU) AND ACUTE INTERSTITIAL NEPHRITIS (AIN) IN THE DRY ZONE REGIONS OF SRI LANKA

Shakila Premarathne[1], Nishantha Nanayakkara[2], Rohana Chandrajith[3], R.M.S.K Rathnayake[4], Neelakanthi Rathnathunga[5], Zeid Badurdeen[6], Hemalika Abeysundara[7], Nalaka Elladeniya[8] , Kumudumali Guruge[9], Sudath Madushan[4], Udaga Samrasiri[4], H.P.M. Hewavitharane[10]

[1]Center for Education Research and Training on Kidney Diseases (CERTKID), Faculty of Medicine, University of Peradeniya, Department of Microbiology, Kandy, Sri Lanka, [2]National Hospital Kandy, Nephrology and Kidney Transplant Unit, Kandy, Sri Lanka, [3]Department Of Geology, Faculty of Science, University of Peradeniya, Sri Lanka, Department of Geology, Kandy, Sri Lanka, [4]National Hospital, Kandy, Kandy, Sri Lanka, [5]Faculty of Medicine, University of Peradeniya, Department of Pathology, Kandy, Sri Lanka, [6]Center for Education Research and Training on Kidney Diseases (CERTKID), Faculty of Medicine, University of Peradeniya, Kandy, Sri Lanka, [7]Faculty of Science, University of Peradeniya, Department of Statistics ad Computer Sciences, Kandy, Sri Lanka, [9]Centre for Education, Research and Training on Kidney Diseases, Peradeniya, Sri Lanka and [10]Centre for Education, Research and Training on Kidney Diseases, Community Medicine, Kandy, Sri Lanka

Background and Aims: An environmental nephropathy which is widely known as Chronic Kidney Disease of uncertain aetiology (CKDu) has been reported in dry zone of Sri Lanka and few other tropical countries. It is already become a major public health problem resulting immense social, economic and health impacts. In recent past, symptomatic presentation of CKDu with tubulitis (CKDuT)/ Acute Interstitial Nephritis indicating activity (AIN) has been reported from Sri Lanka and Central America. The AIN is a nonspecific response of kidney to an injurious agent. Usually the responsible aetiology is obvious in AIN, but not in CKDu cases, however, believed to be a sequel of interstitial nephritis. The aim of this study was to identify the occupational exposures or risk factors associated in AIN cases.

Method: In a two years of a comprehensive investigation, 60 individuals who reported with AIN were investigated. Once a case is reported, a home visit was carried out and behavioural pattern associated risk factors were assessed by a structured questionnaire in which working behaviours and conditions, spraying of agrochemical, usage of Personal Protective Equipment (PPE) and probable exposed environmental conditions were considered.

Results: Majority of AIN patients were male (90:10%) with the mean age of (44 $\pm$ 1.2) ranging from 26 - 62years. Among the study group, 53% were full time farmers while 77% of were doing farming either full time or part time. 55% of patients applied agrochemicals by themselves. 52% of individuals have used Personal Protective Equipment (PPE). 12% of individuals were sand miners while 7% and 5% were full time masons or labourers. 2% were engaged both farming and mason as full time employment. 15% were doing other employment except the above. Smoking, alcohol consumption and betel chewing were reported in the group as 50%, 57% and 72% respectively. Majority of patients were reported from Girandurukotte (17%), Wilgamuwa (32%) and Mahiyanganaya (35%) regions where CKDu are widely reported. Study indicated that there was no any significant pattern of AIN incidents over the study period.

Conclusion: Mean age of reported CKDuT were at least ten years younger than the mean age of CKDu. Comparatively higher number of sex ratio has been found in CKDuT indicating the male dominance. Some of the demographic features of AIN patients were similar with CKDu patients and both CKDu and AIN patients are engaged in farming either full time or part time.

P0225 **THE PRESENCE OF SIMPLE RENAL CYST IS ASSOCIATED WITH INCREASED RISK OF ALBUMINURIA IN YOUNG ADULTS**

Hyo Jin Boo[1], SEUNGMIN SONG[1], Jung Eun Lee[1], Hye Ryoun Jang[1], Wooseong Huh[1], Dae Joong Kim[1], Yoon-Goo Kim[1]

[1]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medicine*

Background and Aims: It is well-known that the prevalence of simple renal cyst increases with age. However, simple cysts are occasionally found in adults younger than 40 years of age. This cross-sectional study evaluated the clinical significance of simple renal cysts in young adults, focusing on the associations with hematuria and albuminuria.

Method: Adults younger than 40 years who received a comprehensive medical checkup from January 2005 to December 2013 were included. Simple renal cysts were identified by ultrasonography.

Results: Among 5832 subjects, renal cysts were found in 276 (4.7%). Subjects diagnosed with polycystic kidney disease (n=5) or medullary sponge kidney (n=1) were excluded from the analyses. A single cyst and multiple cysts were found in 234 (4.0%) and 42 (0.7%) subjects, respectively. The locations of single cyst were cortex in 187, medulla in 26, and parapelvic region in 21. Age (odds ratio [OR], 1.07; 95% confidence interval [CI], 1.02-1.12 per 1-year increment, P = 0.002), systolic BP (OR, 1.01; 95% CI, 1.00-1.02 per 1-mmHg increment, P = 0.006), and hypertension (OR, 1.85; 95% CI, 1.24-2.76, P = 0.003) were independent predictors of the presence of simple cyst. The presence of cysts was not associated with increased prevalence of hematuria. While, the subjects with cysts had higher prevalence of albuminuria than those without cysts (11.3% vs. 4.5%, P <0.001). Multivariate analyses of albuminuria revealed that the presence of simple renal cyst was associated with a 2.30-fold increase in the prevalence of albuminuria (95% CI 1.512-3.519, P <0.001) independently of other risk factors. The location of the cysts was not related to the prevalence of albuminuria.

Conclusion: The presence of simple renal cysts was independently associated with increased prevalence of albuminuria. The causal relationship between renal cysts and albuminuria needs to be elucidated in further studies.

P0226

CONSEQUENCES OF SUPRAPHYSIOLOGICAL DYALYSATE MAGNESIUM CONCENTRATION ON ARTERIAL STIFFNESS, HEMODYNAMIC PROFILE AND ENDOTHELIAL FUNCTION IN HEMODIALYSIS: A RANDOMIZED CROSS-OVER STUDY AND FOLLOW-UP

Rosaria Del Giorno[1], Soraya Lavorato[1,2], Kevyn Stefanelli[3], Giampiero Allegra[1], Claudia Zapparoli[1], Pedrag Lazarevic[2], Lorenzo Berwert[2], Luca Gabutti[1,5]

[1]EOC Ente Ospedaliero Cantonale, Department of Internal Medicine, Clinical Research Unit, Regional Hospital of Bellinzona and Valli, Ente Ospedaliero Cantonale, Bellinzona, Switzerland, Bellinzona, Switzerland, [2]EOC Ente Ospedaliero Cantonale, Nephrology and Dialysis Service, Regional Hospital of Bellinzona and Valli, Ente Ospedaliero Cantonale, Bellinzona, Switzerland, Bellinzona, Switzerland, [3]Sapienza University of Rome, Roma, Italy and [5]Università della Svizzera italiana, Institute of Biomedicine, Lugano, Switzerland

Background and Aims: Increasing dialysate magnesium improves vascular stiffness in subjects undergoing maintenance hemodialysis. The present findings merit a larger trial to evaluate the effects of a 0.75 mmol/L D-Mg2+ on major clinical outcomes.

Method: A randomized 4-week cross-over study aimed at investigating the consequences of increasing D-Mg^{2+} from 0.50 to 0.75 mmol/L on arterial stiffness, hemodynamic profile, and endothelial function in subjects undergoing hemodialysis. The long-term effect of higher D-Mg^{2+} on mineral metabolism markers was investigated in a six-month follow-up. Data were analysed by linear mixed models for repeated measures.

Results: Pulse wave velocity and pulse pressure significantly decreased on the higher D-Mg^{2+} compared with the standard one by -0.91 m/sec (95% confidence interval: -1.52 to -0.29; p=0.01) and -9.61 mmHg (-18.89 to -0.33, p=0.04), respectively. A significant reduction in systolic blood pressure of -12.96 mmHg (-24.71 to -1.22, p=0.03) was also observed. No period or carryover effects were observed. During the long-term follow-up the higher D-Mg^{2+} significantly increased total serum and ionized Mg (mean percentage change from baseline to follow-up +21%; and + 27%; $p \leq 0.001$ for both), while parathormone (PTH) decreased significantly (-11%, p=0.03).

Conclusion: Increasing dialysate magnesium improves vascular stiffness in subjects undergoing maintenance hemodialysis. The present findings merit a larger trial to evaluate the effects of a 0.75 mmol/L D-Mg^{2+} on major clinical outcomes.

P0227 VITAMIN K ANTAGONIST-ASSOCIATED MICROSCOPIC HEMATURIA: ASSOCIATION WITH INR LEVELS AND PROTECTIVE EFFECT OF RAAS BLOCKADE

Clara Maria Cases Corona[1], Emily Larrea[1], Amir Shabaka[1], Karmele Arribalzaga[2], Carmen Herrero Alonso[3], Patricia Dominguez Torres[1], Yunayka Diaz Enamorado[1], Beatriz Sanchez Alamo[1], Gema Maria Fernandez Juarez[1]

[1]Hospital Universitario Fundacion Alcorcon, Nephrology, Alcorcon, Madrid, Spain, [2]Hospital Universitario Fundacion Alcorcon, Hematology, Alcorcon, Madrid, Spain and [3]Hospital Universitario Fundacion Alcorcon, Clinical Analysis, Alcorcon, Madrid, Spain

Background and Aims: Vitamin K antagonists (VKA) are the most widely used anticoagulants in the daily clinical practice for the prevention of thrombotic events. Several renal adverse effects have been associated with the use of VKA, from hemodynamic effects due to massive urological hemorrhage associated with VKA overdose, to non-hemodynamic effects that include glomerular hemorrhage and renal tubular obstruction due to red cell casts. The main aim of our study was to establish an association between INR levels and microscopic hematuria in patients with VKA, and identify possible risk and protective factors associated with development of microscopic hematuria in these patients.

Method: We performed a transversal study that included patients with oral anticoagulation with coumarin derivatives (warfarin or acenocoumarol), that attended the Hematology outpatient clinic from October to December 2019 for routine INR control. A urine specimen was collected on the day of the INR control. We performed a simple urinalysis to all patients and quantified the precise number of red cells in the urine sediment by flow cytometry. Demographic data, kidney function tests including serum creatinine and albuminuria, comorbidities, anticoagulant dose and concomitant treatment were registered.

Results: 337 patients were included in the study, with an average age of 68.6 $\pm$ 12.2 years, 51% were females, 95% were treated with acenocoumarol and 5% with warfarin. Median INR levels were 2.6 (IQR 2.1-3.3) and the median number of urine red cells in the sediment were 11 RBCs/µl (IQR 0-13). 11.9% of the patients presented microscopic hematuria ($\geq$14 RBCs/µl).

There was a significant correlation between INR levels and the number of RBCs in the urine sediment (Spearman's rho= 0.119, p= 0.029), independent from the type of anticoagulant used. This correlation was stronger after excluding those patients who had concomitant bacteriuria (Spearman's rho= 0.201, p= 0.024). We found no correlation between time elapsed from start of anticoagulation or total weekly dose with the intensity of microscopic hematuria.

In the univariate analysis, microhematuria was associated with having an INR >3.5 (19% vs. 10.2%, p=0.046), bacteriuria (15.2% vs. 3.6%, p=0.015), leukocyturia (14.8% vs. 6.6%, p= 0.026), hypertension (16.2% vs. 9.5%, p=0.053), and the use of RAAS blockers (17.2% vs. 6.9%, p=0.004). After performing a multivariate logistic regression that included the aforementioned variables, the association between microhematuria and RAAS blockade with either an ACE inhibitor or ARB was maintained (OR 0.38, CI 95% 0.163-0.886, p=0.025), independent from INR levels, hypertension, leukocyturia or bacteriuria. We found no association between serum creatinine, albuminuria or antiplatelet treatment with the presence of microscopic hematuria.

Conclusion: INR overdose is significantly associated with the presence of microscopic hematuria, independent from the type of VKA used or the total weekly dose. RAAS blockade is an independent protective factor for the presence of microscopic hematuria in anticoagulated patients.

Variable	Odds Ratio	95% Confidence Interval	
		Lower	Upper
INR >3.5	2.08	0.96	4.50
RAAS blockade (ACEI or ARB)	0.38	0.16	0.89
Hypertension	0.94	0.43	2.07
Bacteriuria	0.63	0.25	1.58
Leukocyturia	0.54	0.22	1.35

P0228

THE NEFIGARD TRIAL: THE EFFECT OF NEFECON® (BUDESONIDE) IN PATIENTS WITH PRIMARY IGA NEPHROPATHY AT RISK OF DEVELOPING END-STAGE RENAL DISEASE

Jonathan Barratt[1], Andrew Stone[2], Jens Kristensen[3]

[1]University of Leicester, Mayer IgA Nephropathy Laboratory, Department of Cardiovascular Sciences, Leicester, United Kingdom, [2]Stone Biostatistics Ltd., Crewe, United Kingdom and [3]Calliditas Therapeutics AB, Stockholm, Sweden

Background and Aims: Since the first description of IgA nephropathy (IgAN) over 50 years ago, it has been recognised that the mucosal immune system plays a crucial role in the pathogenesis of this common global cause of kidney failure. Recently, particular attention has focussed on the importance of the gut-associated lymphoid tissue (GALT) as the potential source of the poorly *O*-galactosylated IgA1 that triggers the formation of nephritogenic immune complexes in IgAN. Pathway analysis based on a large meta-analysis of genome wide association studies identified the intestinal immune network for IgA production as the most enriched KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway in IgAN. Furthermore, separate studies have shown that the IgA in glomerular IgA deposits is indistinguishable from mucosal IgA. The therapeutic potential of selectively targeting GALT was demonstrated in the NEFIGAN trial (NCT01738035), which assessed the safety and efficacy of a novel targeted-release formulation of budesonide (NEFECON®), designed to deliver budesonide to the GALT-rich distal ileum in patients with IgAN. After 9 months' treatment, urine protein–creatinine ratio (UPCR) was reduced by 29.3% in the NEFECON® 16 mg group compared with the placebo group. Estimated glomerular filtration rate (eGFR) dropped 4.7 ml/min/1.73 m^2 in the placebo group with no deterioration seen in the NEFECON® 16 mg group. Incidence of patients reporting adverse events was similar in all groups. These data led to the design of the NefIgArd study which aims to assess the efficacy, safety, and tolerability of NEFECON® 16 mg in patients with IgAN at risk of end-stage renal disease.

Method: The NefIgArd study is a randomised, double-blind, placebo-controlled Phase 3 trial, with two parts – **PART A:** a 15–35-day screening period, 9-month treatment and 3-month follow-up period; and **PART B:** a 12-month no-treatment follow-up period (Figure). The study is recruiting across 146 nephrology clinics in 19 countries. Patients must be at least 18 years old with biopsy-confirmed primary IgAN and persistent proteinuria >1 g/24 h and eGFR between 35 and 90 ml/min per 1.73 m^2 (CKD-EPI) despite optimised renin–angiotensin system blockade. Patients are randomised on a 1:1 ratio to NEFECON® 16 mg/day or placebo. Consistent with the Kidney Health Initiative White Paper "Proteinuria Reduction as a Surrogate End Point in Trials of IgA Nephropathy" published in early 2019, the primary outcome of Part A is to assess the effect of NEFECON® 16 mg on 24 h UPCR at 9 months compared with placebo. The Part B primary outcome is based on data presented at the NKF/FDA/EMA workshop in March 2018 that supported eGFR slope as an endpoint for full approval and will assess the effect of NEFECON® 16 mg on a 2-year eGFR-based endpoint compared with placebo. In comparison with other studies that are recruiting, we believe that the relatively short period required to provide validation of the surrogacy of proteinuria reduction will significantly reduce the risks of non-protocol treatments and loss of patients from the study that could dilute the true treatment effect of NEFECON®.

Results: As of 1 January 2020, 207 patients have been randomised, and Part A is expected to complete in Q4 2020, with Part B completing in 2022. To ensure the NefIgArd study results are fully translatable to the global IgAN population, NefIgArd will also open in China in 2020.

Conclusion: The NefIgArd study builds on the experience of the NEFIGAN trial, the largest commercially sponsored study ever completed in IgAN. The design of the NefIgArd study has used state-of-the-art data to evaluate kidney outcomes, using proteinuria as a reasonably likely surrogate of the effect of NEFECON® on long-term kidney outcomes and confirming long-term renoprotection using an NKF/FDA/EMA-suggested eGFR-based endpoint as a basis for full approval.

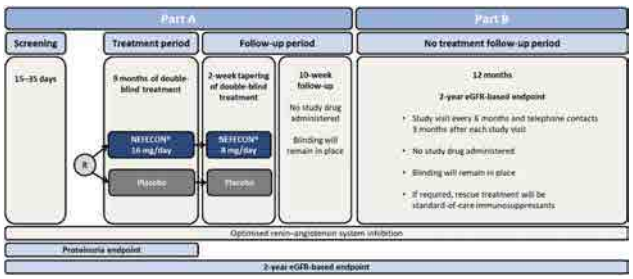


Figure:

P0229

APPLICATION OF A RISK MITIGATION STRATEGY TO PREVENT EXCESS CARDIOVASCULAR RISK IN PULMONARY HYPERTENSION: LARIAT STUDY

R James White[1], Murali Chakinala[2], Melanie Chin[3], Jeremy Feldman[4], Angie Goldsberry[3], Peter McCullough[5], Colin Meyer[3], Megan O'Grady[3], Ronald Oudiz[6], Fernando Torres[7], Daniel Coyne[8]

[1]University of Rochester Medical Center, Department of Medicine, Rochester, United States of America, [2]Washington University School of Medicine, Division of Pulmonary and Critical Care Medicine, St. Louis, United States of America, [3]Reata Pharmaceuticals, Inc., Product Development, Plano, United States of America, [4]Arizona Pulmonary Specialists Phoenix, Phoenix, United States of America, [5]Baylor Scott & White Heart and Vascular Hospital - Dallas, Dallas, United States of America, [6]The Lundquist Institute at Harbor- UCLA Medical Center, Torrance, United States of America, [7]UT Southwestern Medical Center, Department of Internal Medicine, Dallas, United States of America and [8]Department of Pediatrics, Division of Nephrology, St. Louis, United States of America

Background and Aims: Bardoxolone Methyl Evaluation in Patients with Chronic Kidney Disease and Type 2 Diabetes (BEACON) was a multinational, randomized, double-blind, placebo-controlled Phase 3 trial that enrolled patients with type 2 diabetes (T2D) and stage 4 CKD. The BEACON trial was terminated due to a significant increase in the risk of heart failure occurring within the first four weeks of treatment with bardoxolone methyl. Post-hoc analyses identified a history of heart failure and elevated baseline serum concentrations of B-type natriuretic peptide (BNP) as risk factors for these events. A subsequent study, LARIAT (NCT02316821), was designed to evaluate the efficacy and safety of bardoxolone methyl in the treatment of patients with pulmonary arterial hypertension (PAH). Progressive right heart failure is the cause of death for most PAH patients, and PAH patients are at high risk for decompensated right heart failure. LARIAT was designed to mitigate the risk for heart failure, and here we present cardiovascular safety data from this trial.

Method: The LARIAT study was a 16-week double-blind, randomized, placebo-controlled, dose-ranging study that enrolled 208 patients with a confirmed diagnosis of PAH, most of whom had Group 1 Pulmonary Arterial Hypertension and were taking stable doses of at least one approved PAH therapy. Patients were randomized 3:1 to receive bardoxolone methyl or placebo at a starting dose of 2.5 mg, and subsequent doses of 5, 10, or 20mg. In addition to the dose-titration scheme, the initial protocol excluded patients with BNP $>$ 200 pg/mL (later amended to 400 pg/mL), acutely decompensated heart failure in the previous 30 days, or eGFR $<$ 45 mL/min/1.73 m2 at baseline. BNP and NT-proBNP were assessed serially throughout the study. In addition, 24-hour ambulatory blood pressure (ABPM) was monitored in a subset of the patients at baseline, Week 4, and Week 16.

Results: One fluid overload SAE was reported in a placebo patient but not in any bardoxolone methyl patients. Overall, only 2 (1.7%) bardoxolone methyl patients reported cardiovascular SAEs, neither of which were attributed to study drug. Moreover, there were no statistically significant increases in 24-hour ABPM blood pressure, weight, or NT-Pro BNP and BNP levels in bardoxolone methyl-treated patients. Thus, treatment with bardoxolone methyl did not appear to be associated with an increased risk for heart failure hospitalizations or fluid overload adverse events in the LARIAT study.

Conclusion: Despite the real risk for fluid retention and acutely decompensated heart failure in PAH patients, use of BNP $<$ 400 pg/ml and HF history can be used to safely select patients with PAH to receive bardoxolone methyl. There was no increased risk of heart failure or other signs of overt fluid overload; we did not observe subclinical measures of fluid retention (increases in blood pressure or weight). These data support the use of a risk-mitigation strategy in the continued development of bardoxolone methyl for patients at risk for decompensated heart failure.

P0230

IMMUNOSUPPRESSIVE TREATMENT DOES NOT IMPROVE KIDNEY SURVIVAL IN PATIENTS WITH HCV CRYOGLOBULINAEMIA TREATED WITH DIRECT-ACTING ANTIVIRALS

Pérez de José Ana[1], Javier Carbayo[2], Anna Pocurull[3], Ana Huerta[4], Clara Maria Cases Corona[5], Teresa Bada Bosch[6], Amir Shabaka[7], Natalia Ramos Terrada[8], Laura Martinez Valenzuela[9], Marian Goicoechea[10]

[1]University Hospital Gregorio Marañón, Nephrology, MAdrid, , [2]University Hospital Gregorio Marañón, Nephrology, MAdrid, Spain, [3]Hospital Clínic de Barcelona, Gastroenterology and hepatology, Barcelona, , [4]Hospital Universitario Puerta del Hierro Majadahonda, Nephrology, MAdrid, , [5]Hospital Universitario Fundacion Alcorcon, Nephrology, Madrid, , [6]Hospital Universitario Doce de Octubre, Nephrology, Madrid, Spain, [7]Hospital Clinico Universitario San Carlos, Nephrology, Madrid, Spain, [8]Hospital Vall d'Hebron, Nephrology, Barcelona, Spain, [9]Hospital Universitari de Bellvitge,, Nephrology, Barcelona, Spain and [10]University Hospital Gregorio Marañón, Nephrology, Madrid, Spain

Background and Aims: Since the introduction of direct-acting antivirals (DAAs), few data have been published about kidney outcome in hepatitis C virus related mixed cryoglobulinaemia (HCV-MC) patients treated with combined DAAs and rituximab.

We aimed to asses if combined treatment with DAAs and rituximab in patients with HCV-MC improves kidney survival and immunological response.

Method: Observational, multicentre, cohort study of 100 patients with HCV-MC from 14 Spanish centres treated with DAAs. Patients were followed up for a median duration of 138 months (11.5 years).

Long-term kidney survival and immunological response were evaluated based on immunosuppressive treatment received. Kidney event was defined as duplication of creatinine level or 50% decrease in glomerular filtration rate, dependence on renal replacement therapy or non-reduction of proteinuria by 50% compared to baseline. Immunological response was defined as the decrease in cryocrit $\leq$1%.

Results: Sustained virological response was attained in 98 (98%) patients. 49 patients were treated with immunosuppressive treatment associated with DAAs, 26 with rituximab and the rest (23) with steroids and/or cyclophosphamide. Patients receiving immunosuppressive treatment had higher basal cryocrit (6.3$\pm$4.5 vs 3.8$\pm$3.9%, p=0.011), lower glomerular filtration rate (55$\pm$27 vs 68$\pm$25 ml/min/1.73 m^2) and more haematuria (p=0.001). The 26 patients treated with rituximab had more severe disease: higher viral load (p=0.001), cryocrit (p=0.011), proteinuria (p=0.004), microhaematuria (p=0.012) and hypertension (p=0.012) and lower glomerular filtration rate (p=0.001). 15 patients had a kidney event at the end of follow-up. Predictive variables of kidney events were lower age (HR 0.94, 95%CI 0.89-0.99; P= 0.038) and lower glomerular filtrate rate (HR 0.97, 95%CI 0.94-0.99; p=0.026), in a model adjusted to proteinuria and microhaematuria. Immunosuppressive treatment with or without rituximab did not change kidney survival.

Regarding the immunological response, only 19 patients had a cryocrit >1% at the end of follow-up. There were no differences in age, viral load, proteinuria and basal glomerular filtration rate between these patients with no immunological response and those who had a sustained immunological response over time. The only differences between these two groups were a higher basal cryocrit and a minor C4 levels. Immunosuppressive treatment with or without rituximab did not changed the immunological response.

Conclusion: Patients with more severe HCV-MC are those receiving immunosuppressive treatment. However, immunosuppressive treatment does not change kidney survival nor immunological response of these patients in the long term.

P0231 **PREGNANCY AND DELIVERY OUTCOMES IN PATIENTS WITH COMPLEMENT GENE VARIANT MEDIATED THROMBOTIC MICROANGIOPATHY**

Natalja Haninger[1], Martina Gaggl[2], Christof Aigner[3], Kain Renate[4], Zoltán Prohaszka[5], Georg A. Böhmig[6], Piggott Leah Charlotte[7], Sunder-Plassmann Raute[8], Gere Sunder-Plassmann[7], Schmidt Alice[9]

[1]Medical University of Vienna, Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria, [2] Medical University of Vienna, Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria, [3] Medical University of Vienna, Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria, [4]Medical University of Vienna, Clinical Institute of Pathology, Vienna, Austria, [5]Hungarian Academy of Sciences and Semmelweis University, Research Laboratory, 3rd Department of Internal Medicine, and MTA-SE Research Group of Immunology and Hematology, Budapest, Hungary, [6] Medical University of Vienna, Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria, [7]Medical University of Vienna, Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria, [8]Medical University of Vienna, Genetics Laboratory, Department of Laboratory Medicine, Vienna, Austria and [9]Medical University of Vienna, Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria

Background and Aims: In pregnancy and the postpartum period, complement gene variant mediated thrombotic microangiopathy (P-cTMA) can be life threatening for the mother and the child. We describe pregnancy and delivery outcomes of pregnancies a) before cTMA manifestation, b) complicated by P-cTMA, and c) after first manifestation of cTMA in such women.

Method: This study provides an update of patients enrolled in the Vienna TMA Cohort (VTC) as of January 2020. Demographic and clinical data were retrieved from the electronic and paper-based health care records of our institution and from the Austrian Mother-Child Health Passport. Pregnancy outcomes include live births (full term, moderate to late preterm, very preterm, extremely preterm) or deaths (miscarriage, foetal death, stillbirth, neonatal death). Among delivery outcome we ascertained spontaneous vaginal delivery; Caesarean section, gestational age, birth weight and birth weight categories, birth height, head circumference, Apgar scores, admission to a neonatal intensive care unit, and the presence of malformations.

Results: We recorded 58 pregnancies (41 live births/21 women, including one set of twins; 4 abortions and 1 stillbirth in 3 women without live births; 1 ongoing pregnancy; successful pregnancies: 40/57=70%) of 25 women (mean age [years] at first pregnancy 28.2±7.4, at cTMA manifestation 33.2±16.5). Currently 6 women have a kidney transplant and 4 have died (each death not related to pregnancy). Detailed pregnancy outcomes are shown in Figure 1. Table 1 indicates delivery outcomes of 41 live births. 6/8 neonates of pregnancies complicated by cTMA were female. Caesarean sections (female: 11/19, 58%; male: 9/24, 38%; p=0.11), preterm deliveries (female: 7/19, 37%; male: 5/24, 21%; p=0.09), and low birth weight (female: 6/19, 32%; male: 3/24, 13%; p=0.02) were more frequent among 43 pooled live births and stillbirths with known sex.

Conclusion: Overall, pregnancy and delivery outcomes were poor in pregnancies complicated by cTMA as compared to pregnancies before or after cTMA manifestation. The rate of Caesarean section, preterm delivery, and low birth weight was somewhat higher among female as compared to male neonates and stillbirths. Furthermore, neonatal female gender should be explored as risk factor for cTMA manifestation.

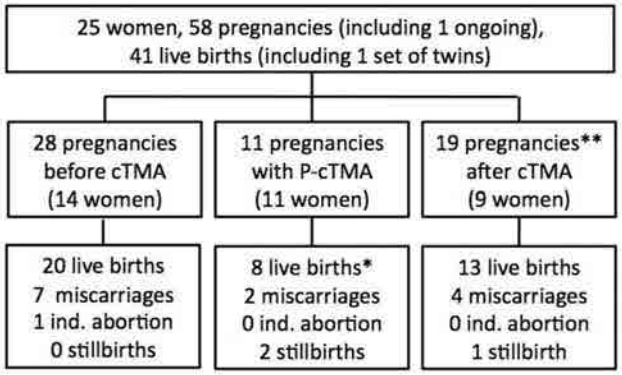


Figure 1. Pregnancies before cTMA manifestation, pregnancies resulting in cTMA (P-cTMA), and pregnancies after manifestation of cTMA (*, including 1 set of twins; **, including 1 ongoing pregnancy; ind., induced).

Table 1. Delivery outcomes of 41 live births

Characteristic	All	Before cTMA	Pregnancy With cTMA	After cTMA	P*
Women, n	21	12	7	6	1.0
Live births, n	41	20	8**	13	-
Gestational age, weeks	38 + 2	39 + 2	34 + 2	37 + 2	0.01
FT/MLP/VP/EP/u, n	29/5/3/1/3	16/1/0/0/3	3/1/3/1/0	10/3/0/0/0	0.01
Mode of delivery, C/V, n	19(46%)/22	10(50%)/10	6(75%)/2	3(23%)/10	0.07
Female/u, n	18(44%)/1	7(35%)/1	6(75%)	5(38%)	0.06
Weight, g	3,061±833	3,357±496	2,188±1,213	3,101±578	0.07
LBW/VLBW/ELBW/u, n	3/3/1/5	1/0/0/4	0/3/1/1	2/0/0/0	0.01
SGA/AGA/LGA/u, n	4/30/2/5	2/14/0/4	2/4/1/1	0/12/1/0	0.04
Length, cm	49±3.8	50±2.1	44.6±6.2	49.8±2.4	0.09
Head circumference, cm	33.8±2.1	34.6±1.4	31.9±3.5	33.8±1.4	0.11
Apgar score at 1 minute	8.5±0.9	8.9±0.6	8.2±0.7	8.3±1	0.11
Apgar score at 5 minutes	9.6±0.7	9.9±0.3	9.5±0.5	9.4±1	0.24
Apgar score at 10 minutes	9.6±0.4	9.9±0.3	9.6±0.5	9.8±0.4	0.28
Admission to NICU/u, n	7/4	0/3	6(75%)/1	1/0	0.01
Malformations, n	5	3	1	1	0.92

Data are given as mean±SD unless not specified otherwise

*, with cTMA vs. before & after cTMA;

**, including 1 set of twins

n, number; u, unknown; g, grams; cm, centimeter; NICU, neonatal intensive care unit

FT, full term; MLP, moderate to late preterm; VP, very preterm; EP, extremely preterm

C, Caesarean section, V, vaginal

LBW, low birth weight; VLBW, very low birth weight; ELBW, extremely low birth weight

SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age

P0232

REFERENCE INTERVALS FOR SERUM CREATININE, CYSTATIN C AND EGFR LEVELS IN THE HEALTHY ADULT POPULATION IN SOUTH CHINA

Junzhe Chen[1], Ying Tang[1], Zhenjian Xu[1], Qiuyan Huang[1], Li Ling[2], Anping Xu[1]

[1]Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Department of Nephrology, Guangzhou, P.R. China and [2]School of Public Health, Sun Yat-sen University, Faculty of Medical Statistics and Epidemiology, Guangzhou, P.R. China

Background and Aims: Serum creatinine (SCr), serum cystatin C (SCyc) and estimating GFR (eGFR) calculated by calculation formula are the most popular parameters to estimate renal function in clinical setting. Reference intervals (RIs) of these important indices are very essential for prompt and precise clinical diagnosis, treatment and management especially for early asymptomatic chronic kidney injury or acute kidney injury. There are few reports on RI for these renal function indices in Chinese healthy population. Hence, it is important to establish the RIs for Chinese. Our study was performed to determine the RIs of SCr, SCyc and eGFR in healthy adult population in South China in large sample size by age and sex group.

Method: Apparently healthy Chinese ethnic individuals without diagnosis of chronic diseases and medications according to the record of our hospital's outpatient service system, aged between 18 and 89 years old and performed health screening in Sun-Yat Sen Memorial Hospital in the last 5 years from Jan 01, 2014 to Dec 31, 2019 were recruited into this study. Individuals with abnormality of urinary system checked with ultrasound, abnormal dipstick urine test including proteinuria, hematuria, urinary infection and low urine osmolality, ALT or AST exceeds the upper limit of reference levels, fasting blood sugar>7.0 mmol/l, Hb<110 g/L or dyslipidemia, gout or hyperuricemia were excluded.

Results: A total of 3480 healthy individuals (female 1645 and male 1835) were enrolled in this study (Table 1). We analyzed the median, 2.5 and 97.5 percentile of SCr, SCysc and eGFR in each age group by sex. The RIs for SCr with respect to age (Table 2) (ranges of 18-29, 30-39, 40-49, 50-59 and 60+ years) were 52.00-87.47, 52.20-82.80, 53.00-86.00, 63.78-88.20 and 53.80-95.20μmol/L for females, and 72.38–112.00, 73.00–111.00, 71.00–112.00, 69.00-114.82 and 70.00-113.00μmol/L for males, respectively. Meanwhile, the RIs for SCysc with respect to age (Table 3) (ranges of 18–29, 30–39, 40–49, 50-59 and 60+ years) were 0.51-1.00, 0.47-1.03, 0.49-1.13, 0.51-1.19 and 0.63-1.25 mg/L for females, and 0.57-1.10, 0.57-1.23, 0.57-1.21, 0.60-1.28 and 0.67-1.39 mg/L for males, respectively. The levels of Scr in female were significantly lower than male ($P<0.001$) and remained relatively stable across different age group both in male and female (Figure 1). However, our results showed that the levels of SCyc were abruptly increased from 50 years old in healthy population especially in female, and the differences between male and female disappeared in more than 60 years old age group (Figure 2). The medians of reference GFRs(CKD-EPI$_{2012Scr-SCy}$) (Table 4) are 108.68, 104.25, 97.80, 91.11 and 82.89 mL/min/1.73 m^2 for males, and 113.35, 111.64, 104.74, 92.22 and 77.72 for females, in healthy adult aged 18-29, 30-39, 40-49, 50-59 and 60+ years, respectively. Our results showed that higher eGFR and lower decline rate per year of eGFR in female compared with male whose age were under 40 years old, as shown in Figure 3. However, thereafter, the decline rate of eGFR was faster in female than male, which shown as 0.77 in 40-49, 1.39 in 50-59 and 1.12 mL/min/1.73 m^2 per year in over 60 years old in female and 0.65 mL/min/1.73 m^2 in 40-49, 0.74in 50-59 and 0.82 mL/min/1.73 m^2 per year in more than 60 years old in male. The levels of eGFR in female were decreased and lower than male after 60 years old. Similar trend was confirmed by CKD-EPI$_{2009Scr}$.

Conclusion: In conclusion, this study provides sex and age specific normal reference values for SCr, SCyc and eGFR of healthy adult population in South China. Our results remind clinicians should consider the important effects of sex and age when evaluate the real renal function of patients and local RIs should be established in clinical setting.

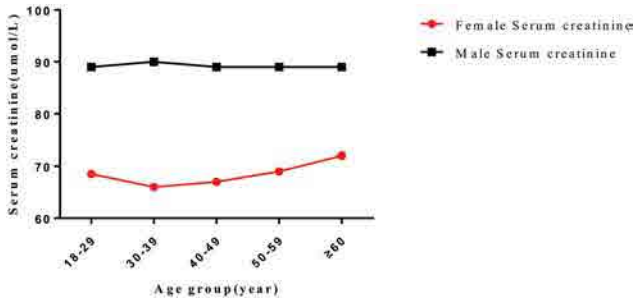


Figure 1. The level of serum creatinine in different age group by sex

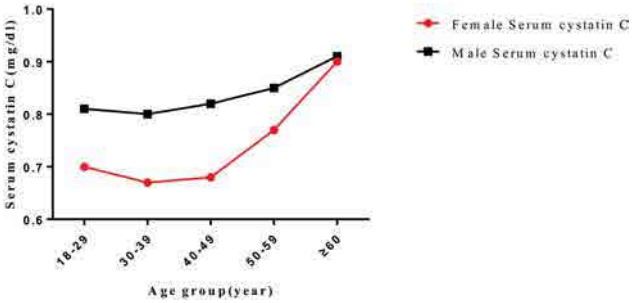


Figure 2. The level of serum cystatin C in different age group by sex

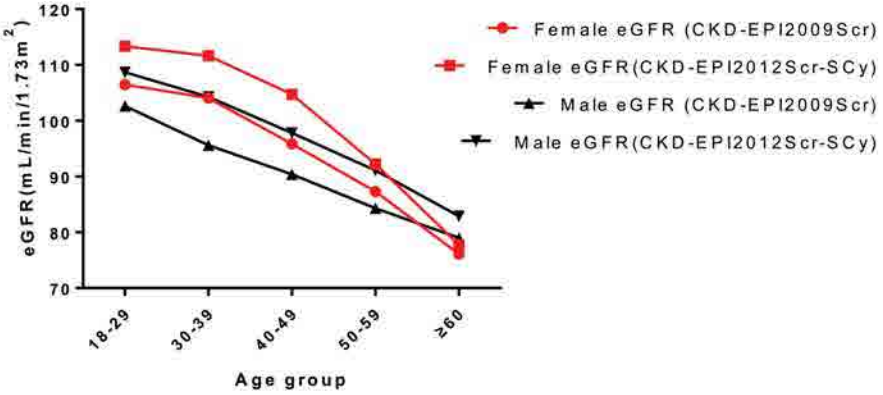


Table 1. The baseline characteristics of the 3480 healthy Chinese adult population

Parameters	Total (n=3480)	Female (n=1645)	Male (n=1835)
WBC	5.84(4.97-6.87)	5.66(4.78-6.65)	5.96(5.17-7.08)
Hb, g/L	140.00(130.00-150.00)	131.00(123.00-137.00)	152.00(145.00-159.00)
PLT	246.00(211.00-285.00)	258.00(221.00-297.50)	234.00(202.00-271.00)
AST, U/L	19.00(16.75-23.00)	18.00(16.00-21.00)	20.00(18.00-24.00)
ALT, U/L	17.00(12.00-23.00)	14.00(11.00-18.00)	20.00(15.00-26.00)
TBIL, umol/L	12.90(10.20-16.30)	11.60(9.25-14.30)	13.95(11.10-17.80)
ALB, g/L	43.70(41.70-45.60)	42.90(41.20-44.70)	44.30(42.20-46.20)
TG, mmol/ L	0.98(0.75-1.33)	0.87(0.69-1.17)	1.09(0.83-1.43)
CHOL, mmol/ L	4.70(4.22-5.09)	4.70(4.24-5.13)	4.69(4.21-5.08)
LDL-C, mmol/ L	2.96(2.61-3.27)	2.91(2.55-3.21)	3.01(2.65-3.30)
HDL-C, mmol/L	1.32(1.13-1.54)	1.44(1.24-1.64)	1.22(1.07-1.40)
Glu, mmol/L	5.00(4.70-5.40)	5.00(4.70-5.30)	5.10(4.80-5.40)
UA, umol/L	338.00(286.00-388.00)	293.00(255.00-337.00)	373.00(334.00-411.00)
Urine Specific Gravity	1.018(1.016-1.023)	1.016(1.013-1.021)	1.02(1.016-1.024)

Figure 3. The decline of eGFR in different sex group

P0233

ISOLATED MICROHEMATURIA IN ADOLESCENTS IS NOT ASSOCIATED WITH RENAL OR URINARY TRACT CANCER IN MIDDLE AGE

Adi Leiba[1], Boris Fishman[2]

[1]Samson Assuta Ashdod University Hospital, Nephrology and Hypertension Institute, Ashdod, Israel and [2]Tel HaShomer Hospital, Department of Medicine D, Ramat Gan, Israel

Background and Aims: Chronic or persistent isolated microhematuria (microhematuria without proteinuria) is not as benign as originally thought. It has been associated with an almost 20-fold risk of developing ESRD (End Stage Renal Disease) in adulthood. It is still unclear if this chronic glomerular bleed increases the risk of renal or urinary tract tumors, secondary to ongoing irritation and inflammation. This is a valid question, especially as an adult with long standing isolated "glomerular" microhematuria can appear with an event of macrohematuria. In order to answer these questions, we studied the association between adolescent microhematuria and renal or urinary tract tumors in adulthood.

Method: A retrospective study based on a cohort of 2,172,866 Jewish adolescents (60% men) aged 16-19 who underwent a mandatory physical examination between ages of 16 and 19 years from 1967 to 2007 prior to their conscription. Urothelial Transitional cell carcinoma (TCC) and Renal cell carcinoma (RCC) incidence through December 31, 2012 was identified by linkage to the national cancer registry. Multivariable-adjusted Cox regression models were used to estimate hazard ratios (HRs) for RCC and TCC among adolescents who were diagnosed with persistent asymptomatic isolated hematuria after comprehensive medical evaluation. The models were adjusted for: Sex, age, year of birth, socio-economic status, BMI, years of education and country of origin.

Results: Over a median of 22 years (interquartile range of 13-31 years) of follow-up, 2007 and 1112 incident cases of TCC and RCC, respectively, occurred amongst the study population. Persistent hematuria was not associated with TCC with crude HR 1.15 (95% CI, 0.37-3.57) and adjusted HR of 1.08 (95% CI, 0.35-3.36), nor with RCC with crude HR 1.11 (95% CI, 0.28-4.457) and adjusted HR of 0.93 (95% CI, 0.23-3.75).

Conclusion: Isolated persistent microhematuria, while carrying a small risk of kidney disease progression, is not associated with either renal or urinary tract tumors. Screening guidelines among these patients should follow the general age and sex-matched approach.

P0234

LOW URINARY CITRATE LEVELS ARE NOT SPECIFIC OF AUTOSOMAL POLYCYSTIC KIDNEY DISEASE (ADPKD) AND ARE PRESENT WHEN RENAL FUNCTION IS IMPAIRED IN ALL NEPHROPATIES.

Francisco-Jose Borrego-Utiel[1], Enoc Merino Garcia[1], Isidoro Herrera[2], Clara Moriana Dominguez[1], Victoria Camacho Reina[2], Esther Ocaña Perez[2], Maria José García Cortés[1]

[1]UGC DE NEFROLOGIA. HOSPITAL UNIVERSITARIO DE JAEN, Spain and [2]UGC ANALISIS CLINICOS. HOSPITAL UNIVERSITARIO DE JAEN, Spain

Background and Aims: In polycystic kidney disease (PKD) it is frequently found a reduction in urinary citrate that is related with degree of renal impairment but it is unknown if this alteration is specific or if it is also present in other nephropathies. Recently it has been suggested that urinary citrate could be a marker of covert metabolic acidosis and reflects acid retention in chronic kidney disease (CKD). Our aim was to compare urinary citrate in PKD with other renal diseases and to show its relation with serum bicarbonate and excretion of uric acid and calcium.

Method: We determined citrate, calcium and uric acid in 24-hour urine in patients with PKD and with other nephropathies with varied degree of renal impairment followed in a outpatient clinic of nephrology.

Results: We included 291 patients, 119 with glomerular diseases, 116 with PKD, 21 with other nephropathies, and 35 patients with normal renal function. Urinary citrate was higher in women (Females 309±251 mg/gCr vs. males 181±145 mg/gCr, $p<0.001$) and in patients with normal renal function (normal 380±210 mg/gCr; PKD 203±166 mg/gCr; glomerular 279±282 mg/gCr; $p<0,001$). PKD patients showed similar values of urinary citrate to patients with glomerular diseases and with other nephropathies. We observed a progressive reduction in urinary citrate parallel to degree of renal impairment, in a comparable way among patients with PKD and glomerular diseases. We did not observe a relationship between urinary citrate and serum bicarbonate levels. Calcium and uric acid elimination in ADPKD patients was similar to other nephropathies and lower to patients with normal renal function. However, serum uric acid was significantly higher in glomerular patients than other nephropathies after adjust with glomerular filtration rate and sex.

Conclusion: Hypocitraturia is not specific of PKD but it is also present in all nephropathies. Urinary citrate are related to degree of renal impairment and it is not related with serum bicarbonate. We think that it could be interesting to study urinary citrate as a marker of renal function and its role as prognostic factor of renal deterioration.

P0235 LOW SERUM 3-METHYL HISTIDINE LEVEL IS ASSOCIATED WITH AORTIC STIFFNESS IN HEMODIALYSIS PATIENTS

Yu-Chi Chang[1], Chi-Chong Tang[1], Bang-Gee Hsu[1,2]

[1]Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Division of Nephrology, Hualien, Taiwan, R.O.C. and [2]Tzu Chi University, School of Medicine, Hualien, Taiwan, R.O.C.

Background and Aims: 3-methyl histidine (3MH) is a non-proteinogenic amino acid and an index of muscle breakdown. Subclinical protein malnutrition is an independent association with arterial stiffness. The aim of this study was to evaluate the relationship between serum 3MH levels and carotid-femoral pulse wave velocity (cfPWV) values in chronic hemodialysis patients.

Method: Fasting blood samples and baseline characteristics were obtained from 136 chronic hemodialysis patients. Serum 3MH was performed with high-performance liquid chromatography and mass spectrometry. Aortic arterial stiffness was defined as cfPWV values >10 m/s according to the ESH-ESC 2013 guidelines.

Results: Among 110 chronic hemodialysis patients, 45 patients (40.9%) were in the aortic arterial stiffness group. When compared to those in the control group, the aortic arterial stiffness group had high prevalence of diabetes mellitus ($p < 0.001$), hypertension ($p = 0.006$), older age ($p = 0.002$), higher systolic blood pressure ($p = 0.016$), and lower serum 3MH level ($p = 0.001$). Multivariable logistic regression analysis of the factors significantly associated with aortic arterial stiffness revealed that serum 3MH levels (odds ratio (OR): 0.791, 95% confidence interval (CI): 0.691–0.906, $p = 0.001$) was the independent predictor of aortic arterial stiffness in chronic hemodialysis patients. Multivariable forward stepwise linear regression analysis also showed that logarithmically transformed 3MH level (log-3MH, $\beta = -0.322$, adjusted R^2 change = 0.127, $p < 0.001$) was an independent predictor of cfPWV values in chronic hemodialysis patients. The area under the receiver-operating characteristic (ROC) curve indicates the diagnostic power of 3MH at predicting aortic stiffness of chronic hemodialysis patients was 0.691 (95% CI: 0.595-0.775, $p = 0.0002$).

Conclusion: Serum-free 3MH level is negatively associated with aortic arterial stiffness in chronic hemodialysis patients.

P0236

COMPARISON OF THE CHARACTERISTICS AND SEVERITY OF RESTLESS LEG SYNDROME AND INSOMNIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND RENAL TRANSPLANT RECIPIENTS

Maria Pappa[1], Haralambos Pappas[2], Elisabeth Kokkolou[3], Andrikos Aimilios[3], ANILA DUNI[2], Karolos Pavlos Rapsomanikis[2], Olga Balafa[2], Georgios Dimakopoulos[2], Paschalis Steiropoulos[4], Ioannis Pnevmatikos[5], Athanasios Konstantinidis[6], Michalis Mitsis[7], Evangelia Ntounousi[2]

[1]Laiko General Hospital, Nephrology, Athens, Greece, [2]University of Ioannina, Nephrology, School of Medicine, Ioannina, Greece, [3]General Hospital Hatzikosta, Nephrology, Ioannina, Greece, [4]Democritus University of Thrace, Respiratory, Alexandroupolis, Greece, [5]Democritus University of Thrace, Intensive Care Unit, Alexadroupolis, Greece, [6]University of Ioannina, Pneumonology, Ioannina, Greece and [7]university of Ioannina, Surgery, Ioannina, Greece

Background and Aims: Symptoms of restless legs syndrome (RLS) are common in patients with chronic kidney disease (CKD) and on dialysis, affecting up to 25% of patients when the international RLS diagnostic criteria are applied. RLS has been associated with disordered sleep, impaired quality of life, increased cardiovascular morbidity and mortality risk in patients with CKD. The aim of our study was to examine the relationship between RLS and the prevalence and severity of insomnia in non-dialysis CKD patients (CKD stage IV and V), in haemodialysis and PD patients, in renal transplant recipients (RTRs) as well as to identify the risk factors independently associated with RLS prevalence and severity in each group.

Method: 436 patients were included in the study (152 patients with CKD stage IV and V, 117 haemodialysis patients, 78 PD patients and 89 RTRs). RLS diagnosis was made according to IRLSSG diagnostic criteria. The questions of the IRLSSG Severity Scale were answered. Athens Insomnia Scale (AIS) was used for the diagnosis of insomnia. Statistical analysis was performed with appropriate parametric and non-parametric tests and regression analysis models.

Results: Applying the IRLSSG criteria for diagnosis, the prevalence of RLS was 17%, 25.9%, 26.5%, 32.1% and 16.9% in patients with CKD stage IV, CKD stage V, hemodialysis patients, PD patients and RTRs respectively. The mean severity of the syndrome was higher in PD patients (14.64), followed by haemodialysis patients (12), CKD stage V patients (11.9), KTRs (11.3) and patients with CKD stage IV patients (10.5). Prevalence of RLS did not significantly differ between groups. CKD patients displayed the lowest presence of insomnia, while PD patients showed the relatively highest presence of insomnia. The mean severity of insomnia differed between the pairs: RTRs vs PD patients, RTRs vs haemodialysis patients and PD patients vs patients with CKD stage IV and V ($p < 0.05$). RLS in all groups correlated with the presence of peripheral neuropathy and female gender. By regression analysis models we found that among CKD patients, presence of RLS independently correlated with number of pregnancies in women, previous cerebrovascular disease, hypothyroidism requiring treatment and antidepressant drugs use, whereas RLS severity independently correlated with the presence of peripheral neuropathy. Regarding hemodialysis patients, presence of RLS independently correlated with body mass index (BMI), female gender, antidepressant drugs use and serum PTH levels. RLS severity in the same group independently correlated only with female gender. Regarding PD patients, RLS presence was independently associated with number of pregnancies in women and left ventricular ejection fraction. RLS severity in the same group was independently associated only with the presence of peripheral arterial disease. Among RTRs, RLS presence independently correlated with female gender and a lower GFR. We were the first to find that presence of RLS was associated with a higher bone mass density and lower levels of 25-OH vitamin D.

Conclusion: The prevalence and severity of RLS and insomnia worsen as kidney function deteriorates in CKD patients, being most burdensome among patients with stage V CKD, haemodialysis and PD patients. The severity of insomnia is especially increased in PD patients. Although the frequency of RLS decreases in KTRs, it still occurs at higher rates compared to the general population. Further studies are needed to investigate the relationship between RLS and associated risk factors in patients with CKD and following kidney transplantation.

P0237 COMPARISONS OF CLINICAL FEATURES IN GITELMAN SYNDROME PATIENTS WITH DIFFERENT URINARY CALCIUM EXCRETIONS

Lei Zhang[1], Bingbin Zhao[1], Xiaoyan Peng[1,2], Ying Wang[1], Limeng Chen[1]

[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Nephrology and [2]Children's Hospital Affiliated to Capital Institute of Pediatrics, Nephrology

Background and Aims: Hypocalciuria is considered typical in Gitelman syndrome (GS). However, a few GS cases diagnosed by gene testing presented as normocalciuria have been reported in recent years. Our study is to observe the clinical features in GS patients with different urinary calcium excretions, and investigate the value of urinary calcium excretion in the clinical classification for GS.

Method: GS cases from the National Rare Diseases Registry System of China (NRSC) (2016-2018) with SLCl2A3 gene screened in Peking Union Medical College Hospital were collected. The features of urinary calcium excretion were analyzed, and the phenotypes of patients with hypocalciuria were compared to those with normocalciuria. Hydrochlorothiazide (HCT) test was performed and the maximal increasement of chloride excretion fraction (△FECl) was calculated to evaluate the extent of NCC dysfunction.

Results: A total of 83 genetically proven GS patients was included, with the mean age at diagnosis of 31.0±13.0 years, and the male/female ratio was 1.4:1. Among them, 53 (63.9%) patients had hypocalciuria. The ratio of urinary calcium/creatine was significantly lower in patients with hypocalciuria (0.08±0.06mmol/mmol) compared to those with normocalciuria (0.47±0.28mmol/mmol), with a *P* value of <0.001. Age, gender, estimated glomerular filtration rate, blood pressure, alkalosis, and serum and urinary electrolytes including potassium, magnesium, natrium, chloride, and phosphorus were all comparable between patients with hypocalciuria and normocalciuria. Based on a standardized symptom questionnaire, fatigue (52.8% vs. 76.7%, *P*=0.03) and polyuria (9.4% vs. 30.0%, *P*=0.02) were less frequently reported in hypocalciuria patients, while all the other clinical symptoms were comparable. Sixteen patients in each group underwent HCT test, and the △FECl value was comparable between patients with hypocalciuria and normocalciuria (median, 0.54% vs. 0.83%, *P*=0.88), both of which indicated a blunt response to HCT (<2.86% according to our previous study).

Conclusion: The results show that 63.9% of the GS patients in this study had hypocalciuria. There is no definite relationship between urinary calcium excretion, phenotype and the extent of NCC dysfunction.

P0238 **LONG-TERM OUTCOME OF CHILDHOOD IDIOPATHIC NEPHROTIC SYNDROME**

Myriam Dao[1,2], Aurélie Hummel[1,2], Olivia Boyer[2,3], Marina Charbit[2,3], Dominique Joly[1,2], Kathleen Dessaix[1,2], Rémi Salomon[2,3], Bertrand Knebelmann[1,2], Aude Servais[1,2]

[1]Necker Enfants Malades, Adult nephrology, Paris, France, [2]Centre de référence du Syndrome néphrotique idiopathique de l'enfant et de l'adulte and [3]Necker Enfants Malades, Pediatric Nephrology, Paris, France

Background and Aims: Little is known about the long-term outcome of childhood idiopathic nephrotic syndrome (INS), in particular long-term complications, rate of relapses, frequency of prolonged steroid (S) and immunosuppressive treatment (IS). The choice of immunosuppressive drug remains discussed. Our aim was to study the long-term outcome in adulthood of patients with INS diagnosed during childhood.

Method: In this monocentric retrospective study, we included all adult patients (>18 years) admitted in our nephrology department between 2013 and 2019 with INS diagnosed during childhood. Patients who reached ESRD during childhood were excluded. Data regarding the outcome in adulthood were obtained through clinical database and medical charts.

Results: Eighty-two patients (M/F = 2/1) were included. Sixty-height patients had steroid-sensitive nephrotic syndrome (SSNS), including 52 with steroid-dependant nephrotic syndrome (SDNS). The other 14 patients had steroid-resistant nephrotic syndrome (SRNS). The median age at diagnosis was 3.9 years (1.2-16.5). The median number of relapses during childhood was 12 (0-52), 0.9/patient/year. 89% of patients received IS therapy in addition to S during childhood: median number of successive therapeutic lines was 3 (0-10) per child.

Median follow-up during adulthood was 4.6 (0.1-25) years. 67% of patients experienced at least one relapse during adulthood, with a median number of relapses of 0.53 (0-3.7)/patient/year. Risk of relapse during adulthood was significantly associated with the total number of relapses during childhood (p=0.015) and with the number of relapses per year during childhood (p=0.007). 45% of patients received IS in addition to S during adulthood, mainly mycophenolate mofetil (23/82), calcineurin inhibitors (21/82) and rituximab (12/82). High blood pressure was observed in 22% of patients.

At last follow-up, median eGFR was 90 (64-117) mL/min/1.73㎡ in SSNS patients, 86 (57-126) mL/min/1.73㎡ in SDNS patients and 70 (23-113) mL/min/1.73㎡ in SRNS patients. Only 4/82 patients presented with eGFR lower than 60 mL/min/1.73㎡. Among them, 3 had SRNS. Only 1 thrombo-embolic event and 3 severe infections were reported.

Bone densitometry was performed in 26 adult patients and osteopenia was found in 19 of them (73%).

Conclusion: The incidence of relapses in adulthood was relatively high in our study. However bias related to inclusion criteria could play a role. Whereas renal function remained normal in most patients, high blood pressure and osteopenia were frequent but major complications were rarely reported.

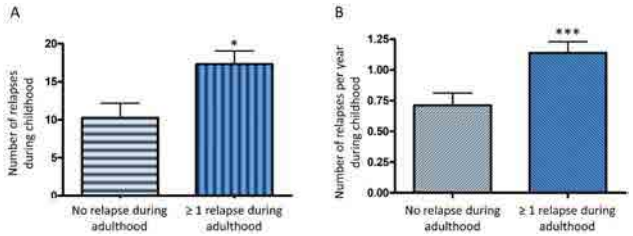


Figure:

Risk of relapse during adulthood was significantly associated with the total number of relapses during childhood (A) and with the number of relapses per year during childhood (B). * $p < 0.05$; *** $p < 0.001$.

P0239

THE EFFECT OF CHRONIC KIDNEY DISEASE AND DIALYSIS MODALITIES ON THE EXPRESSION OF T REGULATORY (CD4+CD25+FOXP3+) AND NATURAL KILLER (CD56+CD16+) CELLS

Erasmia Sampani[1], MARIA STANGOU[2], Dimitra Vasileia Daikidou[1], Despoina Asouchidou[1], Vasiliki Nikolaidou[1], Evangelos Memmos[1], Panagiotis Giamalis[1], Chrysostomos Dimitriadis[1], Asimina Fylaktou[1], Aikaterini Papagianni[2]

[1]Ippokrateio - General Hospital of Thessaloniki, Thessaloniki, Greece and [2]Aristotle University of Thessaloniki, Thessaloniki, Greece

Background and Aims: Tregs regulate immune responses and maintain self-tolerance, while Natural Killer cells (NK) are cytotoxic lymphocytes critical for both adaptive and innate immunity. The presence of chronic kidney disease (CKD) is often characterized by disturbances in immune responses, including dysregulation between tolerance and cytotoxicity. Aim of the present study was to evaluate the influence of CKD on the Tregs (CD4+CD25+FoxP3+) and NK cells, as well as the effect of hemodialysis (HD) and peritoneal dialysis (PD) on these subtypes.

Method: A total of 40 CKD Stage V patients and 15 healthy volunteer subjects were recruited into our study. Peripheral Tregs and NK cells were isolated from whole blood samples using flow cytometry, and the results were compared to those of age and gender matched controls. The immunologic profile of CKD patients was repeated 6 months after HD initiation (n=20) and PD (n=20) in order to investigate the effect of different dialysis methods.

Results: Patients with CKD had significantly reduced populations of CD4+CD25+ FoxP3+ Tregs (47.5± 28.8 vs 71.5±24.7) p=0.01, while there was no difference in NK cells between patients and controls (16.4±8.1% vs. 13.4±9.1%), p=NS, respectively. There were no differences between patients started on HD or PD in terms of clinical and laboratory parameters. Frequencies and total numbers of Tregs were significantly reduced after 6 months of HD, from 7.6±2.1% to 5.2±2.3%, p=0.009, and from 53.6±26K/μL to 36.9±19K/μL, p=0.02, respectively, while showed no differences on PD patients, from 5.3±3.3% to 5.6±2%, p=NS and 33.2±27K/μL to 45.6±28K/μL, p=NS, respectively. NK cells were increased in HD patients, not reaching statistical significance (245±156K/μL to 261±128K/μL). Frequencies of NK cells were positively correlated with CRP (r=0.56, p=0.009) and Intimal media thickness (IMT) (r=0.48, p=0.03)

Conclusion: The results of our study show that initiation of hemodialysis (HD) seems to reduce the expression of CD4+CD25+FoxP3+ T cells while peritoneal dialysis (PD) doesn't seem affect this cell population. The immune alterations observed in hemodialysis patients may have a clinical impact on chronic inflammation and atheromatosis.

P0240

ACQUIRED THROMBOTIC THROMBOCYTOPENIC PURPURA IN HIV POSITIVE PATIENTS SUCCESSFULLY TREATED WITH CAPLACIZUMAB: ABOUT TWO CASES.

Dulciane Baes[1], Paul Nicolazzi[1], Florence Moulonguet[1], Philippine Simphal[1], Marc Hazzan[1], Mehdi Maanaoui[1], François Provôt[1]

[1]*CHU Lille, Department of Nephrology, Lille, France*

Background and Aims: Acquired thrombotic thrombocytopenic purpura (aTTP) is a thrombotic microangiopathy still nowadays associated with a high risk of death. Standards of care included at first the association of plasmatic exchanges, Rituximab and steroids. The emergence of Caplacizumab, a nanobody targeting the A1 receptor of Von Willebrand Factor (VWF), significantly changed the prognosis of the disease. Thrombocytopenia is frequent in HIV positive patients, and aTTP is frequently considered. Prevalence of HIV positive in aTTP patients ranges from less than 1% in western countries, up to more than 50% in African countries. The pathophysiology still remains partially understood, leading to the development of autoantibodies targeting the ADAMTS13 metalloprotease. For now, no specific recommendations are available, and standards of care consist in treating HIV positive patient the same as other aTTP patients. We present the first description of two HIV positive patients, successfully treated with caplacizumab.

Method: We report there two cases of black women, respectively aged 31 (Patient 1) and 52 years old (Patient 2), both positive for HIV for several years. The first one had stopped any antiviral treatment few months ago, and had a positive blood viral load of 110764 copies/ml. Her CD4+ rate was 30/mm^3. The second one was under antiviral medication, with a negative viral load and a CD4+ rate of 295/mm^3. Both were admitted in our department because of low platelet levels and hemolysis, associated with inflammatory triggers. Bacteriema for *Streptococcus mitis* was discovered on admission in Patient 1 and Patient 2, who had a long-term follow-up for Still disease, presented with a flare-up.

Results: Both patients had positive anti-ADAMTS13 autoantibodies (Patient 1: titer 42 UI/ml, Patient 2: 45 UI/ml), with undetectable ADAMTS-13 activities. They were treated with plasmatic exchanges until platelets levels reached over 150 G/L, steroids 1.5 mg/kg/j, Rituximab 375 mg/m^2 at day 1, 4 and 8 and finally caplacizumab 10 mg before the 2nd plasmatic exchange and every day until the ADAMTS13 activity reached over 20%. Antiviral therapy and antibiotics were initiated in Patient 1 and antiviral therapy was maintained in Patient 2. The evolution was promptly favorable with normalization of platelets levels at Day 4 in Patient 1, and Day 15 in Patient 2. Patient 1 stopped caplacizumab at Day 12 and Patient 2 at day 17, when ADAMTS 13 reached over 20%. None of them relapsed after treatment, with a respective follow-up of 4 and 2 months.

Conclusion: Caplacizumab seems to be a safe and efficient treatment for aTTP in HIV positive patients.

P0241 **ACUTE KIDNEY INJURY AFTER NEPHRECTOMY: A NEW NOMOGRAM TO PREDICT POSTOPERATIVE RENAL FUCTION**

Lingyu Xu[1], Chenyu Li[1], Chen Guan[1], Yue Zhang[1], Yan Xu[1]

[1]*The Affiliated Hospital of Qingdao University, Department of Nephrology, Qingdao, P.R. China*

Background and Aims: Acute kidney injury (AKI) due to nephrectomy is associated with adverse prognosis. The study aimed to develop a nomogram based on preprocedural features for early prediction of AKI and to assess the prognosis in patients after nephrectomy.

Method: The study included a development cohort of 1111 patients and an additional validation cohort of 356 patients who underwent nephrectomy. Stepwise and logistic regression analyses were used to evaluate the association between predictors and AKI. Incorporating all independent predictors, a nomogram for postoperative AKI was developed and validated. Patients were followed up for 5 years to assess renal fuction, acute kidney disease (AKD), chronic kidney disease (CKD), hospital readmission and death were key prognostic outcomes we focused on.

Results: Radical nephrectomy (odds ratio (OR) = 3.57, $p < 0.001$), aspirin (OR = 1.79, $p = 0.008$), systolic blood pressure (OR = 1.41, $p = 0.004$), triglyceride (OR = 1.26, $p = 0.024$) were independent risk factors for postoperative AKI, while albumin (OR = 0.72, $p = 0.031$) was a protective factor for postoperative AKI. Patients with a higher estimated glomerular filtration rate (eGFR) (60-90 ml/min/1.73 m^2, OR = 0.41, $p = 0.004$; $\geq$ 90 ml/min/1.73 m^2, OR = 0.37, $p < 0.001$) were less prone to AKI than those with a lower eGFR ($<$ 15 ml/min/1.73 m^2). These predictors were all included in the final nomogram to calculate the probability of postoperative AKI. The incidence of AKD and CKD were 27.12% and 18.64% in AKI group, which were much higher than those in no AKI group ($p < 0.001$).

Conclusion: The nomogram had excellent predictive ability and might have significant clinical implications for the early detection of AKI in patients undergoing nephrectomy.

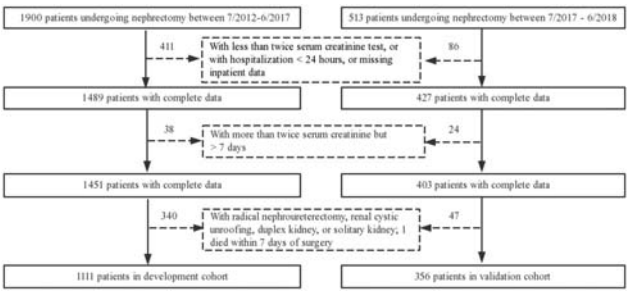


Figure 1 Flow diagram of patients enrollment.

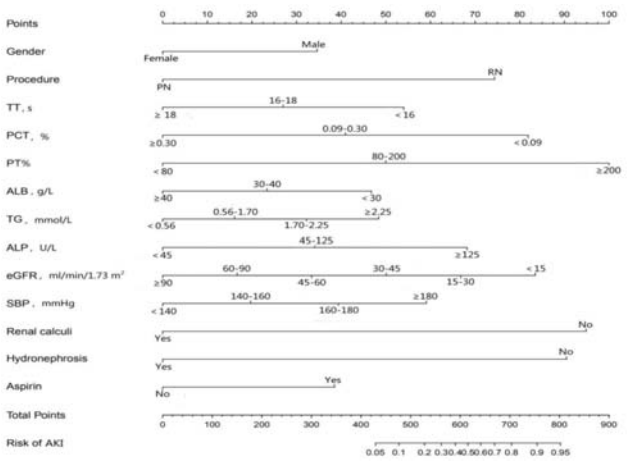


Figure 2 A logistic regression-based nomogram to predict the possibility of AKI after nephrectomy. To obtain the predicted probability of postoperative AKI,locate patient values on each axis.Draw a vertical line upward to the "Points" axis to determine the points of the variable.Sum the points for all variables and locate the sum on the "Total Points" axis.Draw a vertical line down to the "Risk of AKI" axis to find the patient's possibility of AKI after nephrectomy. The predicted range of developing postoperative AKI was from 5% to 95%.

P0242

SUBGROUP EFFICACY ANALYSIS OF SODIUM ZIRCONIUM CYCLOSILICATE (SZC) IN HYPERKALAEMIC HAEMODIALYSIS PATIENTS IN THE DIALIZE STUDY

Kieran McCafferty[1], Steven Fishbane[2], Bruce Spinowitz[3], Anjay Rastogi[4], Martin Ford[5], Nicolas Guzman[6]

[1]Barts Health NHS Trust, London, United Kingdom, [2]Zucker School of Medicine at Hofstra/Northwell, Hempstead, United States of America, [3]New York-Presbyterian Queens, New York, United States of America, [4]David Geffen School of Medicine, Los Angeles, United States of America, [5]King's College Hospital NHS Trust, London, United Kingdom and [6]AstraZeneca, Gaithersburg, United States of America

Background and Aims: Patients with end-stage renal disease have severely reduced renal potassium excretion and many require haemodialysis (3 days/week) to maintain normal serum potassium (sK^+). The phase 3b DIALIZE study (NCT03303521) showed that sodium zirconium cyclosilicate (SZC) reduces predialysis sK^+ after the long interdialytic interval and is well tolerated in haemodialysis patients with hyperkalaemia. This *post-hoc* analysis of the DIALIZE data assessed the efficacy of SZC in patient subgroups.

Method: The DIALIZE study randomised 196 patients 1:1 to placebo (n=99) or SZC (n=97). The study consisted of an 8-week treatment period, comprising a 4-week SZC dose titration phase followed by a 4-week evaluation phase. The starting dose of SZC was 5 g orally once daily on non-dialysis days (4 days/week) for the 4-week dose titration phase (titrated in 5 g increments to a maximum of 15 g) to achieve predialysis sK^+ 4.0–5.0 mmol/L. Patients maintained a stable SZC dose for the 4-week evaluation phase (SZC 5, 10 or 15 g). Here, we assessed the proportion of treatment responders, i.e. those who during the 4-week evaluation phase achieved predialysis sK^+ of 4.0–5.5 mmol/L during ≥3 of 4 haemodialysis treatments after the long interdialytic interval and who did not require potassium-lowering rescue therapy. Treatment responders were stratified by patient subgroups: sex, country, race, age (years), baseline weight (kg) and baseline sK^+ (mmol/L).

Results: For patients receiving SZC, at baseline 59% were male, mean age was 55.7 years, 52% were white, 11% were Black or African American and 34% were Asian, and mean predialysis sK^+ was 5.8 mmol/L. Using a predialysis sK^+ range of 4.0–5.5 mmol/L, 69.1% (n=67/97) of SZC patients and 19.2% (n=19/99) of placebo patients were deemed treatment responders. Response to SZC was generally consistent across patient subgroups vs placebo for sex, country, race, age, baseline weight and baseline sK^+, with some variation between subgroup subcategories (**Table**).

Conclusion: Our results suggest that SZC is generally effective across all groups of haemodialysis patients with hyperkalaemia. SZC responder rates for some patient subgroup subcategories were limited by low patient numbers.

Subgroup analysis for SZC treatment responders

Subgroup	N	Responders, n (%)	Subgroup	N	Responders, n (%)
Country			**Baseline weight (kg)**		
Great Britain	15	8 (53.3)	≥40–<60	19	14 (73.7)
Japan	28	27 (96.4)	≥60–<80	44	31 (70.5)
Russia	33	25 (75.8)	≥80–<100	23	14 (60.9)
USA	21	7 (33.3)	≥100–<120	8	5 (62.5)
Race			≥120–<190	3	3 (100)
White	50	31 (62.0)	**Baseline sK^+ (mmol/L)**		
Black or African American	11	6 (54.5)	≥5.5–<6.0	49	35 (71.4)
Asian	33	30 (90.9)	≥6.0–<6.5	32	25 (78.1)
Age (years)			≥6.5–<7.0	8	4 (50.0)
≥20–<40	17	10 (58.8)	≥7.0–<7.5	6	2 (33.3)
≥40–<60	36	22 (61.1)	Missing baseline sK^+ at Day −7	2	1 (50.0)
≥60–<90	44	35 (79.5)			
Sex					
Male	57	44 (77.2)			
Female	40	23 (57.5)			

Responders were defined as those who during the 4-week evaluation phase achieved predialysis sK^+ of 4.0–5.5 mmol/L during ≥3 of 4 haemodialysis treatments after the long interdialytic interval and who did not require potassium-lowering rescue therapy. All other patients were defined as non-responders, i.e. those who had >1 missing sK^+ measurement and/or if they received rescue therapy. sK^+, serum potassium; SZC, sodium zirconium cyclosilicate

P0243

WOMEN WORKERS THAT DO NOT HAVE A WATER BOTTLE AT THE WORKPLACE HAVE HIGHER PREVALENCE OF URINARY TRACT SYMPTOMS AND INFECTION.

FABIANA NERBASS[1], Cintia Santo[1], Edilaine Fialek[1], Viviane Calice-Siva[1], Marcos Vieira[1]

[1]*Fundação Pró-Rim, JOINVILLE, Brazil*

Background and Aims: Hydration and toilet behavior at work are associated with urinary tract symptoms (UTs) and infection (UTI) in women. We aimed to evaluate the association between self-reported hydration habits, water access and toilet adequacy at work with UTs and UTI in female workers from five dialysis clinics in Southern Brazil.

Method: All women employed were invited (n=258), and 69.4% (n=179) agreed to participate. For this analysis, we included female workers employed for at least 12 months who were not pregnant or breastfeeding in the last year. Weekly work shift varied from 30 to 42 hours, divided into five or six weekdays. Participants answered an online questionnaire comprising questions regarding UTs (burning feeling; frequent or intense urge to urinate; bloody urine; lower abdomen pain) and UTI episodes in the last year; usual daily beverage intake, usual urine frequency and color according to urine color chart; water access and toilet adequacy perception at work. Workers were divided into two groups according to the employee permission in having a water bottle (WB) at the workplace. Administrative and multidisciplinary staff are allowed (WB group) and nurse staff can not have (non-WB group) due to infection control regulation in dialysis rooms.

Results: We included 133 women (age=36.9±9.5 years old). Self-reported usual daily beverage intake= 6.6±2.9 cups/day (∼1320 ml); daily urine frequency= 5.1±2.1; urine color chart score= 3.0±1.2. At least one UTs was reported by 53% (n=70) and UTI episode by 34% (n=45) in the last year. Participants with UTs had a lower urine frequency (4.7±2.3 versus 5.5±1.7 times/day; P=0.03) and a higher urine color score (3.3±1.2 versus 2.6±1.1;P=0.002). Non-WB workers (N=66/49.6%) reported a lower beverage intake (6.0±2.6 versus 7.3±3.0 cups/day;P=0.01), had a higher prevalence of UTs (65% versus 45%; P=0.02) and UTI (42% versus 25%; P=0.04). Among non-WB participants, 47% considered that the distance to water supply from the workplace spot impairs adequate hydration, and 39% answered that the number of toilets available also as a barrier. A higher prevalence of UTs was reported by these subgroups that perceived environment infrastructure barriers (77% versus 54%; P=0.04 and 92% versus 47%; P<0.001, respectively). Non-WB who responded that toilet hygiene impairs hydration (11%) had a higher prevalence of UTI (86% versus 37%; P=0.03). No significant association between work environment perception and urinary problems was found in the WB group.

Conclusion: Lower urine frequency and darker urine color were associated with UTs in this population. Workers who do not have a water bottle at the workplace reported a lower beverage intake, higher UTs and UTI prevalence. Non-WB participants that perceived work barriers to adequate hydration had a higher prevalence of urinary problems.

P0244

OVERTURNING THE CONVENTIONAL PYRAMID OF AL AMYLOIDOSIS MANAGEMENT: DARATUMUMAB ADMINISTERED AS MONOTHERAPY IN SEVERE PATIENTS WITH BIOPSY PROVEN RENAL INVOLVEMENT.

Dario Roccatello[1], Roberta Fenoglio[1], Elena Rubini[2], Carla Naretto[3], Simone Baldovino[1], Savino Sciascia[1], Michela Ferro[1], Daniela Rossi[1]

[1]CMID-Nephrology and Dialysis Unit (ERK-net Member)-Center of Research of Nephrology, Rheumatology, and Rare Diseases, Interregional Coordinating Center of the Network of Rare Diseases,, G. Bosco Hospital and University of Turin, Italy, Turin, Italy, [2] CMID-Nephrology and Dialysis Unit (ERK-net Member)-Center of Research of Nephrology, Rheumatology, and Rare Diseases, Interregional Coordinating Center of the Network of Rare Diseases,, G. Bosco Hospital and University of Turin, Italy, Turin, Italy and [3]CMID-Nephrology and Dialysis Unit (ERK-net Member)-Center of Research of Nephrology, Rheumatology, and Rare Diseases, Interregional Coordinating Center of the Network of Rare Diseases, G, G. Bosco Hospital and University of Turin, Italy, Turin, Italy

Background and Aims: Immunoglobulin light chain amyloidosis (AL) with multi-organ involvement is characterized by poor outcome. Current treatment of AL targeting the underlying plasma cell clone has been adapted from the multiple myeloma (MM). Novel powerful drugs are expanding the therapeutic options. Daratumumab is a first-in-class anti-CD38 human antibody (IgG1κ) which proved to be effective in combination with bortezomib in MM refractory to conventional bortezomib-based regimens. Its effectiveness as a single agent and its safety in the treatment of AL amyloidosis is under study. Aim of the study: This study reports the experience with Daratumumab monotherapy in a series of severe patients with AL amyloidosis and multiorgan and biopsy-proven renal involvement.

Method: Five patients (2 males and 3 females), mean age 64 years (range 52-69) were treated with Daratumumab following antibody testing and extended RBC antigen phenotyping. Treatment protocol was as follows: 16 mg/kg Daratumumab i.v. administered weekly for 8 weeks, then 8 times every two weeks, and then monthly for 1 year. Premedication included oral paracetamol, and i.v. chlorphenamine and methylprednisolone.

Results: In patient #1, in dialysis, who was refractory to conventional therapies Daratumumab administration resulted in normalization of the FLC ratio with disappearance of serum M-component and Bence-Jones (BJ) proteinuria. In patient #2 who had a relapsing disease, Daratumumab treatment resulted in a rapid decrease of proteinuria (from 6.8 to 2.7gr/24 hours at the 16th dose) and N-terminal propeptide (NT-pro-BNP) levels (from 1844 pg/ml to 330 pg/ml) with disappearance of serum M-component and BJ proteinuria and normalization of the FLC ratio. Patient #3 was treated front-line. He had an impressive decrease of proteinuria from 9.3 to 2.2 gr/24 hrs and NT-proBNP levels (from 850 pg/ml to 225 pg/ml) with normalization of FLC ratio and disappearance of serum M-component. In patient #4, who was intolerant to conventional regimens, Daratumumab therapy resulted in decrease in proteinuria, disappearance of serum M-component and improvement in the FLC ratio, which were paralleled by a reduction of NT-proBNP levels. Patient #5 had a relapsing disease. Daratumumab achieved a decrease of proteinuria (from 2.5 to 1 gr/24 hrs9, a decrease of serum M-component with increase of FLC ratio (0.29, nv: 0.31 – 1.56). This was the only patient who experienced an infusion reaction during the first dose (grade 1). The 4 patients with still preserved renal function also showed renal response with sCr improvement or stabilization and a decrease in proteinuria levels These data were paralleled by the reduction of NT-proBNP values in the 3 patients with cardiac involvement.

Conclusion: Daratumumab monotherapy resulted in the disappearance of M-proteins in every patient with FLC ratio normalization in 4 out of 5 subjects and impressive decrease of proteinuria and pro-BNP values proving to be an effective therapeutic option for pretreated/naïve patients with severe AL with renal involvement.

P0245 **PERCUTANEOUS RENAL BIOPSY IN FRAIL AND HIGH RISK PATIENTS**

Dario Roccatello[1], Roberta Fenoglio[1], Joelle Kamgaing[1], Emanuele De Simone[1], Giulio Del Vecchio[1], Michela Ferro[1], Giacomo Quattrocchio[1], Gianluca Rabajoli[1], Maria Rosaria Concas[1]

[1]CMID-Nephrology and Dialysis Unit (ERK-net Member)-Center of Research of Nephrology, Rheumatology, and Rare Diseases, Interregional Coordinating Center of the Network of Rare Diseases,, G. Bosco Hospital and University of Turin, Italy, Turin, Italy

Background and Aims: : Many patients with End Stage Kidney Disease do not undergo percutaneous kidney biopsy (KB) and do lack a definite diagnosis. Whether KB is beneficial in the extreme patients' categories, i.e., age >75 years and very late referrals with kidney disease requiring renal replacement therapy at the first evaluation, remains controversial. Aim: To analyse the benefit/risk balance in terms of therapeutic options and general outcome of KB procedure in these borderline categories.

Method: Files for all biopsies performed in our Centre between 2013 and 2019 (# 903 inpatients' native kidney) were retrospectively analysed with special focus on histological diagnosis, biopsy complications, and post-biopsy patient's outcome. Two groups of high risk patients were identified 1. >75 years old patients, and 2. patients requiring dialysis at the first clinical evaluation. A rigorous protocol of screening of the bleeding risks was adopted.

Results: Of the 903 biopsies, 217 cases (24%) had group 1, and 92 (10%) group 2 criteria. Group 1: mean age 80 years (range 75-92), main histological diagnoses: ANCA associated vasculitis (AAV) (12,4%); membranous nephropathy (MN) (11,5%), diabetic nephropathy (10,1%), IgA glomerulonephritis (IgAGN) (9,2%), cast nephropathy (9,2%), renal amyloidosis (9.2%), focal segmental glomerulosclerosis (FSGS - 7,8 %). Group 2: mean age 60 years (range 20-92), most frequent histological diagnosis: AAV (26,1%); cast nephropathy (19,6 %), nephroangiosclerosis (9,8%), IgAGN (7,6 %), diabetic nephropathy (6,5%), renal amyloidosis (5,4%); FSGS (4,3%). Five major complications (2,3%), including AV fistula with spontaneous resolution in 4 patients and 1 case of severe bleeding requiring arterial embolization, and 14 minor complications (6,5%), including post biopsy haematomas <2cm in 12 patients and haematuria in 2 patients were observed in group 1. Only 1 (1%) major complication (AV fistula) and 4 minor complications (4,3%), including post biopsy <2cm haematomas in group 2 were identified in group 2. Histological diagnosis conditioned or changed treatment strategy in 71% of elderly patients (group 1), and 63% of patients in dialysis (group 2). Dialysis discontinuation was achieved in 30 out of 92 patients (36,6%) with a sparing of over 1 million euro/year.

Conclusion: Given its high diagnostic value (especially in patients who are willing to be transplanted), the prognostic significance (and the assessment of the extent of the renal sclerotic changes), and the potential impact on the treatment policy, indications to percutaneous kidney biopsy in elderly and dialysis patients should be probably revised.

P0246 MEMBRANOUS NEPHROPATHY IN THE ELDERLY : EPIDEMIOLOGY, DIAGNOSIS AND MANAGEMENT

Nessrine Breik[1], Mouna Jerbi[2,3], Raja Aoudia[1,3], Soumaya Chargui[1,3], Hanen Guaied[2,3], Imen Gorsane[1,3], Rim Goucha[2,3], Taieb Benabdallah[1]

[1]Charles Nicolle Hospital, Department of Nephrology, Dialysis and Transplantation, Tunis, Tunisia, [2]Mongi Slim Hospital, Department of Nephrology, La Marsa, Tunisia and [3]Charles Nicolle Hospital, Research Laboratory of Kidney Diseases (LR00SP01), Tunis, Tunisia

Background and Aims: The aging of the population and the increase in life expectancy have led to increasing numbers of elderly patients so greater numbers of elderly patients with chronic kidney diseases are surviving longer. Membranous nephropathy (MN) is the most important cause of glomerular disease in older patients (≥65 years). The aim of this study is to describe the epidemiological and clinical profile of elderly patients with MN and to analyze the diagnostic and management approach.

Method: We conducted a retrospective descriptive study in the nephrology department at Charles Nicolle hospital over a period of 44 years. All older patients (≥65 years) with histologically proven MN were included in this study.

Results: Thirty patients were collected. The mean age was 69.43 years (65-78 years) with a male predominance (sex ratio: 2.3) and low socio-economic level in 83.3% of cases. Sixteen patients were smokers (55.3%), 5 ethyl patients (16.7%), diabetes was present in 3 patients (10%) and hypertension in 11 patients (36.7%). Two cases of neoplasm were present, namely one case of prostatic adenocarcinoma and one case of gallbladder adenocarcinoma, all were diagnosed and treated along one year and ten years respectively, before the diagnosis of MN. The circumstances of discovery was dominated by oedema in 27 cases (86.27%), hypertension in 11 cases (36.7%) and elevated creatinine level in 9 cases (30%). Deep venous thrombosis was the circumstance of discovery in one case. At the time of diagnosis, the clinico-biological picture was dominated by high systolic blood pressure in 21 cases (67.6%), anasarca in 7 cases (23.3%), proteinuria in all cases and hematuria in 20 cases (66.6%). Biology revealed nephrotic syndrome (NS) in 28 cases (87.11%), hypercholesterolemia in 23 cases (76.6%), high serum creatinine in 14 cases (46.6%) with an average creatinine level of 123,85 µmol/l, anemia in 17 cases (56.6%) and anti-neutrophil cytoplasmic antibodies were positive in one case. MN was confirmed by a kidney biopsy in all cases. Twenty-two patients had idiopathic MN (IMN) and 2 patients had secondary MN. In fact, MN was associated with multiple myeloma in one case and secondary to hepatitis B in other case. Symptomatic treatment was indicated in all patients. Patients with secondary MN received etiopathogenic treatment. For the IMN, immunosuppressive therapy started early for 12 patients (40%) because of the severe NS and the deterioration of renal function. Eight patients (26.6%) received corticosteroids alone, three patients received corticosteroid with mycofenolate mofetil and one patient received corticosteroid with ciclosporin. We noted complete remission in 6 patients and end renal stage disease in 5 patients.

Conclusion: In studies of glomerular disease in the elderly, MN was the most common cause of NS. The clinical presentation is similar in older and younger patients, but older patients more often present with kidney failure and severe NS.

P0247 **PREGNANCY IN WOMEN WITH NEPHROTIC-RANGE PROTEINURIA**

Shuli Svetitsky[1], Liz Lightstone[2]

[1]Imperial College Healthcare NHS Trust Renal and Transplant Centre, Hammersmith Hospital, London, United Kingdom and [2]Faculty of Medicine, Imperial College London, Centre for Inflammatory Disease, Division of Immunology and Inflammation, London, United Kingdom

Background and Aims: The adverse effects of chronic kidney disease on pregnancy and pregnancy on renal function have been described, but the effect of severe proteinuria in early pregnancy is not known. The aim of this study was to evaluate the obstetric and renal outcomes of pregnant women with severe proteinuria manifesting in early pregnancy.

Method: We retrospectively assessed the records of over 400 women with renal disease who were cared for during pregnancy in Queen Charlottes and Chelsea hospital and identified women with nephrotic range proteinuria in early pregnancy. Their records were reviewed and outcomes were compared to women with CKD and little or no proteinuria in early pregnancy.

Results: The study included 99 women with renal disease, of these 37 with severe proteinuria, and 62 patients who had mild or no proteinuria. The baseline GFR and blood pressure in the groups was similar. There were significantly more women with glomerular diseases in the group with proteinuria. The group with severe proteinuria had significantly higher rates of delivery by C-section, and prematurity including severe prematurity (<34 weeks). They had lower average birth weight and more babies born with very low birth weight. Their renal outcomes were poorer, with a lower eGFR at 3 years and a higher rate of advanced CKD and renal replacement therapy.

In the women with proteinuria, the level of scarring on renal biopsy was found to be a significant predictor of several poor outcomes, including premature birth and developing advanced kidney disease.

Conclusion: Severe proteinuria early in pregnancy is associated with lower birth weight, greater prematurity and poorer renal function in the long term.

Physicians treating these women must be aware that they are at a higher risk of complications than women with renal disease without severe proteinuria.

Pregnancy outcomes stratified by severity of proteinuria

	Severe proteinuria (n=37)	**mild/no proteinuria** (n=62)	P-value
Need for RRT during pregnancy	2	0	0.137
Caesarian section [number]	21 [37]	16 [50]	**0.021**
Birth week*	35w +6d (5wks)[63]	38w +1d (3w) [38]	**0**
Prematurity (<=37weeks)	19	18	**0.026**
Severe prematurity (<=34 weeks)	11	7	**0.021**
Birth weight (grams)	2213	2753	**0.003**
low birth weight (<2,500 gr)	21	19	**0.017**
Very low birth weight (<1500 gr)	10	3	**0.004**
APGAR			**0.012**
APGAR<9	7	3	0.03
Perinatal death	2 (5.2%)	3 (4.8%)	0.9
Neonatal death up to 6 weeks	4 (10.5%)	3 (4.8%)	**0.419**

Renal outcomes stratified by severity of proteinuria

	Severe proteinuria (n=37)	mild/no proteinuria (n=62)	p
Creatinine			
1 year post partum	115 (106)	73 (39)	0.198
3 years post partum	107 (181)	73 (18)	**0.008**
GFR at 3 years	56 (97)	93 (34)	**0.02**
Decline in GFR one year post preg	11(20)	6.5 (22)	0.1
Decline in GFR 3 years post pregnancy	16.6 (32)	6.1 (21)	**0.056**
Renal replacement therapy at 3 years post-partum	5	1	**0.035**
CKD Stages 4 and 5 at 3 years post partum	11	3	**0**

Outcomes:Scarring on renal biopsy >=30%

	OR	95% CI	p value
Prematurity<=37 weeks gestation	**All were born <37 weeks**		**0.001**
Prematurity<=34 weeks gestation	**8.9**	1.344-58.79	**0.027**
Advanced CKD	**30**	2.216-405.9	**0.006**

P0248 **HEPARIN-INDUCED THROMBOCYTOPENIA (HIT): A POSSIBLE CAUSE OF VENOUS THROMBOEMBOLISM IN ACTIVE SYSTEMIC VASCULITIS**

Francesca Boni[1], Alessandra Gina Gregorini[1], Chiara Salviani[1], Sara Merelli[2], Nicola Portesi[2], Giuliana Martini[2], Federico Alberici[1], Francesco Scolari[1]

[1]ASST Spedali Civili of Brescia, Nephrology Unit, Brescia, Italy and [2]ASST Spedali Civili of Brescia, Hemostasis Center Clinical Pathology, Brescia, Italy

Background and Aims: Increased incidence of venous thromboembolism in active phase of vasculitis has been found by several authors. Examining large cohorts of patients, the underlying mechanisms still remain unclear. Patients with active vasculitis are not rarely exposed to heparin mainly because of dialysis, plasmafiltration or ECMO. In the high inflammatory context of active vasculitis, as in major surgery, heparin exposure could promote the formation of anti-PF4/heparin antibodies and induce HIT.

Method: Description of cases with active vasculitis and HIT observed in our cohort of ANCA-associated vasculitis patients from 1994 to 2019. Review of cases reported in the literature.

Results: We observed 18 patients with systemic vasculitis and HIT (10 M and 8 F, median age: 69.5 yo). Fourteen had ANCA antibodies, one patient had both ANCA and anti-GBM antibodies (double positive), two had positive anti-GBM antibodies, one had negative ANCA and anti-GBM antibodies. Among 15 patients with positive ANCAs, 13 had anti-MPO antibodies and 2 anti-PR3 antibodies (Fig. 1).

All patients were exposed to heparin, 10 because of plasmafiltration and dialysis, 8 for dialysis alone. Mean platelet count nadir was 76100/mm^3 (range 23000-197000/mm^3).

In all patients PF4–heparin antibody immunoassay was strongly positive (optical density >1 in 13 patients).

The most frequent manifestations were thrombocytopenia and repeated clotting of the extracorporeal circuit and dialyzer with thrombosis of the hemodialysis catheter (6/18 patients). Four patients developed deep vein thrombosis almost invariably in the site of the hemodialysis catheter. Pulmonary embolism was observed in only one patient (Fig. 2).

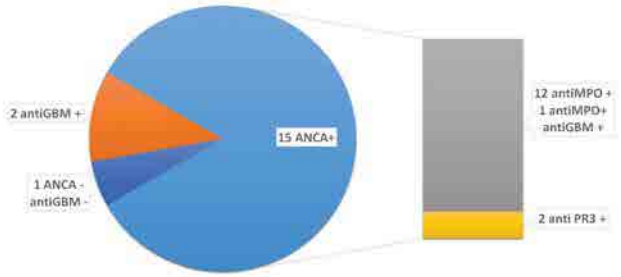


Figure 1. Types of vasculitis in our cohort of HIT patients

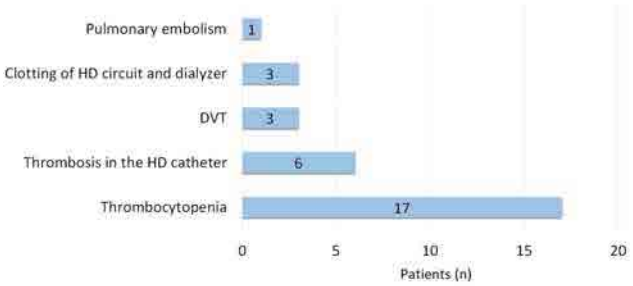


Figure 2. Clinical manifestations in our cohort.
HD = hemodialysis DVT = deep vein thrombosis

Figure:

To our knowledge, only 11 cases of HIT in patients with vasculitis have been reported in literature (Table I). Detailed data are available for 7 patients (6 M and 1 F, median age 69.6 yo). Three patients had anti-PR3 antibodies, 2 anti-MPO antibodies, 1 both ANCA anti-MPO and anti-GBM antibodies (double positive), 1 only anti-GBM antibodies. Mean platelet count nadir was 45625/mm^3 (range 17000-131000/mm^3). Three out of 11 patients developed repeated clotting of the extracorporeal circuit and dialyzer, 2 patients had deep vein thrombosis in the site of the hemodialysis catheter, and one patient had also leukopenia and subarachnoid hemorrhage. Six patients were asymptomatic and developed only thrombocytopenia.

Conclusion: When patients with active systemic vasculitis develop venous thromboembolism and thrombocytopenia after exposure to heparin, or repeated coagulation of the extracorporeal circuit and dialyzer or plasma-filter, HIT should be included in the possible differential diagnosis, and Platelet factor 4–heparin antibody tests should be performed.

P0249 **ESSFSFDSVXVXCVXVVVVDVDDDCVVV**

Francesco Trevisani[1], FEDERICO DI MARCO[1], Andrea Necchi[2], Daniele Raggi[2], Arianna Bettiga[1], Riccardo Vago[1], Umberto Capitanio[1], Andrea Gallina[1], Renzo Colombo[1], Andrea Salonia[1], Alberto Briganti[1], Francesco Montorsi[1]

[1]IRCCS San Raffaele Scientific Institute, Urological Research Institute, Milan, Italy and [2]Fondazione IRCCS Istituto Naizonale dei Tumori, Milan, Italy

Background and Aims: The use of Pembrolizumab, a selective humanized IgG4 kappa monoclonal antibody that inhibits the programmed death-1 receptor, has been largely accepted, especially in a series of trials in patients with advanced melanoma and in other cancers such as renal cell carcinoma (RCC), lymphoma and others. However, few recent studies demonstrated that Pembrolizumab promotes several renal dysfuncion such as acute tubular injury, acute interstitial nephritis and minimal change disease. To better elucidate this topic, we analyzed the renal function's aspects from the PURE-01 protocol's data, a phase 2, open label study of neoadjuvant Pembrolizumab before radical cystectomy (RC) for muscle invasive urothelial bladder cancer (MIUB).

Method: PURE-01 study (NCT02736266) enrolled preliminary 143 patients (pts). Eligibility criteria included: T2-T4N0 stage and residual disease after transurethral reduction of bladder. Pts received 3 cycles of Pembrolizumab 200 mg 3 weekly before RC. Computed tomography scan, FDG-PET/CT scan, and bladder multipara metric magnetic resonance imaging were performed during screening and before RC. Radiologically non-responders to pembro (per investigator decision) are given 3 additional courses of dose-dense MVAC chemotherapy. The collected data consisted in: the serum creatinine at baseline, after the first, second and last cycle in order to obtain the renal function by using eGFR formula (CKD-EPI-2009) for each time step; urine test analysis data after each cycle; the T stage from cTNM (AJCC TNM system-2019) before the treatment; clinical data such as presence of Diabetes, Hypertension, Hydronephrosis, BMI. The main outcome of the study was to correlate the renal function variation (from the pre-treatment to each treatment cycle) with the other clinical variables. Data analysis were performed using linear model, Kruskal-Wallis test and Wilcoxon test with holm's correction.

Results: The median age of the patients was 68 years (62-73), with the 13% of the pts as female. We observed the presence of Hypertension, Hydronephrosis, Diabetes, Overweight (BMI≥25 and BMI<30) and Obesity (BMI≥30) respectively at 54%, 20%, 22%, 50% and 10% in the total population. According pre-treatment T stage we divided the cohort as follows: 17% with stage 0, 32% with stage 2, 47% with stage 3 and 4% with stage 4. The renal function of pts according to the CKD classification was: 26% as stage I (≥90 mL/min/1.73 m^2), 55% as stage II (<90 mL/min/1.73 m^2 and ≥60 mL/min/1.73 m^2), 11% as stage IIIa (<60 mL/min/1.73 m^2 and ≥45 mL/min/1.73 m^2) and 8% as stage IIIb-IV-V (<45 mL/min/1.73 m^2). We observed that eGFR after the first, second and last cycle, remained stable from the pre treatment values, with a median variation of respectively +1.45 (IQR -2.32,6.46), +1.35 (IQR -2.42, 6.74) and +1.75 (-2.83, 6.5) mL/min/1.73 m^2 and without the onset of nephrotic-range proteinuria. Considering the variation after the first cycle, a significative positive correlations were found with the presence of hydronephrosis (+4.4 mL/min/1.73 m^2, CI = 0.9:7.9, p=0.02), T stage 3 (+4.5, CI= 0.7:8.3, p=0.02) and T stage 4 (+14.8, CI=7.0:22.6, p=0.0003); after the second cycle we observed positive correlation with T stage 4 (+8.6, CI=0.5:16.8, p=0.04); after the last cycle the variation correlated with hydronephrosis (+4.2, CI=0.5:7.8, p=0.03) and T stage 4 (+10.7, CI=2.2:19.1, p=0.02).

Conclusion: We observed that the treatment with neoadjuvant pembrolizumab, in patients with bladder cancer, does not correlate with a decay of eGFR, but on the contrary, from our data, is associated with a small improvement of renal function, especially for those patients who presented higher stage of T and hydronephrosis before the treatment suggesting the Permbrolizumab's safety in neoadjuvant therapy before RC for MIUBC from the nephrological point of view. This results needs more in-depths studies to be confirmed.

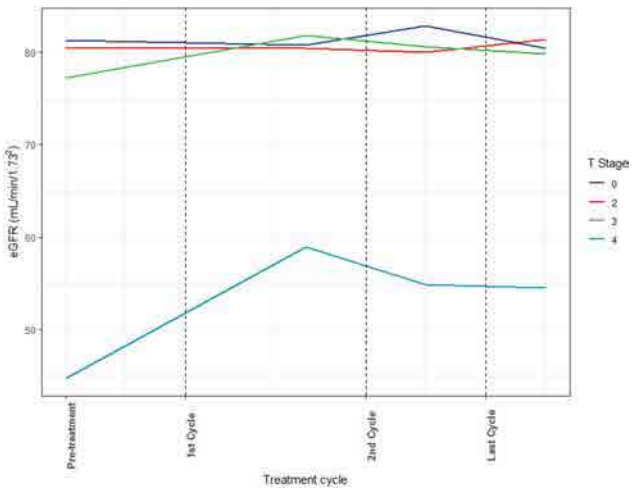


Figure:

P0250 COLD DIURESIS DURING TARGETED TEMPERATURE MANAGEMENT AFTER CARDIAC ARREST, MYTH OR FACT?

Min-Jeong Lee[1], Minjung Kathy Chae[2]

[1]Ajou University School of Medicine, Nephrology, Suwon, Korea, Rep. of South and
[2]Ajou University School of Medicine, Emergency Medicine, Suwon, Korea, Rep. of South

Background and Aims: Therapeutic hypothermia or targeted temperature management (TTM) has been standard treatment for cardiac arrest survivors with suspected hypoxic ischemic brain injury for improvement in both survival and neurological outcomes. TTM is consisted of an induction phase of quickly lowering the temperature to target temperature (ranging from 32°C -36°C) as soon as possible, a hypothermia maintenance phase of keeping the body temperature at target temperature for at least 24 hours, a rewarming phase of slowly rewarming the temperature to normothermia, and a normothermia phase of keeping the body temperature at normothermia. During the dynamic changes in body temperature, cold-diuresis is a commonly described phenomenon. However, limited studies have characterized cold-induced diuresis during TTM. In this study, we sought to determine urine output changes during post cardiac arrest therapeutic hypothermia.

Method: This retrospective cohort study included adult patients who underwent TTM after out-of-hospital cardiac arrest and were admitted to the intensive care unit for post cardiac arrest care between January 2012 and August 2018. The exclusion criteria of this study were as follows: 1) deceased status before the completion of all phase of TTM; 2) previous end stage kidney disease patients, 3) undergoing renal replacement therapy due to AKI within 48 hours of TTM termination; 4) terminal cancer less than 6 months of life expectancy or previously cerebral performance category (CPC) 3 or more. The neurologic outcome was assessed using the CPC score after 1 month. Good neurologic outcome was defined as a CPC score of 1, 2 and poor neurologic outcome as a CPC score of 3 to 5. The post cardiac arrest protocol recommends a target temperature of 33°C unless the patient is hemodynamically unstable or has a bleeding tendency or severe infection. Rewarming rate was 0.15°C/hr or 0.25°C/hr. TTM was conducted with the use of temperature managing devices with a feedback loop system (Artic Sun Energy Transfer Pads, Medivance Corp., Louisville, CO, USA; Cool Guard Alsius Icy Heat Exchange Catheter, Alsius Corporation, Irvine, CA, USA). We calculated the hourly IV fluid input and urine output rates for each TTM phase. To compare the mean of urine volume between each TTM phase, we used repeated measure analysis of variance (ANOVA).

Results: 178 Patients included in the analysis. We observed a increase in urine output rates during hypothermia induction. This effect persisted even after adjustment for variable clinical confounders, including intravenous fluid input rate, mean arterial pressure (MAP), initial shockable rhythm, SOFA score, body mass index, and IV furosemide use. However, we did not detect any evidence of urine output increases or decreases during the hypothermia maintenance or rewarming phases. By repeating measures ANOVA and a linear mixed model, it was confirmed that there is a difference in urine output for each TTM phase. Even after the post hoc analysis was calibrated with several variables, only the hypotheria induction phase differed significantly from the urine output of the phase.

Conclusion: Although our results are some limitations, the findings support the potential presence of cold-induced dieresis, but not rewarm anti-diuresis during TTM. Our study may not fully capture the extent of renal impairment in post cardiac arrest undergoing TTM. However, our objective was to characterize urine output during TTM in post cardiac arrest patients. This has important implications for fluid management in patients undergoing TTM.

Table 1. Fluid and Output during Therapeutic Hypothermia (156 Hypothermia Patients)

	Induction	Maintenance	Rewarming	Normothermia
IV fluid input rate (mL/hr)	522.4	478.5	328.1	240.2
Urine output rate (mL/hr)	238.3	144.2	101.4	118.8
Urine output rate, adjusted¶ (mL/hr)	236.1	139.3	93.1	111.9
MAP* (mmHg)	102.4	94.8	89.9	86.9

P0251

PERCUTANEOUS ANGIOPLASTY OF RENAL ARTERY STENOSIS IN PATIENTS WITH ACUTE KIDNEY INJURY REQUIRING HEMODIALYSIS

Nabil Abu amer[1,1], Dganit Dinour[1]

[1]*Chaim Sheba Medical Center, Tel Hashomer and Sackler School of medicine, Nephrology and Hypertension, RMAT GAN, Israel*

Background and Aims: Atherosclerotic renal artery stenosis (RAS) is a common disease, associated with significant morbidity and mortality. Several studies have shown that percutaneous angioplasty with stenting (PTA/S) is not superior to medical treatment. The benefit of endovascular intervention among acute kidney injury (AKI) patients requiring hemodialysis secondary to RAS has not been studied. We investigated the effects of PTA/S in patients with atherosclerotic RAS, specifically those who presented with AKI indicated for hemodialysis.

Method: We collected data between 2003 and 2019. We defined a subgroup of patients who presented with AKI and underwent the procedure after starting hemodialysis. Data collected included demographic parameters, medical background, indication for intervention, technical procedure parameters and complications and long term data including dialysis treatment and mortality. Patients who underwent PTA/S due AKI with dialysis were categorized as responders or non-responders based on improvement in kidney function and weaning off dialysis.

Results: We identified 109 PTA/S performed in 92 patients. Technical success was 97% and complication rate was 15.5%. Creatinine and blood pressure improved in 8.9% and 32% respectively, based on predetermined criteria. A subgroup of 11 patients underwent PTA/S for hemodialysis-dependent AKI. 8 patients (73%) improved kidney function and discontinued dialysis. The average time on dialysis was 17 days (range 3-35 days) to PTA/S and 22 days (range 3-42 days) to recovery of kidney function, which occurred 6.5 days (range 1-24 days) after PTA/S. two of the 8 patients required long term hemodialysis after 12 and 22 months post procedure. Only two cases were reported with mild complications (pseudo-aneurysm and brachial hematoma). Factors associated with response to PTA/S include a higher baseline eGFR, less proteinuria, larger kidney size and better contrast enhancement on imaging.

Conclusion: In patients with hemodialysis dependent AKI, PTA/S should be considered as a rescue treatment and may recover kidney function even after prolonged time on dialysis.

P0252

TROPONIN T AND LEFT ATRIAL VOLUME INDEX ARE ASSOCIATED WITH THE OCCURRENCE OF NEW-ONSET ATRIAL FIBRILLATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGE 4-5

Markus Hakamäki[1], Tapio Hellman[1], Roosa Lankinen[1], Niina Koivuviita[1], Jussi Pärkkä[2], Petri Kallio[2], Tuomas Kiviniemi[3], Juhani Airaksinen[3], Mikko Järvisalo[4], Kaj Peter Metsarinne[1]

[1]Turku University Hospital, Kidney Center, Turku, Finland, [2]Turku University Hospital, Department of Clinical Physiology, Turku, Finland, [3]Turku University Hospital, Heart Center, Turku, Finland and [4]Turku University Hospital, Department of Anaesthesiology and Intensive Care, Turku, Finland

Background and Aims: Atrial fibrillation (AF) and chronic kidney disease (CKD) are common and often co-existing conditions. However, little is known on the prevalence and incidence of AF in patients with CKD stage 4-5.

Method: We prospectively recruited 210 consecutive non-dialysis patients with CKD stage 4-5 between 2013 and 2017. Follow-up data on AF occurrence as well as baseline medical history, laboratory tests and echocardiography were collected.

Results: At baseline, mean age was 62 years, 73/210 (34.8%) of the participants were female, mean estimated glomerular filtration rate was 12.8ml/min and 41/210 (19.5%) patients had a prior diagnosis of AF. After median follow-up of 46 [IQR 27] months, new-onset AF was detected in 33/169 (19.5%) patients (69.9 events/1000 person-years). Overall, 22/33 (66.7%) of patients with new-onset AF were identified with a triggering condition, most commonly severe infection or surgery, and 21/33 (63.6%) were receiving renal replacement therapy (dialysis or acquired kidney transplant) at the time of AF detection, respectively. In Cox proportional hazard model age >60 years (HR 4.27, CI95% 1.57-11.64, p<0.01), elevated troponin T (TnT) >50ng/l (HR 3.61, CI95% 1.55-8.37, p<0.01) and left atrial volume index (LAVI) >30ml/m^2 (HR 4.82, CI95% 1.11-21.00, p=0.04) independently predicted the occurrence of new-onset AF. Furthermore, the predictive effect of the covariates was cumulative (Figure 1).

Conclusion: The incidence rate of AF was remarkably high in this prospective study on patients with CKD stage 4-5. Elevated TnT and increased LAVI are associated with the occurrence of new-onset AF in patients with severe CKD.

Figure 1

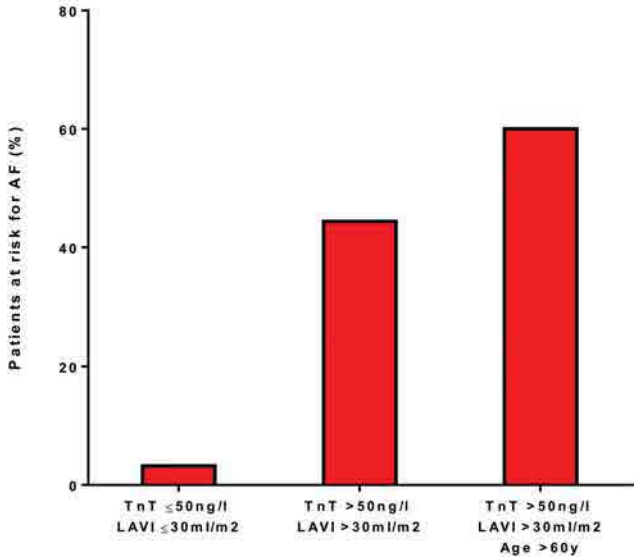


Figure:

P0253 **FRAILTY SCREENING TOOLS, FUNCTIONAL STATUS AND LIFE EXPECTANCY IN ELDERLY PATIENTS WITH PRE-DIALYSIS ADVANCED CHRONIC KIDNEY DISEASE.**

Hani Hussien[1,2], Mugurel Apetrii[1], Mihai Onofriescu[1], Andra Nastasa[1,2], Gabriel Mircea[2], Iuliana Teodor[2], Irina Apascaritei[2], Adrian Covic[1,2]

[1]Grigore T. Popa University of Medicine and Pharmacy, Renal medicine, Iași, Romania and [2]Hospital Doctor C.I. Parhon, Renal medicine, Iași, Romania

Background and Aims: Patients with chronic kidney disease (CKD) are at high risk of being frail, which is associated with poor outcomes including falls, low functional status, decreased quality of life, hospitalization, and mortality. Furthermore, the presence of frailty might decrease the potential benefits of renal replacement therapy initiation or even leads to worse outcomes. Currently, there are over 51 known tools for screening of frailty in the general population. The aim of this study was to describe the prevalence of frailty in elderly patients with pre-dialysis advanced CKD (G4 and G5) according to different frailty assessment tools from the 4 main categories of frailty screening: self-reporting questionnaires, subjective scores, simple single physical tools and complex scores. Also, we compared the functional status and the 10-year survival expectancy in frail Vs non-frail patients.

Method: In this cross-sectional study, we included patients from the Outpatient Department from Nephrology unit in a tertiary health facility "Dr C. I. Parhon Clinical Hospital" who were $\geq$65 years old with CKD G4–5 (eGFR $<$ 30 ml/min/1.73 m^2 using the CKD-EPI formula) on at least two occasions in the previous 3 months prior to the time of inclusion. The frailty was assessed using one method from each frailty screening category: self-reporting score as PRISMA-7, subjective score as Clinical Frailty Scale (CFS), a complex score as Frailty Phenotype (FP) and two simple single physical tools as gait speed in 4.5 meters (GS) and handgrip strength using a dynamometer (HGS). All participants had the Charlson Comorbidity Index (CCI) score calculated and the Karnofsky Performance Status Scale (KPS) performed.

Results: We included a total number of 201 patients, of which 53.23 % were males with a mean age of 73.9 $\pm$ 6.8 years. Mean eGFR was 19 $\pm$ 6.21 ml/min/1.73 m^2. Using the three proposed scores, 69.15% of patients were at risk of frailty using PRISMA-7, compared to 45.77% and 40.3% who were frail according to CFS and FP respectively. HGS was weak in 51.74% of the patients while only 35.82% had slow GS. Half of the patients (50.25 %) had a Karnofsky score of $\leq$ 60, which corresponds to different degrees of losing autonomy.

Comparing functional status in frail Vs. non-frail patients, we found that the mean KPS points for non-frail patients was similar regardless of the used tool: 73 according to FP, 75 according to CFS and 76 points according to PRISMA 7. Same results were obtained in patients with normal GS or with a normal HGS with mean KPS of 71 points.

The 10-year survival expectancy was significantly lower in frail patients with similar mean values: 20% for both CFS and FP and 26 % for PRISMA-7, compared to non-frail patients with a predicted survival of 43% for CFS, 41% for FP and 47% for PRISMA-7. Similarly, in patients with slow GS and weak HGS, the mean CCI was 24 % for both groups, in comparison with 42% and 37 % in patients with normal HGS and normal GS respectively.

Conclusion: To the best of our knowledge, this is the first study to compare five frailty assessment tools in terms of functional status and life expectancy in elderly patients with pre-dialysis advanced CKD, but taking into consideration that those tools must be from different frailty assessment categories. Our study has shown that non-frail elderly patients with pre-dialysis advanced CKD have enjoyed a significantly higher degree of autonomy as well as higher 10-year survival expectancy in comparison with frail patients. The proposed frailty assessment tools have shown very close results in terms of functional status and life expectancy regardless of the complexity of the tool being used. Therefore, we suggest that using a simple self-reporting tool as PRISMA-7 or a simple single physical tool like handgrip strength or gait speed would be appropriate for screening of frailty in elderly patients with pre-dialysis advanced CKD who are at a high risk of losing autonomy and lower life expectancy.

P0254 **MYOCARDIAL TISSUE CHARACTERIZATION IN LIVING KIDNEY DONORS 5 YEARS AFTER NEPHRECTOMY**

Anna Price[1,2], Victoria Stoll[1,2], Ravi Vijapurapu[1,2], Kirsty McGee[2], Roman Wesolowski[1], Manvir Hayer[1,2], William Moody[1], Nicola Edwards[2,3], Boyang Liu[1,2], Amreen Kaur[2], Luke Pickup[1,2], Ashwin Radhakrishnan[1,2], Jonathan Law[1,2], Richard Steeds[1,2], Charles Ferro[1,2], Jonathan Townend[1,2]

[1]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom, [2]University of Birmingham, Birmingham, United Kingdom and [3]Green Lane Cardiovascular Service, Auckland, New Zealand

Background and Aims: Uraemic cardiomyopathy is characterized by left ventricular (LV) hypertrophy, diastolic dysfunction and myocardial fibrosis. Diffuse interstitial fibrosis of the myocardium, assessed using cardiac magnetic resonance imaging (CMR) techniques of native T1-mapping and extracellular volume (ECV), has been demonstrated in end stage chronic kidney disease (CKD) and in patients with stage 3 CKD and normal left ventricular mass. In living kidney donors estimated glomerular filtration rate (eGFR) declines by a third after donation, with 60% having a resultant eGFR comparable with stage 3 CKD. Recent studies have demonstrated small increases in LV mass at 12 months after donation as well as functional sequelae of reduced global circumferential strain and apical torsion. We sought to establish whether living kidney donors had CMR evidence of diffuse interstitial cardiac fibrosis which might contribute to observed functional correlates.

Method: A cross sectional blinded study of living kidney donors (n=50) and healthy controls (n=45) who underwent 3 Tesla CMR and blood samples for biomarkers of fibrosis. A modified look-locker inversion recovery (MOLLI) 5(3)3 sampling scheme was used for T1 mapping followed by T2 mapping sequences at the mid LV slice. Five minutes after the administration of gadolinium (Gadovist®) contrast (0.15mmol/kg), standard T1-weighted gradient echo inversion recovery images were repeated for the assessment of late gadolinium enhancement (assessment for focal fibrosis). Post contrast MOLLI images were acquired using identical slice positions as native images using a 4(1)3(1)2 sampling scheme 15 minutes after the administration of gadolinium. Native and post contrast T1 time was used to calculate ECV.

Results: There were no differences in demographics between groups; age (donors 54 ± 12yrs vs. healthy controls 50 ± 13yrs, p=0.128), ethnicity (89% Caucasian) or male gender (37%). LV mass and volumes were not significantly different. Forty four donors and 34 controls consented to receive gadolinium contrast. Native T1 in the septal mid LV slice was not significantly different between groups (donors 1223 ± 35ms vs. controls 1210 ± 36ms, p=0.102). There was also no difference in T2 time of the septal mid LV slice (donors 40 ± 2ms vs. controls 40 ± 4ms vs. p=0.455).

Late gadolinium enhancement was seen in five living kidney donors in a right ventricular insertion point pattern but there was no mid wall or ischaemic pattern enhancement. There was no difference in septal ECV at the mid LV slice (donors 25 ± 2% vs. controls 25 ± 2%, p=0.896). There was also no corresponding difference in fibroblast growth factor-23 (RU/ml) in donors 74 [58-105] vs. controls 59 [47-75], p=0.081 or soluble α-klotho (pg/ml) in donors 610 [503-810] vs. controls 703 [550-955], p=0.061.

Conclusion: Septal T1 times and ECV in living kidney donors at 5 years from donation are no different from healthy controls. Biomarkers of cardiac fibrosis are also comparable to healthy controls in this small cohort. We found no CMR evidence of the ultrastructural changes reported in uraemic cardiomyopathy in the hearts of living kidney donors at 5 years from donation.

P0255 **THE SHORT TERM MATERNAL OUTCOME OF PREGNANT CHRONIC KIDNEY DISEASE PATIENTS**

Christopher thiam seong Lim[1], Yun Jin Ong[1], Shao Wei Yong[1], Wee Ven Hing Weeven94@hotmail.com[1], Mohammad Zulkarnain Bidin[1], Bak leong Goh[2]

[1]Universiti Putra Malaysia, Seri Kembangan, Malaysia and [2]Serdang Hospital, Kajang, Malaysia

Background and Aims: Pregnancy in chronic kidney disease (CKD) is associated with increased risk of adverse maternal outcomes and fetal outcomes. The risks are noticeable even in early stages of CKD. Despite the rising concern, there are few follow-up studies in this high-risk group.

Method: We followed up and analysed 538 pregnancies in 173 women with pre-existing of primary renal disease who were seen at a tertiary nephrology centre from January 2007 until December 2015. We sought to investigate the changes in laboratory and clinical parameters, maternal and fetal outcomes.

Results: Figure 1 showed the changes of parameters intra and post-partum period. Increase in weight *(p=0.034, OR 1.135, 95% CI 1.01-1.276)*, antibiotics consumption *(p=0.022, OR 0.088, 95% CI 0.011-0.0703)*, pregnancy-related hypertension *(p=0.056, OR 0.161, 95% CI 0.025-1.05)* and gromerulonephritis *(p=0.049, OR 14.22, 95% CI 1.009- 200.52)* were associated with worsening of proteinuria intra-pregnancy and post-pregnancy period. Age more than 30-year-old *(p=0.024, OR 0.644, 95% CI 0.439-0.945)*, multiple pregnancies (*p = 0.032, OR* 14.4, *95% CI 1.25-165* , antibiotics usage *(p=0.033, OR 27.59, 95% CI 1.302-585.169)*, diuretic usage (p=0.034, OR 0.003, 95% CI

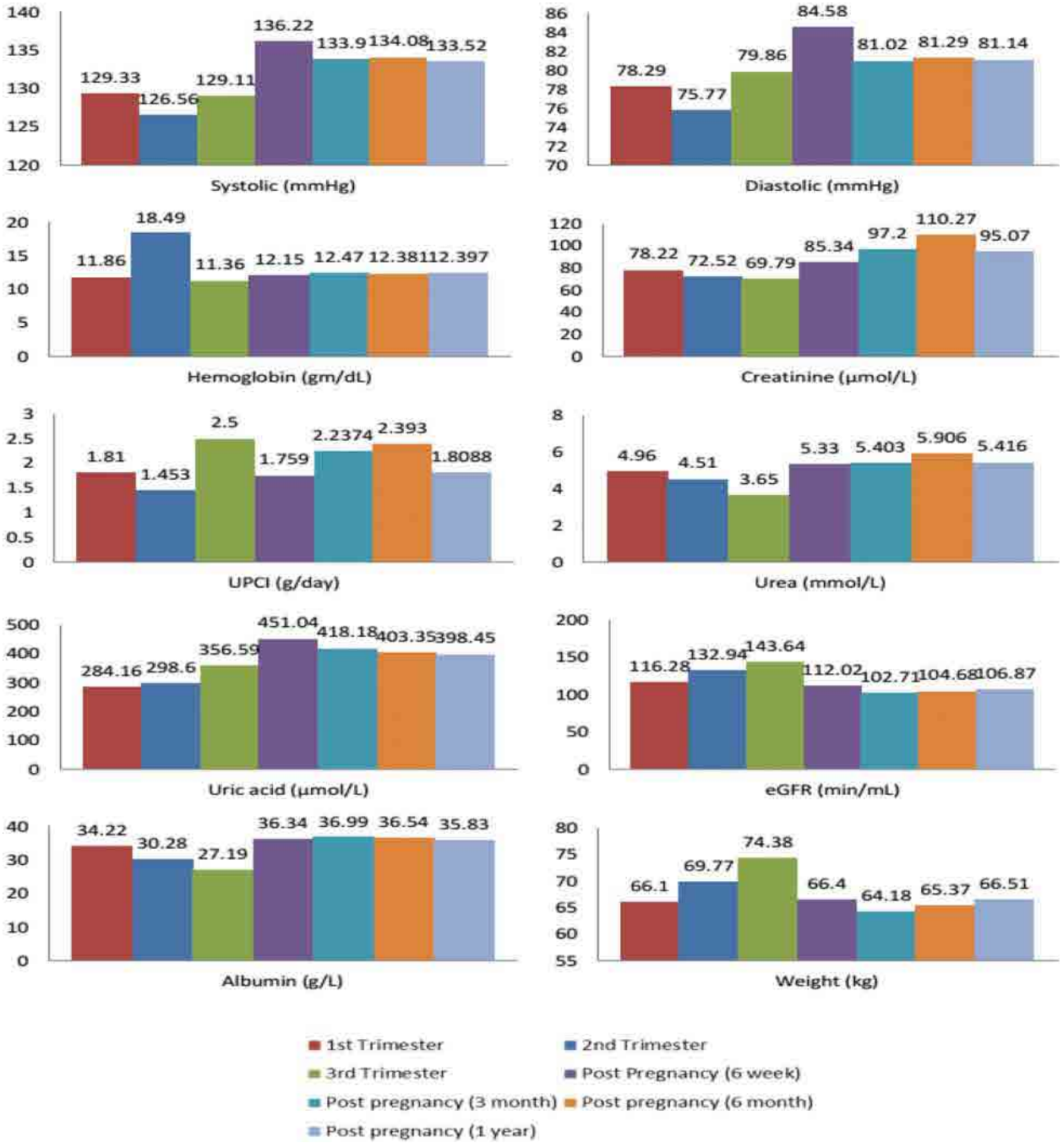


Figure 1: Graph show a mean level of laboratory characteristic taken from pregnancy until 1-year post pregnancy. A) Systolic blood Pressure (sBP), B) Diastolic Blood pressure (dBP), C) Hemoglobin, D) Serum creatinine, E) Urinary protein creatinine Index (UPCI), F) Urea, G) Uric acid, H) eGFR level, I) Serum Albumin, and J) weight

1.26-0.646), pregnancy-related hypertension *(p=0.06, OR 21.838, 95% CI 0.878-543.376)* and proteinuria (> 1.5g/d) *(p=0.025, OR 0.235 95% CI 0.067-0.717)* and fetal complications such as fetal death (*p=0.013, OR 3.608 95% CI 1.311-9.930)* was associated with rapid renal function decline of 25-50% . Elevation of serum uric acid is associated with a higher risk of adverse fetal outcome *(r=0.845 p=0.004*).

Conclusion: Multiple pregnancies, antibiotic usage, pregnancy-related hypertension are strong predictors of rapid maternal rapid function decline. Pre-conception counselling, minimization of antibiotic usage and aggressive blood pressure monitoring and treatment should be part of the standard treatment for this high-risk population.

P0256 RESEARCH OF GUT MACROBIOTA IN PATIENTS WITH CHRONIC KIDNEY DISEASE.

Kamila Olimxanova[1]

[1]*Tashkent Medical Pediatric Institute, Internal disease, Tashkent, Uzbekistan*

Background and Aims: Currently, it is estimated that the intestinal microbiota has hundreds of species of bacteria. It is known that intestinal dysbiosis contributes to the development of many diseases, such as obesity, diabetes mellitus, cardiovascular diseases, including CKD. The question of the relationship between bacterial contamination and the process of endogenous inflammation in patients with chronic kidney disease of the pre-dialysis stages is not completely clear. The aim of the study the composition of the intestinal microbiota in fecal samples and the level of inflammatory markers (CRP, IL-6, leukocytes) in patients with pre-dialysis stages of CKD.

Method: 60 patients with CKD of the pre-dialysis stages (C2-C4) were examined. The diagnosis of CKD was made on the basis of clinical, instrumental, and laboratory data. To study the relationship between the composition of the intestinal microbiota and inflammation in patients with CKD, we studied markers of inflammation such as CRP and IL-6. CRP was determined in blood serum by a highly sensitive method on a Humareader Single analyzer, IL-6 by enzyme-linked immunosorbent assay on a solid-phase analyzer. eGFR was calculated using the formula CKD-EPI-2011. The control group consisted of 30 healthy subjects. Statistical processing was carried out using methods of variation statistics. The results were processed using Microsoft Exel 2002 & Statistica 6.0.

Results: The average age of patients was 59 years. Of these, 25 women (40%) and 35 (60%) men. The estimated glomerular filtration rate varied from 30 to 60 ml / min / 1.73 m2, which corresponded to the indicators of the pre-dialysis stages of CKD. Analysis of intestinal microbiota showed a deficiency of Bifidobacterium bacteria ($<$108 CFU), and an increase in the number of Escherichia ($>$ 108 CFU) in patients with CKD of the pre-dialysis stages. According to the results of the study, in the group of patients with CKD, the level of inflammatory markers was higher (CRP-55%, IL-6-60%, leukocytes 62%) than in the control group (CRP-45%, IL-6-40%, leukocytes 38%) However, in men, the IL-6 index was higher than in women. In patients with CKD with obesity, the titer of pathogenic bacteria and their spectrum showed the worst results, although unreliable.

Conclusion: All examined patients had dysbiosis of the 2nd degree. At the same time, an imbalance of the intestinal microbiota is combined with an increased level of CRP, IL-6, and white blood cells.

P0257 CLINICOPATHOLOGICAL SPECTRUM OF KIDNEY INVOLVEMENT IN MONOCLONAL GAMMOPATGY

Hadj Brahim Mayssa[1], Meriem Ben salem[1], Ouni Amal[1], Handous Insaf[1], Bensalah Manel[1], Letaief Ahmed[1], Hammouda Mouna[1], Aloui Sabra[1], Boukadida Amine[1], Skhiri Habib[1]

1

Background and Aims: The occurrence of kidney diseases associated with a monoclonal gammopathy is increasingly recognized.Renal biopsy and evaluation by light microscopy, electron microscopy and immunofluorescence,in association with adequate clinical examination are essential in accurate diagnosis. The objective of our study is to describe the types of kidney damage secodary to monoclonal gammopathies and to study its renal prognosis.

Method: It is a monocentric RETOSPECTIVE DESCRIPTIVE STUDY carried out in the nephrology department of CHU FATTOUMA BOURGUIBA MONASTIR spread over a period of 7 years from January 2012 to December 2018.

Results: we collected 40 cases of monoclonal gammopathies. The median age was 61 years.The sex ratio was 0,9. the circumstances of discovery were dominated by renal failure. it revealed the diagnosis in 77.5% of cases. the renal presentation proteinuria in 70%, microscopic hematuria in 12.5%, edematous syndrome in 27.5% and nephrotic syndrome in 37,5%. The mean creatinine level was 500 umol / L and proteinuria at 4,3 g / 24 h with a maximum rate of 17.5 g / 24h. the electrophoresis of serum proteins showed the presence of a monoclonal peak in 90% of the cases in the gamma zone. The plasmocytosis was less than 10% in 15% of cases and more than 60% in 22,5% of the cases. Radiology showed bone localizations in 32,5% of cases. These gammopathies were classified as Multiple myeloma in34 patients, POEMS in one case and 5 MGRS. Kidney biopsy was performed in 10 patients showing cast nephropathy, AL amyloidosis and vasculites(endocapillary glomerulonephritis with hyaline thrombi in all vessels and double contour appearance of the glomerular basement membrane) in respectively 12,5%, 7,5% and 2,5% of cases. the main indications were rapidly progressive renal failure, unexplained acute renal failure and nephrotic syndrome. The renal involvement retained was a myeloma tubulopathy in 28 patients, 3 of whom were confirmed histologically . AL amyloidosis was found in 5 patients and the confirmation was histological. Type 1 cryoglobulinemia was diagnosed in only one patient. Glomerular nephropathy remained undetermined in 6 patients whose PBR was indicated but not made in the presence of hemostasis disorders. The chemotherapy was started in 34 patients based on bortezomide-thalidomide-dexamethasone in 30% of cases. An autograft of the bone marrow was done in one patient. Hemodialysis was required in 15 patients. The renal function was improved in 42.5% of the cases and a passage on chronic hemodialysis in 10% of cases. 10% of patients have achieved complete hematological remission.

Conclusion: Patients with MG can develop a large variety of related renal lesions.Renal involvement darkens the prognosis hence the need for adequate care .

P0258

EVALUATION OF ACUTE - PHASE REACTANTS IN MONITORING DISEASE ACTIVITY AND RESPONSE TO IMMUNOSUPPRESSIVE THERAPY IN IDIOPATHIC RETROPERITONEAL FIBROSIS

Katarina Obrencevic[1], Marijana Petroviä‡[1], Nemanja Rancic[2], Jelena Tadiä‡[1], Neven Vavic[1], Bojan Nikolic[3], Milorad Radojevic[1], Violeta Rabrenovic[1], Mirjana Mijuskovic[1]

[1]Military Medical Academy, Clinic of nephrology, Belgrade, Serbia, [2]Military Medical Academy, Centre for Clinical Pharmacology, Belgrade, Serbia and [3]Military Medical Academy, Institute of radiology, Belgrade, Serbia

Background and Aims: Idiopathic retroperitoneal fibrosis (IRF) is a rare disease characterized by fibroinflammatory periaortic tissue that affects the ureters, causing obstructive nephropathy and impairment of renal function. Findings strongly suggest an autoimmune etiology. Medical treatment includes immunosuppressive drugs, but the optimal treatment has not been established. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) represent markers of active inflammation in the early phase of the disease, and hence could be sensitive predictors of the treatment response.

Method: This retrospective case series study includes patients with IRF treated with two different protocols: corticosteroids in combination with mycophenolate mofetil (MMF) and corticosteroids combined with azathioprine (AZA). The total number of 28 patients (13 in the first group and 15 in the second group) were treated and followed in the Clinic of nephrology in Military Medical Academy.

Results: At presentation 92.3% of patients had elevated levels of ESR and CRP, and 67.8% of them had acute renal insufficiency. Systemic symptoms resolved after four weeks in all patients. The kidney function improved significantly in both groups after first moth of treatment, although the creatinine level was higher in the MMF group because of the disease recurrence in 23% of the patients. In MMF group was observed faster reduction in the periaortic mass after six months and 53.8% of patients achieve 100% of the mass reduction at the end of the treatment while 33.3% in AZA group. The levels of ESR and CRP after one month of treatment in AZA group correlated with the fibrotic mass reduction after six months and after one year. In MMF group, only the CRP level after one month correlated with the fibrotic mass reduction achieved after one year.

Conclusion: MMF had more rapid and complete effect in hydrnephrosis withdrawal and total reduction of the fibrotic tissue, comparing with AZA whose effect was slower and without complete mass reduction. CRP strongly correlated with the remission of the disease in both therapeutic protocols.

P0259

PARAPROTEIN-RELATED RENAL LESIONS IN NEWLY DIAGNOSED MULTIPLE MYELOMA: CLINICAL AND PATHOLOGICAL CHARACTERISTIC OF 51 PATIENTS WITH KIDNEY BIOPSIES

Zishan Lin[1], Xiaojuan Yu[1], Suxia Wang[1], Xinan Cen[2], Fude Zhou[1], Minghui Zhao[1]

[1]Institute of Nephrology, Peking University, Renal Division, Department of Medicine, Peking University First Hospital, Beijing, and [2], Department of Hematology, Peking University First Hospital

Background and Aims: Renal involvement is common in multiple myeloma (MM). In this study, we examined kidney biopsy findings in patients with newly diagnosed MM (NDMM) and correlated them with clinical characteristics and survival.

Method: Renal pathological findings were retrospectively studied in 56 patients with NDMM. Clinical and laboratory data as well as outcomes were collected from 51 patients with paraprotein-related renal lesions in NDMM. Patients were categorized according to the with or without myeloma cast nephropathy (MCN).

Results: Among 56 patients with NDMM, 51 had paraprotein-related renal lesions, of which MCN was the most common lesion in 31 patients (60.8%), followed by amyloidosis in 12 patients (23.5%) and light chain deposition disease (LCDD) in 8 patients (15.7%). Five patients had nonparaprotein-associated lesions, of which minimal change disease was the most common diagnosis, seen in 3 patients (60%). Patients with MCN had significantly higher serum creatinine levels, a lower eGFR, a higher percentage of requiring dialysis at diagnosis, a higher incidence of progressing to end-stage renal disease (ESRD), lower hemoglobin levels, a lower percentage of albumin in urine protein, a higher level of serum albumin and were more likely to have a detectable M-spike but less likely to have a detectable monoclonal whole immunoglobulin than patients without MCN. Compared with patients with MCN, the median overall survival time of patients without MCN was significantly longer (not reached vs 39 months (95% CI: 9–69 months); P=0.047; Fig.1). According to the multivariate analysis, the independent predictors of overall survival were the number of myeloma casts (HR: 1.12, 95% CI: 1.07-1.25; P=0.014) and male sex (HR: 4.99, 95% CI: 1.36-18.38; P=0.016).

Conclusion: Patients with MCN suffer from more serious and more urgent renal damage and can also present with high-grade albuminuria but without hypoalbuminemia. The number of myeloma casts and male sex are independent predictors of overall survival.

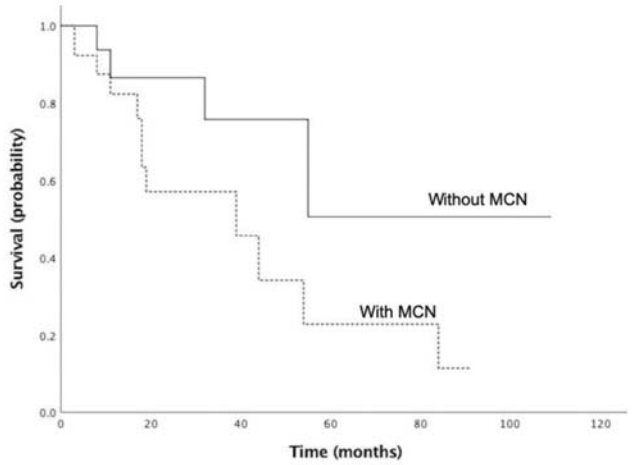


Figure 1. Overall survival divided according to renal histology. Log rank $p = 0.047$. Median overall survival not reached in Without MCN group and 39 months in With MCN group.

P0260 **CLINICAL PROFILE OF PATIENTS INITIATING EVOLOCUMAB IN SPANISH NEPHROLOGY UNITS: A RESTROSPECTIVE, OBSERVATIONAL STUDY IN CLINICAL PRACTICE (RETOSS-NEPHRO).**

Marian Goicoechea[1], Vicente Álvarez[2], Alfonso Segarra[3], Manuel Polaina[4], Guillermo Martín[5], Nicolas-Roberto Robles-Perez[6], Veronica Escudero Quesada[7], Cristhian Orellana[8], Jose Luis Gorriz[9], Santiago Villamayor[10]

[1]Hospital Gregorio Marañon, Madrid, Spain, [2]Hospital Universitario La Princesa, Madrid, Spain, [3]Hospital Arnau de Vilanova, Lleida, Spain, [4]Complejo Hospitalario de Jaén, Jáen, Spain, [5]Hospital Regional Universitario Carlos Haya, Málaga, Spain, [6]Hospital Universitario Infanta Cristina, Madrid, Spain, [7]Hospital Universitario Dr. Peset, Valencia, Spain, [8]Hospital Puerta del Mar, Cádiz, Spain, [9]Hospital Clínico Universitario de Valencia, Valencia, Spain and [10]Amgen, Medical department, Barcelona, Spain

Background and Aims: Cardiovascular disease is the primary cause of morbidity and mortality in patients with chronic kidney disease (CKD). Evolocumab is a monoclonal antibody that inhibits proprotein convertase subtilisin-kexin type 9 (PCSK9) and lowers serum low density lipoprotein cholesterol (LDL-C) levels. Evolocumab is indicated for adult patients with hypercholesterolaemia or mixed dyslipidaemia who are unable to reach LDL-C goals with the maximum tolerated dose of statin or are statin intolerant. This study was conducted to describe clinical characteristics, reasons for therapy initiation and treatment effects in patients treated with evolocumab in Spanish Nephrology units.

Method: Retrospective, observational, chart review of consecutive patients initiating evolocumab (Feb-2016 to Aug-2018) in 15 Spanish Nephrology Units. Patient characteristics, lipid modifying therapies and lipid profiles over time were retrospectively collected at 24 weeks pre- and 12 ± 4 weeks post-evolocumab initiation.

Results: 60 patients were enrolled: 53.3% women; mean (SD) age, 56.9 (12.8) years; mean (SD) body mass index, 28.0 (4.7) kg/m2; 45.0% had familial hypercholesterolemia (FH) (5.0% homozygous, 23.3% heterozygous, 16.7% undetermined FH); from the total population, 35% were in primary prevention and 65.0% started evolocumab after previous Atherosclerotic Cardiovascular Disease [ASCVD]. Regarding renal function, mean (SD) eGFR was 62.6 (30.0) ml/min/1.73m2; 51.7% of patients had eGFR $<$60 ml/min/1.73m2 (CKD stage$>$2), 50.0% had proteinuria ($>$300 mg/g) and 10.0% had nephrotic syndrome. Other CV risk factors were hypertension (75.0%), diabetes (25.0%), and smoking (21.7%); 40.0% of patients were statin intolerant. At evolocumab initiation, 41.7% of patients were on a high intensity statin, 18.3% on moderate intensity statin and 50.0% were receiving ezetimibe. Mean (SD) LDL-C at evolocumab initiation was 179.7 (62.9) mg/dL (53.4% of patients with LDL-C$\geq$160; 29.3% $\geq$190). Mean (SD) baseline HDL-C and total cholesterol were 48.5 (15.0) mg/dL and 273.1 (82.7) mg/dL, respectively. After 12 weeks, evolocumab resulted in LDL-C reductions of 60.1%, to a mean (SD) of 72.7 (80.3) mg/dL, with similar results observed in patients in primary/secondary prevention, with CKD stage $>2/\leq2$ or with/without proteinuria. Conversely, patients with/without FH showed significant differences between their reductions (46.6% vs 76.6%, respectively, p=0.0276). At week 12, 90.0% of patients reached LDL-C levels $<$100 mg/dL, 70.0% $<$70 mg/dL, and 55.0% $<$55mg/dL, while eGFR levels and statin use remained stable.

Conclusion: In Spanish Nephrology Units, evolocumab was predominantly prescribed in patients with FH, ASCVD and/or CKD stage $>$2. Initial evolocumab use was aligned with ESC/EAS dyslipidaemia guidelines, but with higher baseline LDL-C levels than the recommended thresholds. After 12 weeks of evolocumab treatment, LDL–C levels were more than halved and the majority of patients achieved both the 2016 and 2019 EAS/ESC targets of LDL-C control.

P0261 NARRATIVE NEPHROLOGY: A BIO-PSYCHO-SOCIAL APPROACH WITH CDK PATIENTS

Marco Lombardi[1], Alessandro Toccafondi[1], Umberto Caraccia[2], Leonardo Mari[3], Pietro Claudio Dattolo[1]

[1]Division of Nephrology and Dialysis, Firenze 2, Azienda USL Toscana Centro, Italy, [2]Hospital & Clinical Risk Managers, Società Scientifica, Roma, Italy and [3]Pharmacy Borgo San Lorenzo Hospital, Azienda USL Toscana Centro, Italy

Background and Aims: Poor medication adherence in CKD patients can reach up to 80%. Non-adherence is associated with high mortality and morbidity and it is a negative criterion for the inclusion in the transplant waiting list. Poor adherence increases also the costs for health care in terms of diagnostic procedures, dialysis in emergency, etc. Therefore, to increase patients' adherence to medical treatments is one of the priority of clinical nephrology.

According to the WHO adherence behaviors are associated to several factors (e.g. organization of health services, doctor-patient relationship, patients' psychosocial factors). The most efficacy interventions descried in the literature to increase patients' adherence to treatments are conducted by a multi-professional team and with the active participation of patients.

In the last years, narrative evidenced-based medicine has been proved as a useful methodology in the care of chronic patients also in promoting adherence to treatments.

Aim of this clinical project is to obtain the best control of the evolution of chronic kidney disease through a multidisciplinary approach of narrative medicine.

Method: Within the pre-dialysis service of the Division of Nephrology and Dialysis Firenze 2, it has been integrated the clinical care for CKD patients with a protocol based on a narrative medicine approach (Fig.1).

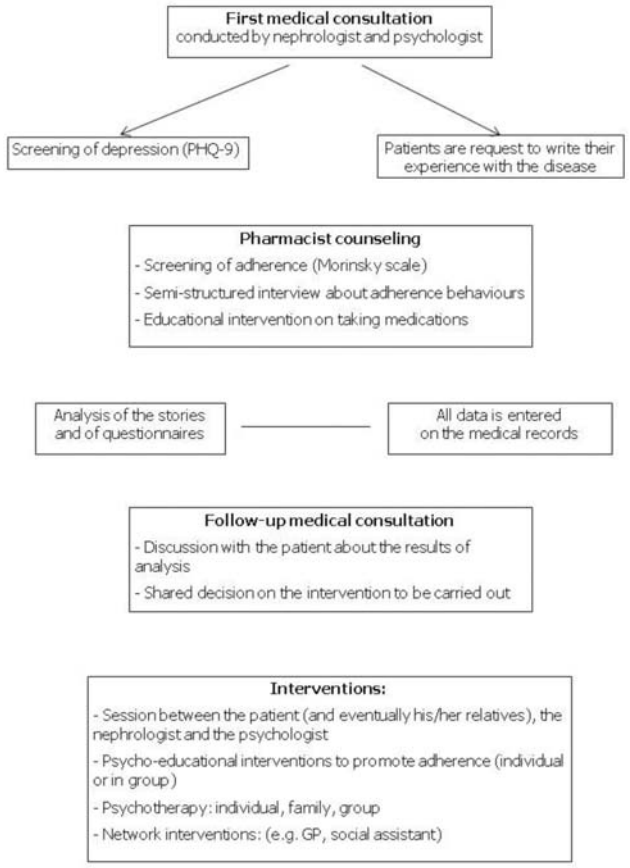


Figure: Protocol of the Narrative Medicine intervention with CDK patients

The clinical protocol is composed by the following procedures:

1. All CKD patients are invited to a first medical consultation at the presence of the nephrologist and a psychologist. During this medical examination, patients are invited to write at home a brief history related to their experience with the CKD and the treatments. These stories are analyzed according to evidence-based narrative medicine procedures. The patients' medical record is integrated with the narrative stories and related analysis.
2. Screening for depression. During this first session, the psychologist administers the PHQ-9 for assessing depression. Patients who obtain a score above the cut-off are invited to a individual session with the psychologist.
3. Pharmacist counseling. Patients are invited to a pharmacist counselling intervention. The pharmacist administers the Morinsky scale (questionnaire for adherence) and conduct a semi-structured interview exploring patients' attitudes and behaviors about taking medications.
4. Sharing decision-making. During the follow-up visit the results of the narrative stories and of questionnaires are discussed with the patients. In case of poor adherence, possible interventions to promote adherence are discussed with the patients (psycho-educational, psychotherapy, etc.).

Results: This project begun around 2 months ago. In this period 15 patients were met, collecting stories by 12 of them (80%). Most of the stories were rich of contents and useful from a medical point of view. None patients refuse the medical consultation at the presence of psychologist, and 5 of them asked for psychotherapy sessions. In line with the literature, 30% of patients presented symptoms of depression. Due to logistic reasons we are going to start the pharmacy counseling intervention at the end of January. All patients were grateful to have been included in this protocol. In the following months we will be able to assess the impact of this protocol in terms of medical outcome.

Conclusion: To promote an active role of patients in taking care of themselves and follow medical prescriptions, it has been implemented a clinical protocol based on narrative medicine approach in which the biological, psychological and social needs of patients are considered and discussed with them. The empirical results obtained in these first months indicate a positive response from patients in terms of wish to write the experience with the disease and to receive the medical visit with the nephrologist at the presence of a psychologist.

P0262

DIAGNOSIS OF PNEUMOCYSTIS PNEUMONIA BY METAGENOMIC NEXT-GENERATION SEQUENCING IN PERIPHERAL BLOOD OF PATIENTS WITH KIDNEY DISEASE

Peng GU[1], Shutian XU[1], Xue JIANG[1], Zhouyu CHAO[1], Yun ZHOU[1], Zhe LI[1], Shijun LI[1]

[1]*National Clinical Research Center of Kidney Diseases, Jinling Hospital, Nanjing University School of Medicine, Nanjing, P.R. China*

Background and Aims: Pneumocystis jirovecii is an opportunistic infectious pathogen that can cause pneumocystis pneumonia in HIV patients. The kidney transplant recipients and patients with kidney diseases receive immunosuppressive therapy, PCP is not uncommon in such patients, but early etiological diagnosis is difficult. Metagenomic next-generation sequencing (mNGS) has higher sensitivity for pathogen identification in a variety of infections. In this study, mNGS was used to detect peripheral blood samples of patients with kidney disease complicated with PCP, and to evaluate the diagnostic value of mNGS in peripheral blood for the etiology of PCP.

Method: From August 2018 to December 2019, We collected 37 cases with kidney disease complicated with pulmonary infection and clinically diagnosed with PCP after receiving immunosuppressive therapy. mNGS was used to analyze the pathogen types and sequences in peripheral blood samples to evaluate the detection efficiency to PCP. To compare the efficacy of mNGS and traditional clinical diagnosis (fungal G combined with lactate dehydrogenase detection) of PCP. In addition, patients with Bacterial/fungal pneumonia or viral pneumonia were mNGS positive controls.

Results: 37 peripheral blood samples were collected from 37 patients, results for all samples were obtained within 72 hours. Pneumocystis jirovecii was detected by mNGS in 35 of the 37 samples, with a sensitivity of 94.59%, specificity of 100%. 31 patients had mixed infection. Cytomegalovirus (CMV) was detected in 19 of the 37 cases (51.4%), epstein-barr virus (EBV) was detected in 6 cases, herpes simplex virus (HSV) was detected in 5 cases, and Torquetenovirus was detected in 8 cases. There were 8 cases of bacterial infection, including 2 cases of staphylococcus, 2 cases of acinetobacter, 1 case of klebsiella pneumoniae, 1 case of escherichia coli, and 4 cases of other uncommon bacteria. There were 33 patients with positive fungal G test and elevated lactate dehydrogenase (BG/LDH), and 4 patients with multiple negative fungal G test .The sensitivity of BG/LDH was 89.19%, the specificity was 56.0%.

Conclusion: mNGS has obvious advantages over the traditional method of diagnosing PCP. It has the characteristics of accuracy, simplicity and noninvasiveness, and is of great value for the early diagnosis of PCP.

P0263 A NEPHROLOGIST'S LOOK AT HYPERTENSIVE DISORDERS OF PREGNANCY

Bianca Covella[1], Luigi Rossi[1], Domenico Caringella[1], Maurizio Guido[1], Giorgina Piccoli[2], Carlo Lomonte[1]

[1]Miulli General Hospital and [2]Centre Hospitalier - Le Mans, Le Mans, France

Background and Aims: Preeclampsia (PE) is a pregnancy-related syndrome of variable severity that falls under the broad category of hypertensive disorders of pregnancy (HDP). The relationship between PE and chronic kidney disease (CKD) is not entirely understood. Once considered a self-limited disease healed by delivery, it is now acknowledged that PE is a marker of cardiovascular and kidney health in the long term. The aim of this study was to review the data of women with hypertensive disorders of pregnancy at our institution, to identify need and to organize a conjoint nephrology and obstetrical activity in our setting

Method: We retrospectively reviewed all the medical charts of the patients hospitalized in the last two years for hypertensive disorders of pregnancy and who delivered in our Hospital. The cohort was divided into two groups: gestational hypertension (GH) and PE. A descriptive analysis of the clinical-laboratoristic was performed (t-test for continuous data with normal distribution).

Results: We identified 93 cases of hypertensive disorders of pregnancy on a total of 3279 deliveries (2.8%), 47 GH and 46 PE [2 cases of HELLP syndrome and 1 of eclampsia included in the PE group]. These two groups showed similar mean age: 33.5±6 vs 34.9±6 years (p value= 0.25); serum creatinine (sCr) and uric acid at admission were statistically different, and higher in the PE group (sCr 0.57±0.15 and 0.66±0.2 – p=0.01 and uric acid 4.5±1.38 and 5.6±1.47 – p=0.01).

Comorbidities were frequent in the PE group: thyroid disfunction was found in 17% of cases (7 hypothyroidism and 1 hyperthyroidism, all under treatment), coagulation abnormalities were present in 15% of cases (4 MTHFR mutation, 1 protein S deficiency, 1 prothrombin-gene mutation, 1 patient was positive for LLAC); gestational diabetes was diagnosed in 13% of the cases. We identified 1 renal transplant recipient, 1 IgA-vasculitis patient, 1 patient with family medical history positive for PE (in her twin sister); none of these patients had been identified as at high risk for PE. At hospital admission, 54% of the patients were on antihypertensive treatment, 7 of them for chronic hypertension and 18 for gestational hypertension (12 of these patients underwent a previous hospitalization during the same pregnancy, diagnosed with gestational hypertension); at admission only 24% of PE patients were treated with anticoagulant or antiplatelet prophylaxis. Caesarean section was performed in 36 cases (78%). All but one children live-born, the exception being a child from a multiple pregnancy (quadruplets).

Conclusion: A multidisciplinary approach and a nephrological follow-up are increasingly indicated in PE. Our series underlines a high prevalence of comorbidity or risk factors, including thyroid disfunction, gestational diabetes and coagulation abnormalities. The high prevalence (7/46) of chronic hypertension and the fact that the two patients with kidney disease were not identified as at risk for PE underlines the potential role for developing a synergic approach between nephrologist and obstetricians.

P0264 **ASSESSMENT OF GFR IN MORBIDLY OBESE PATIENTS USING DIFFERENT EQUATIONS: WHICH IS THE BEST?**

Alaa Sabry[1,1], Amir Basiony[1], Mohamed Kamal[1]

[1]*MANSOURA UNIVERSITY, Egypt*

Background and Aims: Obesity is a potent risk factor for the development of kidney disease. The prevalence of abdominal obesity in Egyptians based upon the European cut-off points was 30.2% for men and 70.9% for women.

To detect the best formula for estimation of glomerular filtration rates in morbidly obese individuals.

Method: In this prospective study 82 morbidly obese patients were included, Age: 15 to 65 years, Morbidly obese patient (BMI > 40 Kg/m2), Creatinine clearance calculated from a 24-h urine was done, ***Estimated glomerular filtration rate (eGFR):*** It was assessed to be correlated with creatinine clearance and detect the most suitable formula for morbidly obese patients.

Cockcroft-Gault formula: *Cockcroft-Gault formula (for total body weight): ockcroft-Gault formula (for adjusted body weight): Cockcroft-Gault formula (for lean body weight),* ***MDRD-eGFR (Modification of Diet in Renal Disease equation) (Shahbaz & Gupta, 2019), CKD-epidemiology (CKD-EPI): (Levey, et al, 2009)***

Results: Demogrphic criteria of the studdied patients

Conclusion: The equations that had the nearest values to creatinine clearance were CG-TBW-GFR and CGAjBW- GFR, both of them had a moderate reliability with more agreement for the CG-TBW-GFR equation . The CG-TBW-GFR formula was the most reliable one to measure GFR, followed by the CG-AjBW-GFR formula, while the CG-IBW, CG-LBW, MDRD-GFR and CKD-EPI-GFR formulae were not reliable at all .

Items	Study group (n=82)
Age *(years)*	37.2 ± 9.7
Gender ➢ Male ➢ Female	 25 (30.5%) 57 (69.5%)
Weight *(kg)*	150.3 ± 28.6
Height *(cm)*	164.1 ± 8.4
Neck circumference *(cm)*	42.5 ± 3.9
Waist circumference *(cm)*	142.1 ± 16.9
Hip circumference *(cm)*	154.7 ± 15.5
Waist hip ratio *"WHR"*	0.92 ± 0.08
Body mass index *"BMI" (kg/m^2)* ➢ < 50 kg/m^2 ➢ ≥ 50 kg/m^2 (super obese) (Mean ± SD) of BMI	 23 (28%) 59 (72%) 55.8 ± 9.5
Body surface area *"BSA" (m^2)*	2.6 ± 0.28
Body adiposity index *"BAI" (%)*	55.9 ± 9.4
Visceral adiposity index *"VAI"*	2.1 (1.7 – 2.7)

Data expressed as mean ± SD, median (IQR) or frequency (%).

Figure:

P0265 SPONDYLODISCITIS IN HEMODIALYSIS PATIENTS: A NEW EMERGING DISEASE? DATA FROM AN ITALIAN CENTER.

Lara Traversi[1], Elisa Nava[1], Brunilda Xhaferi[2], Silvia Tedoldi[1], Tiziana Mazzullo[1], Stefania Martino[1], Giada Giovanna Olga Bigatti[1], Daniele Ciurlino[1], Silvio Bertoli[1]

[1]IRCCS Multimedica, Dialysis and Nephrology Unit, Sesto San Giovanni, Italy and [2]University of Milan-Bicocca, Department Medicine and Surgery, Monza, Italy

Background and Aims: Hemodialysis (HD) patients represent a risk category for infections and for their possible complications, in particular infective spondylodiscitis. Although this is a serious complication, only few cases have been reported in the literature and it is not clear which is the best clinical management.

The aim of this retrospective study was to evaluate the cases of infective spondylodiscitis that occurred among HD patients of our center.

Method: We collected the cases of spondylodiscitis that occurred at our center between May 2005 and October 2019. We focused in particular on the time interval between onset of symptoms and diagnosis, often delayed. The possible risk factors related to the onset of this disease were also considered. The diagnosis of infective spondylodiscitis was based on clinical data, laboratory results and diagnostic imaging tests.

Results: Over more than 10 years, there were 9 cases. The mean age was 69 $\pm$ 12 years. 55.6% of patients were affected by diabetes mellitus, 55.6% by hypertension, 22.2% by bone diseases, 11.1% by cancer and 11.1% by rheumatoid arthritis in chronic treatment with low-dose steroids and azathioprine (Table 1).

All patients had back pain as an initial symptom, 55.6% had fever, while 33.4% had neurological symptoms. At hospital admission 55.6% of patients had leukocytosis and 88.9% of patients had elevated CRP level (Table 2).

Six patients (66.7%) had their diagnoses confirmed by magnetic resonance imaging (MRI), while two patients had performed CT prior to MRI and one patient had his diagnosis confirmed by CT (Table 2). The lumbar region was the most common site of infection (77.8%) (Figure 1).

The mean dialytic age was 33 $\pm$ 38 months. Four patients used an arteriovenous fistula as vascular access for HD, one patient used an arteriovenous graft, three patients used a tunneled cuffed catheter, and one patient used a temporary catheter (Table 3). Two patients had experienced thrombosis of the arteriovenous fistula requiring endovascular surgery.

Blood culture were positive in five patients (four for S. aureus and one for S. agalactiae) and negative in four patients. Three of the patients with positive coltures used a catheter for HD and in two cases it was necessary its removal. Bone biopsy (performed in three cases) confirmed the diagnosis of S. aureus spondylodiscitis in one patient (Table 3).

The mean time interval between onset of symptoms and diagnosis was 34 $\pm$ 42 days (Table 3).

All patients received antibiotic treatment for a mean duration of 6 weeks. In most of the cases it was used vancomycin or teicoplanin plus ciprofloxacin as initial antibiotics (Table 4).

One patients had recurrent infective spondylodiscitis within 2 years; one patient had long-term neurologic sequelae despite surgical treatment. The others 7 cases underwent resolution after a mean of 3.5 months.

Conclusion: Infective spondylodiscitis is a disease to be suspected in the presence of back pain among HD patients, even in the absence of fever or traditional risk factors. It is important to get an early diagnosis, to improve the outcome of patients, avoiding diagnostic delays. Close monitoring of vascular access, paying attention to disinfection procedures and aseptic techniques, is important to avoid this complication.

Figure 1. MRI of the lumbosacral spine without gadolinium contrast showing discitis at the L4–L5 level (Patient n. 6).

Table 1. Characteristics of the patients with infective spondylodiscitis in care at our center.

Table 2. Initial clinical presentation, initial laboratory results, diagnostic tools, location of infection.

Table 3. Dialytic age, vascular access for hemodialysis, culture results, time interval between onset of symptoms and diagnosis.

Table 4. Treatments and outcome of patients.

P0266 **PREDICTIVE FACTORS OF COMPLETE RENAL RESPONSE IN PROLIFERATIVE LUPUS NEPHRITIS: A COLLABORATIVE STUDY**

Beatriz Sanchez Alamo[1], Clara Maria Cases Corona[1], Serena Gatius[2], Patricia Dominguez Torres[1], Elena Valdes[2], Amir Shabaka[1], Gema Maria Fernandez Juarez[1]

[1]Hospital Universitario Fundación Alcorcón, Nephrology, Alcorcón, Spain and [2]Hospital Clinico Universitario San Carlos, Nephrology, Madrid, Spain

Background and Aims: Proliferative lupus nephritis (class III and IV) is the most severe form of lupus nephritis and requires prompt diagnosis and treatment with immunosuppressive therapy. Since it represents the most serious entity and has the greatest functional consequences there is a need to determine which factors in proliferative lupus nephritis are most predictive of good long-term renal function.

Method: Methods We analysed the data of 49 biopsy-proven proliferative lupus nephritis (18,4% class III and 81,6% class IV) of three different Spanish hospitals to find prognostic factors for complete renal response (CRR), defined as loss of <25% of eGFR and the absence of proteinuria and microhematuria at the end of the follow up. Sociodemographic, clinical, laboratory, and treatment-related data at the time of kidney biopsy and during follow-up were obtained. We performed univariate analysis and logistic regression to identify independent risk factors.

Results: The median follow-up was 8 years (IQR: 3-12,5), during which time 18 patients (36,7 %) achieved CRR. In the univariate analysis complete renal response was related to: (1) at the diagnosis to: age [40,52 (11,29) years vs 29,92 (11,93) p=0,004]; (2) in kidney biopsy to less leukocyte infiltration (42,3% p=0,05); (3) during the follow up to: less comorbities (27,8% vs 64,3% p=0,02), less infections (27,8% vs 58,6% p=0,04) and less hospitalizations due to infections (0% vs 33,3% p=0,010), less prevalence of high BP (22,2% vs 60,7% p=0,01), (4) at the end of follow up to : serum albumin [3,97 (0,59) vs 4,31(0,19) mg/dL p=0,03].

In the logistic regression comorbidies (HR : 5,71 95%IC: 1,56-20,93 p=0,008) and age at the moment of diagnosis (HR : 1,046 95%IC:1,001-1,071 p=0,04) were related to complete renal response. We didnt find any differences concerning treatments.

Conclusion: Proliferative lupus nephritis is one of the most severe manifestations of lupus nephritis, resulting in increased morbidity and mortality. Traditionally it has been thought that older patients have a worst prognosis, however we demonstrated that they achieved more frequently CRR. In the management of the patients traditional reno protective measures like strict control of BP must be considered since it is a predictive factor of CRR. We shouldnt forget about the implications of an aggressive immunosuppressive treatment such as hospitalizations due to infections and comorbities.

	NR	CRR	p
Kidney biopsy			
Age (years)	**29,92±11,93**	**40,52±11,29**	**0,00**
Hemogloblin (g/dL)	10,98±1,9	11,15±1,1	0,7
Leukocytes	6615,19±2872,6	7228,33±3704,5	0,5
Lymphocytes	1583,3±855,5	1225,9±501,3	0,1
Albumin	2,98±0,8	2,84±0,6	0,5
Creatinine (mg/dL)	1,05±0,6	1,06±0,4	0,96
eGFR(mL/min/1.73m2)	89,8±39,2	77,7±27,2	0,3
CRP	0,3(0,1-1,1)	0,6(0,0-1,2)	0,4
24h Proteinuria (g/24 g)	1,7(0,7-5,3)	1,6(0,7-3,2)	0,4
UPCR	6,22(2,1-77,6)	1,9(0,6-4,7)	0,2
Anti RNP antibodies	**0,15±0,4**	**1,35±2,8**	**0,04**
C3	54,45±19,1	48,08±17,6	0,3
C4	10,29±7,2	7,25±5	0,1
Leukocite in˚ltrate(n,%)	**11(42,3)**	**13(72,2)**	**0,05**
Subendothelial hyalin deposits (n,%)	10(38,46)	3(17,65)	0,2
Epithelial crescents(n,%)	14(51,9)	8(44,4)	0,6
Treatments			
Induction			
Cyclophosphamide(n,%)	17(58,6)	9(52,9)	0,7
Azathioprine(n,%)	3(10,3)	3(17,7)	0,5
MMF(n,%)	8(27,6)	5(29,4)	0,9
Maintenance			
Cyclophosphamide(n,%)	4(13,8)	0(0)	0,1
Azathioprine(n,%)	5(17,2)	5(27,8)	0,4
MMF(n,%)	17(58,6)	13(72,2)	0,4
End of follow up			
Age (years)	**40,78±12,12**	**48,16±11,59**	**0,05**
Creatinine (mg/dL)	1,1±0,8	0,86±0,2	0,2
Albumine	**3,98±0,59**	**4,3±0,2**	**0,03**
24h Proteinuria (g/24 g)	0,8(0,4-1,8)	0,09(0,1-0,2)	0,1
UPCR (g/g)	1(0,3-72,7)	0,0(0-0,1)	0,4
eGFR(mL/min/1.73m2)	81,2±28,9	87,93±17,8	0,4
Comorbidities(n,%)	**18(64,29)**	**5(27,8)**	**0,02**
Infections(n,%)	**17(58,6)**	**5(27,8)**	**0,0**
Hospitalizations due to infections (n,%)	**8(33,3)**	**0(0)**	**0,0**
Hypertension (n,%)	**17(60,7)**	**4(22,2)**	**0,0**
Death (n,%)	1(3,45)	0(0)	0,4
Adverse events(n,%)	17(62,7)	12(75)	0,4
Relapses(n,%)	13(50)	4(26,7)	0,1

P0267

CLINICAL MANIFESTATIONS, PREVALENCE AND PREDICTORS OF PERIPHERAL NEUROPATHY IN NON DIABETIC CHRONIC KIDNEY DISEASE PATIENTS. A CROSS SECTIONAL STUDY FROM TERTIARY CARE CENTRE.

D PRABHAKAR[1], Satya kumar Kothakota[2], Umashankar Mishra[3]

[1]Sraddha hospital, Nephrology, Visakhapatnam, India, [2]MIMS Hospital, Nellimarla, Medicine, Vizianagaram, India and [3]MKCG Medical College And Hospital, Brahmapur, Medicine, Brahmapur, India

Background and Aims: There is a progressive increase in the prevalence of chronic kidney disease (CKD). The impairment of functions of kidney secondary to CKD leads to uraemia. Peripheral neuropathy is one of the common manifestations of uraemia. The present study focuses on the prevalence, clinical manifestations and predictors of peripheral neuropathy in patients with non-diabetic CKD.

Method: This was a cross sectional study conducted in the Department of General Medicine, Maharaja Krishna Chandra Gajapathi Medical College and Hospital, Berhampur, Odisha, India from October 2015 to October 2017. Patients with serum creatinine >2 mg/dl, estimated glomerular filtration rate <60 ml/min (calculated by using Modification of Diet in Renal Disease equation), kidney size < 8.5cm on ultrasound abdomen were included in the study and patients with age less than 18 years, patients with diabetes mellitus and other recognizable risk factors for peripheral neuropathy (Alcoholism, Drugs, Connective tissue disorders, Sarcoidosis, Vasculitis, Thyroid dysfunction, HIV, Hansen's disease, Paraneoplastic disease etc.) and patients on dialysis were excluded. Peripheral neuropathy was assessed by both clinical methods and nerve conduction studies (NCS). Reduced motor nerve conduction velocity, delayed distal latency, fall in the amplitude of compound muscle action potential on Motor Nerve Conduction Study (MNCS) and delay in the peak latencies, reduced sensory nerve action potential on Sensory Nerve Conduction study (SNCS) were considered as evidence for peripheral neuropathy. From upper limb, median nerve and ulnar nerve were selected for MNCS and SNCS. From lower limb, common peroneal and posterior tibial nerves were selected for MNCS and sural nerve was selected for SNCS.

Results: Total 109 patients were included in the study and 75(68.8%) were proved to have peripheral neuropathy. Majority of the affected patients were in 40 to 50 years age group (n=24;32%). Forty four of 75 (58.6%) were males and 31(41.33%) were females. Patients with both sensory and motor neuropathy were 35(32.1%), 26(23.9%) were affected with only sensory neuropathy, while 14(12.8%) were affected with only motor neuropathy. Patients with clinical neuropathy (patients who have clinical symptoms and signs of neuropathy and also evidence on NCS) were 35(46.6%) and with subclinical neuropathy (only evident on NCS) were 40(53.3%).On univariate analysis, age (p-0.015), hypertension (p-0.031), duration of disease (p<0.0001), serum creatinine (p<0.0001), eGFR (p<0.0001), serum uric acid (p<0.0001), serum parathyroid (p<0.0001), serum phosphorus (p<0.0001), serum calcium (p-0.0003), serum magnesium (p-0.0002) and serum potassium (p-0.0028) were significantly correlated with peripheral neuropathy however on logistic regression analysis, sex [OR-0.058;95%CI(0.004-0.831)], serum parathyroid hormone [OR-1.032;95%CI(2.708-6043.5)], serum phosphorus[OR3.881;95%CI(1.114-13.524)], serum magnesium [OR-127.28;95%CI(0.901-1.113)] and duration of CKD[OR1.109;95%CI(1.005-1.224)] were shown to be independent predictors.

Conclusion: Peripheral neuropathy is one of the frequent complications of uremia. Subclinical presentation is most common. Serum parathyroid, serum phosphorus, serum magnesium and duration of disease are independent predictors of uremia induced peripheral neuropathy

Figure: Binary logistic regression analysis

Risk Factors	Odds Ratio	95% Confidence Interval		P Value
		Lower	Upper	
Age	1.001	0.901	1.113	0.985
Sex	**0.058**	**0.004**	**0.831**	**0.036**
Duration of disease (months)	**1.109**	**1.005**	**1.224**	**0.039**
Sr.Uric acid(mg/dl)	2.314	0.815	5.587	0.123
Sr.Creatinine(mg/dl)	1.222	0.483	3.094	0.672
eGFR(ml/min)	1.017	0.799	1.295	0.888
Sr.Pth(pg/ml)	**1.032**	**1.003**	**1.062**	**0.032**
Sr.Magnesium (mg/dl)	**127.28**	**2.708**	**6043.577**	**0.014**
Sr.Phosphorus(mg/dl)	**3.881**	**1.114**	**13.524**	**0.033**

P0268

A COMPARATIVE STUDY OF CYCLOPHOSPHAMIDE, THALIDOMIDE AND DEXAMETHASONE (CTD) VERSUS BORTEZOMIB AND DEXAMETHASONE (BDEX) IN AL AMYLOIDOSIS: A REAL-WORD STUDY IN CHINESE PATIENTS

Shiren Sun[1], Baojian Liu[1], Yan Wang[1], Ming Bai[1]

[1]*xijing hospital, Nephrology, xi'an, P.R. China*

Background and Aims: Amyloid light-chain (AL) amyloidosis is a plasma cell dyscrasia characterized by the deposition of misfolded immunoglobulin light chains. The prognosis of AL patients is poor. About 70% of patients have renal involvement and one third of patients would progress to dialysis. Cyclophosphamide, thalidomide and dexamethasone (CTD) and bortezomib and dexamethasone (BDex) have shown great efficacy in patients with AL amyloidosis, especially in Chinese patients. But which option is more suitable for Chinese patients is unclear.

Method: We retrospectively evaluated 81 AL patients who received CTD (n = 42) or BDex (n = 39) and used Mayo stage 2012 to match 26 pairs of patients.

Results: In the whole cohort, the overall hematologic responses were 86% vs 91% in the CTD and BDex groups, including a complete response of 56% vs 71%, higher than most of the previously reported chemotherapies. One- and two-year overall survival (OS) was 90.2% and 81.7% with CTD regimen, and 87.6% and 82.7% with BDex regimen. After matching by Mayo stage 2012, BDex regimen showed the advantage in the depth and speed of hematologic response over CTD regimen, but there were no statistically significant differences in OS both based on the ITT analysis (P = 0.24) and 6-month landmark analysis (P = 0.48). Cardiac response was similar, while there was a trend for higher renal response in patients treated with BDex (68% vs 44%, P = 0.09). Additionally, we found that if the patients were limited to Mayo stage III or worse, BDex regimen was associated with improved survival (P = 0.009). Overall toxicities were manageable in both regimens. Severe hematologic toxicities and diarrhea should get more attention in patients treated with BDex.

Conclusion: This is the first comparison of BDex versus CTD in patients with AL amyloidosis. These results indicated that CTD and BDex regimens can be active and safe chemotherapy for Chinese patients, but BDex regimen is superior to CTD in achieving more rapidly and deeper clonal response, as well as in improving OS in selected patients.This conclusion is significant because we confirmed BDex regimen may be an optimal option in treating Chinese patients with AL amyloidosis. The definite advantages on long-term prognosis need to be verified in the further studies.

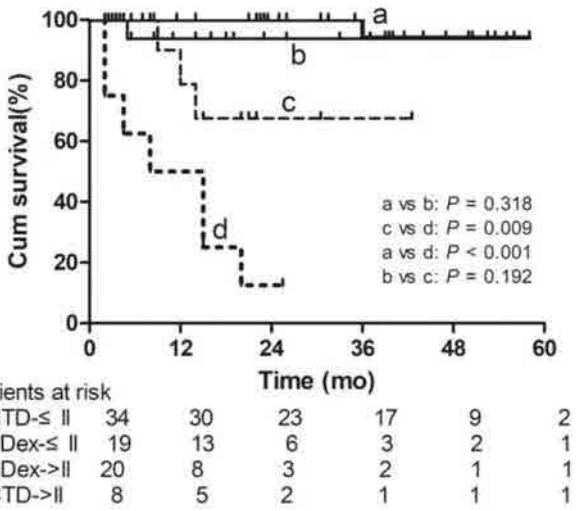


Figure 3. Overall survival of patients according to Mayo stage 2012 and treatment type. (a) Mayo stage ≤ II treated with CTD. (b) Mayo stage ≤ II treated with BDex. (c) Mayo stage > II treated with BDex. (d) Mayo stage > II treated with CTD.

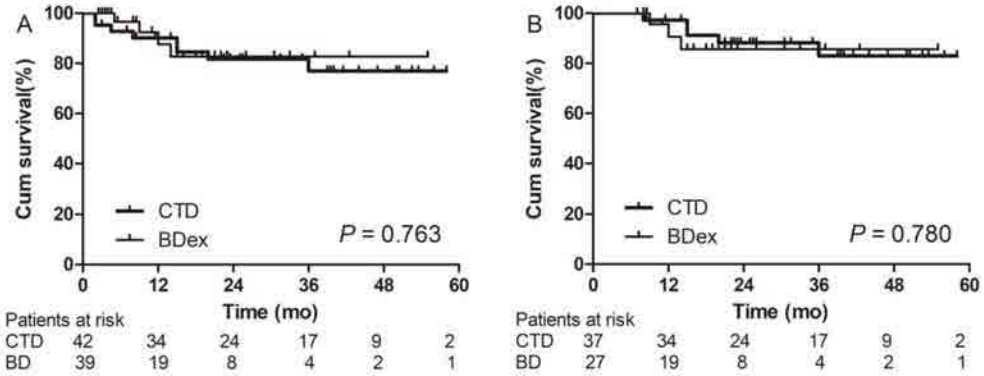


Figure 1. Overall survival of patients according to treatment type based on ITT analysis (A) and 6-month landmark analysis (B) before matching.

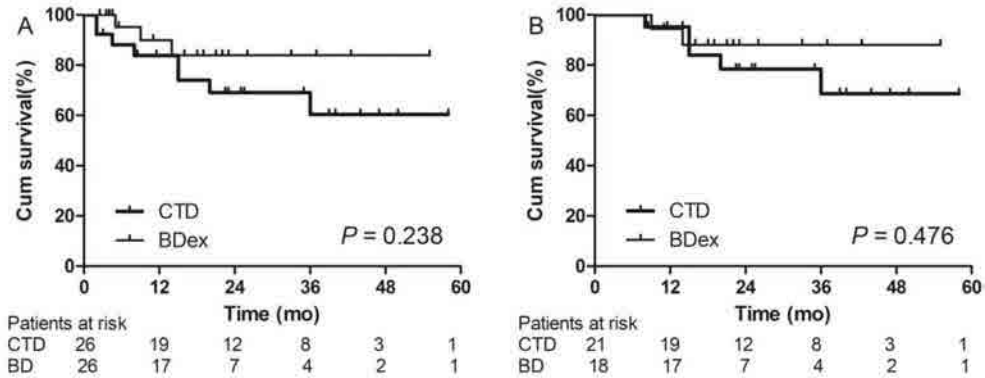


Figure 2. Overall survival of patients according to treatment type based on ITT analysis (A) and 6-month landmark analysis (B) after matching by Mayo stage 2012.

P0269 SYMPTOM-BURDEN IN PEOPLE LIVING WITH FRAILTY AND CHRONIC KIDNEY DISEASE

Andrew Nixon[1,2], Thomas Wilkinson[3,4], Hannah Young[5], Maarten Taal[6,7], Neil Pendleton[8], Sandip Mitra[9,10], Mark Brady[1], Ajay Dhaygude[1], Alice Smith[3,4]

[1]Lancashire Teaching Hospitals NHS Foundation Trust, Department of Renal Medicine, Preston, United Kingdom, [2]The University of Manchester, Division of Cardiovascular Sciences, Manchester, United Kingdom, [3]University of Leicester, Department of Health Sciences, Leicester, United Kingdom, [4]NIHR Leicester Biomedical Research Centre, Leicester, United Kingdom, [5]University of Leicester, Department of Respiratory Sciences, Leicester, United Kingdom, [6]University of Nottingham, Division of Medical Sciences and Graduate Entry Medicine, Nottingham, United Kingdom, [7]University Hospitals of Derby and Burton, Department of Renal Medicine, Derby, United Kingdom, [8]The University of Manchester, Division of Neuroscience and Experimental Psychology, Manchester, United Kingdom, [9]The University of Manchester, Manchester Academy of Health Sciences Centre, Manchester, United Kingdom and [10]NIHR Devices for Dignity MedTech & In-vitro Diagnostics Co-operative, United Kingdom

Background and Aims: Patients with chronic kidney disease (CKD) report high symptom-burden that adversely affects health-related quality of life (HRQOL). Frailty is an independent predictor of poor HRQOL in those with CKD.

Although there is a clear relationship between frailty and HRQOL in patients with CKD, the associated relationship with symptom experience is not well understood. Understanding how living with both frailty and CKD influences symptom-burden could inform management strategies that improve HRQOL of this vulnerable patient group. This study's aim was to evaluate the symptom experience of patients living with frailty and CKD.

Methods: A total of 353 participants were recruited between February 2018 and October 2018 to this cross-sectional observational study. Participants completed physical activity (GP Physical Activity Questionnaire [GPPAQ]), cardiopulmonary fitness (Duke Activity Status Index, providing estimated VO_2 peak), symptom-burden (Kidney Symptom Questionnaire [KSQ]) and HRQOL (Short Form 12 [SF-12]) questionnaires. Frailty was assessed using a modified Frailty Phenotype comprising 3 self-report components:

1) weakness/slowness defined as a SF-12 Physical Functioning score <75; 2) low physical activity defined as 'inactive' by the GPPAQ; and 3) exhaustion defined as a SF-12 Vitality score <55. Participants were categorised as frail if ≥ 2 components were present. Multiple imputation was performed for data considered to be either missing completely at random or missing at random. Regression analyses were used to assess the association between frailty, symptom-burden and HRQOL. Principal Component Analysis (PCA) was performed to explore symptom clusters experienced by non-frail and frail participants.

Results: Two hundred and twenty-five (64%) participants were categorised as frail. Frail participants were significantly older (77.7 vs. 71.5 years, $p<0.001$) and had a significantly lower eGFR (45.8 vs. 50.9 mL/min/1.73m^2, $p<0.001$), albumin concentration (39.2 vs. 41.4 g/L, $p<0.001$) and estimated VO_2 peak (21.7 vs. 33.9 mL/kg/min, $p<0.001$) than non-frail participants. Frailty, when adjusted for age, sex, eGFR and haemoglobin, was independently associated with higher KSQ total symptom score ($p<0.001$) and lower SF-12 Physical Component Summary (PCS) and Mental Component Summary (MCS) scores ($p<0.001$ and $p=0.001$, respectively). Lower eGFR was associated with higher KSQ total symptom score ($p=0.004$) and lower SF-12 PCS score ($p=0.01$). Frailty, when adjusted for age, sex, eGFR and haemoglobin, was independently associated with a two- to over five-fold increase in odds of experiencing all reported symptoms frequently, except loss of appetite and urinary frequency. Lower eGFR was only associated with increased odds of reporting frequent loss of muscle strength ($p=0.04$). PCA revealed two symptom clusters for non-frail participants and three symptom clusters for frail participants. Both non-frail and frail participants had symptom clusters associated with sleep disturbance and musculoskeletal symptoms. There was an additional unique symptom cluster (comprising loss of appetite, tiredness, feeling cold and poor concentration) experienced by frail participants.

Conclusion: Frailty is an independent predictor of high symptom-burden and poor HRQOL. Furthermore, symptom experience for people living with frailty and CKD is distinct from non-frail individuals, reporting a unique symptom cluster that may be a consequence of the frailty syndrome itself. This group of patients should be offered a holistic assessment so that problematic symptoms can be identified and addressed early before they impact more significantly on HRQOL. Future efforts should be focused on evaluating holistic models of care, such as the comprehensive geriatric assessment, for patients living with frailty and CKD.

P0270

SKELETAL MUSCLE AREA AT L3 LEVEL INDEPENDENTLY PREDICTS MORTALITY IN ELDERLY PATIENTS WITH ANCA ASSOCIATED VASCULITIS

Xixi Zheng[1], Peng Xia[1], Jiaying Li[1], Gu-mu-yang Zhang[2], Yan Qin[1], Xuemei Li[1], Hao Sun[2], Limeng Chen[1]

[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Nephrology Division, beijing, P.R. China and [2]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Radiology, beijing, P.R. China

Background and Aims: Infection is the leading cause of death in elderly patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Older patients are more frail and have poorer nutritional reserves. The decrease in skeletal muscle mass and the development of sarcopenia is a pervasive problem among the elderly. Computer tomography (CT) scan provides a practical method to measure muscle mass in hospitalized patients which has been shown to predict the mortality in cancer and ICU patients. In the present study, we aim in to investigate the relationship between skeletal muscle area and clinical outcomes in elderly AAV patients with renal involvement.

Method: Hospitalized AAV patients older than 65 years at the diagnosis in Peking Union Medical Hospital from June, 2014 to June, 2019 were enrolled. Skeletal muscle area was calculated on CT image at the third lumbar vertebra level with previously published method using NIH ImageJ software. Baseline Birmingham Vasculitis Activity Score (BVAS), lab results, intensity of immunosuppressive treatment, follow up time and status of the endpoints (infection or death) were recorded. Characteristics between patients with or without endpoint event were compared. Univariate and multivariate Cox regression model was used to determine the independent predictors of mortality.

Results: A total of 58 patients were included, with. 48.3% male (n=28) and mean age 71.11(65.13, 78.13) years. Baseline BVAS score was 17±4.36 and eGFR was 18.67 (8.306, 34.59) ml/min×1.73m2. Muscle area was 119.6±24.14 cm2 measured on the first CT scan after admission. The baseline serum albumin was 34 (29, 37) g/L, baseline Hemoglobin was 97.83±21.81g/L and baseline immunoglobulin G level was 14.18±4.83g/L. Treatment include glucocorticoid (100%), cyclophosphamide (87.9%), pulse glucocoritcoid (36.2%) and plasma exchange(25.9%).

After a median follow-up of 233.5(56.75, 435.8) days, 30 patients experienced 36 episodes of infections that required either hospitalization or administration of antimicrobial agents, of which 7 episodes were complex infections of more than one site and 10 were infections resulting in ICU admission. Median time to infection was 16 (7.5, 59) days from admission. Pneumonia (n=30) and CMV viremia (n=7) were most common. Seven patients died of infection and 1 died of gastrointestinal bleeding. Median time to death was 44 (25.5,75.3) days from admission.

In univariate analysis, only age (HR=1.198, CI 1.046,1.372, p=0.006) and muscle area (HR=0.945, CI 0.907,0.986, p=0.009) significantly predicted death. Other variables including BVAS score, eGFR at the onset of disease, history of diabetes, history of pulmonary disease, disease affecting the respiratory system and whether receiving glucocorticoid pulse therapy and baseline nutritional markers i.e. BMI, serum albumin level, lymphocyte count, hemoglobin level and immunoglobulin G level were not significant predictors of death or infection. In multivariate survival analysis, muscle area were significant predictor of 6 month death even when controlled for baseline BMI and eGFR.

Conclusion: Muscle area as measured at L3 vertebrae level on non-contrast enhanced CT is an strong predictor of 6 month mortality in elderly AAV patients receiving immunosuppressive therapy

P0271

SERUM VASCULAR ENDOTHELIAL GROWTH FACTOR-D LEVEL CORRELATES WITH RENAL FUNCTION AND ALBUMINURIA IN PATIENT WITH DIABETIC CHRONIC KIDNEY DISEASE

Hyeongwan Kim[1], Jong Hwan Chong[2], Woong Park[1], Sung Kwang Park[3], Won Kim[3]

[1]Chonbuk National University Hospital, Internal Medicine, Jeonju, Korea, Rep. of South, [2]Wonkwang University School of Medicine and Hospital, Internal Medicine, Iksan, Korea, Rep. of South and [3]Chonbuk National University Medical School, Internal Medicine, Jeonju, Korea, Rep. of South

Background and Aims: Biomarkers associated with chronic kidney disease (CKD) may play a crucial role in patients with diabetic kidney diseases. Vascular endothelial growth factor (VEGF)-C and VEGF-D are lymphangiogenic growth factors. It has been well demonstrated that there is lympnagiogenesis in fibrotic kidney disease in human. Previously, we showed that renal VEGF-C and VEGF-D are involved in lymphangiogensis in renal fibrosis model. Recent studies have shown a relationship between sodium load and serum VEGF-C levels in hypertensive patients. Lymphatic endothelial proliferation has been detected in diabetic nephropathy. Thus, serum VEGF-C level has been introduced as a candidate marker of chronic kidney disease. However, until now, there have been few report about serum VEGF-D in patients with diabetic CKD. Thus, we evaluated the relationships between serum VEGF-D and renal function and albuminuria of diabetic CKD.

Method: We divided diabetic CKD patients into four groups: CKD stage 3, CKD stage 4, and CKD stage 5 (without dialysis). Total forty two Asian patients with diabetic CKD (14 patients with CKD stage 3, 14 patients with CKD stage 4 and 14 patients with CKD stage 5) and seven healthy controls without diabetes mellitus have been enrolled in this study. In this cross-sectional study, we performed comparative analysis with serum level of VEGF-D in patients with each group. We measured the levels of VEGF-D through the multiplexing using Luminex® technology.

Results: The serum levels of VEGF-D were higher in the CKD 3, CKD 4 and CKD 5 group compared with the control group (25.9±5.6 pg/ml in control group, 60.3±9.7in stage 3, 62.9±8.5 in stage 4, and 66.5±8.0 in stage 5). However, there was not a significant difference between CKD stage III or IV and CKD stage V in serum levels of VEGF-D. Serum VEGF-D level were negatively correlated with estimated glomerular filtration rate and positively correlated with serum creatinine. At GFR level ≥60 ml/min per 1.73 m^2, serum VEGF-D were biomarkers in ROC analysis. There was a positive correlation between serum VEGF-D level and albuminuria in patient with diabetic CKD. We also found that serum VEGF-D level also correlated with urine protein-to-creatinine ratio in patient with diabetic CKD.

Conclusion: Serum VEGF-D is correlated with renal function in patients with diabetic CKD. VEGF levels in the serum correlate to the severity of proteinuria and albuminuria in diabetic CKD patients. Further large-scale studies are required to confirm these findings.

Table 1. Comparison of serum levels of VEGF-D according to CKD stage

	Control group (N=7)	CKD 3 group (N=14)	CKD 4 group (N=14)	CKD 5 group (N=14)
Serum VEGF-D(pg/mL)	25.9±5.6	60.3±9.7*	62.9±8.5*	66.5±8.0*

Values are means ± SE. CKD, chronic kidney disease; VEGF-D, vascular endothelial growth factor-D; * *p<0.05 vs Control group.*

P0272

COMPARATIVE GUT MICROBIOME DIFFERENCES BETWEEN FERRIC CITRATE AND CALCIUM CARBONATE PHOSPHATE BINDER TREATMENT IN HEMODIALYSIS PATIENTS

Ping-Hsun Wu[1,2,3], Yi-Ting Lin[2,3,4], Po-Yu Liu[5], Mei-Chuan Kuo[1,3,6], Yi wen Chiu[1,3,6]

[1]Kaohsiung Medical University Hospital, Division of Nephrology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C., [2]Kaohsiung Medical University, Graduate Institute of Clinical Medicine, College of Medicine, Kaohsiung, Taiwan, R.O.C., [3]Kaohsiung Medical University, Faculty of Medicine, College of Medicine, Kaohsiung, Taiwan, R.O.C., [4]Kaohsiung Medical University Hospital, Department of Family Medicine, Kaohsiung, Taiwan, R.O.C., [5]National Taiwan University College of Medicine, Department of Internal Medicine, Taipei, Taiwan, R.O.C. and [6]Kaohsiung Medical University, Faculty of Renal Care, College of Medicine, Kaohsiung, Taiwan, R.O.C.

Background and Aims: Gut microbiome alteration increases uremic toxin levels inducing chronic inflammation and leading morbidity and mortality in patients with chronic kidney disease. Phosphate-binding agents may potentially change the composition of the gut microbiota. However, the limited clinical study investigates the microbiome difference between iron-containing and calcium-containing phosphate binders. The aim of this study was to compare the microbiota composition in hemodialysis patients treated with ferric citrate or calcium carbonate.

Method: The stool microbiota was investigated in hemodialysis patients with ferric citrate used (n=8) and calcium carbonate used (n=46) by 16S rRNA next-generation gene sequencing profiling. The altered microbiota between two different phosphate binders was analyzed. Differences in the microbial composition of the two patient groups were assessed using linear discriminant analysis effect size.

Results: Hemodialysis patients with calcium carbonate used revealed significantly reduced microbial species diversity (Shannon index and Simpson index) and increased microbial dysbiosis index compared with ferric citrate users. Compared to patients taking calcium carbonate, a distinct microbial community structure in patients taking ferric citrate, with an increased abundance of *Bacteroidetes* phylum and decreased abundance of phylum *Firmicutes*. In comparison between two phosphate binder users, members of the order *Lactobacillales* were prominent in calcium carbonate therapy, including family *Streptococcaceae* and genus *Streptococcus*. In contrast, taxa of the genus *Ruminococcaceae*, *Flavonifractor*, and *Cronobacter* were enriched in ferric citrate phosphate binder users.

Conclusion: The fecal microbiota was richer and more diverse in the ferric citrate group than in the calcium carbonate group. Hemodialysis patients with ferric citrate used were associated with differences in the gut microbiome composition compared to calcium carbonate users.

P0273 **THE EFFECT OF END STAGE RENAL DISEASE AND RENAL REPLACEMENT THERAPY ON B LYMPHOCYTE SUBPOPULATIONS**

Dimitra Vasileia Daikidou[1], MARIA STANGOU[1], Erasmia Sampani[1], Vasiliki Nikolaidou[2], Despoina Asouchidou[2], Chrysostomos Dimitriadis[1], Georgios Lioulios[1], Eva Pella[1], Aikaterini Anastasiou[2], Asimina Fylaktou[2], Aikaterini Papagianni[1]

[1]Aristotle University of Thessaloniki, Hippokration Hospital, Department of Nephrology, Thessaloniki, Greece and [2]Hippokration Hospital, National Peripheral Histocompatibility Center, Immunology Department, Thessaloniki, Greece

Background and Aims: End-stage renal disease (ESRD) is linked to immunodeficiency, which makes a significant contribution to morbidity and mortality. Disturbances in innate and adaptive immunity have been described in patients on dialysis, although their association with the therapy itself is yet to be defined. The present study aimed to assess the impact of dialysis on B cell subpopulations

Method: B cells (CD19+) and their subsets B1a (CD19+CD5+), naive (CD19+CD27−), memory (CD19+CD27+), (CD19+BAFFR+) and (CD19+IgM+), were quantified using flow-cytometry of in the peripheral blood of ESRD patients, the first day on dialysis (T0), and repeated 6 months later (T6). The results were compared to age-matched healthy control group. Exclusion criteria were age <18 or >75 years, active autoimmune or chronic inflammatory disease, medical history of malignancy, corticosteroids or immunosuppresive treatment for the last 12 months

Results: Pre dialysis ESRD patients had reduced lymphocyte count ($1527\pm646\mu$/L vs. $2459\pm520\mu$/L, $p<0.001$) and B cell (CD19+) count ($82.7\pm59.5\mu$/L vs. $177.6\pm73.8\mu$/L, $p<0.001$) compared to controls, whereas the percentages of B cell subsets were not particularly affected, except for B1a subset which presented a significant increase ($4.1\pm3.6\%$ vs. $0.7\pm0.7\%$ $p<0.001$). In 17 patients who had a follow-up sample 6 months later, the percentage of most subsets was reduced (CD19+CD5+: $1.02\pm0.8\%$ from $3.6\pm4.6\%$, p=0.015, Naive: $40\pm22.3\%$ from $61\pm17.4\%$, p=0.001, CD19+BAFF+:$75.8\pm12.6\%$ from $82.1\pm9.1\%$, p=0.04,), apart from memory B cells percentage, which was increased ($49.4\pm52.1\%$ from 32,9$\pm$35,5%, p=0.01) and CD19+ IgM+ percentage, which was unaffected .

Conclusion: A significant reduction of almost all subsets of B cells was noticed in patients with ESRD on pre-dialysis stage. Furthermore, the initiation of renal replacement therapy may be linked to further alterations in B cells subpopulations, especially at their early stages.

P0274 A NOVEL METHOD FOR THE ASSESSMENT OF RENAL BIOPSY WITH THE ACTIVATABLE FLUORESCENT PROBE

Takuji Iyama[1], Tomoaki Takata[1], Yukari Mae[1], Sosuke Taniguchi[1], Ayami Ida[1], Masaya Ogawa[1], Marie Yamamoto[1], Satoko Fukuda[1], Hajime Isomoto[1]

[1]Tottori University Faculty of Medicine, Division of Medicine and Clinical Science, Yonago, Japan

Background and Aims: Renal biopsy is one of the most important procedures in nephrology. The histological analysis of biopsy tissues is important for the diagnosis and prognosis assessment of renal diseases, as well as determining the treatment strategy. It is necessary to obtain biopsy specimens containing renal cortex for such purpose. Although renal biopsy is the undisputed diagnostic procedure, there always is a need to weigh the benefits against the potential complications. A novel activatable fluorescent probe that reacts with a peptide, which is highly expressed in the renal cortex, has been developed. We evaluated the feasibility of this probe for assessing renal biopsy specimens.

Method: The fluorescent probe was firstly applied to renal proximal tubular cells in order to evaluate the fluorescent emission. Then the probe was applied to mouse kidneys *ex vivo*. Finally, it was applied to human biopsy specimens (n=12). Fluorescent images were acquired using commercially available digital camera equipped with optical interference filter. Fluorescent intensities were quantified and the intensities in cortex and medulla were compared.

Results: We observed fluorescent emission from the renal proximal tubular cells immediately after the administration of the fluorescent probe. The fluorescent intensity gradually increased with time. The fluorescence signal was detected in the mouse kidneys ex vivo without markedly affecting the tissue morphology. The probe on human biopsy specimens also emitted fluorescent and the fluorescent could be detected in all the patients examined. In addition, the cortico-medullary junction could be identified in the fluorescent image (Figure). The fluorescent intensities in renal cortex were remarkably stronger than in medulla.

Conclusion: Renal biopsy specimens can be assessed by fluorescent image using this activatable fluorescent probe. This novel fluorescent probe is useful in clinical nephrology.

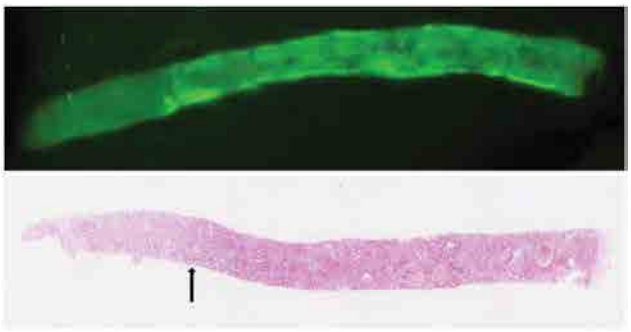


Figure: Fluorescent and hematoxylin-eosin staining images from a representative case. Arrow indicates the cortico-medullary junction.

P0275

SCOPE AND CONSISTENCY OF OUTCOME MEASURES FOR PHYSICAL FITNESS IN TRIALS IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW

Dev Jegatheesan[1,2], Richard Modderman[3], Rathika Krishnasamy[2,4], Allison Tong[5,6], Jeff Coombes[7], Andrea Viecelli[1,2], David W Johnson[1,2], Nicole M Isbel[1,2]

[1]Princess Alexandra Hospital, Nephrology, Brisbane, Australia, [2]University of Queensland, Centre for Kidney Disease Research, Brisbane, Australia, [3]Princess Alexandra Hospital, Physiotherapy, Brisbane, Australia, [4]Sunshine Coast University Hospital, Nephrology, Birtinya, Australia, [5]The University of Sydney, Sydney School of Public Health, Camperdown, Australia, [6]The Children's Hospital at Westmead, Centre for Kidney Disease Research, Sydney, Australia and [7]The University of Queensland, School of Human Movement and Nutrition Sciences, St Lucia, Australia

Background and Aims: Impaired physical fitness is prevalent across the spectrum of kidney disease and is associated with an increased risk of mortality, progression to end-stage kidney disease, falls and hospitalisation. Physical fitness outcomes have been extensively reported in randomised trials involving patients with kidney disease. This study aimed to assess the scope and consistency of physical fitness outcomes and outcome measures reported in kidney disease trials.

Method: A systematic review of randomised trials reporting physical fitness outcomes in adults with chronic kidney disease not requiring kidney replacement therapy, receiving maintenance haemodialysis or peritoneal dialysis, and kidney transplant recipients was conducted. The scope, frequency and characteristics of physical fitness outcome measures were categorised and analysed. Trials were identified from MEDLINE, Embase and the Cochrane Library from March 2000 to March 2019.

Results: From 115 relevant trials, 171 outcome measures for 32 outcomes were identified and categorised into five domains of physical fitness: exercise capacity (reported in 83% of trials), physiological-metabolic (57%), neuromuscular fitness (52%), body composition (45%) and cardiorespiratory fitness (19%). Exercise capacity had 53 different outcome measures and at 15 separate time points. The most common outcome measures were the 6-minute walk test (29%), peak oxygen uptake (20%), 1-repetition maximum (19%) and hand-grip strength (11%), with marked inconsistency in the reporting of outcomes between trials. Outcomes were assessed by field-based tests (65%), lab-based tests (31%) and patient-reported measures (4%).

Conclusion: There is large heterogeneity in the reporting of physical fitness outcomes, with inconsistencies in the use of validated, relevant and patient-important outcome measures.

P0276 **SERUM C3 LEVELS AND THE PROGNOSIS OF ANCA-ASSOCIATED VASCULITIS: A SINGLE-CENTER RETROSPECTIVE STUDY.**

Annalisa Carta[1], Elisa Russo[1], Leda Cipriani[1], Daniela Picciotto[1], Michela Saio[1], Francesca Costigliolo[1], Daniela Verzola[1], Giacomo Garibotto[1], Alberto Sanna[1], Pasquale Esposito[1], Ernesto Paoletti[1], Francesca Viazzi[1]

[1]Ospedale Policlinico San Martino, Nephrology, Dialysis and Transplantation, Genoa, Italy

Background and Aims: Despite improved survival, patients affected by ANCA-associated vasculitis (AAV) presenting with rapidly progressive glomerulonephritis (RPGN) still remain at a higher risk of death relative to the general population. Recent findings suggest a role for the activation of the complement alternative pathway in the pathogenesis of the disease. We aimed to retrospectively evaluate the presentation and outcome of a cohort of patients with AAV and RPGN according to ANCA specificity, investigating the role of complement pathways.

Method: We retrospectively examined 1,547 biopsies performed between 1996 and 2019 in our center, which included 124 patients presenting with paucimmune RPGN.

Table 1. Baseline characteristics of n=68 with ANCA associated vasculitis	
F/M, n [%]	36 [53] / 32 [47]
MPO/PR3, n [%]	30 [44] / 21 [31]
Age at diagnosis, yrs	64.5 (14.5)
eGFR (ml/min)	15 (20)
Serum creatinine (mg/dl)	3.7 (4)
Urea (mg/dl)	124.5 (115)
Uric acid (mg/dl)	7.1±2
Hemoglobin (g/dl)	9.6±1.7
Thrombocyte count, x10^9/l	288 (148)
Urinary proteins (g/day)	1.4 (2.3)
Protein C reactive (mg/dl)	31 (68.4)
VES (mg/dl)	94.5 (51)
LDH (mg/dl)	222 (84)
Fibrinogen (g/l)	5.3±1.6
Ferritin (mg/dl)	417 (279)
C3 (g/l)	1.1±0.2
C4 (g/l)	0.2±0.1
Albumin (g/dl)	30 (10.5)
Patients requiring acute RRT n [%]	21 [30.8]
Death, n [%]	8 [11.7]
NRRT during follow-up n [%]	27 [39.7]
Data are mean±SD or median and interquantile range (when not normally distributed). MPO:myeloperoxidase; PR3: proteinase 3; eGFR:estimated GFR (CKD-EPI 2009).	

Table 2. Baselines characteristics of patients with AAV according to ANCA serotype			
	PR3-ANCA, n=21	MPO-ANCA, n=30	p-value
F/M, n [%]	10 [47.6] / 11 [52.3]	12 [40] / 18 [60]	0.58
Age at diagnosis, yrs	61 (14)	69 (11)	0.02
eGFR (ml/min)	19 (29)	15(14)	0.20
Serum creatinine (mg/dl)	3.3 (4.2)	3.7(5)	0.33
Urea (mg/dl)	119 (120)	(134 (120)	0.95
Uric acid (mg/dl)	6.2 ±2	7.4±2.2	0.17
Hemoglobin /g/dl)	9.8±1.4	9.5±1.7	0.50
Thrombocyte count, x10^9/l	364 (209)	275 (103)	0.01
Urinary proteins (g/day)	1.2 (1.8)	1 (1.4)	0.16
Protein C reactive (mg/dl)	55 (88)	22 (53)	0.21
VES (mg/dl)	90 (43.5)	104 (52)	0.46
Fibrinogen (g/l)	5.3(3.4)	5.4 (1.7)	0.96
Ferritin (mg/dl)	438(348)	365 (364)	0.2
C3 (g/l)	1.25±0.2	1±0.22	0.009
C4 (g/l)	0.3±0.1	0.28±0.08	0.50
Albumin (g/dl)	29.5(8)	30 (11.5)	0.62
Data are mean±SD or median and interquantile range (when not normally distributed).n MPO:myeloperoxidase; PR3: proteinase 3; eGFR:estimated GFR (CKD-EPI 2009).			

Figure:

Patients without ANCA serology and/or with missing data (n=44), ANCA negative RPGN (n=15) and anti-GBM disease (n=2) were excluded from our analysis. Seventy-eight patients with AAV and RPGN (63 biopsy proven) were analysed and compared according to ANCA serotype (n=30 MPO, n=21 PR3). Furthermore, data were analysed on the basis of median levels of serum C3 (1.05 g/l).

Statistical analysis

Data are mean ± SD or median and interquartile range for variables not normally distributed. Groups were compared using ANOVA after logarithmic transformation of skewed variables. Primary endpoint was renal survival defined as need for renal replacement therapy (NRRT); secondary outcome was patient survival. Cumulative and renal survivals were calculated using Kaplan-Meier method and differences between groups were analysed with the log-rank test. Multivariate Cox proportional hazard analysis for time to NRRT was performed to determine the significance of different risk factors in renal outcome. A p value of < 0.05 was considered statistically significant.

Results: Patients had a mean age of 64± yrs and eGFR ±15 ml/min at diagnosis. Patients with MPO-AAV were older (69±11 vs. 61±14 yrs, p=0.02) and showed lower levels of C3 (1.0±0.22 vs 1.25±0.2 g/l, p=0.009) as compared to PR3 patients. Moreover, those presenting with C3 levels lower than median value had more advanced renal damage at diagnosis (eGFR 7± ml/min vs 15.5± ml/min, p= 0.04). Serum C3, but not C4 levels, significantly correlated with eGFR, proteinuria and serum uric acid at diagnosis. Twenty-seven (39.7%) reached ESRD requiring RRT. The 1-, 5- and 10- yrs patients renal survivals were 81%, 62.9 % and 52.4%. Renal outcome was neither influenced by ANCA serotype nor gender but patients with C3 levels below median value exhibited a worse renal prognosis (Log rank p=0.02) and a 5 times higher risk of NRRT (HR 5.1, 95% CI 1.4-18.7, p=0.01) independently by potential confounding factors.

Conclusion: Referral to the nephrologist was late, at an advanced stage of disease, indicating the need to improve the awareness of AAV and RPGN in order to favour early treatment. In this cohort, low C3 indicated a more severe renal damage and predicted poorer renal outcome thus suggesting a role of complement activation in the pathogenesis and progression of these nephritides.

P0277 **PATIENTS WITH PYELONEPHRITIS PRESENTING ONLY WITH LOWER URINARY TRACT SYMPTOMS.**

Fazal Rehman[1], Farrukh Umair[1]

[1]*Aga Khan University Hospital, Nephrology, Karachi, Pakistan*

Background and Aims: The rate of acute pyelonephritis (APN) is assessed at almost 9–11 cases for every 10,000 tenants. Its prevalence is more in developing countries and among those having low socioeconomic status. The demographics of the population in our region is different from the western population with multiple factors such as delayed presentation to hospital, varying socioeconomic status, malnutrition and lack of knowledge about basic treatment leads to increased morbidity and mortality as compared to western population. To the best our knowledge this will be the first study of its kind to describe the frequency of pyelonephritis without upper urinary tract symptoms in hospital setting.

AIM To determine the frequency of pyelonephritis in patients presenting only with low urinary tract symptoms, at a tertiary care hospital, Karachi.

Method: Study is conducted at a tertiary care hospital charts and files were reviewed from 01-11-2018 to 28-02-2019 for all the patients having diagnosis of APN from medical record files.

Results: In our study total five hundred and twenty-one (n=521) patients were included (n=492 (94%) of the participants were suffering from pyelonephritis. Approximately, 22.8% of the patients showed absence of both flank pain and costo-vertebral tenderness but were diagnosed with pyelonephritis on the basis of CT/MRI as presented. While 27% of the patients reported both upper urinary tract symptoms and were also positive on CT-MRI. It is also witnessed that 24% and 16% of the patients either reported flank pain or costo-vertebral tenderness respectively. Insignificant association between gender, age, comorbid with pyelonephritis. While, the total leucocytes count was significantly related with CT/MRI.

Conclusion: Our study showed significant number of patients having pyelonephritis in the absence of any upper tract symptoms. Ignoring the diagnosis as serious can lead to under treatment, possibility of higher rate of re-admissions or poor selection of initial antibiotics. Whereas, other side of the spectrum haunts with higher investigation cost of imaging and broad spectrum use of antibiotic for every patient presenting with just urinary tract infection in Emergency department. A balance should be devised to equilibrate the balance between two extremes.

Table 1: Frequency of urinary tract infections and Comorbids with respect to pyelonephritis in tertiary care hospital of Karachi, Pakistan, (n=521). Values reported in n (%)

SYMPTOMS	**PYELONEPHRITIS**	
Fever	Yes	No
Yes	300	17
No	192	12
	492 (94.3%)	29 (5.3%)
Upper urinary tract (UUT) symptoms		
• Flank Pain		
Yes	283 (100)	0 (0.0)
No	209 (87.8)	29 (12.1)
• Costo-vertebral tenderness		
Yes	238 (100)	0 (0.0)
No	254 (89.7)	29 (10.2)
Lower Urinary tract symptoms		
• Increased Frequency		
Yes	240 (93.3)	17 (6.6)
No	252 95.4	12 4.5
• Dysuria		
Yes	235 (93.2)	17 (6.7)
No	257 (95.5)	12 (4.4)
• Urgency		
Yes	198 (93.8)	13 (6.1)
No	294 (94.8)	16 (5.1)
• Incomplete voiding		
Yes	223 (94.4)	13 (5.5)
No	269 (94.3)	16 (5.6)
Comorbids		
• Diabetes mellitus (DM)		
Yes	251 (94.0)	16 (5.9)
No	241 (94.8)	13 (5.1)
• Hypertension (HTN)		
Yes	241 (94.5)	14 (5.4)
No	251 (94.3)	15 (5.6)

Table 3: Frequency of urinary tract symptoms and Comorbid with respect to CTMRI in tertiary care hospital of Karachi, Pakistan, (n=521).

Urinary Tract Symptoms and Comorbid	**CT/MRI**	
	Positive	**Negative**
Presence of both Upper urinary tract symptoms*	131 (27.0)	17 (3.0)
Absence of both Upper urinary tract symptoms*	119 (22.8)	29 (5.5)
Presence of only flank pain	118 (22.6)	17 (3.0)
Presence of Costo-vertebral tenderness	77 (14.7)	13 (2.5)
Hypertension (HTN)	221 (42.4)	34 (6.5)
Diabetes mellitus (DM)	227 (43.5)	40 (7.67)

n (%) for categorical variable, Upper urinary tract symptoms includes flank pain & Costo-vertebral tenderne

P0278 CARDIOVASCULAR RISK FACTORS AND THE LONG TERM OUTCOME OF LUPUS NEPHRITIS

Marwa Omrane[1], Raja Aoudia[1], Mondher Ounissi[1], Soumaya Chargui[1], Mouna Jerbi[2], Hanene Gaied[2], Hafedh Hidri[1], Amel Harzallah[1], Taieb Ben Abdallah[1], Rim Goucha[2]

[1]Charles Nicole Hospital, Internal medicine A, Tunis, Tunisia and [2]Mongi Slim Hospital, Nephrology, La Marsa, Tunisia

Background and Aims: Systemic Lupus Erythematosus (SLE) is associated with an increased risk of cardiovascular morbidity and cardiovascular mortality. The risk of cardiovascular events is 1.3–2.7 times higher in SLE patients than in the general population, and even higher in patients with lupus nephritis (LN). Traditional risk factors as well as SLE-specific and treatment-related factors all contribute to the increased risk of cardiovascular disease. The primary aim of the present study was to evaluate cardiovascular risk factors, morbidity and mortality in patients with LN.

Method: This is a retrospective study of patients over the age of 16, with LN proved by kidney biopsy and followed up in our department over a period of 17 years. The diagnosis of lupus was made according to criteria of The American College of Rheumatology revised in 1997. Demographic, clinical and para-clinical data were collected from medical observations.

Results: We collected 155 women and 19 men with a sex ratio F / H of 8.2. The mean age at the time of the discovery of LN was 32.6 years [15-45 years]. Overall median follow-up time was 81.2 months. Renal symptomatology was dominated by proteinuria noted in all patients with an average proteinuria at 3.3 g / 24h, associated to a nephrotic syndrome in 68% of patients, hematuria was present in 69% of patients and renal failure was present in half of cases with an average serum creatinine of 110 µmol / l. At the time of diagnosis of LN, hypertension was noted in 48.9% of cases, diabetes in 2.8% of cases and obesity in 57.4% of cases with an index average body mass of 28.5 Kg / m2. Smoking was reported in 17.2% of the cases. The average cholesterol level was 5,5 ± 2,1 mmol/l, the average triglycerid level was 2,5 ± 1,1 mmol/. Antiphospholipid syndrome was found in 14.9% of cases. We performed 243 renal biopsies with 174 initial and 69 iterative biopsies. The histological lesions were polymorphic dominated by LN class IV (54.3%), arteriolosclerosis was observed in 47.7% and lesions of thrombotic microangiopathy in 29.8%. Corticosteroid therapy was prescribed in all patients combined with immunosuppressive therapy in 54.6% of cases. The overall survival of the patients at 10 years was 85%. During follow-up, cardiovascular complications found in our series were mainly strokes (6.3%) and coronary insufficiency (5.2%) and transient ischemic attack (6.9%). After a univariate analysis, the additional cardiovascular risk factors identified in our study were antiphospholipid syndrome ($p = 0.01$), renal failure ($p = 0.01$), long-term corticosteroid therapy ($p = 0.009$), the chronicity of the disease (evolution of lupus> 10 years) ($p = 0.014$), proliferative forms ($p=0.001$), arteriolosclerosis ($p=0.0002$) and lesions of thrombotic microangiopathy ($p=0.018$). Survival in patients without cardiovascular risk factors was better (96% vs 88%).

Conclusion: In conclusion, in addition to traditional risk factors SLE patients have several disease related risk factors that explain increase cardiovascular disease. A careful control for this risk factors is essential to continuously improve survival in SLE.

P0279

DIABETIC KIDNEY DISEASE VERSUS CHRONIC KIDNEY DISEASE IN ADULTS WITHOUT DIABETES MELLITUS: A RENAL SURVIVAL ANALYSIS

Gabriel Stefan[1,2], Ligia Petrescu[1,2], Simona Stancu[1,2], Gabriel Mircescu[1,2]

[1]Nephrology Hospital Dr. Carol Davila, București, Romania and [2]Carol Davila University of Medicine and Pharmacy, București, Romania

Background and Aims: Diabetic kidney disease (DKD) is the most common cause of end-stage renal disease, but the decline in kidney function varies considerably between chronic kidney diseases (CKD), and determinants of renal function loss, early in the course of the disease, are still a matter of debate.

Method: We retrospectively examined the renal outcome at 31 July 2017 of 309 CKD patients (age 59.1 (50.1-68.6) years; 60% male; eGFR 32.7 (21.7-44.8) mL/min) admitted in our hospital during January 2007-December 2012 with a median follow up time of 7.2 (95%CI, 6.8-7.6) years. Only patients who had at least 3 admissions and who were alive during the study period were included. CKD was defined as the presence of an eGFR <60ml/min/1.73m^2 or the presence of albuminuria >30mg/g creatinine for more than 3 months. The primary endpoint was renal survival defined as renal replacement therapy (RRT) initiation. Factors affecting renal survival were evaluated in a Cox proportional hazard model.

Results: DKD (24%), glomerular (GN, 24%), tubulo-interstitial (TIN, 27%) and vascular nephropathies (VN, 25%) were the causes of CKD. Patients with DKD (66.8 (56.5-72.2) years) and VN (68.5 (59.7-76.2) years) were older than those with GN (50.3 (37.4-59.0) years) and TIN (55.6 (45.8-61.8) years). Moreover, the highest cardiovascular comorbidity score was found in patients with VN and DKD (p<0.001). Median eGFR decline was -1.23 (-3.39 – 0.35) mL/min/year; 29% of the patients had CKD progression of >3mL/min/year and 14% had rapid progression (>5mL/min/year). Patients with GN had the lowest eGFR (26.8 (19.1-38.9) versus DKD 36.2 (23.4-47.7), VN 34.9 (22.4-51.0), TIN 32.4 (21.8-44.8) mL/min, p<0.001), the fastest eGFR decline (-3.1 versus DKD -1.9, VN -1, TIN -1,2 mL/min/year, p 0.5) and the highest proteinuria (2.7 versus DKD 1.4, VN 0.4, TIN 0.6 g/24h, p<0.001). During follow up, 29% of the studied patients started RRT; mean renal survival time for the entire cohort was 7.4 (95%CI, 7.0-7.8) years. CKD cause (versus DKD p=0.04, **Figure 1**), lower eGFR (HR 0.89 (95%CI, 0.85-0.93)), elevated albuminuria (HR 1.4 (95%CI, 1.2-1.7)), higher total serum cholesterol (HR 1.00 (95%CI, 1.00-1.01)) and elevated mean arterial blood pressure (HR 1.03 (95%CI, 1.00-1.06)) were associated with RRT initiation in the Cox regression model.

Conclusion: Patients with DKD and VN had similar poorer renal survival as compared with GN and TIN. Earlier referral to the diabetic renal clinic and intensive management of the modifiable risk factors (albuminuria, hypercholesterolemia, hypertention) are necessary to retard progression of CKD and, subsequently, prolong renal survival.

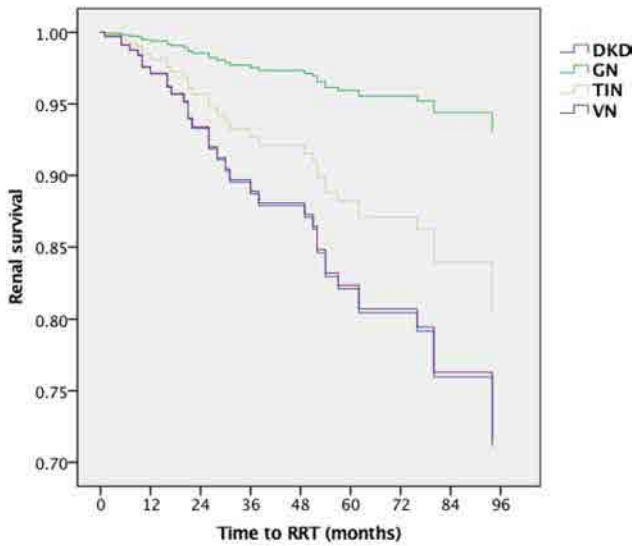


Figure 1. Adjusted renal survival for CKD cause; DKD and VN have similar poorer renal survival as compared to GN and TIN

P0280 **ENVIRONMENTAL AND OCCUPATIONAL EXPOSURES IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS. A CASE-CONTROL STUDY.**

Federica Maritati[1], Francesco Peyronel[2], Paride Fenaroli[2], Giuseppe Daniele Benigno[2], Alessandra Palmisano[2], Giacomo Emmi[3], Maria Letizia Urban[3], Federico Alberici[4], Paolo Fraticelli[5], Massimo Corradi[6], Augusto Vaglio[7]

[1]Nephrology, Dialysis and Kidney Transplant Unit, Ospedali Riuniti, Ancona, Italy, [2]Nephrology Unit, Parma University Hospital, Parma, Italy, [3]Internal Medicine, University of Firenze, Firenze, Italy, [4]Department of Medical and Surgical Specialities, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy, [5]Internal Medicine Department, Ospedali Riuniti, Ancona, Italy, [6]Department of Medicine and Surgery, University of Parma, Parma, Italy and [7]Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Firenze, Firenze, Italy

Background and Aims: Eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss Syndrome) is a rare systemic disease, included in the group of antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV), characterized by adult-onset asthma, blood and tissue eosinophilia with organ involvement, and small-vessel vasculitis. The pathogenesis of the disease is poorly understood, but it is likely that immunogenetic factors play a crucial role in its development. However, it has been suspected that the disease may be triggered by exogenous factors including environmental agents, infections, vaccinations, and drugs. Data about the association between individual, environmental and occupational risk factors and the development of EGPA are scarce. In this study we aimed to investigate the role of occupational agents (such as silica, farming, organic solvents and chemical agents) as well as individual agents (such as smoking habits) and their interactions, as potential risk factors for EGPA.

Method: The study has a case-control design. We enrolled 111 patients with EGPA and 333 healthy controls, matched for age, sex and geographical origin. Occupational history was obtained using a structured questionnaire administered by blinded specialists in occupational medicine. The exposures to non-occupational risk factors potentially predisposing to EGPA were assessed through the interview and through the examination of medical records. All exposures were considered until the time of EGPA diagnosis.

Results: At a multivariate logistic regression analysis, EGPA was associated with silica exposure (OR 2.26 [95% CI 1.10-4.62], p=0.026), farming (OR 2.10 [95% CI 1.19-3.73], p=0.011) and with the exposure to organic solvents (OR 2.20 [95% CI 1.14-4.2], p=0.018). There was a positive relationship between the duration of exposure to silica, chemical agents and the risk of developing EGPA (Figure 1). A multiplicative effect on risk was found for the co-exposure of silica and farming (OR 7.49 [95% CI 2.77-20.25], p<0.0001) (**Figure 2**). The exposure to tobacco smoke appeared protective against EGPA (OR 0.49 [95% CI 0.29-0.70], p<0.0001).

Conclusion: This is, to our knowledge, the first study investigating the role of environmental, occupational and individual risk factors in the development of EGPA, through the comparison of a group of EGPA patients with a group of healthy controls, matched for age, gender and geographical origin. Our results demonstrate that occupational factors may significantly contribute to the development of the disease. In particular, we found a significative association between exposure to silica, farming, organic solvents and EGPA. In addition, our findings reveal that tobacco smoking has a protective role against the disease. Further studies are necessary to investigate the biological effects of such risk factors on disease pathogenesis.

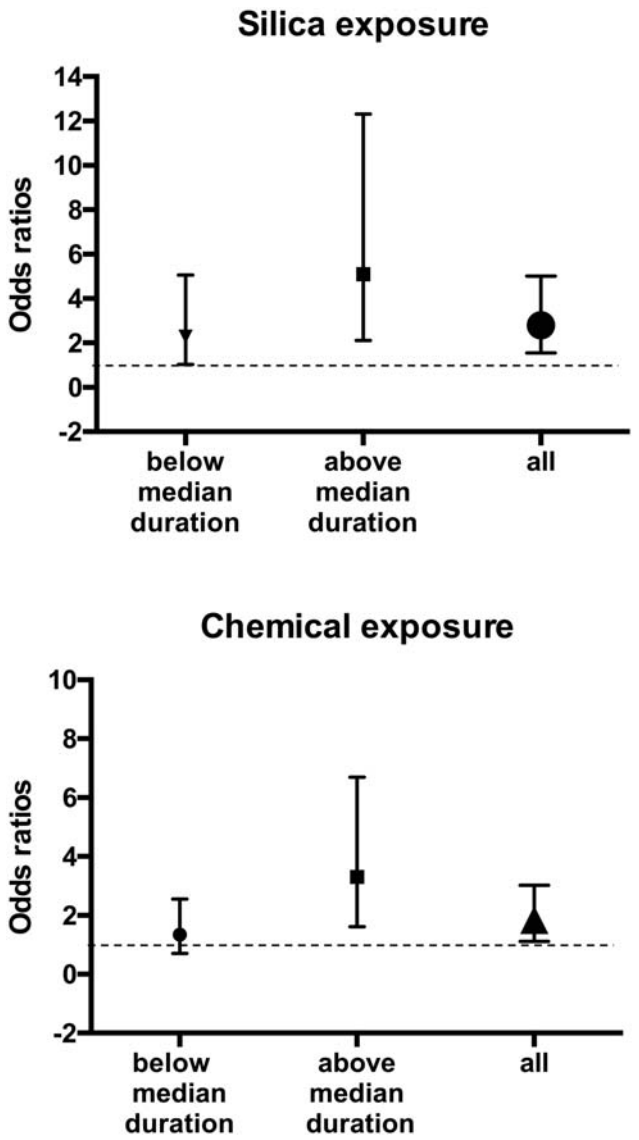


Figure 1. Odds ratios for EGPA associated with duration of silica and chemical exposures. Top. Compared to subjects not exposed to silica, those below the median duration of silica exposure had an OR lower than those above the median duration of the exposure. Bottom. The analysis of the duration of chemical exposure revealed an association with a long-term exposure while no association was demonstrated between EGPA and chemical exposure lasting less than the median duration of the exposure.

Exposure	Participants, *n* Case	Controls	OR (95% CI)	p value
Farming	36	64	2.68 (1.61-4.45)	0.0002
Silica	13	19	3.26 (1.51-7.02)	0.004
Farming and Silica	11	7	7.49 (2.77-20.25)	<0.0001

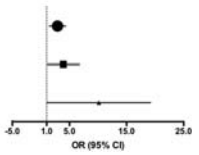


Figure 2. Coexposure to farming and silica. The coexposure to farming and silica led to an OR higher than the addition of the single OR, suggesting a multiplicative (rather than just an additive) effect between these two variables.

P0281 **THE EFFECT OF DIRECT ANTIVIRAL AGENTS ON GLOMERULAR FILTRATION RATE**

Iman Sarhan[1], Reem Elsharabasy[2] , Fatma Ahmed[1], Mohamed Hassan[1]
[1]ain shams university, faculty of medicine, nephrology, Cairo, Egypt

Background and Aims: HCV infects 170 million individuals approximately worldwide. The kidney is a major component of the HCV clinical syndrome. This viral infection imposes itself as a cause of kidney disease, a major risk in hemodialysis units and a significant threat in kidney transplantation. In 2011, direct acting antivirals (DAA) had been developed, which represented a huge boom in the treatment of HCV. Some doubtful data suggest possibility of association between some DAA administration and AKI occurrence, but larger prospective studies are recommended for confirming this suggestion.

Method: Retrospective cohort study of 118 adult HCV infected patients with normal baseline kidney functions (GFR $\geq$ 60ml/min) were included. Patients coinfected with HBV and those with impaired kidney functions at beginning of treatment were excluded. Patients were divided into 3 groups according to their DAA-combination treatment regimen. Patients' eGFR were measured at baseline, at the end of treatment and one year later.

Results: Our results showed that patients who received Sofosbuvir/Daclatasvir/Ribavirin, their pre-treatment eGFR Mean $\pm$ SD. was (86.15$\pm$16.37). Post treatment eGFR showed an insignificant change after end of treatment (84.73$\pm$17.41) and 1 year after treatment (82.0$\pm$18.07) (P-value: 0.998 and 0.220 respectively). Those who received Sofosbuvir/Daclatasvir, their pretreatment eGFR Mean $\pm$ SD was (94.60$\pm$19.32). Post treatment eGFR showed an insignificant change after end of treatment (89.39$\pm$18.39) and 1 year after treatment (89.17$\pm$20.27). (P-value: 0.156 and 0.097 respectively). As for patients who received Sofosbuvir/Simeprevir, their pretreatment eGFR Mean $\pm$ SD was (92.71$\pm$15.11). Post treatment eGFR showed an insignificant change after end of treatment (88.36$\pm$16.27) and 1 year after treatment (89.01$\pm$15.72). (P-value: 0.620 and 0.676 respectively).

Conclusion: The new direct antiviral agents (sofosbuvir, daclatasvir and simeprevir) are effective and safe regarding glomerular filtration rate in patients with normal renal function. However, a meticulous monitoring of kidney function is mandatory during the use of these medications to early detect any untoward side effects.

P0282 SARCOIDOSIS WITH RENAL INVOLVEMENT: APPROACH TO DIAGNOSIS AND MANAGEMENT.

Imen Chemli[1], Meriem Ben salem[1], Ahmed Letaief[1], Mouna Hammouda[1], Sabra Aloui[1], Manel Ben Salah[1], Habib Skhiri[1]

[1]*hospital of Fattouma Bourguiba Monastir, nephrology, monastir, Tunisia*

Background and Aims: Renal involvement in sarcoidosis is rare. It is most often the consequence of calcium metabolism disorders, interstitial granulomatous damage or secondary glomerular damage. It can progress to kidney failure in around 3% of cases.

In this study, we determined the clinical presentation of sarcoidosis with renal involvement and we described the histological lesions. We report our experience about the management and the follow-up.

Method: we analyzed all cases of renal failure caused by sarcoidosis in our department during the period of 13 years (2006-2019). There were five patients (one man and four women) at the time of diagnosis. The middle age was 53.8 years.

Results: The renal involvement was revealing in 60% of the cases. The extrarenal localizations were: pulmonary (100%), cutaneous (knotty erythema 20%), ocular (dry eye syndrome (60%) and anterior uveitis (20%)), the reticuloendothelial system (adenitis (20%) and medullary (20%)), exocrine glands (sialadenitis (40%), nasal (20%), nervous (optic neuritis 20%)). The middle renal clearance (eGFR) at the time of diagnosis of renal involvement was 33ml / min / 1.73 m. Moderate proteinuria was observed in four patients (median: 0.99 g / 24 hours), aseptic leukocyturia in one patient. No patient had microscopic hematuria. Hypercalcemia was noted in 60% of patients with hyper calciuria (median: 3 mmol / kg / 24 hours). Nephrolithiasis was noted in only one patient. No cases of nephrocalcinosis was noted. Renal biopsy showed tubulointerstitial nephropathy with granulomatous in 2 cases (40%), absence of granuloma in one case, extra-membranous glomerulonephritis in one patient and moderate interstitial fibrosis with tubular atrophy in two patients, fibrous andarteritis in a single case. A granuloma without caseous necrosis was objectified on the osteo-medullary biopsy in a single case. All patients received oral corticosteroids (Prednisone: 1 mg / kg / day for 4 patients; 0.5 mg / kg / day for one patient) associated with the treatment of hypercalcemia (hydration and diuretics). The follow-up varied from 2 to 156 months with an median of 56.4 months. 3 patients improved their renal function with a middle clearance : M0: 29 ml / min, M1: 42 ml / min, M3: 68 ml / min, M6: 67 ml / min, M12: 95 ml / min. A non-recovery of renal function was noted in only one patient. An end-stage renal disease was observed in two patients. A renal and extrarenal (lymph node) relapse was noted in a single patient with an interval of 7 years after the initial presentation.

Conclusion: Renal involvement in sarcoidosis is probably underestimated. Treatment is based on corticosteroid, which must be introduced early to prevent progression to renal failure.

P0283 **LONG-TERM FOLLOW-UP OF CRYOGLOBULINEMIC SYNDROME WITH RENAL INVOLVEMENT AFTER DAA**

Stefania Affatato[1], Ester Pollastri[2], Elena Belotti[3], Roberta Zani[1], Serena Zaltron[2], Angiola Spinetti[2], Francesco Castelli[2], Francesco Scolari[1]

[1]ASST Civil Hospital of Brescia, Nephrology, Brescia, Italy, [2]ASST Civil Hospital of Brescia, Infectious Disease, Brescia, Italy and [3]ASST Vallecamonica, Nephrology, Esine, Italy

Background and Aims: To date, the literature shows that HCV eradication with DAA leads to remission from HCV-related cryoglobulinemic syndrome (CS). The goal of our study is to evaluate the effect of DAA treatment on cryoglobulinemic kidney disease.

Method: Since 2015, 58 patients (pts) have been treated in our Centre; among them we have selected 12 pts with active kidney disease at the time of treatment. Clinical

Characteristics	
Male, % (n)	25 (3)
Age, median	68 (43-77)
Follow-up (months), average	36±15
HCV genotype, % (n)	
1	83 (10)
2	0
3	17 (2)
4	0
Hepatitis B serology, % (n)	
Lymphoma, % (n)	33 (4)
IS 6 months before, %(n)	67 (8)
Antiviral treatment, % (n)	
SOF-Simep	27 (3)
RBV-SOF-Dacl	27 (3)
Dasa-OPR	45 (5)

Table 1. Main characteristics of the population.
IS: immunosuppressive therapy; SOF: sofosbuvir; Simep: simeprevir; RBV: ribavirin; Dacl: daclatasvir; Dasa: dasabuvir; OPR: Ombitasvir/paritaprevir/ritonavir.

	T0	EOT	6M	12M	24M	36M	48M
Purpura, %(n)	42 (5)	25 (3)	18 (2)	22 (2)	14 (1)	13 (1)	50 (2)
Arthralgia, % (n)	58 (7)	0	0	11 (1)	14 (1)	0	50 (2)
Weakness, % (n)	50 (6)	25 (3)	27 (3)	0	14 (1)	0	50 (2)
Peripheral Neuropathy, % (n)	33 (4)	8 (1)	9 (1)	22 (2)	28 (2)	13 (1)	50 (2)
Sicca syndrome, % (n)	0	0	0	0	0	0	0
Cutaneous Ulcers, % (n)	33 (4)	8 (1)	0	0	0	0	0

Table 2. Clinical manifestations of cryoglobulinemic syndrome from baseline (T0) to the end of follow-up (48M).

manifestations, renal function and immunological tests were monitored during follow-up (range 6-48 months).

Results: General characteristics of the population are shown in Table 1.

At the time of treatment 6 pts had nephritic syndrome (sdr), 1 had nephrotic sdr and 5 pts had mixed nephritic-nephrotic sdr.

It should be noted that 8/12 pts had been treated with Rituximab (RTX) in the 6 months preceding the DAA; despite that they had active disease at baseline.

Ten out of 12 pts went into complete remission after HCV-eradication, 1 went into partial remission. One pt, never treated, did not respond clinically to HCV eradication and therefore underwent RTX therapy.

Other 2 pt with a recent diagnosis of cryoglobulinemic syndrome came to our attention with a clinical picture of nephritic sdr: they'd never been treated with immunosuppressive therapy and get remission only whit HCV eradication.

One pt, although complete CS remission, started hemodialysis for ESRD secondary to ADPKD.

During follow-up 3 pts underwent CS relapse: 2 pts, one with lymphoma, were retreated with RTX after 12 and 48 months respectively; 1 pt, with type I cryoglobulinemia and clinical manifestation of vasculitis, died of acute disease reactivation in Cameroon after 9 months from the end of DAA.

By evaluating the overall population there is a rapid and prolonged clinical response to DAA therapy, in particular a complete resolution of skin ulcers (Tab 2).

Cryocrit decreases and C3 and C4 increase early and persistently after treatment; vice versa the rheumatoid factor does not undergo significant variations.

Proteinuria is reduced at the end of the treatment (EOT) and shows a decreasing trend also afterwards; urinary sediment is drastically reduced at EOT and further decreases during follow-up up to the presence of only isolated urinary anomalies in almost all patients (Tab 3).

Conclusion: The eradication of HCV, and therefore the removal of the immunological stimulus underlying the cryogloblinemic syndrome, appears to be crucial in the control of cryoglobulinemic glomerulonephritis, also after failure of RTX treatment.

However, relapses at variable interval from DAA therapy do not allow us to lose these patients to follow-up even after several years from disease remission.

P0284 RENAL FUNCTION AFTER DISCONTINUATION OF CHRONIC LITHIUM TREATMENT: FINDINGS FROM THE LISIE RETROSPECTIVE COHORT STUDY

Filip Fransson[1], Ursula Werneke[2], Andreas Jonsson[1], Michael Ott[1]

[1]Umeå University, Department of Public Health and Clinical Medicine, Umeå, Sweden and [2]Umeå University, Department of Clinical Sciences, Division of Psychiatry, Umeå, Sweden

Background and Aims: Current guidelines consider lithium a first-line treatment for bipolar disorder to prevent relapse and suicide. Lithium, however, has renal adverse effects that can accumulate over decades of treatment. Studies have found a positive association between duration of lithium use and incidence of chronic kidney disease and prevalence of end stage renal disease. When the kidney function declines the treating clinician is presented with a choice of either continuing lithium, despite the risk of renal failure, or discontinuing lithium, despite an increased risk of relapse of the underlying affective disorder. One recent study showed that concerns about reduced renal function may account for 9% of reasons for lithium discontinuation. Yet it remains unknown, whether after lithium discontinuation, decline of renal function will continue unchanged, become less steep, or whether renal function can even improve.

The aim of our study was to investigate the effect of lithium discontinuation on renal function.

Method: A retrospective mirror-image study, examining the decline of renal function five years before and after lithium discontinuation. Our study was part of LiSIE, a retrospective cohort study of patients with bipolar disorder, schizoaffective disorder and depression in the Swedish county of Norrbotten 1997 - 2017. We included all patients who had discontinued lithium between 1997 and 2013. We excluded patients who (a) had renal diseases possibly affecting renal function acutely (e.g. glomerulonephritis) or (b) used lithium less than 90% of the 5 years of the pre-mirror period. The patients provided informed verbal consent. In accordance with the ethical approval, deceased patients were also included. Patients were followed for 5 years after lithium discontinuation, until they initiated renal replacement therapy, restarted lithium treatment or died. To evaluate renal function, we calculated eGFR by the CKD-EPI -formula from all creatinine measurements taken during out- or in-patient care in the county of Norrbotten. We censored values for episodes of acute kidney injury or values not reflective of the underlying kidney function, such as in terminal cancer and cachexia. All data was manually validated in the medical records.

A mixed effects model was fitted including eGFR as dependent variable. Age, hypertension and diabetes mellitus were included as fixed effects.

Results: Of 1340 patients with lithium treatment 579 patients had discontinued lithium. 172 patients (55.2% women, 44.8% men) with 5335 creatinine samples were eligible for inclusion. Mean age at discontinuation was 61.5 (min. 24.5 max. 91.3). Mean duration of lithium treatment was 15.8 (min. 4.5, max. 42.5) years. 19.2% of patients had diabetes and 48.9% had hypertension diagnosed before or during the study period. There was a statistically significant change in annual decline of renal function ($p<0.001$), from -1.96 ml/min/year before (95% CI -2.22 to -1.70) and -0.22 ml/min/year (95% CI -0.50 to 0.07) after discontinuation. Diagnosed hypertension added -1.27 ml/min/year in decline of eGFR ($p<0.001$). Diabetes mellitus did not affect the decline.

Conclusion: Mean annual decline of renal function is significantly steeper during lithium treatment than after discontinuation. However, decline still occurs. In patients with hypertension, the decline of renal function is accelerated irrespective of lithium discontinuation. The implications for renal function in individual patients considering lithium discontinuation remain unclear. The decision of whether to discontinue lithium depends on a careful trade-off of potential psychiatric risks against potential renal benefits.

P0285 **A COMPARISON OF URINE MICROSCOPY AND CULTURE IN HIV-INFECTED AND NON HIV-INFECTED INDIVIDUALS IN THE ANTI-RETROVIRAL ERA.**

EIY Madela[1,2], Alain Assounga[1,2]

[1]University of KwaZulu-Natal, Dept of Nephrology, Durban, South Africa and [2]Inkosi Albert Luthuli Central Hospital, Dept of Nephrology, Durban, South Africa

Background and Aims: Urinary tract infection is among the most common causes of sepsis presenting in hospitals. The aim was to collect data to enable empirical treatment of urinary tract infections in HIV negative and positive nephrology patients while waiting for urine culture results in order to reduce hospital stay. Our aim is also to assess incidence and antimicrobial susceptibility of urinary tract infections in HIV negative and positive patients.

Method: A retrospective chart review of nephrology patients admitted from January to December 2014 in Nephrology ward and the first consecutive 200 outpatients seen in Nephrology clinic in 2014 at Inkosi Albert Luthuli Central Hospital was conducted. Information was gathered with the use of a data collection sheet and urinary tract infection was based on urine culture results. All data was analysed using Statistical Package for Social Sciences version 23. Percentages of basic characteristics were calculated between groups. Logistic regression analysis was used to identify factors associated with positive urine culture.

Results: There were 654 patients in the study, 514 (79%) were HIV negative and 139 (21%) were HIV positive. The incidence of UTI in nephrology patients was 9%, 10.1% in inpatients and 6.5% in outpatients. 22% were HIV positive (p value 0.883, 95% CI 0.550-2.003). 19% had Diabetes mellitus, 15% had Systemic Lupus Erythematosus and 5% were post renal transplant patients. Escherichia coli and Klebsiella pneumonia were the common causes of urinary tract infection at 40.7% and 15.3% respectively with 22% cases on extended beta lactam resistance.

Conclusion: There was no statistically significant difference on the incidence and antimicrobial isolates between HIV infected and HIV negative nephrology patients with urinary tract infection. Hence, empirical treatment for UTI should remain the same in the 2 groups. Escherichia coli and Klebsiella pneumoniae were the most commonly cultured organisms in both groups. There is microbial resistance to commonly used antibiotics. Constant assessment of anti-microbial sensitivity of urinary tract infections is of paramount importance.

P0286

B CELL REPOPULATION AFTER REMISSION INDUCTION WITH RITUXIMAB IN NEWLY DIAGNOSED PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: DOES ONE SIZE FIT ALL?

Chiara Salviani[1], Alessandra Gina Gregorini[1], Guido Jeannin[1], Federico Alberici[2], Giovanni Cancarini[2], Francesco Scolari[2]

[1]ASST Spedali Civili of Brescia, Nephrology Unit, Brescia, Italy and [2]ASST Spedali Civili and University of Brescia, Nephrology Unit, Brescia,

Background and Aims: Rituximab (RTX) is one of the mainstays of ANCA-associated vasculitis (AAV) treatment. Nevertheless, studies specifically addressing the B cell repopulation in AAV patients after remission induction with RTX are still scanty and with conflicting results. Moreover, the role of B cell monitoring in the management of RTX-based maintenance therapy still remains to be fully elucidated. In this study, we evaluated B cell repopulation after a single course of RTX in treatment-naïve patients with AAV.

Method: We included all consecutive patients with new diagnosis of AAV from December 2009 to December 2017, treated with a single course of RTX for remission induction, with a follow-up ≥12 months. B cell recovery, re-treatment for relapse or rise in ANCA titer and scheduled re-treatment were considered as the termination of observation period. B cell count was performed by flow cytometry (Beckman Coulter Navios©) every 2 weeks during the 1st month, every 4 weeks until the 6th month, then every 12 weeks. B cell recovery was defined as CD19 count ≥10 cells/μl.

Results: Seventy-four patients (38% M, 62% F) met the inclusion criteria. Mean age was 63±21 years. MPA, GPA and EGPA were diagnosed in 49 (66%), 24 (33%) and 1 (1%) patients, respectively. ANCA were positive in 65 (88%) patients, with 50 (68%) anti-MPO and 15 (20%) anti-PR3. Overall median follow-up was 40 months (IQR 25-60). All patients achieved remission and complete B cell depletion after RTX. Twenty-two (31%) patients received plasma-exchange and 20 (29%) steroid pulses. Maintenance therapy with azathioprine or methotrexate was started in 10 (14%) patients. Seventeen (23%) patients received re-treatment with RTX (10 patients for relapses, the remaining cases for B cell recovery and/or a rise in ANCA titre or scheduled re-treatment). B cell recovery was observed in 39 (53%) patients, after a median time of 27 months (IQR 20-38). Particularly, only 7% of patients recovered B cells at 12 months (Figure 1). Univariate analysis showed significant correlation of persistent B-cell depletion with diagnosis of MPA vs GPA (p<0.001), ANCA anti-MPO vs anti-PR3 (p=0.009), higher serum creatinine (p<0.0001) and older age (p=0.004) (Figure 2). Sex, plasma-exchange at induction, steroid pulses, cumulative dose of RTX and maintenance therapy did not affect B cell recovery. Multivariate analysis confirmed significant association between B cell recovery and better renal function (RR 2.655, IC 1.254-5.615, p= 0.011) and clinical diagnosis of GPA (RR 2.466, IC 1.211-5.021, p=0.013).

Conclusion: After a single course of RTX for remission induction, we observed a very long-lasting B cell depletion in the large majority of our patients. Clinical diagnosis of MPA and a worse renal function were significantly correlated to persistent B cell depletion. These data question the need for scheduled RTX re-treatments in all AAV patients regardless of clinical diagnosis and features.

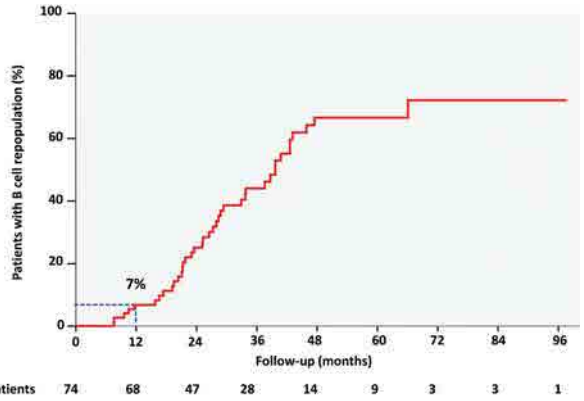


Figure 1. B cell repopulation after a single course of Rituximab in our cohort of AAV patients.

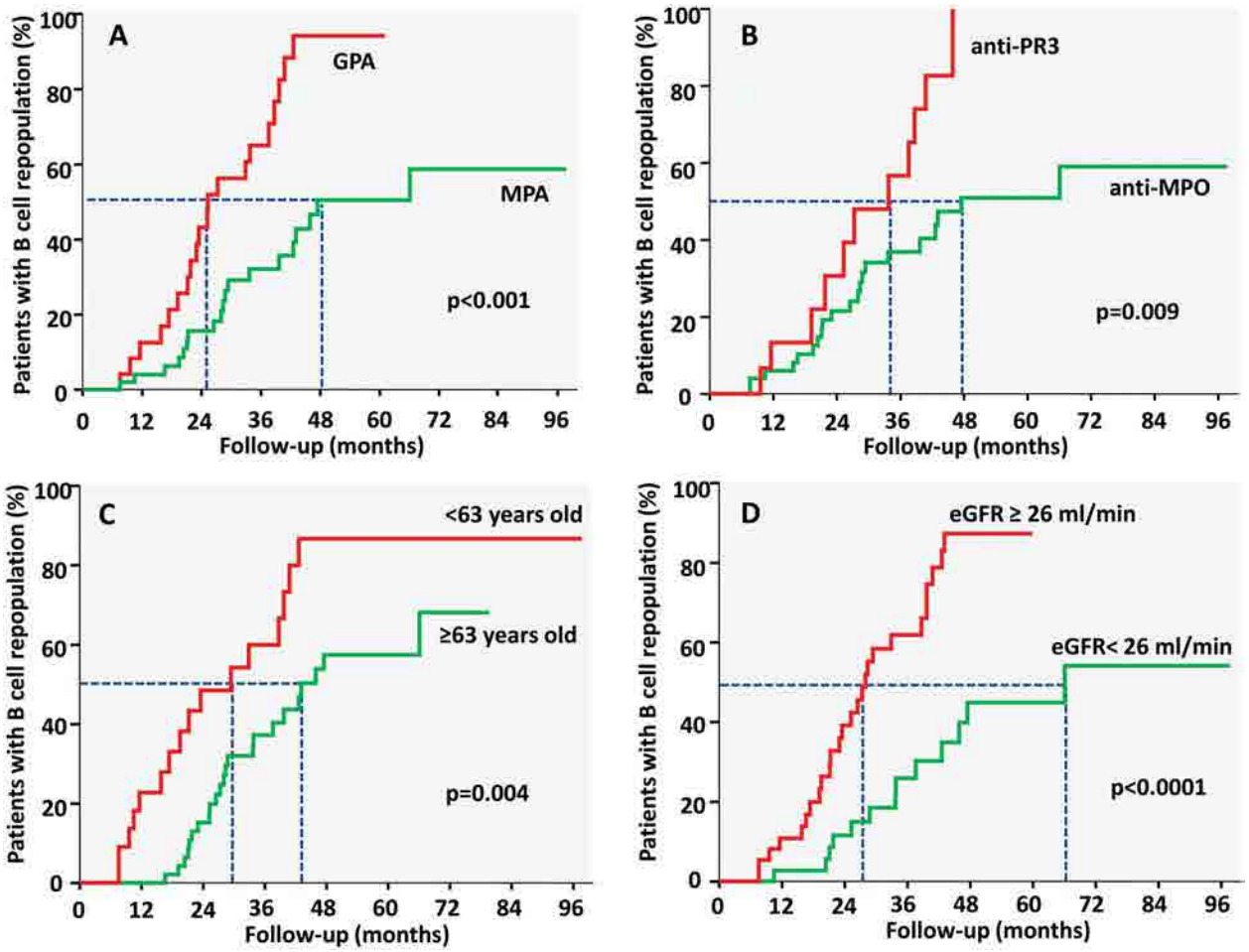


Figure 2. B cell recovery according to clinical diagnosis, ANCA specificity, age, eGFR.

P0287 LONG-TERM CLINICAL OUTCOMES IN IDIOPATHIC MEMBRONOUS NEPHROPATHY TREATED BY CYCLOSPORINE AND PREDNISOLONE

Chiharu Ito[1], Yasuhiro OTSUKA[1], Asami Takeda[1]

[1]*Nagoya daini red cross Hospital, nephrology, Nagoya City, Japan*

Background and Aims: Membranous nephropathy (MN) is the most common primary glomerular disease diagnosed in older patients. MN in adults is most often idiopathic, and risk factors of clinical findings for progressive idiopathic MN (iMN) seems to be older age at onset, male sex, and nephrotic-range proteinuria persisting for several months. Immunosuppressive therapy should be applied to the patients with iMN who have risk factors for progression, however little is known about the most effective regimen of immunosuppressive therapy. In addition, long-term prognosis of iMN for each immunosuppressive regimen is unclear. Most of the patients with iMN at our center were treated by prednisolone (PSL) and cyclosporine (CYA) combination therapy, and commencement of therapy was around the time of renal biopsy. The objective of this study is to assess medium to long-term outcome of treated iMN patients with CYA at our center.

Method: Retrospective data were collected from January 2000 to December 2014 on all consecutive 1080 native renal biopsy at our center. 102 cases were diagnosed as MN. Of 102 MN cases, 43 cases were iMN, which was IgG4 dominant or codominant in immunofluorescence of IgG subclass. Secondary MN is diagnosed by clinical history of possible drug use, the presence of malignancy, positive serologic tests for both infection and connective tissue diseases, hepatitis B or hepatitis C virus positive, and full house immunofluorescence.

Results: Of 43 iMN cases, there were 4 cases who were treated with only nonimmunosuppressive therapies, 5 cases who were treated with PSL, and 34 cases who were treated with CYA combination. Immunosuppressive therapy commenced within one month before and after renal biopsy. Immunosuppressive regimen was determined by each doctor. CYA was administered once-daily, and the area under the concentration-time curve up to 4 hour after administration of CYA (AUC0-4h) was determined in each patient. No infectious complications were found. The duration of CYA use was 194.7±848.9 days (median 786.5 days), and follow-up period of CYA group was 3026.4±1608.0 days.

There were no significant differences between PSL group and CYA group in age (53.4±20.6 years vs. 64.1±10.6 years, p=0.162), sex (1 male 4 female vs. 23 male 11 female ,p=0.162), urinary protein (1.37±0.65 g/gCre vs. 5.44±3.64 g/gCre, p=0.0679), serum creatinine at the time of renal biopsy (0.66±0.19 mg/dl vs. 1.09±0.57 mg/dl, p=0.352), a 30% eGFR decline (0 cases vs. 2 cases), cases achieved complete remission (CR) (5 cases vs. 26 cases, p=0.196), and time from commencement of immunosuppressive therapy to CR (748.2±795.5 days vs. 422.2±379.9 days, p=0.242).

There were no significant differences between non-remission cases in CYA group (8 cases) and remission cases in CYA group (26 cases) in age, sex, and urinary protein, but serum creatinine was significantly greater in non-remission cases than remission cases in CYA group (1.75±1.01 mg/dL vs. 0.94±0.29mg/dL, p=0.0251).

There were no significant differences between non-recurrent cases in CYA group (16 cases) and recurrent cases (10 cases) in CYA group in age, sex, urinary protein, and serum creatinine at the time of renal biopsy.

Conclusion: Between PSL group and CYA group, there were no significant differences in age, and sex at the time of biopsy, and there was a trend that urinary protein was greater in CYA group than in PSL group (p=0.0679). Due to the tendency that urinary protein at the biopsy was greater in CYA group, no significant differences were seen in the remission rate and the time from commencement of immunosuppressive therapy to remission between PSL group and CYA group. Despite long duration of CYA use, infectious complications and renal function deterioration were not seen, so CYA can use safely by dose adjustment by AUC0-4h. Further study is needed to provide enough evidence of effectiveness of CYA combination therapy.

P0288

CLINICOPATHOLOGICAL FEATURES OF FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS: STEPS FOR AN ACCURATE CLASSIFICATION - A SINGLE CENTRE CASE SERIES

Afonso Santos[1], Pedro Campos[1], Anna Lima[1], Ana Gaspar[1], Catarina Brás[1], Karina Soto[1]

[1]*Hospital Fernando Fonseca, Amadora, Portugal*

Background and Aims: Focal and segmental glomerulosclerosis (FSGS) is a histological pattern that is defined by the presence of segmental sclerosis of at least one glomerulus in the kidney biopsy. However, the etiological classification of this lesion remains challenging in clinical practice. FSGS can be divided into primary/idiopathic, genetic or secondary. Nowadays here is no biochemical marker that allows clinicians to distinguish between these categories nor a pathognomonic feature associated to a particular subtype of FSGS. Also, genetic testing is not suitable for all patients. Although it is crucial to determine the cause of FSGS, this is not easily done in clinical practice. Herein we present a series of patients with histologic diagnosis of FSGS in which clinical and histological criteria were applied in order to establish the etiologic classification of FSGS.

Method: A retrospective analysis of 359 patients who performed kidney biopsy from January 2010 to December 2018 was performed. Patients with histological features of FSGS were identified. Clinical, laboratorial and pathological data were collected, including treatment and outcome. Patients were classified as having genetic FSGS if they accomplished at least one of the following: a) nephrotic syndrome resistant to corticosteroids; b) non-nephrotic proteinuria or nephrotic syndrome with normal serum albumin; c) non-nephrotic proteinuria or nephrotic syndrome with focal foot process effacement or d) non-nephrotic proteinuria with diffuse foot process effacement. The remaining patients were classified as secondary FSGS (if they presented a disease known to be associated with FSGS) or primary FSGS. Each group was divided according to treatment with corticoid, other immunosuppressive agents or and RAAS blockage. Renal outcomes were assessed (progression to ESKD).

Results: A total of 359 kidney biopsies were performed between January 2010 to December 2018, 66 with a histological pattern of FSGS. 65% (N=43) were males, 71% (N=47) were Caucasian and 23% (N=15) were black. 74% (N=49) had past medical history of hypertension, 26% (N=17) diabetes mellitus and 5% (N=3) had HIV. The majority of patients were classified as having secondary FSGS (52%, N=34), 23% (N=15) were classified as primary and as 25% (N=17) genetic/idiopathic. From the genetic group 58.8% (N=10) were treated with corticoid, 12% (N=2) with other IS agents and 71% (N=12) with ACE/ARB. 29% (N=5) evolved to ESKD (median time to dialysis 11 IQR 1-30).

In the primary FSGS group 40% (N=6) were treated with corticoid, 7% (N=1) with other IS agents and 80% (N=12) with ACE/ARB. 27% (N=4) evolved to ESKD (median time to dialysis 0 months, IQR 0-33).

In the genetic group 59% (N=10) were treated with corticoid, 12% (N=2) with other IS agents and 71%(N=12) with ACE/ARB. 29% (N=5) evolved to ESKD (median time to dialysis 11 months, IQR 1-30).

Conclusion: FSGS is a very prevalent glomerular disease and its correct etiologic classification aids in better treatment choice. Although its etiology is not straightforward in most of the patients, some clinical and histological characteristics aid in FSGS classification.

P0289 **MULTI-PARAMETRIC RENAL MAGNETIC RESONANCE IMAGING IN EARLY KIDNEY TRANSPLANTATION**

Keith Gillis[1], Alastair Rankin[1], Sarah Allwood-Spiers[2], Rosemary Woodward[3], Giles Roditi[3], Aleksandra Radjenovic[1], Bernd Kuehn[4], Rajan Patel[5], Patrick Mark[1]

[1]University of Glasgow, Institute of cardiovascular and medical sciences, Glasgow, United Kingdom, [2]NHS Greater Glasgow and Clyde, Department of clinical physics, Glasgow, United Kingdom, [3]NHS Greater Glasgow and Clyde, Department of Radiology, Glasgow, United Kingdom, [4]Siemens, Erlangen, Germany and [5]NHS Greater Glasgow and Clyde, Glasgow Renal and Transplant Unit, Glasgow, United Kingdom

Background and Aims: Existing methods of investigating renal transplant dysfunction do not provide reliable information regarding diagnosis nor prognosis. Multi-parametric magnetic resonance imaging (MRI) may provide novel biomarkers for evaluation of transplant dysfunction. We aim to determine how MRI parameters change over the first year of transplantation, and how these relate to future renal function.

Method: Patients receiving a kidney transplant attended for study visits at 6, 26 and 52 weeks post operatively, comprising measurement of clinical and biochemical parameters, together with research multi-parametric MRI. Imaging measurements comprised kidney volume, arterial spin labelling (ASL) perfusion, T1 relaxation time, T2*, apparent diffusion coefficient (ADC) and fractional anisotropy (FA). Imaging was performed at 3.0 Tesla using a Siemens MAGNETOM Prisma system. Regions of interest were drawn in whole kidney (WK), cortex (Cx) and medulla (Md) (figure 1).

Results: 20 patients were included: 16 were male, with age 55.5±12.8 years, baseline eGFR 54.0±23.6 ml/min/1.73m2, and blood pressure 146/80 ± 15/15 mmHg. 14 received deceased, and 6 received live, donor transplants. Patients were all managed with tacrolimus, mycophenolate and low dose prednisolone, following induction therapy with either basiliximab or anti-thymocyte globulin.

6 week ADC was 1.69±0.14 in WK, 1.65±0.08 in Cx, and 1.67±0.10 $\times 10^{-3}$ mm^2/s in Md. FA was 0.19±0.04 in WK, 0.14 ± 0.04 in Cx and 0.22 ± 0.10 in Md. T2* was 57.6±9.4 in WK, 63.9±8.7 in Cx and 45.0±8.0 ms in Md. Over the 3 visits there was reduction in FA (p=0.008) and medullary T2* (p<0.001). There was no significant change over 12 months in any other MRI parameter.

Over 1 year the median change in eGFR was -2ml/min/1.73m^2. There was correlation between baseline eGFR and the following variables: volume (r=0.29, p=0.04), whole kidney ADC (r=0.36, p=0.01), cortical ADC (r=0.46, p=0.001), representative cortex ADC (r=0.48, p<0.001) and medullary ADC (r=0.29, p=0.04). There was no correlation between eGFR and other imaging biomarkers. There was correlation between baseline whole kidney ADC (r=0.54, p=0.02), cortical ADC (r=0.49, p=0.03), and renal function at 12 months.

Conclusion: Diffusion weighted MRI measurements correlate with eGFR and may allow improved prognostication regarding future renal function. Certain MRI parameters including FA and R2* vary depending on time point of transplantation which may reflect changes in transplant microstructure in the early postoperative period. Multi-parametric MRI provides a novel method of evaluating renal transplants non-invasively and may allow more accurate prediction of future transplant function than existing biochemical measures.

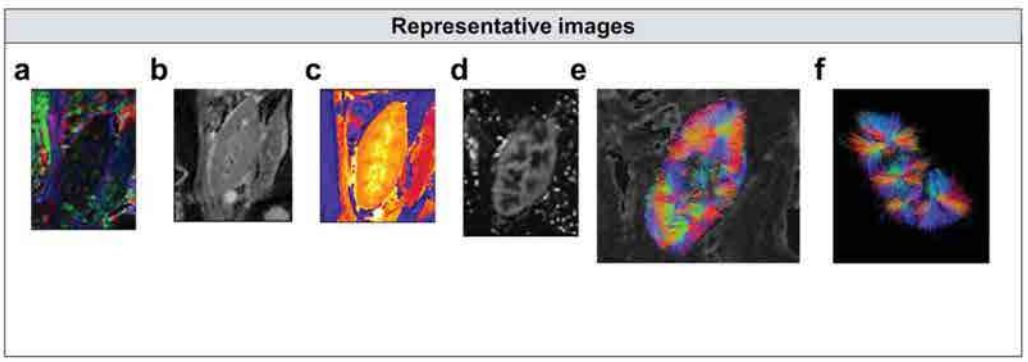


Figure 1 Representative images; a.FA, b. ADC, c.T1, d. ASL, e & f. tractography derived from DTI

P0290 THERAPEUTIC PLASMAPHERESIS EXPERIENCE DUE TO NEPHROLOGICAL INDICATIONS

İsmail Baloglu[1], Hatice Ozge Serin[2], Halil Zeki Tonbul[1], Nedim Yılmaz Selcuk[1], Kultigin Turkmen[1]

[1]Necmettin Erbakan University, Meram Medical School, Nephrology, Konya, Turkey and [2]Necmettin Erbakan University, Meram Medical School, Internal Medicine, Konya, Turkey

Background and Aims: Therapeutic plasma exchange (PEX) has an increasingly long list of indications in recent years, in addition to immunosuppressive therapies in many life-threatening immune activations, it provides significant improvements in mortality and morbidity. In this study, we aimed to investigate the laboratory and clinical effects of PEX performed with nephrologic indication in our clinic.

Method: The records of 67 patients (36 females, 31 males; mean age, 45.7±15.8 years) who underwent PEX with nephrological indication between 2012 and 2017 in our clinic were retrospectively reviewed. Characteristics of the patients such as, indications of PEX, laboratory values and number of PEX sessions were recorded. In addition, clinical responses were also evaluated.

Results: When a total 398 PEX sessions were examined, the most common indication (40.3%) was acute humoral rejection after renal transplantation, followed by granulomatosis with polyangiitis (19.4%) and thrombotic microangiopathy (9%), respectively. The average of the PEX sessions was 5.94. There was a statistically significant increase in the bicarbonate value when the arterial blood gas of the patients was evaluated after PEX (p=0.002). However, no significant difference was observed in the pH and ionized calcium values (p=0.135, p=0.969, respectively) (Table 1).

When all the patients were evaluated, there was no significant change in hemoglobin values (p=0.174), but platelet values decreased significantly (p=0.011) after PEX. However, when the patient group admitted with thrombotic microangiopathy was examined, it was observed that platelet count increased and LDH level decreased significantly (p=0.063, p=0.028, respectively).

When the serum creatinine values of all patients were evaluated, a significant decrease was observed in the serum creatinine values after PEX (p=0.001). In addition, after 2 years following PEX treatment, 70.1% of patients were still alive and 12.5% of patients undergoing PEX for acute humoral rejection were undergoing on hemodialysis treatment.

Conclusion: According to the results of our study, patients should be followed up especially for acid-base and electrolyte changes after PEX. In addition, therapeutic PEX might be effective in terms of improving morbidity and 2 year-mortality of these patients.

Table 1. Clinic parameters of patients

	Before plasma exchange Mean±SD	After plasma exchange Mean±SD	p
Hemoglobin (gr/dl)	9,35±1,95	9,70±1,76	0,174
Platelet (n/mm^3)	178.300±101.600	145.150±74.650	0,011
Creatinine (mg/dl)	4,49±1,76	3,55±1,97	0,001
Ionized calcium mmol/l	0,93±0,21	1,10±0,63	0,969
ph	7,38±0,06	7,40±0,09	0,135
$HCO3^-$ mmol/l	20,18±4,88	23,59±4,79	0,002

P0291 **MYELOMA CAST NEPHROPATHY, LIGHT CHAIN DEPOSITION DISEASE, AND BOTH IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA.**

Zishan Lin[1], Xiaojuan Yu[1], Suxia Wang[1], Fude Zhou[1], Minghui Zhao[1]

[1]*Peking University First Hospital, Nephrology, Beijing, P.R. China*

Background and Aims: The pathological patterns of myeloma-related kidney disease are various, in which myeloma cast nephropathy (MCN) and light chain deposition disease (LCDD) are two of the main patterns. Of note, in patients with multiple myeloma (MM), these two patterns of pathology can occur at the same time. However, there are limited data available showing the difference of clinical characteristics and outcomes among newly diagnosed MM patients with these three patterns of pathology. In this study, we retrospectively reviewed 42 newly diagnosed MM patients with renal biopsy-proven pure MCN, pure LCDD or MCN with coexistent LCDD in Peking University First Hospital, to describe the clinical characteristics, treatment, and outcomes, in order to help define the spectrum of prognostic profiles.

Method: All the native renal biopsies between September 1999 and October 2019 at Peking University First Hospital were retrospectively restudied. A total of 42 newly diagnosed MM patients with pure MCN (n=24), pure LCDD (n=8) and MCN with coexistent LCDD (n=10) were enrolled. The clinical features, as well as prognostic risk factors for renal survival and overall survival were retrospectively investigated.

Results: The 42 parents consisted of 26 men and 16 women with a mean age of 53.2± 10.9 years. There was no significant difference in age and gender among the 3 groups. Patients with pure LCDD had significantly higher hemoglobin levels, a higher percentage of albumin in urine protein, a lower incidence of progressing to ESRD and more likely to present with AKD than patients with pure MCN or with MCN+LCDD. Patients with pure LCDD had significantly higher serum creatinine levels, a lower eGFR, a lower incidence of death and more likely to present with nephrotic syndrome than patients with pure MCN, but no different than patients with MCN+LCDD. No significant difference between pure MCN and MCN+LCDD.

Median renal survival in LCDD group (not reached) was significantly higher compared to MCN (11 months, $p = 0.002$) group and MCN+LCDD group (1months, $p = 0.012$, Figure 1). Median overall survival in LCDD group (not reached) was significantly higher compared to MCN (39 months, $p = 0.014$) group, but had no difference with MCN+LCDD group (not reached, $p = 0.199$, Figure 2).

According to the multivariate analysis, the independent predictors of renal survival were hemoglobin (HR: 0.957, 95% CI: 0.922-0.994; $p = 0.022$) and eGFR (HR: 0.940, 95% CI: 0.880-0.995; $p = 0.034$), the independent predictors of overall survival were hemoglobin (HR: 0.943, 95% CI: 0.895-0.993; $p = 0.025$) and pure MCN (HR: 7.597, 95% CI: 1.171-49.272; $p = 0.034$).

Conclusion: Patients with MCN+LCDD presented similar in clinical characteristics to patients with pure MCN and both suffer from more serious and more urgent renal damage than patients with pure LCDD. However, the overall survival in patients with MCN+LCDD was similar to patients with pure LCDD while the renal survival was worse. Hemoglobin and eGFR were independent predictors of renal survival and hemoglobin and pure MCN were independent predictors of overall survival.

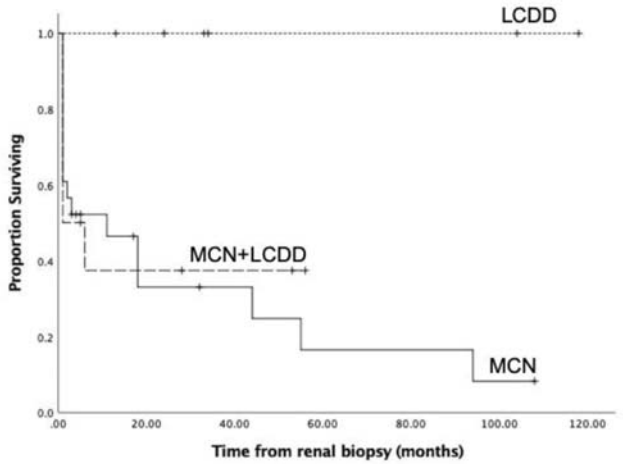


Figure 1. Renal survival of patients divided according to renal histology. Log rank $p = 0.009$ (MCN vs. LCDD $p = 0.002$, MCN+LCDD vs. LCDD $p = 0.012$, MCN+LCDD vs. MCN $p = 0.082$). Median renal survival not reached in LCDD group, 39 months in MCN group and 1 months in MCN+LCDD group.

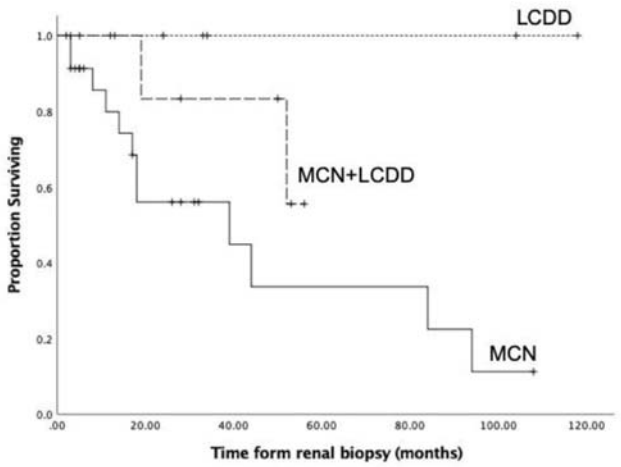


Figure 2. Overall survival divided according to renal histology. Log rank $p = 0.019$ (MCN vs. LCDD $p = 0.014$, MCN+LCDD vs. LCDD $p = 0.199$, MCN+LCDD vs. MCN $p = 0.15$). Median overall survival not reached in LCDD group, 39 months in MCN group and not reach in MCN+LCDD group.

P0292 **CONSTIPATION IN CHINESE ELDERLY: A HIDDEN CAUSE OF CHRONIC KIDNEY DISEASE AND THE RISK OF RAPID RENAL FUNCTION DECLINE**

Guihua Jian[1], Dongsheng Cheng[2], Zhi Wang[3,4], Junhui Li[2], Qi Yang[5], Huan Chen[6], Niansong Wang[2]

[1]Affiliated Sixth People's Hospital, Shanghai Jiao Tong University, Nephrology, Shanghai, P.R. China, [2]Affiliated Sixth People's Hospital, Shanghai Jiao Tong University, nephrology, Shanghai, P.R. China, [3]Shanghai University of Traditional Chinese Medicine, nephrology, Shanghai, P.R. China, [4]Affiliated Sixth People's Hospital, Shanghai Jiao Tong University, nephrology, Shanghai, , [5]Changqiao Community Health Center, Xuhui District, nephrology, Shanghai, P.R. China and [6]Kangjian Community Health Center, Xuhui District, nephrology, Shanghai, P.R. China

Background and Aims: Both constipation and chronic kidney disease (CKD) are common among seniors. However, the association between constipation and CKD remain unclear. This study investigates the correlation between the two to provide a new basis for clinical treatment.

Method: Data from Shanghai community elderly physical examination database (2010-2018) were used to conduct a cross-sectional study and a retrospective cohort to evaluate the relationship between constipation and the prevalence of CKD and rapid renal function decline in the elderly community.

Results: The cross-sectional study covered 16,177 participants, with an average age of 71.3. Comparing to no constipation group, seniors with constipation have a higher proportion of suffering from CKD stage 3. Constipation is an independent risk factor contributing to the high prevalence of CKD stage 3 (OR:1.238,95% CI,1.045-1.466). This finding was further tested through a retrospective cohort study that included 4,203 participants with a medium following time of 6.1 years. As a result, 9.5% (n=401) reported to have rapid progression of renal function. After adjustment of confounding factors, the logistic regression analysis indicates that, constipation is an independent predictive variable of rapid renal function decline among aged population.

Conclusion: Constipation is an independent risk factor for the prevalence of CKD and an independent predictor of rapid renal function decline among seniors in the community. Prevention and treatment for constipation should be taken at an early stage, which may reduce the incidence of CKD and delay the progression of CKD.

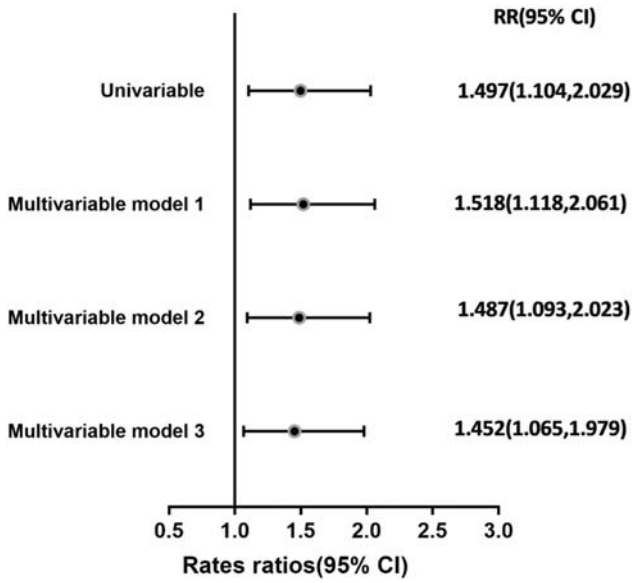


Figure:

P0293

FRACTIONAL EXCRETION OF TOTAL PROTEIN IS AN ACCURATE INDICATOR OF PROTEINURIA IN NPHROTIC PATIENTS

Shori Takahashi[1], Shoichi Shimizu[2], Hiroshi Saito[3], Tamaki Morohashi[4], Ichiro Morioka[2], Riku Hamada[6]

[1]Itabashi Chuo Medical Center, Pediatrics, Itabashi City, Japan, [2]Nihon University School of Medicine, Pediatrics, Itabashi City, Japan, [3]Massachusetts General Hospital, Endcrine unit, Boston, United States of America, [4]Nihon University School of Medicine, pediatrcs, Itabashi City, Japan and [6]Tokyo Metropolitan Children's Medical Center, Fuchu, Japan

Background and Aims: Urinary total protein/creatinine ratio (U-TP/Cr) is a simple and useful indicator of proteinuria. And it had been shown to correlate well with 24-hour urinary protein test (24hr UPT). However, U-TP/Cr is not always accurately reflecting the degree of proteinuria, especially in cases with heavy proteinuria.

Proteinuria in nephrotic syndrome could be defined as the result of changed sieving coefficient (SC) of plasma total protein through the glomerular capillary wall. Therefore, we studied fractional excretion of total protein (FETP; total protein clearance/creatinine clearance %) instead of directly unmeasurable SC. The accuracy of the FETP was verified by 24hr UPT in comparison with U-TP/Cr.

Method: Sixty-three serum and urine samples were collected from 35 pediatric patients with various age (age: 3 − 20 y; mean: 10.3 y, 22 male, 13 female) with hypoproteinemia (TP≦ 5.0 mg/dL), heavy proteinuria (FETP≧ 0.01%), and normal GFR (creatinine clearance ≧ 100 ml/min). The correlations between 24hrUPT and U-P/Cr and FETP were studied using samples obtained the same time and the superiority was statistically examined.

Results: Mean±SE of 24hUPT, U-TP/Cr and FETP (%) were 5.53±0.71 (g/day), 10.23±1.26 (g/gCr), and 0.12±0.016 (%) respectively. R values for the correlation between 24hrUPT and U-TP/Cr and 24hr UPT and FETP were 0.64 and 0.86 respectively. FETP showed a statistically better correlation with 24hrUPT than with U-TP/Cr (P: 0.0001).

Conclusion: FETP is an accurate indicator of 24hr UPT for nephrotic patients under conditions of heavy proteinuria and hypoproteinemia in comparison with UTP/CR.

Figure 1

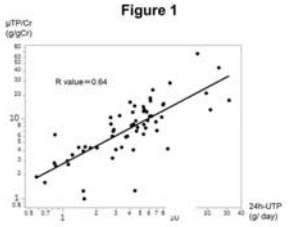
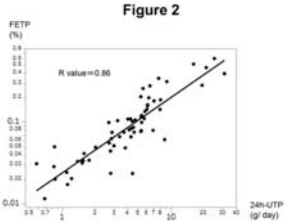


Figure 2



P0294 WHEN DO WE HAVE TO SUSPECT THAT A PREECLAMPSIA MASKS A GLOMERULOPATHY?

Isabel Galceran Herrera[1], Andrés Ribas Closa[1], Susana Vázquez González[1], Laia Sans Atxer[1], Clara Barrios[1], Sara Outón[1], Adriana S. Ochoa[1], Julio Pascual Santos[1], Eva Rodriguez[1]

[1]*Hospital del Mar, Nephrology, Barcelona, Spain*

Background and Aims: Between the 2-8% of pregnancies suffer preeclampsia (PE). In the literature, there have been reported cases of glomerulopathy debuted by pregnancy (GDP) which are initially missdiagnosed as PE. These cases are unusual and not well-defined. We aimed to evaluate clinical and analytical factors that allow us to suspect that a PE masks a GDP.

Method: Retrospective study that included pregnant patients with a postpartum histological diagnosis of glomerulopathy who had been missdiagnosed as PE during pregnancy. We compared them with patients who suffered PE with full recovery after childbirth. We evaluate demographic variables of pregnant women and newborns, clinical variables related to pregnancy and childbirth, blood pressure (BP) and analytical variables before pregnancy and postpartum (serum creatinine (sCrea), estimated glomerular filtration rate by CKD-EPI equation (eGFR), serum uric acid (sUA), ratio of urine protein to creatinine (UPCR)).

Results: Thirty patients were included in the study ,10 patients with a postpartum histological diagnosis of glomerulopathy who had been diagnosed as PE during the pregnancy and 20 patients with a diagnosis of PE without GDP, baseline characteristics are described in attached table. Glomerulopathy was diagnosis through renal biopsy, main indication of renal biopsy was the persistence of proteinuria and/or sediment abnormalities after 4 months of childbirth. The diagnoses were: IgA nephropathy (3, 33.3%), focal and segmental hyalinosis (2, 22.2%), X-linked Alport syndrome (2, 22.2%), diabetic nephropathy (1, 11.1%), lupus nephritis (1, 11.1%) and chronic interstitial nephropathy (1, 11.1%).

Pregnant women with GDP showed higher prevalence of smoking habit and major value of sCrea and sUA (figure). Regarding to pregnancy factors, patients with GDP had significant higher prevalence of primiparous gestation (100% vs 40%, p=0.002), twin gestation (20% vs 0%, p=0.03), premature newborn (50% vs 15%, p=0.01) and higher weight gain during pregnancy (13.9±5.8 vs 9.5±3.6 kg, p=0.01). Furthermore, in the postpartum data we objected a higher value of systolic/diastolic BP (145.6±10.3 / 89.4±12.1 vs 128.5±10.0 / 80.0±6.3 mmHg, p<0.05), sCrea (0.83±0.3 vs 0.54±0.2 mg/dl, p=0.02), sUA (5.8±1.3 vs 3.4±0.8 mg/dl, p<0.001) and UPCR (3046 [613-4179] vs 802 [281-948] mg/g, p=0.05) in patient with NPD.

Conclusion: Our results suggest that clinical and analytical variables in pregnancy and post-partum allow clinicians suspect a glomerulopathy in the setting of PE. Patients diagnosed as PE who develop GDP had higher prevalence of smoking habit, primiparous gestation, twin gestation and premature newborns. In addition, they also have higher weight gain during pregnancy, worse renal function and major sUA before pregnancy and after childbirth, and major UPCR and BP after childbirth; compared with patients with PE and full recovery after childbirth.

Figure: Baseline characteristics.

	With NDP (n=10)	Without NDP (n=20)	P
Age (years) (mean±SD)	29.1 ± 5.8	30.3 ± 4.9	0.5
Smoker (n, %)	4 (33.3%)	1 (5%)	0.01
BMI (kg/m2) (mean±SD)	24.1 ± 4.2	27.1 ± 4.5	0.1
HT (n, %)	2 (20%)	2 (10%)	0.4
DM (n, %)	1 (10%)	0 (0%)	0.1
Gestational DM (n, %)	0 (0%)	3 (15%)	0.1
Dyslipidaemia (n, %)	1 (10%)	1 (5%)	0.6
Familiar HT (n, %)	4 (40%)	10 (50%)	0.6
Familiar DM (n, %)	1 (10%)	3 (15%)	0.7
sCrea (mg/dl) (mean±SD)	0.73 ± 0.1	0.53 ± 0.1	0.001
eGFR ml/min/1.73m2 (mean±SD)	105.8 ± 19.8	128.2 ± 10.1	<0.001
sUA (mg/dl) (mean±SD)	4.7 ± 1.2	3.0 ± 0.9	0.003

BMI: body mass index, DM: diabetes mellitus, HT: hypertension, eGFR: estimated glomerular filtration rate, NDP: nephropathy debuted by pregnancy, sCrea: serum creatinine, SD: standard deviation, sUA: serum uric acid.

P0295 IMPROVED LEFT VENTRICULAR FUNCTION EVALUATION AFTER KIDNEY TRANSPLANT

Milagros Melissa Flores Fonseca[1,2], Viridiana Rodriguez Ugarte[1], Priscila Berenice Villalvazo Osoria[1], Norma Cecilia Ruiz Cruz[1], Sandra Fabiola Velasco Ramirez[3], Ana Cristina Ramirez Anguiano[3], Benjamin Gomez Navarro[1]

[1]Centro Medico Nacional de Occidente, Nefrologia y Trasplante, Guadalajara, Mexico, [2]Universidad de Colima, Posgrado de Ciencias Medicas, Colima, Mexico and [3]Centro Universitario de Ciencias Exactas e Ingenierias, Quimica, Guadalajara, Mexico

Background and Aims: Chronic kidney disease (CKD) represents a major risk factor for cardiovascular (CV) disease. CKD pro inflammatory state evokes structural and functional cardiac and vascular changes, such as chronic dysregulation of nitric oxide in vascular muscle, results in left ventricular hypertrophy (LVH), LV dilatation, LV systolic and diastolic dysfunction, endothelial dysfunction and atherosclerosis. Recent advances in echocardiographic methods allows to evaluate changes in cardiac structure and function after KT. The aim of this study was to assess changes in LV structure and function after renal transplantation in patients with end-stage renal disease (ESRD).

Method: All subjects were prospectively recruited prior to kidney transplantation in our center at Centro Medico Nacional de Occidente, Jalisco, Mexico. Demographics, echocardiographic evaluation, clinical and biochemical studies were performed before and after KT. Patients with transplant failure after KT were excluded. Thirty patients were included in the final analysis. Statistical analysis: Results are expressed as means and standard deviation (SD). Accordingly, paired T test or Wilcoxon test were used for comparison of paired observations. Categorical variables were compared using chi-square test or Fisher's exact probability test, as appropriate. Multivariate logistic regression models including the variables changes in LVEF, LV systolic and diastolic function and LV mass index. Statistical analyses were performed using SPSS v26.0 (IBM Corporation, NY, USA); $p < 0.05$ was considered statistically significant.

Results: Mean age was 31.99 $\pm$ 11.28 years, and 65% were women. Before transplant, LVEF was 58% and pulmonary arterial pressure was 32 mmHg. Ventricular dysfunction was associated with unclamping donor renal vessels at 107.8 $\pm$ 7.96mmHg, and lower perioperative hemodynamics values. The LVEF group increased from 25% to 72.5%, and serum creatinine decrease from 2.25 $\pm$ 3.76 mg/dl to 1.98 $\pm$ 2.65 mg/dl ($p<0.001$) by 6 months after kidney transplant. The best set of predictors in multiple regression analysis of renal function were the onset of diuresis and the use of diuretics ($R2 = 0.4$; $p < 0.001$).

Conclusion: We observed a significant reversal of LV dysfunction. This was accompanied by a significant improvement on kidney graft function. These findings highlight the dynamics between cardiac and renal function, and support the application of adequate echocardiographic evaluation on CKD patients with low LVEF undergoing KT.

P0296 LAST HIT '' INFECTIONS'' BROUGHT THE END: CHRONIC KIDNEY DISEASE TO RENAL REPLACEMENT TREATMENT

Feyza Bora[1], Emine Asar[1], Fatih Yılmaz[2], Ümit Çakmak[1], Fevzi F. Ersoy[1], Gultekin Suleymanlar[1]

[1]Akdeniz University, Nephrology department, Antalya, Turkey and [2]Antalya State Hospital, Nephrology department, Antalya, Turkey

Background and Aims: It is evident that Chronic Kidney Disease (CKD) influences the risk of developing AKI (Acute Kidney Injury) and recent studies suggest that CKD patients who experienced an episode of AKI are more likely to progress to end stage renal disease (ESRD) than patients without CKD. AKI-CKD association might originate from common comorbidities associated with both AKI and CKD, such as diabetes and/or hypertension, and concurrent increase in interventions leading to frequent exposure to various nephrotoxins. AKI in the elderly has been shown to increase the risk of progression to CKD to ESRD. AKI is common in critically ill patients, and those patients with the most severe form of AKI, requiring RRT, have a mortality rate of 50–80 %. Patients with an eGFR <45 ml/min per $1.73m^2$ who experienced an episode of dialysis-requiring AKI were at very high risk for impaired recovery of renal function. Our aim was to determine the reasons that initiate hemodialysis (renal decompensation) in patients with regular follow-up in the low clearance polyclinic without renal replacement treatment (RRT).

Method: The retrospective study included predialysis CKD patients who had followed up regularly and had undergone RRT in recent 4 years. Data on baseline characteristics and medical history were obtained from patient hospital records.

Results: Of the 228 patients, 155 (68%) were male and 73 (32%) were female. The mean age was 58 years (45-66). Diabetes Mellitus was the first in the etiology of CKD (26,3 %), the second was unknown (12,7 %), the third was hypertension (11,8 %). 145 patients (63,6%) underwent regular hemodialysis (HD) (62 years, 55-69), 25 patients (11%) began peritoneal dialysis (PD), 58 patients (25%) had renal transplantation. 52 patients underwent HD with renal decompensation, 22 (%42,3) had working arteriovenous fistula (AVF). There was no decompensation in patients with PD or transplantation plan. 34 patients started HD because of infections (65%), 8 patients (15%) after operations (4 was Coronary Artery Bypass Grafting-CABG), 6 patients (%11,5) after coronary angiography, 4 patients (7,5%) with cardiac decompensation. 2 patients died during the hospitalisation for infections. Of 145 HD patients, 89 (%61,4) had AVF. The patients who had renal decompensation were more older 63 (58-70), have lower Hgb 9,7 g/L (9,1-10,7) and albumin 3,5 g/L (3,2-3,9) level ($p<0,05$). There was no difference in eGFR at the beginning of HD between renal decompensation and other HD patients. 42 patients did not undergo HD at the time we suggested during visits. Of them 9 patients (%21) had renal decompensation (6 infections,3 CABG), 17 patients (%40) had AVF. 3 of them died. The others underwent HD for uremic complications.

Conclusion: We have shown that infections are as the leading cause of renal decompensation. Most of our patients who started to RRT from our low clearance outpatient clinic have chosen HD for RRT. Prevention of infections via vaccination programs or early diagnosis at regular policlinic or telephone visits, and informing patients adequately about nephrotoxic drugs or the conditions that may cause renal decompensation are among the first tasks of the predialysis outpatient clinic. Transition of CKD patients to RRTs, with proper preparation, neither late nor early- at the most appropriate time- should be among in our goals. This may reduce the cost of ESRD patients.

P0297

CHANGES OF CD4CD28NULL AND CD8CD28NULL T CELLS IN CHRONIC KIDNEY DISEASE AND THE IMPACT OF DIFFERENT DIALYSIS MODALITIES

Erasmia Sampani[1], MARIA STANGOU[2,3], Dimitra Vasileia Daikidou[2], Vasiliki Nikolaidou[2], Despoina Asouchidou[2], Chrysostomos Dimitriadis[2], Danai Faitatzidou[2], Asimina Fylaktou[2], Aikaterini Papagianni[2,3]

[1]Ippokrateio - General Hospital of Thessaloniki, Nephrology, Thessaloniki, Greece, [2]Ippokrateio - General Hospital of Thessaloniki, Thessaloniki, Greece and [3]Aristotle University of Thessaloniki, Thessaloniki, Greece

Background and Aims: Chronic Kidney Disease (CKD) affects both the innate and adaptive immunity, although clinical consequences, and the effect of different renal replacement methods on those alterations remain unclear. The purpose of this prospective observational study was to investigate the alterations of T cell immunity in CKD patients, as well as the effect of different dialysis methods on T lymphocyte subtypes.

Method: T cell subpopulations namely CD3+CD4+, CD3+CD8+, CD4+CD28- and CD8CD28- cells, were isolated from whole blood samples using flow cytometry in 40 CKD patients at predialysis state (ESRD-T0). The immunological profile was repeated six months later after initiation of renal replacement therapy (hemodialysis (HD) or peritoneal dialysis (CAPD)). Fifteen age and gender matched healthy individuals served as controls.

Results: Both CD4+ and CD8+ T cells were significantly reduced in ERSD-T0 patients compared to controls, 604(105-3551) vs. 943(584-1867) μ/L, p=0.001, and 352(103-1561) vs. 422.4(263-1453) μ/L, p=0.05. The percentage of both CD4+CD28null and CD8+CD28null cells, 6.4(0.3-30) % vs. 2.7(0.1-7.8) %, p=0.04 and 58.2(12.8-85.4) % vs. 39(7.8-57.1) %, p=0.01 was increased in ERSD-T0 patients comparing to controls. Furthermore the percentage of CD4+CD28null cells correlated with CRP (r=0.4, p=0.04) and serum albumin levels (r=-0.5, p=0.007), while, significant differences were noticed between patients with and without cardiovascular disease, regarding both, CD4+CD28null and CD8+CD28null cells, 8.6(1-30) % vs. 2.1(0.1-19.8) %, p=0.04 and 62.5(12.8-85.4) vs. 45.5(5.7-73.7), p=0.02, respectively.

Changes in the population of CD4+CD28null after 6 months on dialysis showed significant differences between HD and CAPD methods, 110.11(-27.1 to 311.4)% vs. -28.1(-100 to 30)%, respectively, p=0.003, as were in CD8+CD28null cells, 55.23(-29.06 to 197.93)% vs. -8.34(-54.99 to 66.72)%, respectively, p=0.05.

Conclusion: CKD seem to affect specific T cell subtypes, at a pre-dialysis stage, and levels correlate with chronic inflammatory markers and the presence of CVD. These disturbances are further enhanced in HD, while they are alleviated in CAPD.

P0298 EMPHYSEMATOUS PYELONEPHRITIS: SEVEN YEAR EXPERIENCE OF MANAGING CONSECUTIVE 22 PATIENTS IN A SINGLE CENTER OF BANGLADESH

Muhammad Abdur Rahim[1], Ishrat Jahan[1], Samira Humaira Habib[2], Tufayel Ahmed Chowdhury[1], Mehruba Alam Ananna[1], Md Mostarshid Billah[1], Abdul Latif[1], Md. Anisur Rahman[1], Sarwar Iqbal[1], Khwaja Nazim Uddin[3], Zafar Ahmed Latif[4]

[1]Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Nephrology, Dhaka, Bangladesh, [2]Bangladesh Diabetic Somiti, Health Economic Unit, Dhaka, Bangladesh, [3]Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Internal Medicine, Dhaka, Bangladesh and [4]Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Endocrinology, Dhaka, Bangladesh

Background and Aims: Emphysematous pyelonephritis (EPN) is an uncommon, severe, necrotizing infection of the renoureteral unit and is recognized by accumulation of gas within the collecting system, renal parenchyma and/or perinephric tissue. Common risk factors for EPN are diabetes mellitus, renal stone, obstructive uropathy and immunosuppression. Principles of treatment include resuscitative measures, antibiotics, strict glycaemic control and interventions in selected cases. This study aimed to describe clinical, laboratory and imaging characteristics of EPN patients with special emphasis on in-hospital outcome.

Method: This cross-sectional study included consecutive 22 EPN patients, managed in the Department of Internal Medicine and the Department of Nephrology of a tertiary care hospital in Dhaka, Bangladesh from January 2013 to December 2019. Patients' selected socio-demographic, clinical and laboratory parameters and in-hospital treatment-outcome were recorded in case record forms at the time of discharge or death, if were any.

Results: Total patients were 22 (mean age 46.8±12.5, range 34.0–55.0 years) including 16 (72.7%) females. All (22, 100%) were diabetic [one (4.5%) patient was newly detected as diabetic during EPN diagnosis]. Three (13.6%) patients had renal stones (bilateral in one), two (9.1%) had obstructive uropathy, six (27.3%) had chronic kidney disease, 12 (54.5%) had hyponatreamia and 16 (72.7%) were complicated by acute kidney injury (AKI). Patients presented with fever (22, 100%), loin pain/renal angle tenderness (19, 86.4%), vomiting (19, 86.4%) and dehydration (8, 36.4%). One (4.5%) patient had pneumaturia. One (4.5%) patient presented with uraemic encephalopathy and none had shock. One (4.5%) patient had tender ectopic (pelvic) right kidney. Patients had leukocytosis (mean total white cells 19917±7549, range 10250–37630/cmm of blood) and four (18.2%) patients had thrombocytopaenia. All patients had high erythrocyte sedimentation rate (mean 65.7±20.8, range 35–120 mm in 1st h) and C-reactive protein (mean 68.9±60.3, range 18–209 mg/L). Glycaemic status was poor [mean random blood glucose at admission 17.4±6.0, range 10.6–35.5 mmol/L and mean glycated haemoglobin (HbA1c) 9.8±2.1, range 6.9–15.5%]. Diagnosis of EPN was confirmed by abdominal ultrasonography and computed tomography scan. One patient had EPN in ectopic right kidney, one patient had EPN along with air in ureter, two patients had associated emphysematous cystitis and one had psoas abscess. Ten (45.5%) patients had EPN in right kidney (including pelvic kidney), 11 (50%) had EPN in left kidney, one (4.5%) had bilateral EPN and three (13.6%) patients had concomitant contralateral pyelonephritis. According to Huang and Tseng classification, one (4.5%) patient had class 4 EPN, three (13.6%) patients had class 3B, five (22.7%) patients had class 3A and thirteen (59.1%) patients had class 2 EPN. *Escherichia coli* was the most common (13, 59.1%) organism identified on urine culture [including four (4/13, 30.8%) cases with extended-spectrum beta-lactamase positive *E. coli*] and four (18.2%) patients were complicated by bacteraemia. Five (22.7%) patients required surgical interventions [nephrectomy in three (13.6%) and open drainage in two (9.1%)]. All patients were treated with intravenous antibiotics and other supportive measures. One patient required three sessions of haemodialysis. Mean hospital stay was 16.1±6.4 (range 7–31) days. AKI resolved in 3 (3/16, 18.8%) patients and in others renal function was improving at the time of discharge and there was no death.

Conclusion: Most EPN patients were successfully managed by conservative approach in this study, two-thirds had AKI, one-fourth required surgical interventions and there was no death. Though conservative approaches for managing EPN is becoming popular, we emphasize interventions should not be delayed, as and when indicated, and may appear life-saving.

P0299

EVALUATION OF THE CORRELATION BETWEEN VITAMIN D LEVELS AND THROMBOCYTE MARKERS IN PATIENTS WITH DİALYSİS, CHRONIC RENAL DISEASE AND RENAL TRANSPLANTATION PATIENTS.

KÖNÜL AHMEDOVA[1], Garip SAHIN[2], Cengiz Bal[3], Rüya Mutluay[4]

[1]Eskişehir Osmangazi University Faculty of Medicine, Department of Internal Medicine, Eskişehir, Turkey, [2]Eskişehir Osmangazi University Faculty of Medicine, Department of Nephrology, Eskişehir, Turkey, [3]Eskişehir Osmangazi University Faculty of Medicine, Department of Biostatistics, Turkey and [4]Eskisehir Osmangazi University Faculty of Medicine, Department of Nephrology, Turkey

Background and Aims: 25(OH)D3 levels are known to be lower in patients with chronic renal disease (CRD). Vitamin D supplementation has been shown to have beneficial effects on mortality in these patients. In our study, we have evaluated the pleiotropic effect of vitamin D on thrombocyte markers, which is known very little by most.

Method: The main thrombocyte function markers (MPV, PDW and PCT) were obtained in patients which underwent dialysis, renal transplantation and patients with grade 3-4 CRD before and after vitamin D supplementation. 40 healthy individuals were chosen as control group and 24 patients underwent renal transplantation, 25 patients underwent dialysis for at least 3 months, 32 patients were diagnosed as Grade 3-4 CRD. All of the patients above had 25(OH)D3 levels $<$20ng/mL ($<$50nmol/L). Thrombocyte markers were evaluated before and after vitamin D supplementation (which was given 50.000 IU orally once a week for 8 weeks).

Results: Statistically no significant difference were found between MPV values in- and across- group comparison before and after vitamin D supplementation. After the correlation analyses were reviewed, statistically significant negative correlation was found ($r=-0,422$ $p<0.05$) between ΔMPV and ΔVitamin D in renal transplantation group. Also statistically significant positive correlation was found between ΔPDW and ΔVitamin D. In the control group with healty participants, a statistically significant negative correlation was found ($r=-0,493$ $p<0.05$) between ΔVitamin D and ΔThrombocyte count. In the dialysis group a statistically significant negative correlation was found ($r=-0,422$ $p<0.05$) between ΔVitamin D and ΔMPV.

Conclusion: A significant correlation was found particularly between Vitamin D and MPV in dialysis and renal transplantation patients. In order to prevent cardiovascular events due to thrombosis caused by Vitamin D deficiency which increases MPV, it has been thought that Vitamin D supplementation and antiaggregant therapy might be beneficial.

P0300

CEPHALOSPORINS COMPARED TO OTHER ANTIMICROBIALS FOR CKD-PATIENTS WITH PYELONEPHRITIS INFECTED BY PMRG-PRODUCING ENTEROBACTERIACAE OR NOT

Olga Chub[1], Oleksandr Bilchenko[1], Olga Godlevska[1], Fedir Moshel[2], Oleg Chub[3]

[1]Kharkiv Medical Academy of Postgraduate Education, Dep. of Internal Medicine and Nephrology, Kharkiv, Ukraine, [2]Kharkiv Medical Academy of Postgraduate Education, Dep. of General, Pediatric and Oncologic Urology, Kharkiv, Ukraine and [3]Kharkiv city polyclinic number 19, Kharkiv, Ukraine

Background: Chronic kidney disease (CKD) is associated with significant major infectious complications, which occur at rates 3 to 4 times the general population. Urinary tract infection (UTI) is one of the major nosocomial infections, reaching 150 million episodes per year and accounting for $6 billion. Pyelonephritis is the leading cause of hospitalization among all UTIs. Recent years, steady increase in the rate of uropathogen resistance to commonly prescribed antibiotics is associated with plasmid-mediated resistance genes (PMRG) existence. **The aim** of the study is to compare the effectiveness of cephalosporins versus fluoroquinolones for pyelonephritis among non-dialysis CKD-patients.

Method: A cross-sectional study of 105 adult CKD patients with pyelonephritis, who were admitted in Kharkiv City Clinical Emergency Hospital, Ukraine, was carried out. Antimicrobial susceptibility was determined by the Kirby Bauer disk diffusion method and screening for PMRG was performed by the polymerase chain reaction. Subjects were randomized to receive either 3d generation of cephalosporins (n=56), or fluroquinolones (n=49) intravenously. The treatment duration was 7-10 days. After IV treatment, patients were switched to oral levofloxacin 500 mg up to 3-5 days.

Results: Out of 105 patients, 31 (29.5%) were infected with PMRG-producing bacteria. Among 81 gram negative bacterial isolates, 39 (48.1%) were identified to carry different types of PMRG, among which 27 (69.2%) were found to be extended spectrum beta-lactamases producers (ESBLs), and 12 (30.8%) – were positive for PMQR. Clinical outcome was assessed at the day 5 (D5), end of treatment (EOT), test of cure visit (TOC). At the D5, clinical cure was observed in 41.9% (13/31) patients infected with resistance bacteria compared to 75.7% (56/74) patients infected with PMRG-negative bacterial strains (RR 0.4 95% CI [0,21; 0,75]). At the EOT, the favorable clinical response was seen in 51.6% (16/31) patients infected with PMRG-bacteria compared to 87.8% (65/74) patients infected with PMRG-negative bacterial strains (RR 0.91 95% CI [0.8;1.03]). At the TOC, composite cure was observed in 82.6% (19/23) and 96.3% (79/82) patients, respectively (RR 0.86 95% CI [0.71;1.04]). There was no significant difference between levofloxacin and ceftriaxone efficiency, except for the D5, when the clinical efficacy of levofloxacin was significantly higher. In the cephtriaxone group, clinical cure rates were significantly higher among patients, infected with PMRG-negative strains compare to patients infected with resistant bacteria at the D3 ($p \leq 0.001$), D5 ($p \leq 0.001$), EOT ($p=0.013$), TOC ($p=0.016$) visits. In the levofloxacine group, there wasn't find any significant differences between patients infected with PMRG-producers or not. Rates of microbiologic eradication were significantly higher among patients infected with PMRG-negative strains at the day 5 (OR 0.05; 95% CI [0.01;0.25]), EOT (OR 0.05; [0.01;0.21]), TOC visits (OR 0.03 [0.01;0.13]).

Conclusion: Composite cure rates were significantly higher in patients infected with PMRG-negative bacterial strains. Further clinical studies are needed to establish the guideline for the management of patients with plasmid-mediated resistance and to expand the number of options available for empiric therapy of these multi-drug resistance infections.

P0301

FIT FOR PURPOSE VALIDATION OF A CLINICAL ASSAY FOR THE DETECTION OF SERUM LEVELS OF GALACTOSE-DEFICIENT IMMUNOGLOBULIN A1 (GD-IGA1) IN PATIENTS WITH IGA NEPHROPATHY (IGAN)

Laura Sponton[1], Hulin Jin[1], Markus Fluck[1], Yusuke Suzuki[2], Amy Kao[3]

[1]Merck KGaA, Clinical Biomarkers & Companion Diagnostics, TxM, Global Development, Darmstadt, Germany, [2]Juntendo University, Tokyo, Japan and [3]EMD Serono Research & Development Institute, Inc. (A business of Merck KGaA, Darmstadt, Germany.), Global Clinical Development – Immunology, Billerica, United States of America

Background and Aims: Analysis of serum or plasma from patients with IgA nephropathy (IgAN) has confirmed the presence of elevated levels of circulating immune complexes containing Gd-IgA1 (Czerkinsky 1986). New sensitive and reasonably specific noninvasive tests are emerging to guide the therapeutic strategy that is applicable to all stages of IgAN (Suzuki 2014).

Here we are reporting the fit for purpose validation of an ELISA method for the quantitative determination of Gd-IgA1 in human serum samples to support biomarker investigations in clinical studies of Merck KGaA, Darmstadt.

Method: The assay was developed based on a commercially available immunoassay kit. The dynamic range of the calibration curve was determined from 1.56 ng/mL (LLOQ) to 100 ng/mL (ULOQ). With a minimum required dilution of 200-fold and standard assay volume of 50.0 µL, the range of the method in matrix was from 312 ng/mL to 20, 000 ng/mL.

In assay validation phase, multiple validation parameters were evaluated, which included minimum required dilution (MRD), calibration curve, matrix effect, Intra- & Inter run accuracy & precision, selectivity, and parallelism. Additional validation parameters include sample stability (short/long term, freeze-thaw) and batch-to-batch comparison.

Results: All samples measured for intra & Inter - assay precision, accuracy, fulfilled the specifications according to the acceptance criteria. The selectivity was assessed using blank serum matrix from 10 individuals: the result indicated that matrix components in serum did not interfere with the detection of Gd-IgA1. Parallelism assessment was performed successfully for both samples from healthy donors and IgAN patient samples up to dilution factor (DF) 3200 (serum samples from healthy donors were determined up to DF 1600). All DF-corrected results within the assay range were determined with %CV $\leq$ 30.0%. Batch to batch comparison was assessed successfully based on the known shelf life of the kit. Short term stability using QC samples were given for up to 24hrs at room temperature. Freeze-thaw stability was given for up to 3 cycles at -20°C±5°C and -75°C±15°C.

The investigations were performed according to general guidelines for method validation and applicable regulations. The results of investigated validation parameters fulfilled the requirements and recommendations, generally accepted for bioanalytical projects.

Conclusion: The present validation qualified the method for the quantitative determination of Gd-IgA1 in human serum samples from clinical studies.

P0302 **NEUTROPHIL TO LYMPHOCYTE AND PLATELET TO LYMPHOCYTE RATIO IN PATIENTS UNDERGOING KIDNEY TRANSPLANT**

Sandra Fabiola Velasco Ramirez[1], Milagros Melissa Flores Fonseca[2,3], Ana Cristina Ramirez Anguiano[1], Martha Rosa Cueto Casilla[1], Yolanda Diaz Burke[4], Luz Margarita Baltazar Rodriguez[3], Priscila Berenice Villalvazo Osoria[2], Norma Cecilia Ruiz Cruz[2], Miguel Medina Perez[2], Benjamin Gomez Navarro[2]

[1]Centro Universitario de Ciencias Exactas e Ingenierias, Quimica, Guadalajara, Mexico, [2]Centro Medico Nacional de Occidente, Nefrologia y Trasplante, Guadalajara, Mexico, [3]Universidad de Colima, Posgrado de Ciencias Medica, Colima, Mexico and [4]Centro Universitario de Ciencias Exactas e Ingenierias, Guadalajara, Mexico

Background and Aims: Inflammation plays a central role before and after a kidney transplant recipients (KTR). Despite survival improvement, several factors are associated with poor outcomes after transplantation. In search of a cost effective inflammatory marker neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR) have shown a prognostic value. Therefore, the objective of this study was to determine the association of NLR and PLR and acute kidney allograft dysfunction as markers of inflammatory state in KTR.

Method: A single center, retrospective study. Our study group included 41 KTR with acute kidney allograft dysfunction from our center at Centro Medico Nacional de Occidente, Jalisco, Mexico. NLR and PLR were collected and evaluated 1 month prior KT, at the time, 6 months and one year after transplantation. Statistical analysis: Data were expressed as the mean $\pm$ SD, median and range or frequency, as appropriate. Intergroup comparisons were performed with a chi-squared test for categorical variables and Student's t test or the Mann-Whitney test for continuous variables. Putative associations between clinical factors, biological factors and mortality were assessed in univariate and multivariate Cox models. Statistical analyses were performed using SPSS v26.0 (IBM Corporation, NY, USA); $p < 0.05$ was considered statistically significant.

Results: Mean age was 29.54 $\pm$ 7.32 years, and 56% were women. Of those patients, all received living donor kidney transplantation. All patients in the study groups received standardized immunosuppressive regimen consisting of calcineurin inhibitors, mycophenolate mofetil and steroids. Median serum creatinine levels after KT were between 1.11 $\pm$ 0.36 mg/dl. The median NLR and PLR levels were significantly higher in the study group, with a median of 3.34 (1.83 –5.14) and 8.65 (343.47 – 360.59), not statistically associated. The best set of predictors in multiple regression analysis of higher levels of NLR were serum albumin ($r = -0.432$; $p = 0.007$) and C reactive protein ($r = 0.641$; $p = 0.002$). The best set of predictors in multiple regression analysis of higher levels of PLR were hematocrit ($r = -0.313$; $p = 0.055$) and serum glucose ($r = 0.360$; $p = 0.026$).

Conclusion: Our data showed that higher values of NLR and PLR are associated with inflammatory markers, leading to the conclusion that this finding must be confirmed with larger, prospective and controlled follow up.

P0303 IS THERE ANY UTILITY OF USING A RATIO BETWEEN SERUM BIOMARKERS AND PREDIALYSIS SERUM CREATININE IN ESKD PATIENTS TREATED WITH HEMODIALYSIS?

Adalbert Schiller[1,2], Flaviu Bob[1,2], Oana-Marina Schiller[3], Lazar Chisavu[1,2], Adelina Mihaescu[1,2], FLORICA GADALEAN[1,2], Iulia Dana Grosu[1,2], LUCIANA MARC[1,2]

[1]Timişoara County Emergency Clinical Hospital, Nephrology, Timişoara, Romania, [2]Victor Babeş University of Medicine and Pharmacy, Timişoara, Romania and [3]"Avitum" Hemodialysis Center Timisoara,, Romania

Background and Aims: Serum creatinine is mainly used to estimate GFR in a patient with steady state kidney function. In ESKD patients on HD therapy however it may be used as a surrogate muscle mass indicator The predialysis serum creatinine decreases in time with HD therapy duration and low pre dialysis concentrations have been associated with increased all cause and cardiovascular mortality probably related to protein energy wasting. Under these conditions our working hypothesis was that exploring blood cytokine biomarkers (BM) and their significance in HD patients the correction of BM blood values to a prognosis marker (as pre dialysis serum creatinine) may change the results of our findings.

Method: 63 G5D patients (21 female and 42 male median age 61years.) have been included in a prospective study concerning assessment of 5 blood cytokine biomarkers (KIM-1,TGF beta, IL-6, soluble Klotho and VEGF) and their prognosis significance. At inclusion, the median duration of HD therapy was 3.2 years. Patients have been assessed for cardiovascular disease (including history, EKG and cardiac ultrasound, PVW). Standard blood biochemistry and blood count have been performed. Enzyme-linked immunosorbent assays were used for the assessment of blood BM. Statistical correlations of cytokine values and cytokine/predialysis serum creatinine with the collected data were performed

Results: The average plasma levels of the investigated biomarkers were: KIM-1 267.1+/-482.9 pg/ml, IL-6 7.3+/-5.1 pg/ml, TGFβ 298.9+/-609.5 pg/ml, VEGF 1371.3+/-787.5 pg/ml, Soluble Klotho 305.7+/-341.6 pg/ml. The average predialysis serum creatinine (SCr) was 8.4+/-1.9 mg/dl.

KIM-1 levels correlated with CRP (r=0.28, p=0.028) and Left Ventricular Hypertrophy (LVH) (r= - 0.28, p=0.026). The correlations of KIM-1/SCr did not significantly differ (with CRP r= 0.29, p=0.023 and LVH r= - 0.25, p= 0.047). IL-6 levels correlated with sKlotho (r=0.37, p=0.003), IL-6/SCr however correlated with iPTH (r=0.26, p=0.045), sKlotho (r=0.90, p=0.001), Alc.P (r=0.32, p=0.012), Ferritin (r= - 0.28, p=0.029), monthly EPO dose (r= - 0.26, p=0.044), TGFβ (r=0.36, p=0.023), VEGF/SCr (r=0.43, p= 0.000). TGFβ correlated with SCr levels (r= - 0.32, p=0.047) but TGFβ/SCr correlated with sKlotho (r=0.36, p=0.005), IL-6 (r=0.98, p=0.000), Ferritin levels (r= - 0.28, p=0.027). VEGF did not correlate with any of our investigated data however when reported to SCr, VEGF/SCr correlated with sKlotho (r=0.34, p=0.008), monthly EPO dose (r= - 0.27, p=0.035), PWW results (r= - 0.33, p=0.034), IL-6/SCr (r= 0.43, p=0.000), sKloto/SCr (r=0.39, p=0.002). sKlotho correlated with IL-6 (see above), daily EPO dose (r= - 0.31, p=0.013). sKlotho/SCr correlated with eKt/V (r=0.25, p=0.048), TGFβ (r=0.34, p=0.034), IL-6 (as above), iPTH (r=0.26, p=0.043), Ferritin (r= - 0.27, p=0.024).

Conclusion: With the exception of KIM-1 our working hypothesis was confirmed and it seems that in HD patients statistics are modified if blood biomarkers (BM) are referred to predialysis serum creatinine. More research is needed in order to verify the validity and significance of our observations.

P0304 **POINT OF CARE ULTRASOUND IN NEPHROLOGY: THE SOONER THE BETTER!**

Mirela Liana Gliga[1,2], Mihail Gheorghe Gliga[3], Cristian Chirila[4], Raluca-Maria Lie-Ungurean[5], Paula Chirila[6]

[1]University of Medicine and Pharmacy Science and Technology "George Emil Palade" of Târgu Mureş, Nephrology, Târgu Mureş, Romania, [2]Diaverum Dialysis Center Tirgu Mures, Romania, [3]University of Medicine and Pharmacy Science and Technology "George Emil Palade" of Târgu Mureş Nephrology, Physiology, [4]University of Medicine and Pharmacy Science and Technology "George Emil Palade" of Târgu Mureş, Nephrology, TARGU MURES, Romania, [5]Diaverum Dialysis Center, Brasov, Romania and [6]University of Medicine and Pharmacy Science and Technology "George Emil Palade" of Târgu Mureş, Endocrinology, TARGU MURES, Romania

Background and Aims: Point of care ultrasound (POCUS) is performed at the bedsite of the patient by de treating clinician. In nephrology a particular situation is related to severly ill patients, immobilized with elevated creatinine, which can not be deffered to imaging investigations such as CT scan or MRI. Using a small portable device, important clinical problems can be solved in no time.

Method: We examined 360 out of 670 patients admitted to the nephrology departament in a period of one year. They were severely ill due to following pathologies: 35 severe sepsis with hypotension, 53 decompensated heart failure, 24 stroke, 248 with renal failure and acido-basic or electrolitic disturbances. Evaluation was made using a portable US device with a 10 MHz linear probe and 3.5 MHz convexe probe with abdomen and thoracic software. Diameter of inferior vena cava (IVC), respiratory collapse of IVC, effusions in pleura, pericardium or peritoneum, liver dimensions, kidneys and spleen were described.

Results: 31 out of 35 patients with hypotension had collapsed IVC, diameter less than 1cm, PPV 88.5%; 48 from 53 heart failure had enlarged IVC with reduced respiratory collapse, PPV 90.6% and 201 from 248 renal failure patients had kidney changes, 81.04%. As compared with standard diagnostic tools (echocardiography, native CT scan and clinical examination, Sensitivity was over 98% in all cases.

Conclusion: POCUS is a very usefull test for the rapid bed-site examination of kidney patients, were a rapid decision has to be made using a portable device. Sensitivity of the method proved to be comparable as with standard diagnostic tools.

P0305 DIAGNOSTIC VALUE OF TGF-B-1 AND ANG II EXCRERION IN URINE IN CHILDREN WITH VESICOURETERAL REFLUX DEPENDING ON THE THERAPEUTIC APPROACH

Natalia Zaicova[1,2], Tatiana Sudareva[2], Vladimir Dlin[2], Lilia Sinitsina[3], Anatolii Korsunskiy[4]

[1]Sechenov University, pediatric nephrology, Moscow, Russia, [2]Pirogov Russian National Research Medical University, pediatric nephrology, Moscow, Russia, [3]Institute of Mother and Child Care, pediatric nephrology, Kishinev, Moldova and [4]Sechenov University, of pediatrics, Moscow, Russia

Background and Aims: to determine the diagnostic value of profibrogenic cytokines of transforming growth factor (TGF-β1) and angiotensin II (AngII) in urine to detect the severity of tubulointerstitial fibrosis in children with vesicoureteral reflux (VUR) depending on the therapeutic approach.

Method: 117 patients aged 3 to 16 years (mean age 10.2 ± 4.5, 70.1% of girls) with VUR were examined. The control group consisted of 20 healthy children. All children underwent a complete nephrological examination. The levels of TGF-β1 and AngII were determined in morning urine using the ELISA method and counted for urine creatinine. To identify the severity of the lesion of the renal parenchyma, a static DMSA scintigraphy was performed.

Results: depending on the therapeutic approach, the children were divided into 2 groups: 1 gr. - children on conservative treatment (63.2%), 2 gr. - children, after surgical correction of VUR (36.8%). In each group, 3 subgroups were identified depending on the development of tubulo-interstitial fibrosis according to DMSA: A subgr. - without signs of sclerosis (15.4%), B subgr. - 1-2 foci (44.74%) and C subgr - > 3-4 foci of sclerosis (40.1%). All patients with VUR had a high urinary excretion of TGF-β1/Cr and AngII/Cr when compared with the control group ($p<0.05$). Regardless of the therapeutic approach, in subgroups A (without foci of sclerosis) and B (1-2 foci of sclerosis), patients had a statistically significantly lower level of excretion of these cytokines when compared with patients from subgroup C ($p<0.05$). No significant difference was found in the urinary excretion of TGF-β1/Cr and AngII/Cr depending on the therapeutic approach.

Conclusion: we established a reliable dependence of the excretion of TGF-β1/Cr and AngII /Cr in the urine on the severity of tubulo-interstitial fibrosis according to DMSA scintigraphy in children with VUR. At the same time, we did not note the dependence of the excretion of TGF-β1/Cr and AngII/Cr in the urine on the method of the therapeutic approach. Therefore, the study of the excretion of TGF-β1/Cr and AngII/Cr in the urine as non-invasive markers can be used as a criterion for the progression of nephropathy in VUR, regardless of treatment methods.

P0306 ACUTE KIDNEY INJURY AFTER CHECKPOINT INHIBITOR TREATMENT: FACING THE FUTURE

Clara Garcā-a Carro[1], Mónica Bolufer[1], Diana Oleas[1], María A. Azancot[1], Irene Agraz[1], Natalia Ramos Terrada[1], Eugenia Espinel[1], Daniel Seron Micas[1], María José Soler[1]

[1]*Vall d'Hebron Hospital, Nephrology Department, Barcelona, Spain*

Background and Aims: Checkpoint inhibitors (CPI) are used to treat solid organ metastatic malignancies. They act on by triggering a vigorous immune response against tumoral cells, preventing their proliferation. CPIs reinvigorate antitumor immune responses by interrupting co-inhibitory signaling pathways and promote immune-mediated elimination of tumor cells.This is not a selective response, deriving in immune related adverse events (irAEs). The kidney can potentially be damaged with an incidence of 13-29%. The most frequent type of toxicity is acute interstitial nephritis (AIN).

Method: We evaluated all the patients with solid organ metastatic malignancies treated with immunotherapy that developed acute renal injury (AKI) and underwent to kidney biopsy from March 2018 to November 2019 at Vall d'Hebron University Hospital.

Results: 11 patients with solid organ metastatic malignancies treated with immunotherapy developed AKI and underwent to kidney biopsy during the study period. The most frequent malignancy was lung cancer - in 6 patients-, followed by 3 patients with melanoma. 8 patients (72%) had already received previous oncological therapy, and for the remaining 3 patients (27%), CPI was the first line therapy. 8 patients (72%) were treated with anti-PD1 (programmed cell death protein 1), 4 patients (36 %) received anti PDL-1 (programmed death-ligand 1) 1 of these patients in combination with an anti CTLA-4 (cytotoxic T-lymphocyte antigen 4) and another patient received both anti PD1 and anti PDL-1. The time between the start of CPI and the onset of the AKI ranged between 2-11 months. The most frequent urine findings were subnephrotic range proteinuria with a mean protein/creatinine (mg/g creatinine) 503.6 $\pm$ 190.5 and leukocyturia in 9 of 11 patients. Mean creatinine (mg/dl) at diagnosis was 3.4 $\pm$ 1.3. 10 out of the 11 patients were diagnosed of AIN after performing a kidney biopsy. The remaining patient presented chronic changes (IFTA and glomerulosclerosis) in the biopsy, performed after receiving steroids for a month. 3 patients who presented AIN received pulses of methylprednisolone 250-500mg as induction treatment and 7 patients received prednisone 1mg/kg/day. Mean prednisone accumulated dose (mg) during the first month of treatment was 1387.5 $\pm$ 540. 9 patients experienced complete recovery of kidney function and two patients progressed to CKD.

Conclusion: We reported 11 patients who presented AKI associated to CPI treatment and underwent to kidney biopsy in the last 20 months at our center. 10 out of 11 presented biopsy confirmed CPI related AIN. In our experience, CPI related AIN is the most frequent renal lesion associated to the novel immunotherapy treatments. This entity seems to have good renal prognosis as long as steroid treatment is early started.

P0307 KIDNEY-HEMOPATHY CONSULTATION: A SINGLE-CENTER EXPERIENCE

Nouvier Mathilde[1], DEEB ABBAS[1], Pelletier Solenne[1], Laetitia Koppe[1], Denis Fouque[1]

[1]HOPITAL LYON SUD, NEPHROLOGY, PIERRE BENITE, France

Background and Aims: Renal involvement in plasma cell dyscrasia has been widely described, including Monoclonal Gammopathy of Renal significance (MGRS). Chronic kidney disease (CKD) in hematological disorders carries major implications for management, prognosis and the potential for progressive renal injury and ESRD.

Specific monthly Kidney-Hemopathy Consultation has been created in 2017 in the department of Nephrology.

The aimed of this was to describe the clinical, biological and histological characteristics of patients with hematological disorders and CKD.

Method: From 01/05/2017 to 31/12/2019 adults with hematological disorders and CKD (eGFR<60ml/min and/or proteinuria or hematuria) were prospectively included.

Results: Fifty-six patients (27 men) were enrolled: Multiple Myeloma (n=30), MGUS (n=11), Lymphoma (n=5), Acute Leukemia (n=4), LMC (n=2), 1 LLC (n=2), Cryoglobulinemia (n=1), Refractory Anemia with Excess blasts (n=1), Bone marrow aplasia (n=1).

This nephrology consultation was the first for 22 patients (39%), referred by a hematologist in 38 cases (68%). Renal injury was confirmed after the hematologic diagnosis in 34 patients (61%) and precedes the diagnosis of plasma cell dyscrasia for 8 patients (14%).

The median eGFR was 54.1ml/min/1.73m̀ (128-4): CKD stage II (n=16), stage III (n=28), stage IV (n=7) and stage V (n=2). Proteinuria was >0.5g/day for 22 (39.3%) patients including a Bence-Jones proteinuria for 15 patients (27%). Acute Kidney Injury (AKI) was confirmed in 34 patients (63%) and 8 (24%) requiring acute dialysis.

Histologic diagnostic of kidney injury was confirmed for 21 patients (38%): 16 kidney biopsies and 5 AL renal amyloidosis confirmed by salivary glands or abdominal fat biopsy.

MGRS was confirmed in 34 patients (61%): Cast nephropathy (n=10;29%), AL amyloidosis (n=7;20%); C3 nephropathy (n=3; 9%), Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposits (n=3), Light Chain Proximal Tubulopathy (n=3), Randall-type monoclonal immunoglobulin deposition disease (n=2, 6%), 1 Minimal Change Disease (n=1; 3%), Glomerulonephritis with Organized Microtubular Monoclonal Ig Deposits (n=1) and exclusive tumoral renal infiltration (n=1).

Associated tumoral infiltration or crystalline podocytopathy was confirmed in 2 and 1 biopsy respectively. Glomerular MGRS was highly suspected for 2 patients, even if no biopsy was performed.

MGRS was excluded for 22 patients (39%): AKI due to antibiotics or sepsis (n=8; 36%), hypovolemia (n=4; 18%) or hypercalcemia (n=3; 14%); 2 renal artery stenosis due to tyrosine kinase inhibitors (n=2; 9%), nephroangiosclerosis (n=1), lithiasis (n=1), CKD post- nephrectomy CKD (n=1), and immunoallergic nephritis (n=1).

Hematological treatment was initiated in 54 patients (96%). All patients with MGRS were treated, whom 17 (50%) completely or partially in the Nephrology department. Proteasome inhibitors, alkylant agents and IMIDs were the main molecule used in first line therapy (56%, 23% and 12% respectively). Eleven patients (20%) had stem cell transplantation.

After a median follow up of 16 months (38-0), complete or very good partial hematologic response was obtained in 48 patients (89%); whom 30 with MGRS (88%). Median eGFR was 45ml/min/1.73m̀ (142-4): CKD stage II (n=18), stage III (n=23) and stage IV (n=9). Only 1/3 CKD stade V patient needed chronic replacement therapy. Eight patients died (14%): 4 uncontrolled hematologic disease (50%) and 3 septic complications (38%).

Conclusion: Very closed collaboration between Nephrology and Hematology Department in our Center contributes to improve early management of patients with hematological disorders associated with CKD, and probably their survey. Hemato-Nephrology is a viable and emergent specialty.

P0308 **IMPACT OF MAJOR SURGICAL OPERATIONS ON CLINICAL OUTCOME IN DIALYSIS PATIENTS**

Rezzan Eren Sadioğlu[1], Gizem Kumru Şahin[1], Sim Kutlay[1], Şule Şengül[1], Kenan Keven[1], Gökhan Nergizoglu[1], Kenan Ateş[1], Neval Duman[1], Şehsuvar Ertürk[1]

[1]*Ankara University School of Medicine, Ibni Sina Hospital, Department of Nephrology, Ankara, Turkey*

Background and Aims: We aimed to study the impact of major surgical operations on clinical outcome in patients with end-stage kidney disease treated with haemodialysis (HD) or peritoneal dialysis (PD).

Method: We retrospectively evaluated the records of all patients on HD and PD, who had been treated for at least 3 months at our outpatient clinics between January 1, 2014 and December 31, 2018. In addition to clinical and laboratory parameters, data on all major surgical operations were recorded.

Results: Among the 202 patients, 133 (66%) were on HD and 69 (34%) on PD. The mean age (±SD) was 58.3±14.5 years, 48% were female and 28% had diabetes mellitus. Forty-seven patients (23%) had a major surgical operation. The operation types were cardiovascular in 14 patients, orthopaedic in 11, gastrointestinal in 8, genitourinary in 6, parathyroidectomy in 5 and brain, pulmonary and breast in 1 patient each. Operations were emergent in 10 patients (21%) and elective in the others (79%). Among the whole study population, 59 patients (29%) died during the study period. In Kaplan-Meier analysis (Figure), mean (95% CI) survival time in operated patients was 43 months (37 to 49 months), while it was 49 months (46 to 52 months) in the others (p=0.023). Fifteen out of 23 deaths (65%) among the operated patients occurred in the first month after surgery. Severe perioperative complications (arrhythmias, hypervolemia, hypotension, bleeding, acute coronary syndrome, respiratory failure and cerebrovascular event) were recorded in 17 (36%) of the operated patients, of whom 16 died (p=0.001). Although did not reach a significant level, mortality rate tended to be higher after emergent operations than that after elective operations. Cox regression analyses revealed that age (RR 1.033, 95% CI 1.010-1.057, p=0.005), diabetes (RR 2.581, 95% CI 1.474-4.521, p=0.001), preoperative C-reactive protein level (RR 1.005, 95% CI 1.002-1.007, p<0.0001) and having a major surgical operation (RR 1.868, 95% CI 1.068-3.268, p=0.028) were the independent predictors of mortality.

Conclusion: Although prospective studies with a higher patient number are needed to confirm, our study shows that, in addition to age, diabetes and inflammatory status, having a major surgical operation is an independent risk factor for mortality in dialysis patients. The prevention and management of perioperative complications properly may result in more favourable outcomes in these patients.

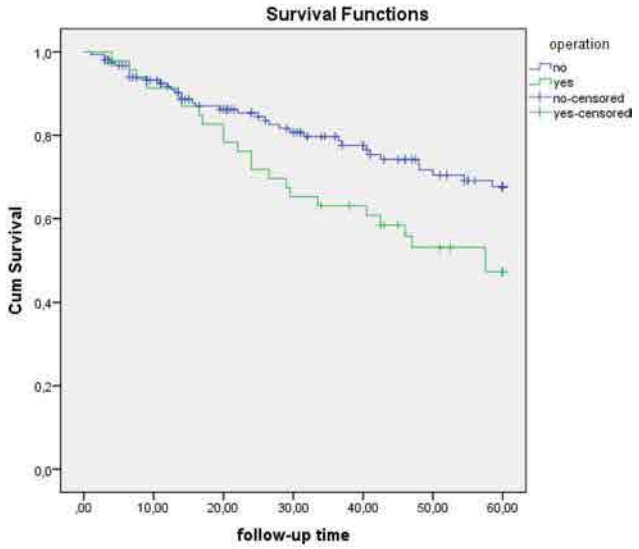


Figure:

P0309

IMPACT OF ACUTE KIDNEY INJURY ON CLINICAL COURSE AND TREATMENT RESPONSE IN PATIENTS WITH MINIMAL CHANGE NEPHROTIC SYNDROME

Hiroki Okushima[1], Yukimasa Iwata[1], Taisuke Takatsuka[1], Daisuke Yoshimura[1], Tomohiro Kawamura[1], Yoshiyasu Ueda[1], Tatsuya Shoji[1], Terumasa Hayashi[1]

[1]*Osaka General Medical Center, division of nephrology and hypertension, Osaka, Japan*

Background and Aims: Minimal change nephrotic syndrome (MCNS) has acute onset and is occasionally complicated with acute kidney injury (AKI) in its clinical course. Few studies concerning factors associated with AKI and impact of AKI on clinical course and response to treatments are available to date. Thus, we assessed the prevalence of and factors associated with AKI and its effect on clinical course in MCNS patients.

Method: Single center retrospective cohort study was conducted on 72 biopsy-proven MCNS patients presented to Osaka General Medical Center, between January 2006 and December 2016. Multivariate logistic regression analysis and Cox proportional hazards analysis were used to assess contributing factors to AKI and its effect on the duration until remission.

Results: Median age was 58 years and 50% were male. At first presentation, the mean albumin and total cholesterol were 1.7±0.5g/dl and 402±118mg/dl, respectively. The mean urinary protein and eGFR were 12.8±8.2g/gCr and 60.1±29.4ml/min/1.73m^2, respectively. A total of 29 patients (40%) had AKI and 10 of them needed renal replacement therapy (RRT). Corticosteroid and cyclosporine A were used in 66 (91%) and 3 (4%) patients, respectively for initial treatment and 3 patients (4%) received neither. 67 patients (93%) achieved complete remission (CR) with a median duration of 18 days after treatment, while 20 of those relapsed during the median follow-up period of 38 months. Logistic regression analysis revealed that older age, lower albumin, and higher urinary protein were significantly associated with AKI. Furthermore, patients with AKI had longer duration to CR induction compared with those without AKI (Log-rank test: p=0.03). Cox proportional hazards analysis showed that older age and RRT induction were associated with the delay of CR.

Conclusion: AKI occasionally occurs in patients with MCNS and need for RRT is associated with the delay of CR.

P0310 **FLUID OVERLOAD AND MARKERS OF CARDIOVASCULAR DAMAGE IN SEVERE NEPHROTIC SYNDROME**

Anna Matyjek[1], Aleksandra Rymarz[1], Stanisław Niemczyk[1]

[1]*Military Institute of Medicine, Department of Internal Diseases, Nephrology and Dialysis, Warsaw, Poland*

Background and Aims: One of the major symptoms of severe nephrotic syndrome is fluid retention. Fluid overload can induce cardiovascular damage. NT-proBNP (N-terminal pro-brain natriuretic peptide) and hsTnT (high sensitivity troponin T) are well known markers of this disorder. The aim of the study was to evaluate the association between volumes of body water compartments and markers of cardiovascular damage in patients with severe nephrotic syndrome (SNS) defined as nephrotic range proteinuria and hypalbuminaemia $\leq$ 2.5 g/dl.

Method: 40 patients with SNS and eGFR >30 ml/min/1.73m^2 formed the study group (SNSG) and 40 healthy volunteers without SNS matched according to age, sex, height, body mass and kidney function formed the control group (CG). In all participants serum creatinine, serum albumin concentration, daily proteinuria, hsTnT and NT-proBNP were measured. Body water compartments such as extracellular water (ECW), intracellular water (ICW), total body water (TBW), overhydration (OH) were assessed using Body Composition Monitor, Fresenius Medical Care. For statistical analysis Spearman's correlation coefficients, chi2 or Mann-Whitney U tests were used (Statistica v 13.1).

Results: SNSG included 28 males (70%) and 12 females. Median age was 55 years (IQR 30-65), the mean daily proteinuria was 10.5 ±5.0 g. The characteristics of the study parameters in two groups are described in the table.

	Severe Nephrotic Syndrome Group (SNSG)	Control Group (CG)	P
Gender	M: 28 (70%) F: 12 (30%)	M: 29 (72.5%) F: 11 (27.5%)	1.0
Age [years]	55 (30-64)	44 (30-64)	0.736
Height [cm]	170 ±10	173 ±10	0.173
Body weight [kg]	80.0 ±15.5	77.5 ±14.5	0.473
eGFR [ml/min/1,73m^2]	73 ±36	82 ±27	0.382
Serum albumin [g/dl]	2.0 ±0.4	4.6 ±0.5	**<0.0001**
hs-TnT [ng/l]	18 (8-40)	6 (3-13)	**0.0001**
NT-proBNP [pg/ml]	294.8 (94-1033)	47.1 (33-168)	**0.0003**
TBW [L]	39.8 ±8.6	38.8 ±7.7	0.603
OH [L]	4.2 (3.0-6.6)	0.3 ((-0.2)-0.6)	**<0.0001**
ECW [L]	20.9 ±5.2	17.4 ±3.3	**0.001**
ICW [L]	18.9 ±4.7	21.4 ±4.8	**0.034**

Significantly higher hsTnT (18 vs 6 ng/l, p=0.0001) and NT-proBNP (294.8 vs 47.1 pg/ml, p=0.0003) levels were observed in the severe nephrotic syndrome group in comparison (SNSG) to CG.

In SNSG extracellular water was significantly higher (20.9 ±5,2 vs 17.4 ±3.3 L, p=0.001) and intracellular water (ICW) was significantly lower (18.9 ±5.2 vs 21.4 ±4.8 L, p=0.034) in comparison to CG. Interestingly total body water (TBW) did not differ between the groups (39.8 ±8.6 vs 38.8 ±7.7 L, p=0.603). Also overhydration which is a derivative of ECW, was higher in SNSG (OH: 4.2 vs 0.3 L, p<0.0001) than in CG. Significant, positive correlation was observed between OH and NT-proBNP (R=0.56, p<0.0001) as well as hsTnT (R=0.60, p<0.0001). We did not observed significant correlation between ECW and NT-proBNP or hsTnT.

Conclusion: In the severe nephrotic syndrome group fluid retention was associated with the increase in ECW and the decrease in ICW whereas TBW was the same in both groups. Such constellation can indicate for intracellular underhydration which was not describe so far. Overhydration, which is a derivative of ECW, positively correlated with markers of cardiovascular damage and can be important for patients with resistant SNS and can influence their prognosis.

P0311 **INFECTION-RELATED GLOMERULONEPHRITIS IN ADULTS: TIME FOR A DEFINITIVE PARADIGM SHIFT?**

Chiara Salviani[1], Mattia Zappa[2], Guido Jeannin[1], Mario Gaggiotti[1], Regina Tardanico[3], Simona Fisogni[4], Giovanni Cancarini[5] , Francesco Scolari[5]

[1]ASST Spedali Civili of Brescia, Nephrology Unit, Brescia, Italy, [2]University of Brescia, Nephrology Unit, Brescia, Italy, [3]University of Brescia, Department of Molecular and Translational Medicine, Section of Pathology, Brescia, Italy and [4]ASST Spedali Civili and University of Brescia, Nephrology, Brescia, Italy

Background and Aims: The recent decades have witnessed significant changes in the epidemiology and clinical course of infection-related glomerulonephritis (IRGN). We analyzed the clinicopathological features and long-term outcome of adult patients with biopsy-proven IRGN followed in a large Italian referral centre.

Method: We included patients with biopsy-proven IRGN diagnosed from 2000 to 2018. Clinical and laboratory findings, histological features, possible risk factors and therapy were assessed for both renal and patient outcome.

Results: Forty-one patients met the inclusion criteria (male:female ratio 3:1, mean age 61±16 years). Smoke habit (47.2%), alcoholism (30.6%), and diabetes (27.5%) were the most common risk factors. The most frequently identified sites of infection were skin, lung and heart (Table 1). *Staphylococci* spp. accounted for 76.5% of positive cultures (Figure 1). Hypocomplementaemia emerged in 48.5% of cases. The most frequent histologic patterns were diffuse proliferative (56.0%) and membranoproliferative (29.3%) glomerulonephritis. Haemodialysis was required by 22.5% of patients at inception. Two thirds of patients developed chronic kidney disease; half of them reached end-stage renal disease (ESRD). By multivariate analysis ESRD was associated with diabetes (HR 13.7; 95% CI, 1.6-121.0; p=0.018), crescents (HR 25.2; 95% CI, 2.7-235.7; p=0.005), and interstitial fibrosis (HR 31.0; 95% CI, 3.3-287.3; p=0.003). Male gender (HR 12.7; 95% CI, 10.8-14.6; p=0.008) hypertension (HR 40.8; 95% CI, 38.6-43.1; p=0.001), gross haematuria (HR 11.8; 95% CI, 9.4-14.2; p=0.047), need for haemodialysis at onset (HR 16.3; 95% CI, 14.7-17.8; p<0.0001), and interstitial infiltrate (HR 13.3; 95% CI, 11.6-15.0; p=0.003) significantly affected survival. Corticosteroids did not affect prognosis.

Conclusion: While traditionally considered a "benign" disease with a favorable course in children, IRGN is a potentially severe disease in adults, particularly when a background of major comorbidities and older age are present. A significant proportion of patients does not recover renal function, with a remarkable risk of ESRD.

Table 1. Sites of infection. Three patients (11.5%) presented multiple infections

	N°/ TOT	%
Pneumonia	9/26	34.6
Skin infection	7/26	26.9
Endocarditis	6/26	23.1
Bone infection	3/26	11.5
Pharyngitis	1/26	3.8
Cholangitis	1/26	3.8
Prosthetic aortic graft infection	1/26	3.8
Urinary tract infection	1/26	3.8
Granulomatous rhinitis overinfection	1/26	3.8

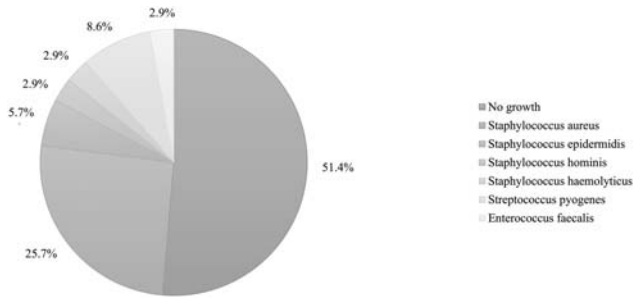


Figure 1. Results from microbiological tests.

P0312 **ALTERATIONS IN THE PROGRESS OF LYMPHOCYTE APOPTOSIS IN PRE- AND POST- DIALYSIS END STAGE RENAL DISEASE PATIENTS.**

Dimitra Vasileia Daikidou[1], MARIA STANGOU[1], Erasmia Sampani[1], Despoina Asouchidou[2], Vasiliki Nikolaidou[2], Chrysostomos Dimitriadis[1], Georgios Lioulios[1], Eva Pella[1], Aikaterini Anastasiou[2], Asimina Fylaktou[2], Aikaterini Papagianni[1]

[1]Aristotle University of Thessaloniki, Hippokration Hospital, Department of Nephrology, Thessaloniki, Greece and [2]Hippokration Hospital, National Peripheral Histocompatibility Center, Immunology Department, Thessaloniki, Greece

Background and Aims: Lymphocyte apoptosis, as a programmed mechanism of lymphocyte death, is essential in maintaining homeostasis and balance between inflammatory and immune reactions. Disturbances in the apoptotic progress, leading to fragmented lymphocytes, "late apoptotic" cells, may result in immunodeficiency, oncogenesis, atheromatosis, etc. Aim of the present study was to investigate the lymphocyte apoptotic progress in End Stage Renal Disease (ESRD) and the effect of dialysis.

Method: The study included patients on ESRD; measurements were performed at the first day of dialysis (T0) and repeated 6 months later (T6), while being on dialysis. Total lymphocytes and B lymphocytes (CD19+) were gated and stained with Annexin V to detect apoptotic cells; early and late apoptotic cells were quantified. The results were compared to age-matched healthy control group.

Results: ESRD patients had reduced lymphocyte and B cell count, $1550 \pm 592\mu/L$ vs. $2692 \pm 690\mu/L$, $p<0.001$ and $120.4 \pm 80\mu/L$ vs. $321.7 \pm 184.7\mu/L$, $p=0.002$, respectively, compared to controls. There was an increase in total lymphocytes and B cells, being on later apoptotic stages (LAS) in ESRD-T0 compared to controls, $0.3 \pm 0.8\%$ vs. $0.06 \pm 0.1\%$, and $0.04 \pm 0.08\%$ vs. $0.01 \pm 0.03\%$, respectively, although differences did not reach statistical significance. After 6 months on dialysis, a reduction was noticed in the population of lymphocytes on LAS, $0.18 \pm 0.2\%$ from $0.34 \pm 0.8\%$, while there was an increase of B cells on LAS, $0.1 \pm 0.2\%$ from 0.02 ± 0.07, with subsequent alterations in total numbers of apoptotic cells were also evident

Conclusion: Late apoptotic changes affecting total and particularly B lymphocytes happen in ESRD, and initiation of dialysis seem to cause further alterations, which may be implicated in the increased morbidity and mortality of disease

P0313 **POLYCLONAL FREE LIGHT CHAINS IN IGA-NEPHROPATHY: CORRELATION WITH CLINICAL AND MORPHOLOGICAL PARAMETERS AND PROGNOSTIC SIGNIFICANCE.**

Anna Churko[1], Maria Khrabrova[2], Vasiliy Sipovskii[2], Alexei Smirnov[2]

[1]Pavlov First Saint Petersburg State Medical University, Department of propaedeutics of internal diseases, Saint Petersburg, Russia and [2]Pavlov First Saint Petersburg State Medical University, Scientific Research Institute of Nephrology, Saint Petersburg, Russia

Background and Aims: Mechanisms of kidney injury by monoclonal free light chains in myeloma kidney are well established. The role polyclonal free light chains (pFLC) in pathogenesis of renal interstitial inflammation and fibrosis in primary glomerulonephritis is still poorly investigated. We hypothesize that increased level of pFLC could have the similar role in activation of interstitial inflammation and fibrosis formation and impact chronic kidney disease (CKD) progression in the most prevalent form of chronic glomerulonephritis - IgA-nephropathy (IgAN).

The aim of this retrospective study was to analyze the association of pFLC kappa (pFLC-κ) and lambda (pFLC-λ) assessed in serum by Freelite® with clinical and morphological parameters and CKD progression in IgA-nephropathy cohort.

Method: In this study we enrolled 23 patients with biopsy-confirmed diagnosis of IgAN. pFLC-κ and pFLC-λ levels were assessed in all cases at the time of kidney biopsy (KBx) by Freelite method. Normal range for pFLC-κ and pFLC-λ was 3,3-19,4 mg/l and 5,7-26,3 mg/l, respectively. The following clinical parameters were evaluated at the time of KBx: estimated glomerular filtration rate (eGFR) by CKD-EPI, daily proteinuria, serum albumin and microhematuria. Morphological findings were investigated by light and immunofluorescence (IgA, IgM, IgG, C3, C1, lambda, kappa, fibrinogen) microscopy. Oxford MEST-C score was evaluated as well as % of sclerotic glomeruli. Additionally we semiquantitatively measured (0- absent, 1- mild, 2 – moderate, 3 - severe) mesangial proliferation, endocapillary proliferation, glomerular basement membrane (GBM) thickening, interstitial inflammation, interstitial edema, tubular atrophy (TA), peritubular capillaritis (PTC), interstitial fibrosis (IF) according to currently accepted criteria. The demographic, clinical and morphological parameters at the time of KBx are presented in Table 1. Patients were treated with nephroprotective agents (n=23) and steroids/cyclophosphamide (n=21). Correlation between parameters were assessed by Spearman's coefficient. Progression of CKD was determined as decline of eGFR >25% from the initial level at the end of follow-up period. Prognostic analysis was performed with Cox proportional hazards regression. Median follow-up was 28 (7; 37) months.

Results: Correlations between clinical and morphological parameters and pFLC levels are presented in Table 2.

Univariate Cox regression analysis has shown that pFLC-κ (Exp(β)=1,051; 95% CI: 1,001-1,104, p=0,045) and FLC- λ (Exp(β)=1,040; 95% CI: 1,001-1,081, p=0,044) as well as other well-known clinical (daily proteinuria (Exp(β)=1,177; 95% CI: 1,003-1,382, p=0,045), eGFR at the KBx time (Exp(β)=2,981; 95% CI:1,112-20,124, p=0,042)) and morphological parameters (% of sclerotic glomeruli (Exp(β)=1,031; 95% CI: 1,001-1,062, p=0,046), T-score (Expβ=10,784; 95% CI: 1,364-85,246, p=0,024) are associated with CKD progression.

Conclusion: In IgAN higher levels of pFLC, both kappa and lambda, are associated with renal interstitial inflammation and fibrosis, tubular atrophy and chronic glomerular injury and could be used as predictors of CKD progression. Mechanisms of pFLC effects on the formation of renal tubular and interstitial inflammation and fibrosis require further studies.

P0314 TREATMENT AND OUTCOMES OF IDIOPATHIC MEMBRANOUS NEPHROPATHY IN ELDERLY PATIENTS

Nessrine Breik[1], Mouna Jerbi[2,3], Raja Aoudia[1,3], Soumaya Chargui[1,3], Hanen Guaied[2,3], Imen Gorsane[1,3], Rim Goucha[2,3], Taieb Benabdallah[1]

[1]Charles Nicolle Hospital, Department of Nephrology, Dialysis and Transplantation, Tunis, Tunisia, [2]Mongi Slim Hospital, Department of Nephrology, La Marsa, Tunisia and [3]Charles Nicolle Hospital, Research Laboratory of Kidney Diseases (LR00SP01), Tunis, Tunisia

Background and Aims: The increase in life expectancy has led to increasing numbers of elderly patients in all medical disciplines, particularly in nephrology. Idiopathic membranous nephropathy (IMN) is common in the elderly and can lead to significant morbidity and mortality because of the complication of nephrotic syndrome (NS) and immunosuppressive therapy. The aim of this study is to analyze the diagnostic, therapeutic and evolutionary approach of IMN in elderly patiets.

Method: We conducted a retrospective descriptive study in the nephrology department at Charles Nicolle hospital over a period of 44 years. All older patients ($\geq$65 years) with histologically proven MN were included in this study. Data collected included demographic, clinical and biological parameters in each patient. Data were entered and analyzed using SPSS software.

Results: Twenty-eight patients were collected. The mean age was 67.03 years (65-78 years) with a male predominance (sex ratio: 2.3) and low socio-economic level in 82.5% of cases. Sixteen patients were smokers (57.14%), 5 ethyl patients (17.8%), diabetes was present in 3 patients (10.7%) and hypertension in 11 patients (39.28%). Two cases of neoplasm were present, namely one case of prostatic adenocarcinoma and one case of gallbladder adenocarcinoma, all were diagnosed and treated along one year and ten years respectively, before the diagnosis of MN. The circumstances of discovery were dominated by oedema in 27 cases (86.27%), hypertension in 11 cases (39.28%) and elevated creatinine level in 9 cases (32.14%). Deep venous thrombosis was the circumstance of discovery in one case. At the time of diagnosis, the clinico-biological picture was dominated by high systolic blood pressure in 21 cases (75%), anasarca in 7 cases (25%), proteinuria in all cases and hematuria in 20 cases (71.14%). Biology revealed nephrotic syndrome (NS) in all cases, hypercholesterolemia in 23 cases (82.14%), high serum creatinine in 14 cases (50%) with an average creatinine level of 127,95 µmol/l, anemia in 17 cases (60.7%) and anti-neutrophil cytoplasmic antibodies were positive in one case. MN was confirmed by a kidney biopsy in all cases. Symptomatic treatment was indicated in all patients. Immunosuppressive therapy was started early in 12 patients (40%) because of the severe NS and the deterioration of renal function. Eight patients (26.6%) received corticosteroids alone (group 1), three patients received corticosteroid with mycofenolate mofetil (group 2) and one patient received corticosteroid with ciclosporin (group3). Fourteen patients received only symptomatic treatment (group 4). We noted partial remission in group 3, however complete remission in 37.5%, 14.28% and 12.5% from respectively group 1, group 4 and group 2. The side effects of immunosuppressive therapy were infectious complication in 8 patients (28.5%), osteoporosis in 3 patients (10.7%) and Steroid diabetes in one case. The side effects of NS were thrombotic complication in 5 patients (17.85%). Two patients had presented coronary syndrome and two other patients had presented hepatitis C. Two cases of death were noted whose etiology was pulmonary infection in one patient and undeterminate etiology in the other case.

Conclusion: Treatment of IMN in older patients has unique challenges, reducing the need for renal replacement therapy. Most studies report that the elderly respond to therapy with rates comparable with younger patients but in the other hand elderly are more susceptible to side effects of immunosuppressive therapy.

P0315 SUCCESFUL TREATMENT OF A STRETOCOCCUS-PNEUMONIAE-ASSOCIATED HAEMOLYTIC URAEMIC SYNDROME BY A SHORT COURSE OF ECULZIMAB

Silvius Frimmel[1], Michael Hinz[1], Joerg Henschel[2], Steffen Mitzner[1], Sebastian Koball[1]

[1]Rostock University Medical Center, Division of Nephrology, Department of Medicine, Rostock, Germany and [2]Rostock University Medical Center, Internal Intensive Care, Rostock, Germany

Background and Aims: Hemolytic uraemic syndrome (HUS) is a known rare complication of Streptococcus pneumonia infections (SP-HUS) and is characterized by microangiopathic hemolytic anemia, thrombocytopenia and renal failure. In adults it is associated with a higher mortality than HUS due to other etiologies.

Method: Case Report

Results: A 33-years old female patient with a history of alcohol abuse was referred to hospital with hypotension and symptoms of infection, including high fever and diarrhea, which had occurred since three days. On admission the patient presented with septic shock and was transferred to the intensive care unit. There she showed signs of hemolytic uraemic syndrome, including severe thrombocytopenia (11 Gpt/l), schistocytosis, elevated lactate-dehydrogenase (LDH; max. 2300 U/l), low haptoglobine (<0,3g/l) and acute anuric renal failure with need of continuous renal replacement therapy. Severe confusion and necrotic lesions of the extremities completed the clinical picture. Plasma exchange (PE) was initiated under suspected thrombocytopenic thrombotic purpura (TTP). Under PE the clinical situation did not ameliorate and signs of severe HUS persisted. A total of four PE were realized, TTP was excluded by Factor VIII-ADAMTS13-activity above the diagnostic limit. In the peripheral blood cultures Streptococcus pneumonia was detected, and antimicrobial was deescalated from piperacillin/tazobactam to penicillin G. Under the clinical picture of a persistent severe pneumococcal associated HUS, without clinical benefit of PE, we decided to start therapy with eculizumab, a monoclonal anti-C5-antibody, approved for the therapy of aHUS and with anecdotical evidence of efficacy in SP-HUS. We started with 1200 mg of ECZ, followed by doses of 900 mg weekly with a total of four doses. Under therapy thrombocyte count normalized, renal function ameliorated and dialysis could be discontinued, the levels of haptoglobin and LDH normalized. The patient could be referred to a rehabilitation clinic, where renal function normalized and no further signs of hemolysis were seen three months after discontinuation of therapy under monitoring. The forefoot remained necrotic with need of surgery in future, the ischemic lesions of the hands completely disappeared.

Conclusion: Eculizumab could provide a therapeutic option of pneumococcal associated HUS. Therapy could be safely discontinued after 1 month under strict monitoring of signs of HUS. Further studies are required to document the benefit of complement blockade therapy in severe forms of SP-HUS.

P0316 RELATION OF RENAL ULTRASONOGRAPHIC MEASUREMENTS WITH BODY HEIGHT

Adrijana Spasovska Vasilova[1], Lada Trajcheska[1], Mimoza Milenkova[1], Aleksandra Canevska[1], Angela Kabova[1], Ana Stojanoska[1], Vladimir Pushevski[1], Irena Rambabova Bushljetikj[1], Igor Nikolov[1], Galina Severova- Andreevska[1], Svetlana Pavleska Kuzmanoska[1], Dzvezdana Petronijevic[1], Biljana Gerasimovska Kitanovska[1], GJULSEN SELIM[1], Aleksandar Sikole[1], Vesna Ristovska[1], Goce Spasovski[1]

[1]*University Clinic of Nephrology, Skopje, Republic Of North Macedonia*

Background and Aims: Kidney size has been found to be correlated with anthropometric features and is different among different ethnicities. In this study, we used ultrasonography for measurement of kidney volumes in healthy individuals and evaluated the relationships with body height, age and gender.

Method: We conducted a cross-sectional observational study and evaluated 108 healthy individuals whose serum creatinine level was within reference range. Patients' medical clinical and laboratory records were reviewed. Age, gender and height were recorded. Pearson correlation coefficients were used to evaluate the strength of association between ultrasonographic parameters with each other and with other parameters, and were expressed as r^2. Variations in left and right renal dimensions between various age groups were compared using a one-way analysis of variance, followed by a post-hoc Tukey's test.

Results: Subjects' age ranged from 16 to 84 years and the mean age was over 50 years. There was an equal distribution among genders. Strong and positive correlations were seen for the measured length, parenchyma thickness and also for both total and parenchymal volumes with subjects' height for both kidneys. The strongest correlations were observed for the left and right kidney length and also for the right kidney parenchymal volume (r=0.536, p=0.001; r=0.469, p=0.001; r=0.44, p=0.001). On the opposite, most of the relations with age were negative, but week and insignificant. When we divided the study subjects into three age groups and compared them for the height, there was no significant difference among them. Regarding the parenchymal and total kidney volumes of both kidneys, the different age groups showed similar findings in the ultrasonographic measurements. The mean calculated volumes were slightly declining with age and showed the largest values in the first group of patients under 30 years and lowest values in patients over 70 years old. Ultrasonographic measurements were also compared among the two genders. Both (men and women) showed similar age (53.55 ± 18.22 *vs.* 50.79 ± 18.13 p= 0.430, respectively). As for the height, men were significantly taller than women (1.734 ± 0.007 *vs.*1.637 ± 0.005, p= 0.001). The kidney length, volume and parenchymal volumes of both kidneys were significantly larger in men.

Conclusion: Renal length and volume are strongly correlated with body height. This relation must be considered in clinical decisions on further investigations regarding kidney disease progression.

P0317 EARLY MARKERS OF RENAL INJURY AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH METABOLIC SYNDROME

Sherzod Abdullaev[1]

[1]*Tashkent pediatric medical institute, Internal medicine, Tashkent, Uzbekistan*

Background and Aims: The definition of subclinical renal damage markers in patients with metabolic syndrome (MS) and evaluation the relations between the indicators of subclinical renal injury and endothelial dysfunction.

Method: The study included 62 patients with MS, 32 (51.6%) men and 30 (48.4%) women aged 51.2±5.4 years. The control group included 25 practically healthy individuals, 13 (52.0%) men and 12 (48.0%) women, aged 47.3±6.1 years. All patients were underwent clinical and laboratory examination, calculation of glomerular filtration rate (GFR) using the formula CKD-EPI, ultrasound of the carotid arteries, determination of the insulin resistance index (IR) (HOMA-IR), as well as determination of the content of endothelin-1 (ET-1) in serum and albumin excretion in a single portion of urine by IFA.

Results: When calculating GFR, hyperfiltration was detected in 10 (16.1%), optimal filtration - in 23 (37.1%), slightly reduced - in 29 (46.8%). At the same time, in patients with MS, a statistically significant excess of urinary albumin excretion (UAE) in a single dose was revealed compared with the control group (26.6±5.8 mcg/ml and 9.2±3.4 mcg/ml, respectively; $p < 0.001$).

Based on the increase in level (ET-1) in patients of the main group, compared with the control (6.3±3.2 fmol/ml and 3.4±1.0 fmol/ml, respectively; p=0.03) may indicate the development in patients of the main group of endothelial dysfunction. A correlation analysis revealed a direct correlation between the level of UAE and ET-1 ($R = 0.45$; $p = 0.005$).

A direct correlation was found between UAE and IR-HOMA ($R = 0.68$; $p < 0.007$), interventricular septum thickness ($R = 0.71$; $p < 0.001$), and intima–media thickness (IMT) ($R = 0.49$; $p < 0.008$) and systolic blood pressure ($R = 0.47$; $p = 0.026$). Similar associations were noted also for the ET-1 level: IR-HOMA2 ($R = 0.78$; $p < 0.001$), with the thickness of the interventricular septum ($R = 0.76$; $p = 0.001$), IMT ($R = 0.46$; $p < 0.033$) and systolic blood pressure ($R = 0.45$; $p = 0.035$).

Conclusion: In patients with metabolic syndrome, in addition to the well-known manifestations, in the early stages, may be a violation of renal function and endothelium, manifested by the change of glomerular filtration rate, increased levels of UAE and increased concentration of ET-1 in the blood. Direct correlation of the level of UAE and ET-1 level, and the coincidence of the correlation relationships of these indicators with a number of clinical and laboratory indicators of the metabolic syndrome will make it possible to consider an increasing of the level of UAE as one of the markers of endothelial dysfunction.

P0318 HYPERKALEMIA: EPIDEMIOLOGY AND MANAGEMENT

Eya Felah[1], Barbouch Samia[1], Hajji Mariem[1], Shedha Ben amor[1], Soumaya Chargui[1], Mohamed Iotfi Amiri[1], Raja Trabelsi[1], Rym Goucha[2], Fethi Ben Hmida[1], Mondher Ounissi[1], Taieb Ben abdallah[1]

[1]Charles Nicolle Hospital. Tunis, Tunisia., Departement of nephrology and Laboratory of kidney pathology LR00SP01, Tunis, Tunisia and [2]Monji Slim Hospital Marsa Tunis, Nephrology and dialysis departement, Tunis, Tunisia

Background and Aims: Hyperkalemia is a dreadful biological event that can immediately compromise the vital prognosis. Etiologies are many and varied. The aim of our study is to better characterize the epidemiological and clinical aspects of this disorder in order to establish adequate diagnostic and therapeutic strategies in order to intervene effectively and in the shortest possible time.

Methods: Cross-sectional study carried out over a period of 12 months [January-December 2017] including all emergency calls for hyperkalemia greater than 5.5 mmol / l and undergoing hemodialysis in the nephrology department.

Results: We collected 185 patients (Sex ratio= 1.43) aged on average 61.8 ± 16.1 years [18-94 years].

70.3% had serum potassium between 5.5 and 7 mmol / l and 29.7% greater than 7. Patients mainly came from emergencies in 71.4% of cases. Main symptoms consisted in oligoanuria, vomiting, chest pain, and febrile syndrome in 38.9%, 10.8%, %, and 5.9% of cases, respectively. Of these patients, 76.2% are known to be chronic renal failure whose 29.7% are in chronic dialysis. Acute renal failure (ARF) was diagnosed in 30.3% of patients. Of these, 39.4% were functional AKI, 41% were obstructive and organic AKI in 19.6% of cases. Mean serum potassium was 6.7 ± 0.9mmol / l [5.5-11] associated with metabolic acidosis in 52.4% of cases. Mean serum creatinine was 988umol / l[184-3270]. The electrical signs of hyperkalemia were noted in 40% (n = 74) of patients: large T in 28.6% of cases, atrioventricular block (AVB) in 3.8% of cases including a 3rd BAV degree in 1.6% of cases, QRS wide in 11.4% of cases and sinus bradycardia in 7% of cases, Ventricular Extrasystoles and a branch block found respectively in 3.2% of cases. 30.8% (n = 57) of the patients were under hyperkalaemic treatment. In fact, 27 % of patients took a blocker of the renin-angiotensin system, 7% were on aldoactone, 13.5% of patients on þetabloquant,1.6 % of whom were on kaleoride and / or admitted to intensive care and infused with KCl. Medical treatment was started urgently in 42.7 % of cases and included the administration of twenty ml 10% ca gluconate that was given intravenously over 5-10minutes, insulin with glucose ,sodium polystyrene sulfate (Kayexalete) and salbutamol, sodium bicarbonate indicated for severe metabolic acidosis (pH<7.20). Overall mortality was 21.1% of cases .

Conclusion: Hyperkalemia remains a frequent metabolic disorder. Renal failure and acidosis were the main factors associated to hyperkalemia in our study. The clinical and therapeutic subtleties must be known by any caregiver in order to effectively mitigate the harmful effects of this disorder, mainly in the cardiac function.

P0319 **DEPRESSIVE BURDEN, QUALITY OF LIFE AND CAREGIVER BURDEN IN END STAGE RENAL DISEASE - A PARADIGMATIC SHIFT IN HOLISTIC MANAGEMENT**

Abdul waheed Khan[1], Shahbaz ali Khan[2], Deepak Shanker Ray[3], Swetanka Prasad[4], Shagufta Khan[5], Aruna Deshpande[6]

[1]Brahmananda Narayana Multispeciality Hospital, Jamshedpur, Nephrology, Jamshedpur, India, [2]Command Hospital (Central Command), Psychiatry, Lucknow, India, [3]Rabindranath Tagore International Institute of Cardiac Sciences, Nephrology, Kolkata, India, [4]Brahmananda Narayana Multispeciality Hospital, Jamshedpur, Laboratory services, Jamshedpur, India, [5]VEER KUNWAR SINGH UNIVERSITY, ARA(BIHAR), Psychology, Arrah, India and [6]EngenderHealth Maharashtra Office, Monitoring and Evaluation specialist, Pune, India

Background and Aims: Depressive illness is not only common in patients of End Stage Renal Disease (ESRD) but also an independent risk factor for morbidity and mortality. The relation between depressive illness, Quality of Life and caregiver burden in this vulnerable group is complex. We attempted to study these 3 important psychosocial domains in patients of ESRD on hemodialysis, peritoneal dialysis as well as those ESRD patients who were not on any dialysis yet

Method: A cross sectional analytical comparative controlled design was done to compare 3 domains of depressive burden, quality of life and caregiver burden in 3 group of patients – ESRD patients on hemodialysis, ESRD patients on peritoneal dialysis and ESRD patients not on any dialysis

Statistical methods used - χ^2 statistic or Fisher's exact test for categorical variables and comparison of group means. ANOVA was used for continuous variables where more than 3 groups were compared. Correlational analysis done using Spearman's correlation coefficient . A p-value of <0.05 was considered significant. SPSS 20.0 was used

Results: Depressive symptoms were present significantly across all 3 groups of ESRD. Depressive disorder was significantly higher in the Hemodialysis group (HD) as compared to peritoneal dialysis (PD) group(p=0.038). Mean QOL was significantly higher for PD. Caregiver burden was higher in the HD group.

The study brought out the huge burden of depressive symptoms and depressive illness in patients on ESRD across all 3 group of patients and the significantly higher burden of depressive illness and lower QoL and higher caregiver burden in the hemodialysis group. This assumes significance because the majority of our ESRD patients are on HD

Conclusion: This depressive burden is the hidden factor behind poor Quality of Life as well as poor overall satisfaction as well as treatment outcome in our patients of ESRD whether or not on dialysis. Apart from the inherent factors related to the illness or the type of dialysis, sociodemographic factors seem to play a role in QoL and CG burden in the hemodialyis group. To address this hidden depressive burden comprehensively, we recommend closer cooperation between nephrologist, psychiatrist and psychosocial workers to improve the overall treatment outcome in ESRD patients.

P0320

KIDNEY DAMAGE IN THE NON-HODGKIN LYMPHOMA/ LEUKEMIA AND HODGKIN'S LYMPHOMA - CLINICAL AND PATHOLOGY SPECTRUM IN THE REAL PRACTICE

Elena V. Zakharova[1], Ekaterina Stolyarevich[2], Tatyana Makarova[1], Olga Vorobyeva[3]

[1]City Clinical Hospital n.a. S.P. Botkin, Nephrology, Moscow, Russia, [2]City Nephrology Centre, Pathology, Moscow, Russia and [3]National Centre of Clinical Morphology Diagnostics, Difficult diagnosis, Saint Petersbourg, Russia

Background and Aims: Kidney damage in non-Hodgkin lymphoma/leukemia (NHL/CLL) and in Hodgkin's lymphoma (HL) are caused by several mechanisms: tumor mass localization, clonal cell expansion, hormones, cytokines and growth factors secretion, metabolic, electrolyte and coagulation disturbances, infectious, drug-induced and radiation complications etc., which can affect urinary tract, renal arteries and veins and all renal parenchyma compartments. Clinical presentation of kidney involvement in the patients with NHL/CLL and HL include both acute kidney injury (AKI) and chronic kidney disease (CKD), the latter - with or without nephrotic syndrome (NS). Pre-renal AKI, tumor-lysis syndrome (TLS), or urinary tract compression by lymph nodes usually diagnosed on the clinical basis, but one cannot differentiate other conditions, particularly NS, in the clinical setting. Importantly, symptoms of kidney damage may dominate or even preclude overt NHL/CLL or HL, and only pathology data give the clue to the main diagnosis. Kidney biopsy or post-mortem pathology findings include various patterns of paraneoplastic glomerulonephritis (GN) as well as amyloidosis; as also as tubulointerstitial damages, mainly specific lymphoid interstitial infiltration and sometimes pyelonephritis

Method: In this retrospective study from a single nephrology centre, we retrieved charts of the patients with NHL/CLL and HL. Collected data were age, gender, main diagnosis, diagnosis of AKI or CKD, CKD stage, NS presence, the cause of AKI and CKD based on the clinical presentation, and pathology pattern, if available.

Results: Study group included 57 patients, 36 males and 21 females, median age 48 [18; 80] years. Kidney biopsy was performed in 22 (39%) of cases. Main clinical data and pathology shown in the Figure.

Patients with B-cell NHL/HLL comprised almost 3/4 of the study group, with AKI and CKD in a roughly equal proportion. Pathology showed specific infiltration in about 1/4 of AKI and in a few CKD cases, and various paraneoplastic GN in every fifth case - minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), membranoproliferative GN (MPGN), and IgA-nephropathy (IgAN); two cases of AA amyloidosis, and one case of tubulointerstitial nephritis.

There were only three patients with T-cell NCL/CLL, pathology findings were MCD in one case and lymphoid infiltration in another.

Four out of 13 cases of HL demonstrated paraneoplastic GN – MCD, FSGS and IgAN, with just one case of AA amyloidosis.

Totally 17 cases of AKI - pre-renal and caused by TLS or urinary tract compression by lymph nodes diagnosed on the clinical basis.

Interestingly, in five cases we found a combination of various clinical settings and pathology patterns – compression with lymph nodes and TLS or acute pyelonephritis, AA amyloidosis and lymphoid infiltration or acute pyelonephritis, and finally IgAN and lymphoid infiltration.

In 14 (24.5%) of the study group, the cause pf CKD remained unknown, as kidney biopsy was not performed due to severe anaemia and/or thrombocytopenia.

Conclusion: It is impossible to decipher many of AKI and most of CKD causes in the patients with NCL/CLL and HL without pathology evaluation. Nephrologist must perform kidney biopsy in all patients with NCL/CLL of HL CKD, and those with AKI of unknown origin, unless contraindicated, especially if the hematological diagnosis is uncertain.

Kidney damage	Main diagnosis	B-cell NCL/CLL	T-cell NCL/CLL	HL
AKI	Hypovolemia	4		3
	TLS	6		
	Compression with lymph nodes	2		
	Lymphoid infiltration	4	1	
	Compression with lymph nodes + TLS	1		
	Compression with lymph nodes + acute pyelonephritis	1		
CKD 1-2, NS	Minimal change disease		1	2
	Focal segmental glomerulosclerosis			1
	AA amyloidosis + lymphoid infiltration	1		
	Unknown	3		
CKD 3-4, NS	Membranous nephropathy	1		
	Membranoproliferative glomerulonephritis	1		
	AA amyloidosis			1
	AA amyloidosis + acute pyelonephritis	1		
	Unknown	3		
CKD 5, NS	Unknown	1		
CKD 1-2 without NS	IgA-nephropathy			1
	Unknown	3	1	1
CKD 3-4 without NS	Membranous nephropathy	1		
	Membranoproliferative glomerulonephritis	1		
	Focal segmental glomerulosclerosis			1
	IgA-nephropathy + lymphoid infiltration	1		
	Retroperitoneal fibrosis	1		
	Unknown	1		2
CKD 5 without NS	Lymphoid infiltration	1		
	Tubulointerstitial nephritis	1		
	Unknown	2		1

Figure:

P0321 OUR EXPERIENCE OF PATIROMER (VELTASSA) USE AND POTENTIAL COST-BENEFITS AT SOUTH TYNESIDE AND SUNDERLAND NHS FT, U.K.

James Coates[1], William Hinchliffe[2]

[1]Queen Elizabeth Hospital (Gateshead), United Kingdom and [2]Sunderland Royal Hospital, Department of Renal Medicine, Sunderland, United Kingdom

Background and Aims: Patiromer is a new medication used to manage hyperkalaemia and acts as a bowel cation-exchange polymer with a simpler dosing and more favourable side effect profile than existing agents. In May 2018, South Tyneside and Sunderland NHS Foundation Trust (STSFT) implemented a protocol for the use of Patiromer in managing chronic hyperkalaemia to enhance options for managing cardio-renal patients in clinic. Conditional on our successful formulary application, was an audit against the protocol aiming to understand utility. Our second aim was to identify potential cost-benefits of patiromer. In particular, we were interested in preventing hospital admissions, bed days saved, temporary venous lines and dialysis sessions. It is important to note this analysis is subject to interpretation based on likely outcome should patiromer not have been given.

Method: To be eligible, patients had to have eGFR <30 and either a potassium >5.5 precluding the use of RAASi/MRAs or a recurrent potassium >6. Using electronic patient record system, we investigated 49 patients commenced on patiromer between October 2018 and October 2019.

Results: Only 14% of the incident prescriptions were in clinic with over half starting at a higher than UK licensed dose (once daily). The distribution of hyperkalaemia was varied as defining hyperkalaemia onset is challenging and what we found as more emergency use. We also identified the following clinical savings: 12 fewer bed days, 15 temporary lines and a minimum of 25 dialysis sessions avoided. Interestingly, we also found that in 2 cases, physicians utilised patiromer and avoided a referral to the renal team. Furthermore, we identified 11 uses of patiromer in the conservative/palliative setting allowing patients to withdraw from dialysis and to prevent discussions on commencing renal replacement therapy for concerns around hyperkalaemia. It would also provide a quality of life benefit avoiding recurrent cannulation to facilitate the standardised medical management of hyperkalaemia.

Conclusion: In conclusion, whilst this may not demonstrate an objective cost benefit, it does show the versatility of patiromer use in clinical practice. We have found an emphasis on usage in the inpatient setting to avoid dialysis and its attendant costs, rather than where its evidence base originates: as a renin-aldosterone blockade enabler in the outpatient setting. We have demonstrated awareness of adhering to the protocol criteria, whilst understanding the pitfalls of the protocol and why the medication has been administered out with of it, especially with regards to dosing. We wish to share our experience with clinicians and raise awareness of their growing armamentarium.

P0322 **OUR EXPERIENCE IN ELECTRONIC CONSULTATION FOR REDUCING WAITING LIST AND OPTIMIZING NEPHROLOGY HEALTHCARE**

Jose Luis Gorriz[1], Rosa De Ramon[2], Isidro Torregrosa Maicas[1], Francesc Moncho[1], Sergio Garcia-Vicente[2], Elena Gimenez-Civera[1], Luis D'Marco[1], Maria Romero-Parra[1], Irina Sanchis[1], Elisa Perez-Bernat[1], Aurora Pérez Ys[1], Isabel Juan-Garcia[1], Miguel Angel Solis[1], Maria Jesã°s Puchades Montesa[1]

[1]University Hospital Clinico. Universidad de Valencia. INCLIVA. Valencia. Spain, Nephrology, València, Spain and [2]University Hospital Clinico., Health information management and Admisision Unit, València, Spain

Background and Aims: Chronic kidney disease (CKD) is recognized as a health problem in the general population; as a result, there is a growing demand for specialist services. This is especially relevant in the Spanish health system which covers the entire population free of charge.

We describe our experience with new e-consultation software that allows specialists to provide clinical recommendations to primary care providers about non-subsidiary patients referred to our Nephrology Department. This system respects current protocols and is based on patient chart review without face-to-face visits, thus avoiding unnecessary time wastage in the healthcare system.

Method: Our Nephrology department covers the metropolitan area of Valencia with 341,972 citizens attended by 16 primary care centers. The Community IT software system allows all doctors (hospitals and primary care) to access the patient's medical records including laboratory, radiology, anthropometric data and treatments. A mailbox, developed as part of the Hospital General's IT system, receives all proposed referrals from primary care doctors to our department. A nephrologist then decides if the e-consultation requires an in-person visit or can be answered as a *non face-to-face* visit. Thus, patient's appointments are scheduled in less than one week (mean 3.8±4.5 days) and the outpatient visit in less than 14 days.

The main referral criteria were: albumin/creatinine ratio> 300 mg/g, eGFR<30 ml/min/1.73 (<45 in <70 years), renal progression, resistant hypertension in CKD patients, electrolyte abnormalities and renal anemia. Patients with conditions that do not meet referral criteria are attended and given the appropriate recommendations via e-consultation. The patient is not required to present at the hospital. We describe the results of e-consultations from 1St September 2017 to 31st December 2019.

Results: A total of 2641 consultations were submitted between September, 2017 to December, 2019 (807 in 2017, 861 in 2018 and 903 in 2019). Of these, 285 (12%) were answered as *non face-to-face* visit (6% of the 2017 e-consultations, 11% from 2018 and 24% from 2019).

The characteristics of the 285 *non face-to-face* e-consultations: mean age: 68.9 ±19.5 years, female: 61.4%, diabetics: 31.2%. The main reasons for referral were: mild/low eGFR (35%), mild albuminuria (10%), administrative questions related to treatments (10%), mild hypertension (4%), mild electrolyte disturbances (2%), subacute renal dysfunction resolved (10%) (mostly NSAIDs), non-nephrology causes (mainly urological) (8%), non-renal pathology (simple renal cysts, other) (10%) and other causes (11%). The re-consult rate was 2% within the first year.

Regarding patients referred with low eGFR, the mean age was 76 ± 14 years (range: 19-98), female sex: 73.9%, eGFR: 39±11 ml/min/1.73m2, serum creatinine 1.4 ± 0.4 mg/dL. Urine alb/creat ratio: 49±127 mg/g. Thirty five percent of them were between 70-79 years and 48% were> 80 years old. For those patients referred with mild albuminuria: mean age was: 57±21 years, male sex: 61%, diabetics: 31%, eGFR: 77±18 ml/min/1.73m2, serum creatinine 0.87±0.27 mg/dL. Urine alb/creat ratio: 83 ± 54 mg/g (range 33-128).

There was a 17 day waiting list to attend an outpatient nephrology clinic in 2016 (previous to the initiation of the e-consultation period). On the contrary, during the study period it was 14 days in 2017 and 4 days each in both 2018 and 2019.

Conclusion: Our experience shows that *non-face-to-face* e-consultation for patients with mild renal pathology promotes the effective management of patients who do not meet remission criteria according to established protocols. It also prevents the remission of a significant percentage of patients, reduces the waiting list and optimizes the healthcare system's resources.

P0323 REVERSIBLE RENAL FUNCTION DECLINE ASSOCIATED WITH NIRAPARIB

Helene Lazareth[1], Nicolas Delanoy[2], COHEN Raphaël[3], Emilie Boissier[2], KARRAS Alexandre[1], Eric Thervet[1], Marie Courbebaisse[3], Nicolas Pallet[4]

[1]Hôpital Européen Georges Pompidou, Nephrology, PARIS, France, [2]Hôpital Européen Georges Pompidou, Oncology, France, [3]Hôpital Européen Georges Pompidou, Physiology, France and [4]Hôpital Européen Georges Pompidou, Biochemistery, France

Background and Aims: Inhibitors of poly-ADP-ribose-polymerase-1 (PARP) are prescribed for the treatment of metastatic breast and ovarian cancers. Clinical data trials suggest that niraparib may not have adverse effects on the kidney.

Method: We present a descriptive case series of renal function parameters of all the patients who received niraparib for maintenance treatment of recurrent ovarian cancer in a tertiary care center. Twenty patients received niraparib for the first time between april 2018 and march 2019 in the Georges Pompidou European Hospital, Paris, France. Four patients were excluded from the analysis because of lack of repeated serum creatinine (Scr) measurements during the first 4 months following niraparib introduction.

Results: The patients ranged in age from 51 to 82 years. All patients were women with high grade serous ovarian carcinoma. Personal medical history of hypertension was present in 68% and diabetes in 18% of patients. All patients received carboplatin and 90% received bevacizumab as maintenance treatment after first-line chemotherapy. Niraparib was introduced on average 3 years (range 2 to 9 years) after the diagnosis of cancer, at a dosage of 200 mg/day in all patients. The median Scr at baseline was 84 µmol/l (range 62 to 114 µmol/l). All patients experienced an increase in Scr level over the 3 months following niraparib introduction. The average max Scr increase was 1.35 times baseline (median Scr 117µmol/l, range 88 to 155 µmol/l, $p<0.0001$ compared to baseline values), and 3 patients (18%) developed stage 1 KDIGO Acute Kidney Injury/ Disease (Scr increase $>$ 1.5-2 fold baseline). None of the cases had biochemical signs of tubular or glomerular injury. Urinary creatinine clearance was higher than urinary clearance of 51Cr-EDTA, making interaction with tubular creatinine secretion unlikely. Kidney biopsy was performed in one patient who developed albuminuria. Microscopic examination identified mild tubular atrophy and interstitial fibrosis without inflammatory lesion Immunofluorescence analysis did not show immune deposits. Mesangiolysis was found in some glomeruli, typical of bevacizumab effects. Niraparib was interrupted in all but 1 patient (95%), because of haematological toxicity (n=7), tumoral progression (n=7) or gastro-intestinal toxicity (n=1). Average Scr level returned to baseline (82 µmol/l, range 62 to 107 µmol/l) over the 2 months following discontinuation.

Conclusion: Niraparib is associated with a systematic and significant increase in Scr (+35%) without obvious sign of tubular or glomerular injury. Renal dysfunction is mainly reversible after discontinuation. Decline of renal function under treatment may not be an incentive to stop treatment automatically. Physicians prescribing this agent should be aware of this complication.

P0324 **SODIUM ZIRCONIUM CYCLOSILICATE TO PREVENT HYPERKALAEMIA IF HAEMODIALYSIS IS POSTPONED DUE TO VASCULAR ACCESS COMPLICATIONS: EXPERIENCE FROM CLINICAL PRACTICE**

Owain Brooks[1], Ashraf Mikhail[1], Chris Brown[1], Mark Gumbleton[2], Justine Jenkins[2], Kaitlin Boyle[2]

[1]Swansea Bay University Health Board, Department of Nephrology, Swansea, United Kingdom and [2]Cardiff University, School of Pharmacy and Pharmaceutical Sciences, Cardiff, United Kingdom

Background and Aims:

Vascular access is a fundamental aspect of haemodialysis (HD) treatment. Vascular access may be compromised due to central venous catheter (CVC) thrombosis, arteriovenous fistula (AVF) or graft (AVG) stenosis, infections or perioperative complications that require urgent resolution or the formation of alternative emergency or definitive access. Sodium zirconium cyclosilicate (SZC) (Lokelma®) is a new oral potassium binder. We offer an insight into SZC treatment to prevent hyperkalaemia in patients where HD is postponed due to vascular access complications.

Method:

Adult prevalent HD patients were included for analysis. Each patient was unable to receive their full scheduled HD treatment due to a vascular access complication. SZC was prescribed on the day HD was not possible (D1) until the vascular access issue was resolved and HD could recommence. The primary efficacy measures were the prevention of increases in serum potassium (sK^+), the safe postponement of HD and the avoidance of emergency hospital admission.

Results:

Four patients receiving thrice-weekly HD (mean age 69 years, all male) received SZC for a mean duration of 3.5 days (min 2 days, max 6 days). No patients were admitted during these acute episodes. The mean pre-dialysis sK^+ on D1 was 6.0mmol/L (K1). No post-dialysis sK^+ values were obtained on D1 because HD was not possible or cut-short (Table 1).

For patients 2 and 3, one and 10 HD treatments preceded the next sK^+ (K2) respectively. sK^+ reduced from 5.8mmol/L (K1) to 4.8mmol/L (K2) for patients 1 and 4 (Table 1). No statistical analyses were undertaken due to the low patient numbers.

HD was delayed beyond the scheduled treatment date for 3 of the 4 patients, with a mean delay of 1.75 days (min 0 days, max 3 days) (Table 2). There was no delay between

Table 1

Patient	HD vascular access type on D1 and summary of complication	Hours of HD received on D1	Pre-dialysis sK^+ (mmol/L) on D1 (K1)	SZC dose from D1	Next recorded pre-dialysis sK^+ (mmol/L) (K2)	The number of HD treatments between K1 and K2	HD vascular access type for the next HD treatment
1	Tunnelled CVC – poor flows, likely thrombosis	0	5.8	10g TDS for 2 days then 10g OD for 4 days	4.8	0	AVF – now ready to use
2	AVF – stenosis	1	6.2	10g OD for 2 days	4.6	1	Non-tunnelled CVC – newly inserted
3	AVF – severe bruising	0	6.2	10g OD for 4 days	5.2	10	AVF – bruising improved
4	Tunnelled CVC – poor flows, likely thrombosis	0	5.8	10g OD for 2 days	4.8	0	Tunnelled CVC – improved flows

Table 1. HD vascular access types at D1 and the next HD treatment, SZC dose, sK^+ K1 and K2 and the number of HD treatments between K1 and K2.

Table 2

Patient	Gap (days) between previous HD and D1	Gap (days) between SZC initiation (D1) and next HD treatment	Total gap (days) between HD sessions in this acute episode	The number of days' delay beyond scheduled HD treatment
1	4	2	6	3
2	0 (1 hour HD on D1)	2	2	0
3	2	3	5	3
4	2	1	3	1

Table 2. Gap (days) between the previous HD treatment and D1, gap (days) between SZC initiation (D1) and the next successful HD treatment, total gap (days) between HD treatments and the number of days' delay after the scheduled HD treatment.

Figure:

HD treatments for patient 2, who only received 1 hour HD treatment on D1. The last full HD treatment for patient 2 was 3 days prior to D1. A gap between SZC initiation (D1) and the next HD treatment was seen for all four patients, with a mean gap of 2 days (min 1 day, max 3 days) (Table 2).

Conclusion:

Sodium zirconium cyclosilicate can be used to successfully reduce, or avoid an increase in sK^+ in mild to moderate hyperkalaemia, avoid emergency hospital admission and allow HD to be postponed for a valuable short period until HD vascular access can be re-established.

P0325

FREQUENCY AND PREDICTORS OF NON URINARY INFECTIONS AMONG THE ADULT PATIENTS WITH STERILE PYURIA ATTENDED IN NEPHROLOGY DEPARTMENT OF BSMMU, BANGLADESH

Hossain Md Ismail[1], Dr. A H Hamid ahmed Hamid[2], Dr.Mirza Sumaiya Tanzin Tanzin[3], Rafi Nazrul Islam[4]

[1]Sir Salimullah Medical College & Mitford Hospital, Dhaka-1100, Department of Nephrology, Dhaka, Bangladesh, [2]Bangabondhu Shekh Mujib Medical University, Department of Nephrology, Dhaka, Bangladesh, [3]Dhaka Medical College Hospital, Department of Anaesthesiology, Dhaka, Bangladesh and [4]BIRDEM, Dhaka, Department of Nephrology, Dhaka, Bangladesh

Background and Aims: Urinalysis is a test commonly ordered, especially when the patient has a febrile illness. In most cases it provides useful information, but it can sometimes be misleading. A significant proportion of patients with acute febrile illness have transient pyuria without bacteuria. Identification and management of such cases could be improved by better predictive models.To determine predictors of non urinary infections in adult patients with sterile pyuria and to develop a preliminary predictive model.

Method: This cross sectional study was done in the department of Nephrology, BSMMU, during the period of September 2016 to August 2017. All adult patients with sterile pyuria were included in the study. A total number of 233 cases who had urinary WBCs >5 per high power field (HPF) with a negative culture were selected as sample by convenient sampling technique. We performed detailed clinical and laboratory investigations to identify potential causes of the sterile pyuria. Patients were then divided into two groups, those with causative factors within the urinary tract and those with causative factors outside of the urinary tract. Logistic regression was used to create a model to predict causative group.

Results: Most 196(84.1%) patients were found to have disorders related to urinary tract (Group A) and 37(15.9%) patients had infections outside of the urinary tract (Group B). Significant proteinuria and urinary casts were more common in Group A, while urinary WBCs>20/hpf and microscopic hematuria were more common in Group(B). All of these differences were statistically significant ($p<0.05$). In the logistic regression model patients with sterile pyuria with fever (OR 32.9) and/or pyuria with urinary WBC>20/HPF (OR 2.14) were more likely to involvement outside of the urinary tract. Those with urinary tract symptoms (OR 0.28) and/or proteinuria (OR 0.20) were more likely to have renal and urinary tract involvement.

Conclusion: In patients attended to the nephrology department, sterile pyuria was more likely to have its origin in the urinary tract if there were urinary tract symptoms and/or proteinuria and less likely if there was fever or urinary WBCs >20/hpf.

Diagnosis	Number of patients	Percentage
Disorders related to urinary tract (Group A)	196	84.1
Infections outside the urinary tract (Group B)	37	15.9

Urinary characteristics	Diagnosis Group A(n=196)		Group B(n=37)		P value
	n	(%)	n	(%)	
Protein					
Nil	75	(38.3)	22	(59.5)	
(+)	32	(16.3)	7	(18.9)	
(++)	26	(13.3)	8	(21.6)	0.002[s]
(+++)	42	(21.4)	0	(0.0)	
(++++)	21	(10.7)	0	(0.0)	
RBC					
0-5/hpf	118	(60.2)	31	(83.8)	
6-15/hpf	54	(27.6)	6	(16.2)	
15-30/hpf	5	(2.6)	0	(0.0)	0.032[s]
≥30 /hpf	19	(9.1)	0	(0.0)	
WBC					
≤20 /hpf	136	(69.4)	19	(51.4)	0.034[s]
>20/hpf	60	(30.6)	18	(48.6)	
Urinary cast	48	(24.5)	3	(8.1)	0.027[s]

s= significant

P value reached from chi square test

	Adjusted OR	95% CI Lower	Upper	P Value
Fever	32.90	10.57	99.96	0.001[s]
Urinary tract symptom	0.28	0.09	0.85	0.024[s]
Dysuria	0.10	0.02	0.47	0.003[s]
Frequency	0.32	0.06	1.60	0.165[ns]
Urgency	0.25	0.01	3.51	0.303[ns]
Flank pain	0.01	0.001	1.42	0.998[ns]
Abdominal pain	0.47	0.04	6.17	0.563[ns]
Renal impairment in terms of Serum creatinine (μmol/l)	5.96	0.65	54.28	0.133[ns]
Urinary cast	0.21	0.04	1.10	0.065[ns]
Proteinuria	0.20	0.05	0.77	0.019[s]
Urinary WBCs (>20/hpf)	2.14	1.05	4.37	0.036[s]
Serum albumin	1.22	0.35	4.32	0.758[ns]
CRP (Raised)	0.84	0.31	2.33	0.742[ns]

s=significant, ns= not significant

Multivariable logistic regression analysis was preformed

Figure: Diagnosis of the study population (n=233)

Figure : Bar diagram shows renal status of the study population

P=0.047

P value reached from chi square test

Multivariable logistic regression analysis for infections outside the urinary tract

P0326 EFFECT OF PRAVASTATIN ON ERYTHROCYTE MEMBRANE FATTY ACID CONTENTS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Sumi Lee[1], DongHo Choi[1], Yu In Jeong[1], Young Ki Son[1], Seong Eun Kim[1], Won Suk An[1]

[1]*Dong-A University, Department of Internal Medicine, Busan, Korea, Rep. of South*

Background and Aims: Treatment with statin has been decreased the risk of cardiovascular events in patients with chronic kidney disease (CKD). Erythrocyte membrane oleic acid contents are significantly higher in patients with acute coronary syndrome than control subjects. Still, there is no report about the effect of statin on erythrocyte membrane fatty acid (FA) including oleic acid. The aim of this study was to evaluate the effect of pravastatin on the erythrocyte membrane FA in patients with CKD.

Method: Sixty two CKD patients were enrolled in this single arm randomized clinical trial and this trial was conducted at two centers from Jan 2017 to March 2019 (NCT02992548). Pravastatin with dose of 20mg was initially treated for 24 weeks. Pravastatin dose was increased to 40mg after 12 weeks, if it is necessary to control dyslipidemia. The primary outcome of this study was the change of erythrocyte membrane FA including oleic acid after pravastatin treatment for 24 weeks. We checked total cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol and adiponectin for secondary outcome at baseline and after 24 weeks. Erythrocyte membrane FA contents were measured by gas chromatography at baseline and after 24 weeks.

Results: Forty-five patients finished this study (age: 59.2±12.4 years, male: 42.2%, diabetes: 48.9%). There was no adverse effect related with pravastatin. Baseline serum creatinine was 1.5±0.7 mg/dL and estimated glomerular filtration rate was 54.2±27.3 ml/min/1.73 m^2. Compared to baseline, total cholesterol (223.1±50.8 mg/dL *vs.* 168.4±32.5 mg/dL), LDL-cholesterol (149.1±35.3mg/dL *vs.* 100.1±25.4 mg/dL) and C-reactive protein were significantly decreased after pravastatin treatment. There were no significant changes in triglyceride, HDL-cholesterol, serum creatinine, amounts of proteinuria and adiponectin levels. Saturated FA, oleic acid and arachidonic acid contents of erythrocyte membrane were significantly increased after pravastatin treatment compared to baseline levels. Polyunsaturated FA (PUFA) and linoleic acid were significantly decreased after pravastatin treatment compared to baseline. Decreased tendency of eicosapentaenoic acid and omega-3 index were found after pravastatin treatment.

Conclusion: Linoleic acid or omega-3 FA supplementations may be necessary to recover erythrocyte membrane FA changes, when pravastatin is used for dyslipidemia treatment in CKD patients. Further study for reducing cardiovascular events are necessary by using combined PUFA and pravastatin treatment.

P0327 **SUCCESSFUL ACHIEVMENT OF LONG-TERM COMPLETE REMISSION OF LUPUS NEPHRITIS IN A PATIENT WITH SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS AND SECONDARY INFECTIOUS COMPLICATOINS.**

Anna Bespalova[1], Tatiana Bondarenko[1], Natalya Kozlovskaya[1]
[1]A.K. Eramishancev City Clinical Hospital, nefrological, Moscow, Russia

Background and Aims: A significant contribution to the structure of mortality in SLE is made by infectious complications, which complicate the course of SLE and complicate the management of patients due to the impossibility of prescribing immunosuppressive therapy in full.

Method: A clinical case of successful achievement of LN remission in a patient with severe SLE and secondary APS is described, despite the development of secondary infectious complications and the inability to fully immunosuppressive therapy.

Results: A 42-year-old woman has been observed at the clinic from autumn 2013 to the present. Since the end of Aug.2013 she got a severe dyspnea, generalized edema, ulcers of the legs, blood pressure persistently increased to 180/110 mm Hg, diuresis decreased.

Laboratory examination at admission in Oct.2013: (table 1), polyserositis, non-inclusive thrombosis of the posterior tibial vein on the left.

An immunological examination: anti-dsDNA 101.6 U/L, ANA 5.2, C3 complement fragment 0.29 g/L, antibodies to beta-2-glycoprotein-1 55.7 U/ml, positive lupus anticoagulant.

Intravenous methylprednisolone at a dose of 1000 mg/day for 3 days plus high dose CYC at a dose of 800 mg/day for 1 days was started, followed by prednisone 60 mg/day. This intravenous pulsewas repeated after 3 weeks.

Renal biopsy in Nov.2013: diffuse proliferative glomerulonephritis with 7% cellular crescents, ISN/RPS class IV LN.

Positive dynamics in Dec.2013 (table 1).

By mid-Dec.2013, the patient had complaints of pain and limited range of motion in the right shoulder joint, the appearance of edema in this region. According to the puncture of the joint cavity, MRI, purulent arthritis of the right shoulder joint was diagnosed with the formation of intermuscular phlegmon of this area.

Sepsis was diagnosed. The patient underwent emergency surgical drainage of phlegmon, followed by repeated revisions of this area. Prescribed meropenem at a dose of 3 g/day.

Implementation of the complete immunosuppressive therapy protocol was impossible; a gradual decrease in the dose of prednisone per os was started. Due to the continued activity of SLE, in January 2014, a repeated intravenous pulse methylprednisolone without CYC was performed.

Since Dec.2013, the patient has not received cystostatics. But despite it positive dynamics in Feb.2014 (table 1) .

In Mar.2014 current treatment was hydroxychloroquine 400 mg/day, prednisone 15 mg/day, azathioprine 100 mg/twid.

After 2 years of complete remission of LN in April 2016: prednisone 10 mg/day, hydroxychloroquine 400 mg/day, azathioprine 50 mg/twid. After another 2 years of complete remission of LN in 2018: prednisone 5 mg/day, hydroxychloroquine 400 mg/day. During the observation, a complete clinical and laboratory remission of SLE was noted.

Laboratory examination at admission in Oct.2019: complete remission of SLE (table 1). The patient takes prednisone 5 mg/day, hydroxychloroquine 400 mg/day.

The patient has limited mobility of the right shoulder joint, but complete loss of function did not occur. According to the control MRI there are the formation of aseptic necrosis of the head of the right humerus.

Conclusion: Infectious complications remain one of the leading causes of mortality in patients with SLE. The uniqueness of this clinical case in the successful achievement of long-term complete remission of SLE, despite the secondary infectious complications. The success of achieving long-term remission of SLE is associated with the onset of immunosuppressive therapy as soon as possible from the debut of the disease, with the conduct in the maximum allowable volumes. The morphological picture with a small % cellular crescents was also a favorable factor.

Table 1.

	Hв, g/L	Leu,10^9/L	Platelets,10^9/L	TP, g/L	Cr,umol/L	Anti-dsDNA,U/L	Proteinuria, g/L	Erythrocyturia
Oct 2013	116	4,2	88	39	138	101,6	6,62	100
Dec 2013	114	6,2	189	42	92		2,3	40
Feb 2014	120	10,9	236	64	86	3,9	0,9	20
Oct 2019	129	6,2	193	71	67	2,3	no	no

P0328

DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME: THE GREAT MIMICKER SECONDARY TO LENALIDOMIDE IN PERITONEAL DIALYSIS

Silvia Cazzato[1], Riccardo Magistroni[1], Elisabetta Ascione[1], Monica Maccaferri[1], Gianni Cappelli[1]

[1]*Policlinico of Modena University Hospital of Modena, Modena, Italy*

Background and Aims:

DRESS syndrome is a rare, idiosyncratic, potentially life-threatening adverse drug reaction, characterized by latent period after intake of the inciting drug (2-6 weeks), fever higher than 38.5°C, skin eruptions (usually pruritic maculopapular rash or diffuse erythematous eruption), eosinophilia (in 66-95% of patients), mononucleosis-like atypical lymphocytes (27-67% of pts), thrombocytopenia, lymphadenopathy (in 54% of pts) and multiple organ involvement. In 50-60% of patients, two or more organs are involved, most frequently liver (hepatomegaly, hepatitis with ALT> 2 times and ALP> 1,5 times the upper limit), kidney (acute interstitial nephritis, most often induced by allopurinol) and lung (interstitial pneumonia). Cardiovascular involvement occurs lately (up to four months after recovery) with myocarditis, decreased LV function and elevated troponin. Different mechanisms have been involved in the pathogenesis of DRESS syndrome, including detoxification defects leading to reactive metabolite formation and subsequent immunological reactions, slow acetylation and reactivation of human herpes, including Epstein-Barr virus and HHV-6. Cacoub et al reported 172 cases of DRESS: the most frequently reported "trigger-drugs" were carbamazepine, allopurinol, sulfasalazine, phenobarbital, nevirapine and HHV-6 infections were positive in 80% of cases. Interestingly, the culprit drug could be able to trigger viral reactivation, inducing a pathogenic anti-viral CD8+ response. According to available literature, the drug should be withdrawn and, in cases of visceral involvement, systemic steroids are indicated (1 mg/kg orally with slow taper over 3-6 months). In severe cases, other therapies include IVIG, plasmapheresis and immunosuppressant drugs.

CASE REPORT

A 72-year-old male, affected by ESKD in peritoneal dialysis and hypokinetic heart disease, started lenalidomide for multiple myeloma with bone involvement. After 18 days he presented a violet maculopapular rash involving >50% of his body, fever (38,5 °C), leukopenia with CRP <0,8 mg/dl. Lenalidomide was withdrawn and started oral steroid, anti-histamine and levofloxacin. One week later he was admitted for a syncopal episode. Laboratory tests revealed leukocytosis (12.250/mm̊), eosinophilia (until 56%, 4.550/mm̊) and cholestatic-cellular liver damage (ALT 1448 U/l, ALP 308 U/l) requiring albumin infusion.

Extensive infectious and autoimmune workup was negative, including ANA test, immunological liver diseases tests, blood cultures, viral/bacterial tests, except for HHV6 reactivation (420 copies/ml). US abdominal study was negative, while DLCO test showed an important diffusive deficit. ECHO showed a reduced LV ejection.

Skin biopsy demonstrated sparse vacuolization of epidermis and dermal-epidermal inflammation with some eosinophils and CD8+ T cells, suggesting a drug reaction.

For clinic and laboratory features RegiSCAR score system and Japanese consensus group categorized this case as "definite DRESS" respectively with score 6 and 7. So we started IVIG (1 gr/Kg for 2 days) and prednisone with reduced dose for comorbidities (0,8 mg/Kg daily, tapered to 0,6 mg/Kg after 1 week); the patient gradually improved but after 1 week, DRESS syndrome relapsed with rash, elevated GOT and GPT and troponin until 330 ng/l with normal ECG; he has just started steroid bolus and IVIG.

Conclusion: The variety of drugs, the clinical course with slow resolution and relapse and HHV-6 reactivation suggest that drugs cannot be the sole etiology of DRESS. Precise mechanism of lenalidomide in DRESS syndrome is not clear and its immunomodulatory activity could contribute in the hypersensivity reaction. Only few cases are reported in literature, but with the increasing use of lenalidomide a broad workup and a careful approach are important for a fast diagnosis

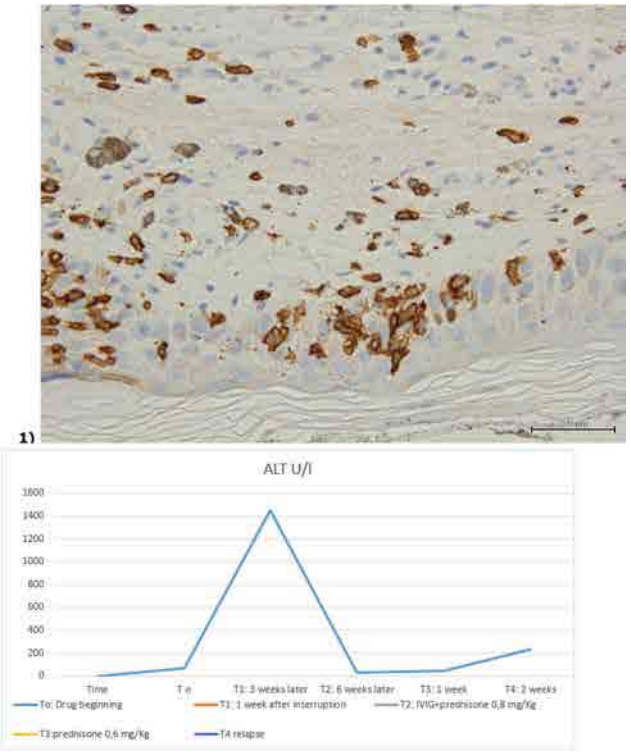


Figure:1

Epidermis and dermal-epidermal inflammation with CD8+ T cells

P0329 CLINICAL SIGNIFICANCE OF CREATININE VARIABILITY AND ITS IMPACT ON CARDIOVASCULAR OUTCOMES

Soojin Lee[1], Yeonhee Lee[1], Sehoon Park[2], Kyungdo Han[3], Yaerim Kim[4], Jung-Hyun Kim[5], Kwon Wook Joo[1,2], Dong Ki Kim[1,2]

[1]Seoul National University Hospital, Internal medicine, Seoul, Korea, Rep. of South, [2]Seoul National University College of Medicine, Seoul, Korea, Rep. of South, [3]Catholic University of Korea, Department of Biostatistics, Seoul, Korea, Rep. of South, [4]Keimyung University Dongsan Hospital, Internal medicine, Daegu, Korea, Rep. of South and [5]PaiChai University, Department of Home Economics Education, Daejeon, Korea, Rep. of South

Background and Aims: Linear decline of glomerular filtration rate (GFR) is associated with aggravating the patient outcomes. Serum creatinine, which is commonly used for estimating GFR, often fluctuates throughout the serial measurement. The clinical significance of creatinine fluctuation among the general population whose renal function is prior to chronic kidney disease (CKD) development had not been demonstrated yet. Thus, we investigated the study to evaluate the impact of creatinine variability on patient outcomes.

Method: A nationwide retrospective cohort study was performed usaing the database of Korean National Health Insurance System. Adult patients who received national health screening program and measured creatinine for $\geq$3 times between 2012 and 2016 were considered. Those who previously developed CKD were excluded. The variability of creatinine values were presented with variability independent of mean (VIM). The patients were classified into quartiles of the VIM and Q4 presented highest variability of creatinine. Then, the risks of myocardial infarction (MI), stroke and death were assessed according to the extent of variability.

Results: During the median follow up of 3.27 years, 3,509,899 participants were examined for association of creatinine variability and cardiovascular outcomes. Participants with higher creatinine variability were significantly associated with elevated risk of MI (hazard ratio (HR) (95% confidence interval (95% CI)) 1.11 (1.04-1.18), stroke (HR (95%CI) 1.06 (1.00-1.13)) and death (HR (95%CI) 1.15 (1.09-1.21)), compared to those with the lowest quartile of creatinine variability.

Conclusion: Increased creatinine variability exhibited association with elevated risk of MI, stroke and death. In general population, whose renal function is prior to CKD development, monitoring of creatinine variability needs to be considered as the parameter of predicting the adverse outcomes, in addition to the decline of GFR.

P0330 RENAL INVOLVEMENT IN OBSTETRIC CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

Yuia Korotchaeva[1], Natalia Kozlovskaya[2], Kseniya Demyanova[2]

[1]I.M. Sechenov First Moscow State Medical University, Russia and [2]Peoples' Friendship University of Russia, Russia

Background and Aims: Catastrophic antiphospholipid syndrome (CAPS) is an uncommon, often fatal, variant of the antiphospholipid syndrome (APS) that defined as multiorgan thrombosis affecting three and more organs confirmed by histopathology of small vessel occlusions in at least one organ or tissue.

The development of CAPS in pregnancy poses many diagnostic challenges as a result of its overlap with other obstetric TMA syndromes. Because of the high associated mortality rate, prompt recognition and treatment are paramount. Some studies have shown that complement activation contributes in antiphospholipid antibodies (aPL) mediated thrombosis in CAPS. Short treatment with eculizumab can result in a rapid improvement of pts with TMAs other than aHUS with persisted hematological and renal symptoms worsened despite treatment of the TMA-inducing condition.

Aims: Analysis of renal involvement, course and outcomes of obstetric CAPS

Method: From 2016 to 2019 we observed 11 pts aged 19 - 38 years with CAPS, occurred during pregnancy (from 16 to 40 weeks) or postpartum period. Only 1 patient had a diagnosis of APS with SLE before pregnancy. 5 out of 11 pts had the first pregnancy, 6 pts already had a history of pregnancy, but all previous pregnancies were failed: miscarriage or antenatal death of the fetus.

Results: Preeclampsia (PE) and/or HELLP syndrome, surgical intervention in combination with obstetric complications (bleeding, manual separation of the placenta, Caesarean delivery, etc.) preceded CAPS manifestation in all pts. Moreover, in 1 patient with SLE, secondary APS and triple aPL positivity, HELLP syndrome developed very early stage of 16 weeks.

In all cases, aPL circulation was detected (anti-cardiolipin antibodies and/or anti-beta-2-glycoprotein-1, lupus anticoagulant). All pts (100%) had complete MAHA (microangiopathic hemolysis): hemoglobin level 73,0 ± 19,2 g/l, LDH level 1066,7 ± 1056,7 U/l, schizocytosis), thrombocytopenia (122,0±157,9x10μL) and multi-organ failure (MOF): kidney damage (81%, 9 of 11), liver (63%, 7 of 18), gastrointestinal tract, heart, lungs, central nervous system - 55% (6 of 11), skin (gangrene 1-9%). A feature of kidney involvement was the development of AKI (mean creatinine level 207,6 ±140,3 mg/dl, oliguria or anuria) not all pts (9 of 11), in 2 case was observed only minimnal urinary syndrome without increasing sCr.

All pts underwent traditional treatment, including plasma exchange and/or plasma infusions+corticosteroids+anticoagulants, which was effective in 6 out of 11 pts. In the 2 most severe plasma-resistant cases complement-blocking treatment with eculizumab was prescribed, with rapid positive dynamics was observed: the relief of MOF, hematological parameters normalization after the first infusion and recovery of kidney function by the end of the induction course.

Favorable outcome with complete normalization of lab parameters and clinical improvement with kidney function normalization was achieved in 8 of 11 women. In 1 patient chronic kidney disease (CKD) stages 3B has occurred as outcome of AKI. 2 pts died despite ongoing therapy with PT + ST+IG+AC from progressive multiple organ failure.

Conclusion:

1. Complicated obstetric history in patients with acute obstetric TMA requires mandatory exception of CAPS

2. Proven role of complement system involvement in the pathogenesis of CAPS gives a reason for the complement-blocking therapy appointment in severe postpartum TMA, which increases the patients' chance of recovery.

P0331

ASSESSMENT OF DELIVERY OF NICE APPROVED USE OF TOLVAPTAN (JINARC) IN ADULTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE IN A UK RENAL CENTRE

Aaron Acquaye[1], Kate Naylor[2], Sunil Bhandari[1]

[1]Hull University Teaching Hospitals NHS Trust, Renal Medicine, Kingston upon Hull, United Kingdom and [2]Hull York Medical School, Undergraduate Medicine, Kingston upon Hull, United Kingdom

Background and Aims: Until recently, the management of ADPKD has largely been limited to lifestyle changes (smoking cessation, salt avoidance and diet with weight loss) and tight blood pressure control, in addition to kidney pain management and prompt treatment of complications such as infections. The approval of Tolvaptan, a highly selective vasopressin V_2 receptor antagonist, by NICE, following the pivotal TEMPO 3:4 trial provides clinicians with an opportunity to modify the progression of ADPKD and preserve kidney function. Tolvaptan works by slowing cyst growth patients with ADPKD (and therefore potentially reducing kidney pain, urinary tract infections and haematuria). During the TEMPO 3:4 trial, a reversible elevation ($>$ 3X upper limit) of liver enzymes was observed in 4.4% patients taking tolvaptan vs 1% on placebo. The onset of liver injury was between 3 – 14 months of initiation of tolvaptan; therefore, monthly blood tests are required to mitigate the potential injury associated with the increase in liver enzymes. The main side effects are polyuria and thirst.

The aims for the audit were

- To assess compliance of tolvaptan therapy
- To assess the tolerability of the side effects of tolvaptan
- To assess the feasibility of a pharmacist led, consultant backed tolvaptan clinic
- To measure the retention rate among patients on tolvaptan therapy

Method: We carried out a prospective questionnaire-based study on all patients who were on tolvaptan therapy. All patients received a comprehensive explanation of the merits and side-effects of Tolvaptan with written literature and a copy of their initial assessment consultation prior to commencement of therapy.

In addition, we reviewed patients' clinic attendances, relevant biochemical results and liver function test as per licence agreement tolvaptan therapy. This was approved by the Hull University Teaching Hospitals (HUTH) NHS Trust Audit department with a signed Clinical Governance Form 1.

Results: In total, 27 patients, consisting of 18 males and 9 females [mean age 44.5yrs] and all Caucasian on tolvaptan therapy were evaluated. The median duration of treatment was 10months.

Two patients [7.4%] dropped out of treatment: one patient opted out of treatment due to the polyuria interfering with his job requirements and the other had relocated to another country; giving HUTH a retention rate of 92.6%.

55.5% of patients responded to not having missed a dose of drug at any time at any time despite a significant number experiencing side-affects (Figure1). Some purposely missed medication due to a social event.

Although 100% of patients did respond to experiencing side effects of tolvaptan, 74% of patients said it did not interfere with their quality of life. 88.8% of patients were on the full dose of 90mg in the morning and 30mg after 8 hours.

The Tolvaptan clinic in HUTH is run as a pharmacist led with consultant oversight. Currently no issues have arisen but the patients' view of a pharmacist led-clinic is currently being studied.

Conclusion: This study demonstrates that despite a number of expected side-affects; with good patient education and follow-up, few patients stopped therapy and most patients remain compliant to tolvaptan therapy. Currently a pharmacist led, consultant backed tolvaptan clinic has not adversely affected this success.

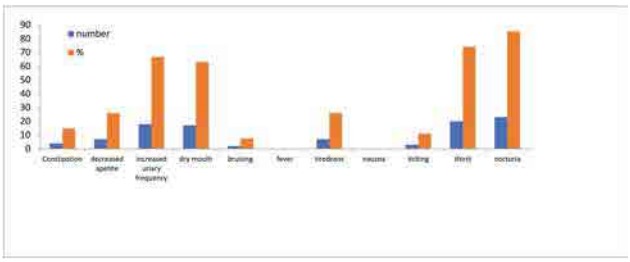


Figure: The percentage of patients experiencing side affects from Tolvaptan therapy.

P0332 DIAGNOSTIC, THERAPEUTIC AND EVOLUTIONARY FEATURES OF KIDNEY DISEASE IN MULTIPLE MYELOMA

Nessrine Breik[1], Barbouch Samia[1], Mariem Najjar[1], Safa Fattoum[1], Sawsen Ben Nsira[1], Seif Azaiez[1], Amel Harzallah[1], Syrine Karoui[2], Imen Gorsane[1], Fethi Benhmida[3], Monther Ounissi[1], Taieb Benabdallah[1]

[1]Charles Nicolle Hospital, Department of Nephrology, Dialysis and Transplantation, Tunis, Tunisia, [2]Mahmoud el Matri Hospital, Department of Nephrology and Dialysis, Ariana, Tunisia and [3]Charles Nicolle Hospital, Research Laboratory of Kidney Diseases (LR00SP01), Tunis, Tunisia

Background and Aims: Multiple myeloma (MM) is a malignant disease of plasma cells. It's is characterized by clonal proliferation of malignant plasma cells producing monoclonal proteins and causing organ damage. Kidney injury is a common complication of multiple myeloma. Multiple pathogenic mechanisms can contribute to kidney injury in the patient with myeloma, some of which are the result of nephrotoxic monoclonal immunoglobulin and some of which are independent of paraprotein deposition.

Method: We conducted a retrospective study, from January 1974 to June 2019, including all cases of multiple myeloma with renal impairment treated in our Department. The objective of this study is to analyze the epidemiological and clinico-biological characteristics of MM with renal impairment and to identify the predictive factors of mortality.

Results: We collected 196 cases. The average age was 63.47 years (31-86 years) with a male predominance (sex ratio 1.27). The circumstances of discovery was dominated by asthenia, anorexia and weight loss in 150 cases (76.5%). Renal involvement was present at the time of diagnosis of myeloma in 138 patients (70.4%) with an average serum creatinine level of 686.42 µmol/l (92-2960 µmol/L). The average hemoglobin level was 8.05 ± 2.4 g/dl. The average 24-hour proteinuria was 2.62 ± 2.11 g/24h. The renal biopsy puncture was performed in 48 patients (24.4%), revealing myelomatous tubulopathy in 16.32% of cases, AL amyloidosis in 5.1% of patients, Randall disease in 3.06% of patients, nodular glomerulosclerosis in 1% of cases and membranous nephropathy in one patient. In our series, 170 patients received chemotherapy. Of the patients, 25.5% required hemodialysis at the time of diagnosis of MM. In our series, 66.83% progressed to the end stage renal disease, 25.5% were in partial remission and 2.05% in total remission. The causes of death were dominated by infectious complications (14.97%). The average renal survival was 4 months. The prognostic factors correlated with poor renal survival were tobacco ($p = 0.01$), serum uric acid> 600 µmol/l ($p = 0.04$) and 24-hour proteinuria> 5g/24h ($p = 0.009$).

Conclusion: Renal involvement is frequent in multiple myeloma. The spectrum of renal lesions is heterogeneous, and it determines the management and prognosis of MM so the factors associated with renal recovery should be studied further.

P0333

ACQUIRED HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN A PATIENT WITH EMPHYSEMATOUS PYELONEPHRITIS AND SEVERE SEPSIS: A CASE REPORT

Mahesh Kota[1], Girish Kumthekar[1], Rajasekara Chakravarthi M[1], Jyothsna G[1], Dinesh Katre[1]

[1]*Star hospital,Road no-10, Nephrology, Hyderabad, India*

Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a rare disorder of uncontrolled immune activation.Incidence in the adult population remains unclear. Primary HLH is caused by genetic mutations affecting the cytotoxic function of T lymphocytes and natural killer (NK) cells and typically presents in young children. Secondary HLH occurs in the setting of infectious, malignant, rheumatologic, or metabolic conditions. Various infections have been described as triggers. The diagnosis of HLH is particularly challenging, as many features overlap with other causes of severe illness including sepsis and hematologic malignancy.

Background: 53-years-old male patient presented to a hospital elsewhere with complaints of fever, dysuria and malaise for 1 week. On evaluation, he was diagnosed as bilateral pyelonephritis with right sided emphysematous pyelonephritis,with urosepsis, acute kidney injury (AKI) on chronic kidney disease (CKD). Due to severe azotaemia and acidosis, patient required dialytic support (SLED) on 2 occasions. Subsequently, patient underwent bilateral DJ stenting, right renal papilla extraction and optical urethrotomy.Due to persistent fever and not improving general wellbeing patient was shifted to Star hospital for further management.

Course in hospital: Patient presented with severe sepsis and empiric antibiotic therapy started after sending appropriate cultures (date of admission 18.7.19). As cultures were suggestive of CRBSI, dialysis catheter removed and antibiotics continued. He improved initially, however he again had high-grade intermittent fever,then right sided PCNL and drainage of perinephric collection was done. Post procedure patient developed septic shock, hyperkalemia and acidemia. Left IJV dialysis catheter was placed and initiated on SLED. He underwent right nephrectomy and left DJ stent exchange in view of persistent fever despite using broad spectrum antibiotics and antifungals. X-ray chest showed pulmonary edema and 2D echo revealed global hypokinesia. Patient further deteriorated, vasopressor requirement increased and required intubation and mechanical ventilation on 1.8.19. Patient received GM-CSF in view of leukopenia. To look for other causes of non-responding sepsis, serum ferritin and interleukin 6 (IL-6) were tested. Ferritin was 4532 ng/ml& IL-6 was 531 pg/ml as on 1.8.19. Bone marrow aspiration and biopsy (3.8.19) revealed acquired hemophagocytosis,hence he was started on corticosteroids (1 mg/kg/day prednisolone equivalent) and other appropriate antibiotics continued. Gradually fever subsided and hemodynamic improved. As patient showed adequate respiratory attempts and acceptable oxygenation, he was extubated on 9.8.19. Patient remained on alternate day haemodialysis.

Patent was discharged from hospital on 19.8.19 with tunnelled right IJV catheter for haemodialysis. Corticosteroids (prednisolone) tapered off gradually over a period of 8 weeks. After 8 weeks; patient remains dialysis dependant but back to work and routine life.

Conclusion: In events of non-responding sepsis, immunological disorders could be screened for and treated accordingly. Seemingly, treating immunological disorders and sepsis is seen antagonistic but might be mutually complementary as is seen in this particular case with acquired HLH where patient responded to immune suppression with corticosteroid. In literature search, we could not find association of HLH with emphysematous pyelonephritis. Hence, this could be a unique case of immune activation in a patient with complicated UTI, AKI and resulting in dialysis dependency. Moreover, antibiotic resistance and scarcity of new antibiotics are two more reasons to search for immune dysregulation in sepsis. As many of these cases could be immune dysregulation and not infection per se.

P0334 **HEMOLYTIC UREMIC SYNDROME: CLINICAL PRESENTATION, LABORATORY FINDINGS, MANAGEMENT AND OUTCOMES**

Issa Al Salmi[1,2], AbdelMasiah Metry[1], SUAD Hannawi[3]

[1]The Royal Hospital, The Renal Medicine Department, Bausher, Muscat, Oman, [2] and [3]Ministry of Health Head Office, Dubai, United Arab Emirates

Background and Aims: Hemolytic-uremic syndrome (HUS) is a disease that has been described as a triad of hemolytic anemia, thrombocytopenia and renal impairment. There are two types of HUS, typical and atypical. HUS remains a leading cause of acute renal injury in children and is increasingly recognized as a cause of renal failure in adults. In our study we evaluated the demographic features, clinical characteristics, management and outcome of HUS.

Method: This is a descriptive study evaluating all cases of Hemolytic Uremic Syndrome (HUS) that have been admitted at Royal Hospital (RH) Oman in the period between 2008 and 2017.

Results: Thirty-six patients identified. The mean age (SD) of 10.68 (14.07) years.

Eighteen (50%) presented with abdominal pain, nausea, vomiting and diarrhea, 9 (25 %) with hypertension, 23 (64 %) with acute kidney injury (AKI), 6 (16.67%) with seizure, 2 (5.56%) with confusion and 1 (2.78%) with cerebrovascular accident (CVA).

Twenty-one (58.33 %) diagnosed as typical HUS of which 19 with Shiga toxin producing Escherichia Coli (STEC) HUS and 2 had post Streptococal HUS.

Six (16.67%) diagnosed with aHUS, 2 (5.56%) with HELLP, 2 (5.56%) with G6PD, 3 (8.33%) with Autoimmune hemolytic anemia (AIHA), one (2.78%) with congenital TTP and 1 (2.78%) with post partum HUS.

Hb	**7.95 (2.35)**	**11.9 (1.76)**	**0.0000**
TLC	**15.22 (9.06)**	**7.13 (2.75)**	**0.0000**
ANC	**8.99 (7.60)**	**2.66 (1.71)**	**0.0001**
L.C	**4.48 (2.80)**	**3.50 (1.64)**	**0.0435**
EC	**0.25 (0.33)**	**0.34 (0.29)**	**0.2119**
MC	**1.46 (1.08)**	**0.60 (0.36)**	**0.0001**
Plt	**95.57 (97.27)**	**282.56 (89.52)**	**0.0000**
RC	**5.26 (4.31)**	**2.42 (1.75)**	**0.0080**
C-reactive protein	**76.40 (66.54)**	**14.64 (21.61)**	**0.0005**
ESR	**50.00 (46.87)**	**43.33 (51.68)**	**0.4226**

Variable	Mean 1 (SD)	Mean 2 (SD)	P value
Calcium	2.38 SD 0.18	2.47 (0.13)	0.0269
phosphorus	2.02 (0.68)	1.63 (0.24)	0.0019
Iron	9.08 (4.94)	14.53 (4.83)	0.0657
Transferrin saturation %	19.22 (8.41)	28.78 (13.60)	0.1755
Bilirubin	33.68 (81.43)	8.65 (5.19)	0.0884
Alanine transferase	100.59 (123.85)	28.78 (38.20)	0.0038
Alkaline phosphatase	187.84 (243.75)	196.16 (83.85)	0.8583
Albumin	27.47 (7.13)	36.47 (4.21)	0.0000
Parathyroid hormone	19.56 (15.59)	9.6 (10.29)	0.2480
Urine protein creatinine ratio	2088.86 (3700.59)	75.46 (133.91)	0.0224
Urea	23.73 (13.33)	7.14 (5.49)	0.0000
Creatinine	304.88 (205.48)	96.33 (129.23)	0.0000
Estimated glomerular filtration rate	22.73 (24.72)	63.33 (25.16)	0.0000
Bicarbonate	16.12 (5.78)	23.36 (3.34)	0.0000
Uric acid	619.75 (248.73)	348.38 (142.21)	0.0420
Compliment 3	862.54 (282.55)	1058.45 (418.99)	0.090

Figure:

Twenty three (63.89%) needed renal replacement therapy (RRT), while remaining 13 (36.11%) did not require RRT.

Eleven (30.56%) received plasma exchange, 5 (13.89%) received Eculizumab while 2 (5.56%) received plasma infusion and 1 (2.78%) patient received Rituximab.

The majority 22 (61.11%) had partial recovery after treatment, 5 (13.89 %) had compelte recovery and 3 (8.33%) ended with end stage kidney disease (ESKD) and 1 (2.78%) died from hypertensive crises.

Conclusion: The study results showed that HUS population were mostly due to Shiga toxin producing Escherichia Coli (STEC). It showed that HUS population were young, mostly male and only 25% have known medical comorbidities at time of presentation. Also, the majority presented with AKI requiring dialysis, of which PD was main stay of therapy. The duration of RRT and recovery time was almost a month period.

P0335 PULMONARY HEMORRAHGE IN IG A NEPHROPATHY: A RARE MANIFESTATION

Abid Hanen[1], Harzallah Amel[1], Trigui Chifaa[1], Chargui Soumaya[1], Goucha Rim[2], Ben Hamida Fathi[1], Ounissi Mondher[1], Ben Abdallah Taieb[1]

[1]Charles Nicolle Hospital, department of medecine A, Tunis, Tunisia and [2]Charles Nicolle Hospital, Laboratory of kidney pathology, Tunis, Tunisia

Background and Aims: Ig A nephropathy is the most frequent cause of glomerulonephritis worldwide. Renal-limited disease is the habitual clinical form of the disease. Pulmonary involvement may also be seen in rare cases. Capillaritis with pulmonary hemorrhage is the most frequent pulmonary involvement and is lifethreatening. We reported the case of patient presenting a rapidly progressive glomerulonephritis with pulmonary hemorrhage revealing Ig A nephropathy.

Method: A case report

Results: A 23 year-old man admitted for a rapidly progressesive glomerulonephritis with sever hypertension. He presented a respiratory distress with hemoptysis. At biology serum creatinine was at 2200µmol/l (eGFR = 2.4 ml/min) and Hemoglobin was at 5g/dl. Immunoassays of anti-glomerular basement antibodies and antineutrophil cytoplasmic autoantibodies were negatives.

Computed tomography scan showed diffuse intra alveolar hemorrhage associated with pleural effusion. Bronchoalveolar lavage confirms this diagnosis. Renal histology showed Ig A nephropathy.

Treatment consisted of daily depleted haemodialysis with blood transfusion and corticosteroids associated with monthly pulses of cyclophosphamide. His hemoptysis gradually resolved with a stable hemoglobin at 11 g/dL. However, renal failure persisted requiring maintenance hemodialysis regularly.

Conclusion: Pulmonary hemorrhage is a rare but serious complication of Ig A Nephropathy which is associated with significant morbidity and mortality. The exact cause for this "extra renal bleed" in Ig A Nephropathy is not known but it possibly represents IgA capillaritis. Though no evidence-based treatment protocol exists, therapeutic options includes steroids, plasmapheresis, cyclophosphamide and rituximab.

GLOMERULONEPHRITIS

P0342 A STUDY OF TREATMENT WITH RITUXIMAB IN REFRACTORY LUPUS NEPHRITIS

Pranab Jyoti Mahanta[1], Manjuri Sharma[1,1], Shahzad Alam[1], Prodip Kumar Doley[1], Gayatri Pegu[1], MASTAKIM AHMED MAZUMDER[1]

[1]*Guwahati Medical College Hospital, Nephrology, Guwahati, India*

Background and Aims: SLE patients have 40% to 70% life time risk of developing lupus nephritis (LN). In LN patients rate of end-stage renal disease is 10%, remaining constant in the last 30 years, even after the emergence of various immunosuppressive therapy.

SLE is an example of classical antibody-mediated disease and hence treatment with B cell depleting agent (like the use of Rituximab) appears to be a promising approach for this unwinnable disease from the Roman era.

The aim of this study was to analyze the outcome in terms of - no renal response (NRR), complete renal response (CRR) or partial renal response (PRR) at week 24 after rituximab treatment initiation in refractory LN.

CRR considered, if serum creatinine (S Cr) level returned to baseline, with a decline in the 24 hour urinary protein to < 500 mg/day. PRR defined as stabilization (+/-25%), or improvement of S Cr, plus a 50% decrease in 24 hour urinary protein (which was < 3.5 gm/day). NRR considered, if participant did not achieve either a CRR or PRR.

Method: It is a single center prospective observational study, comparing short term (24 week) outcomes in resistant lupus nephritis patients of >18 year age group with weekly (total 4) dose of rituximab therapy.

The study was conducted on 25 refractory lupus nephritis patients admitted in Nephrology Department (not responding to conventional immunosuppressive drugs like cyclophosphamide, MMF). Repeat renal biopsy was performed, all baseline investigations were done.

Injection Rituximab 375 mg/m^2 weekly 0,1,2,3 week along with premedication treatment were given to every patient. The clinical outcome was assessed monthly post-treatment.

Results: In the study maximum patients were of class IV, n=21 (84 %). Sustained (6 months post treatment) CRR was achieved in n=6 (24%) patients, n=7 (28%) patients achieved PRR, rest n=12 (48%) patients had NRR. Mean blood absolute CD-19 count was significantly negatively correlated with response to rituximab treatment (p< 0.001) .Mean absolute CD-19 count was 2.33/microliter in CRR, 2.14/microliter in PRR group and 21.25 / microliter in NRR group . No significant side effects of rituximab were observed.

Limitations –Small sample size, single center study, long term follow up not considered.

Conclusion: In refractory LN patients, 24 weeks after Rituximab treatment

- Total sustained renal response was achieved in 52% patients.
- Response to rituximab was inversely related to mean absolute blood CD-19 count.

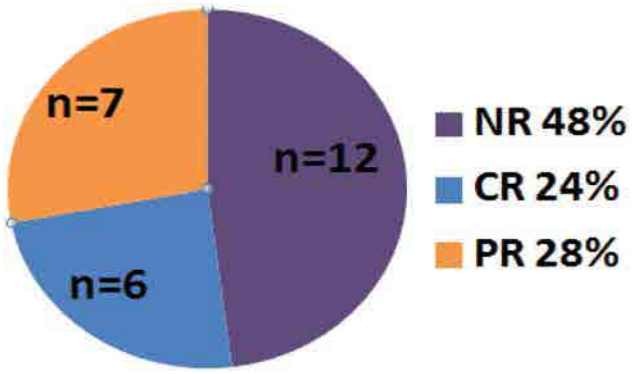


Figure-1, Response of rituximab in refractory lupus nephritis
(NR –no response, CR –complete response, PR – partial response)

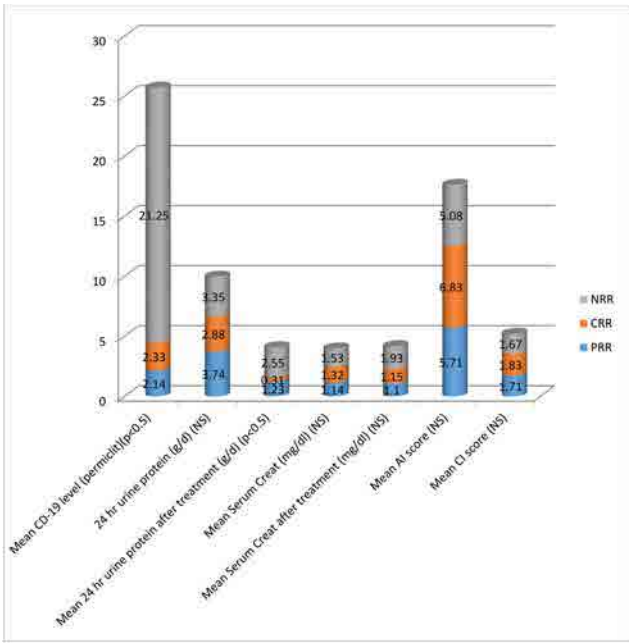


Figure 2: Clinicopathological parameters before and after rituximab treatment in refractory lupus patients.

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P0343 RISK PREDICTION MODELS FOR PREDICTING PROGRESSION OF IGA NEPHROLOGY:A VALIDATION STUDY

Jingyuan Xie[1]

[1]*Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Nephrology Department, Shanghai, P.R. China*

Background and Aims: Risk prediction models for IgA nephropathy (IgAN) containing clinical variables (clinical model) or clinical plus pathological variables (full model) have been established based on a large international collaborative study recently, but external validation of these models are still required before clinical application. The aim of this study is to externally validate previously reported risk prediction models based on our multi-center IgAN cohort.

Method: Biopsy-proven IgAN patients with eGFR $\geq$15 ml/min/1.73 m2 at baseline and a minimum follow-up of 6 months were enrolled. Primary outcome was defined as end-stage kidney disease (ESRD). Cox proportional hazards models were built to validate risk models. R2, Akaike information criterion (AIC) and C statistic were calculated to evaluate model accuracy.

Results: A total of 2300 IgAN patients with a median follow-up of 30 months were enrolled, and 214(9.3%) ESRD occurred during the follow-up period. The median age was 35(interquartile range, 28-44) years, and 1106 cases (48.1%) were men. Our cohort successfully validated the clinical model and the full model based on C statistic (0.90 and 0.91) and R2 (0.32 and 0.32). Our results showed limited improvement in model performance after adding the Oxford classification parameters to clinical parameters. However, both two models performed better than the model consisting only pathological parameters(C statistic 0.83, R2 0.24). We also validated other risk prediction models, including CLIN model (C statistic 0.90, R2 0.32) and CLINPATH model (C statistic 0.91, R2 0.31) derived from Chinese IgAN patients or CKD model (C statistic 0.90, R2 0.32) derived from Canadian CKD patients. It was found that clinical models based on different combinations of clinical parameters performed similarly.

Conclusion: In summary, we successfully validated a recently reported IgAN risk model and we found that clinical parameters alone could accurately predict ESRD risk in IgAN patients.

P0344 NEFECON® (BUDESONIDE) SELECTIVELY REDUCES CIRCULATING LEVELS OF BAFF (BLYS) AND SOLUBLE BCMA AND TACI IN IGA NEPHROPATHY

Karen Molyneux[1], David Wimbury[1], Jonathan Barratt[1]

[1]*University of Leicester, Mayer IgA Nephropathy Laboratory, Department of Cardiovascular Sciences, Leicester, United Kingdom*

Background and Aims: There is increasing evidence to support a pivotal role for the gut-associated lymphoid tissue (GALT) as a major source of the poorly *O*-galactosylated immunoglobulin A1 (IgA1) that triggers the formation of nephritogenic immune complexes in IgA nephropathy (IgAN). Critical to the regulation of IgA synthesis in GALT are two cytokines, which regulate B-cell maturation, function and survival: BAFF (B-cell activating factor [also known as BLyS (B-lymphocyte stimulator)]) and APRIL (A PRoliferation-inducing ligand). BAFF and APRIL bind to specific cell-surface receptors: TACI (transmembrane activator and calcium modulator and cyclophilin-ligand interactor), BCMA (B-cell maturation antigen) and the BAFF receptor. Several studies have shown elevated levels of BAFF and APRIL in IgAN linked to worse clinical outcomes. The therapeutic potential of selectively targeting GALT was demonstrated in the NEFIGAN trial (NCT01738035), which assessed the safety and efficacy of a novel targeted-release formulation of budesonide (NEFECON®), designed to deliver budesonide to the GALT-rich distal ileum in patients with IgAN. The trial comprised a 6-month run-in, 9-month treatment and 3-month follow-up phase: 48 patients received NEFECON® 16 mg/day, 51 patients received NEFECON® 8 mg/day and 50 patients received placebo. The headline result of the study was that NEFECON® 16 mg/day, added to optimised renin–angiotensin system blockade, reduced proteinuria and stabilised estimated glomerular filtration rate in patients with IgAN. In this study, we aimed to determine whether NEFECON® treatment altered synthesis of the BAFF and APRIL B-cell maturation modulators.

Method: Serum levels of BAFF, APRIL, BCMA and TACI were measured using Luminex technology. Changes in the levels of each biomarker between randomisation (T0), end of treatment (T1) and the end of study (T2) and between treatments arms were compared using a one-way analysis of variance. Significance was set at $p<0.05$.

Results: A significant, dose-dependent reduction in serum BAFF levels was seen with NEFECON®, which reversed on cessation of NEFECON®. There were similar significant reductions in the levels of soluble BCMA and TACI with treatment but no effect was seen on circulating levels of APRIL. These changes were mirrored by parallel changes in soluble CD27 levels and are consistent with our previous reports describing a dose-dependent reduction in circulating IgA–IgG immune complexes, secretory IgA and galactose-deficient IgA levels with NEFECON®.

Conclusion: Delivering budesonide to the GALT-rich distal ileum modulates key regulators of GALT B-cell maturation in IgAN. Although the samples available are not sufficient to determine that the observed changes in serum BAFF, BCMA and TACI levels are due to a direct action on GALT, it is intriguing to note that BAFF-transgenic mice develop an IgAN-like disease, principally due to IgA overexpression in the intestinal lamina propria.

P0345 **THE EFFICACY OF THE CORTICOSTEROIDS COMBINED ORAL CYCLOPHOSPHAMIDE FOR IGA NEPHROPATHY WITH REAL INSUFFICIENCY**

Shiren Sun[1], Feng Ma[1], Xiaoxia Yang[1], Ming Bai[1]

[1]*Xijing Hospital, Fourth Military Medical University, Department of Nephrology, xi'an, P.R. China*

Background and Aims: IgA nephropathy (IgAN) is the most type of primary glomerulonephritis and one of the major causes of end-stage renal disease (ESRD). The KDIGO clinical practice guidelines for glomerulonephritis suggest not the use of immunosuppressive drugs in IgAN patients with estimated glomerular filtration rate (eGFR) $\leq$50 mL/min/1.73m^2. However, VALIGA study showed that immunosuppressive drugs were more frequently used in IgAN patients with eGFR $<$ 30 mL/min/1.73m^2 than in those with eGFR $\geq$ 30 ml/ min/1.73m^2 (60% vs. 44 %; p = 0.004). The immunosuppressive drugs could be effective for IgAN with renal insufficiency in few studies, such as corticosteroids combined oral cyclophosphamide (CS + oral CTX). Therefore, in our present study, we evaluated the efficacy and treatment-related complications of the patients with eGFR from 15 ml/min/1.73m^2 to 59 ml/min/1.73m^2 who receive supportive care, or CS, or CS + oral CTX.

Method: 1602 renal biopsy–proven patients were reviewed between January 2008 and December 2016 in the Xijing Hospital. Patients were excluded from the study if they had secondary IgAN. The inclusion criteria were the primary IgAN with eGFR from 15 ml/min/1.73m2 to 59 ml/min/1.73m2 (n = 389). We extracted the patients with receive supportive care, or corticosteroids, or corticosteroids combined oral cyclophosphamide (n = 212). We further excluded patients: $<$ 8 glomeruli (n = 10), diabetes mellitus (n = 4), a follow-up less than 6 months (n = 22), and incomplete data (n = 7). The remaining 169 patients were included in the study (Figure 1). The data included baseline demographic at renal biopsy, renal biopsy, treatment, follow-up parameters and outcomes. The primary endpoint was the combined event of a $\geq$ 50% reduction in eGFR and/or ESRD. Univariate and multivariate Cox regression analyses were conducted to determine which variables were associated with renal survival. Variables were entered into a multivariate Cox regression model using an Enter method, which were derived from adjusted models: model 1 was adjusted for age, sex, MAP, proteinuria, and eGFR; model 2 was adjusted for the variables in model 1 plus RAS; model 3 was adjusted for the variables in model 1 plus M1, E1, S1, T1-2, and C1-2; model 4 was adjusted for the variables in model 3 plus RAS.

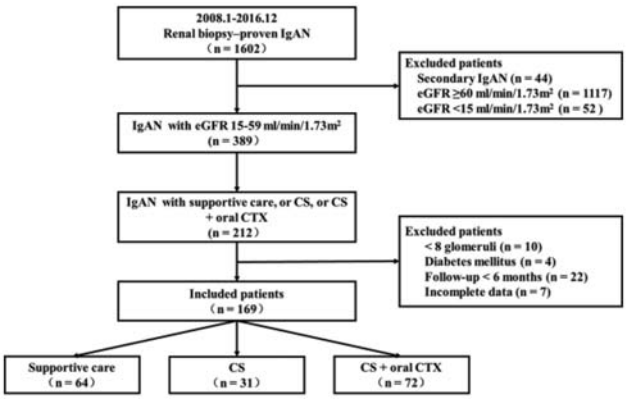


Figure 1 Inclusion flowchart.

Results: In all patients, the mean age was 36.0 years, the median proteinuria at the time of the biopsy was 1.6 g/day, the mean MAP was 108.7 mmHg, and eGFR was 40.4 ml/min/per 1.73 m2, the mean follow-up period was 43.3 months, 75 (44.9%) patients had reached combined event. The cumulative 5-year and 10-year renal survival rate were 39.3% and 9.3%, respectively, in the no-IS group ; 56.5% and 25.1%, respectively, in the CS group and 63.4% and 27.1%, respectively, in the CS + CTX group (Figure 2). Both univariate and multivariate Cox analyses shown that CS did not reduce the risk of combined event, whereas CS + CTX significantly reduced the risk of combined event. CS + CTX (HR = 0.367, 95%CI 0.198-0.682, P = 0.002) was notably associated with the risk of combined event after adjusted for age, sex, MAP, proteinuria, eGFR, M1, E1, S1, T1-2, C1-2, and ARB. The two groups did not differ significantly in treatment-related complications.

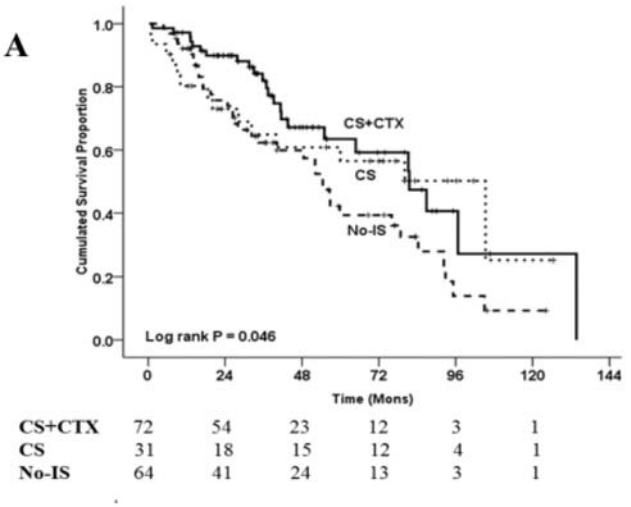


Figure 2 Kaplan–Meier survival curves show the cumulated survival of supportive care, or CS, or CS + oral CTX.

Conclusion: CS + oral CTX is possibly more effective than supportive care, or CS for IgAN patients with eGFR from 15 ml/min/1.73m^2 to 59 ml/min/1.73m^2. Furthermore, randomized controlled trials further verified the findings of the present study.

P0346 THE EFFECTS OF RITUXIMAB MAINTENANCE THERAPY ON LUPUS NEPHRITIS

Matthias Cassia[1], Rachel B. Jones[2], Daniele Cagna[3], Rona Smith[2], Giovanni Casazza[1], Guido Jeannin[4], Roberta Zani[4], Gabriella Moroni[5], Renato A. Sinico[6], Giacomo Emmi[7], Augusto Vaglio[7], Maurizio Gallieni[1], Francesco Scolari[8], David Jayne[2], Federico Alberici[8]

[1]University of Milan, Milano, Italy, [2]University of Cambridge, Cambridge, United Kingdom, [3]ASST Fatebenefratelli Sacco, Milano, Italy, [4]ASST Spedali Civili, Brescia, Italy, [5]Fondazione IRCCS Ca' Granda Ospedale Maggiore, Milano, Italy, [6]University of Milano Bicocca, Monza, Italy, [7]University of Florence, Florence, Italy and [8]University of Brescia, Brescia, Italy

Background and Aims: Lupus Nephritis (LN) is the organ manifestation with the most severe prognosis in Systemic Lupus Erythematosus (SLE). Treatment options are limited due to partial efficacy, intolerance or side effects; moreover 10% of patients reach ESRD despite treatments. Rituximab (RTX) in LN is recommended as second line drug for induction of the remission after failure of Cyclophosphimide or Mycophenolate Mofetil. We have shown a role for RTX as maintenance therapy (RMT) in SLE however the effects of such approach on LN are still unclear. Aim of this study was a sub-analyses of a cohort of SLE patients treated with RTX focusing on the ones with active LN at the moment of the first RTX administration.

Methods: Patients with active LN at the time of the first RTX administration within a cohort of 147 patients with SLE were identified. Patients with SLE and a flare of LN were classified as treated with a "Single RTX course" (any RTX regimen administered within a single month) (SRC) or with RMT. Patients receiving at least three SRCs with the aim of relapse prevention and within 4 to 8 months between consecutive treatments, were classified as receiving RMT.

LN activity was determined according to creatinine, proteinuria and haematuria; complete response (CR) was defined as a decrease of proteinuria to <0.5 g/day, normal creatinine and negative urinary sediment; partial response (PR) was defined as $\geq 50\%$ improvement in creatinine and proteinuria, treatment failure (TF) was any other condition. A renal flare (RF) was defined as an increase of creatinine and/or proteinuria $>30\%$ or the detection of an active urinary sediment due, according to the treating physician, to active disease.

Results: 33 patients were identified; a renal biopsy had been performed in 76% with prevalence of class IV lupus nephritis in 16/33 (48%). Six months after RTX the rate of CR, PR and TF was respectively 36%, 27% and 36%; proteinuria and the prednisolone dose reduced significantly compared to baseline (respectively from a median of 2200 mg/day (IQR 499-5400) to 850 mg/day (IQR 400-1700) (p=0.005)) and from 25 mg (IQR 11-25) to 10 mg (IQR 6.125-15) ($p<0.0001$)). At univariate analyses the only factor associate to the risk of TF was a high number of immunosuppressive drugs employed before RTX (p=0.0077).

Of the 33 patients, 11 received RMT with a median duration of 18 months (IQR 12,6-23,4) and a median RTX dose of 5 g (IQR 4-6). During the RMT 3 patients experienced a renal flare.

The median follow-up after the last RTX administration within the SRC and the RMT groups was respectively 15 months (IQR 13,5-18,4) and 16 months (IQR 3,5-23). Comparing the RF free-survival of the two subgroups after the last RTX infusion, there was a trend towards a longer relapse free survival after the RMT (p=0.057) (*figure, left panel)*. Of interest, the renal relapse free-survival of the 11 patients treated with RMT after the last RTX infusion was significantly longer compared to the one of the same group after the first RTX (p=0.0271) (*figure, right panel)*.

The incidence of SAEs per 100 patient years was 0.31 in the SRC group and 0.74 in the RMT group.

Conclusion: RTX is confirmed as an effective option for patients with LN. A RMT may have a role in improving LN disease control compared to a single RTX administration.

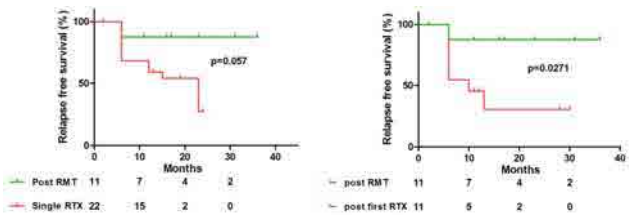


Figure:

P0347 **COMPLEMENT FACTOR BB AND FACTOR C4D IN IGA NEPHROPATHY AND IGA VASCULITIS**

Emelie Westergren[1], Magnus Söderberg[1], Benjamin Challis[2], Annika Wernerson[1], Abdul Rashid Tony Qureshi[3], Annette Bruchfeld[1]

[1]Karolinska Institute, Division of Renal Medicine, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden, [2], Translational Science & Experimental Medicine, Research and Early Development, Cardiovascular, Renal and Metabolism, BioPharmaceuticals R&D, Astra Zeneca, Cambridge, United Kingdom and [3]Karolinska Institute, Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Huddinge, Sweden

Background and Aims: IgA nephropathy (IgAN) is the most common glomerulonephritis worldwide. IgAN and IgA Vasculitis with nephritis (IgAVN) are thought to have related pathogenesis characterized by IgA-containing renal immune complexes contributing to chronic kidney disease (CKD) and renal failure**.** In both diseases, IgA1 immune complexes and complement factors have been shown to be involved, indicating complement activation. However, the individual contribution of the alternative and lectin pathway has of yet not been fully elucidated. Plasma Bb is a marker of the alternative pathway activity and plasma C4d of the mannan-binding lectin pathway. We aimed to investigate the association between circulating plasma *Bb* and *C4d* at diagnosis and potential correlates with clinical features, renal histopathology and renal outcome in patients with IgAN and IgAVN.

Method: A prospective study of 98 patients undergoing renal biopsy was performed. Median age was 43 years, 52% males, 88% were caucasians, Sixty-six patients were diagnosed with IgAN, 15 IgAVN and 17 controls with "non-immunocomplex driven disease including Thin membrane disease, Diabetic Nephropathy, Minimal change disease or renal failure due to hyperfiltration. Blood samples were analyzed for complement factors *C4d* and *Bb* (both ELISA, Termo Fisher Scientific^{TM}). Oxford classification of the renal biopsy was done at baseline and creatinine, estimated glomerular filtration rate (eGFR-CKD-EPI formula) were measured annually. Continuous data are expressed as median (25th to 75th percentile) and nominal or ordinal data as percentage. Comparisons between groups were assessed with the non-parametric Wilcoxon test/ Kruskal-Wallis ANOVA-test for continuous variables and Chi-square test for nominal variables.

Results: Patients with IgAN and IgAVN were significantly younger than the control group. There were no significant differences between the three groups for gender distribution and eGFR. Complement factor *Bb for patients with* IgAN and IgAVN was significantly increased (figure 1) as compared to the control group, whereas there was was no statistical difference for complement factors*C4d* between groups. Estimated GFR decreased significantly only in patients with IgAN after 24 months of follow-up (56.6 ± 3.8 ml/min/1,73m^2 as compared to IgAVN 83.8 ± 8.5 and controls 90.2 ± 8.9).

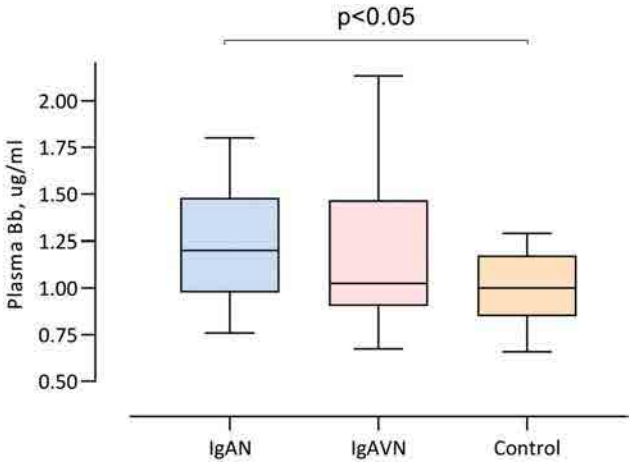


Figure 1. Plasma Bb levels *(ug/ml)* in IgAN, IgAVN and control group at baseline.

Patients with IgAN had more severe histopathological changes in T-score (T-score 0, 1, 2 in IgAN 51 %, 37 % and 12 % respectively) compared to IgAVN. In the IgAN group a more severe T-score was significantly associated with increased levels of complement factor *Bb* (p=0.005) but did not reach significance for complement factor *C4d* (p=0.097). No other difference or correlations were found with regards to M, E, S and C % scores.

Conclusion: Patients with IgAN were younger and had increased levels of complement factor *Bb* and after 24 months follow-up significantly reduced eGFR. The increase in factor Bb was also associated with more severe histopathological changes in T-score. These findings suggest that the alternative complement pathway contributes to the pathogenesis in IgAN and chronic kidney damage. Our findings should motivate studies in a larger population to further clarify the role of complement activity in IgAN and IgAVN.

P0348

THE DUAL ENDOTHELIN ETA AND ANGIOTENSIN AT1 RECEPTOR BLOCKER SPARSENTAN PROTECTS AGAINST THE DEVELOPMENT OF ALBUMINURIA AND GLOMERULOSCLEROSIS IN THE GDDY MOUSE MODEL OF IGA.

Hajime Nagasawa[1], Hitoshi Suzuki[1], Celia Jenkinson[2], Seiji Ueda[1], Yusuke Fukao[1], Maiko Nakayama[1], Tomoyuki Otsuka[1], Kai Liu[2], Radko Komers[2], Yusuke Suzuki[1]

[1]Juntendo University Faculty of Medicine, Department of Nephrology, Tokyo, Japan and [2]Retrophin,Inc., San Diego, CA, United States of America

Background and Aims: gddY mice are an IgA nephropathy (IgAN)-prone mouse model that develops albuminuria by 8 weeks (wks) of age with glomerular IgA, IgG, and C3 deposits and progressive mesangioproliferative glomerulonephritis. A previous study in the ddY mouse model, the more genetically heterogeneous predecessor of gddY mice, using the endothelin type A receptor (ET_AR) antagonist FR139317 resulted in amelioration of proteinuria and preservation of kidney function. Treatment of ddY mice with the angiotensin II type 1 receptor (AT_1R) blocker valsartan resulted in significant protection from glomerulosclerosis (GS) without a significant prevention in proteinuria. Here we examined the effect of sparsentan (SP), a dual ET_AR and AT_1R blocker, currently in phase 3 trials for focal segmental glomerulosclerosis and IgAN, on the development of albuminuria and GS in gddY mice.

Method: gddY mice at 4 wks of age were fed with control (C) chow (n=5) or chow containing 900 ppm (n=10) or 1800 ppm (n=10) SP (approximately 180 and 360 mg/kg/day) for 8 wks. Albuminuria (U-Alb) was assessed at 4, 6, 8, and 12 wks of age and plasma levels of SP were determined at 8 am and 4 pm at wks 6, 8, and 12. Kidney biopsies were taken at the end of the study at 12 wks of age for processing and 30 glomeruli per animal were scored for the percentage of GS.

Results: gddY mice fed SP in the diet for 8 wks from 4 wks of age demonstrated significantly ($*P<0.05$) decreased U-Alb compared to mice fed the C diet in a dose-dependent manner (Figure 1). The development of GS in mice fed the diet containing 1800 ppm SP was significantly ($*P<0.05$) attenuated compared to C diet (Figure 2). Plasma levels of SP taken at 8 am and 4 pm after 8 wks of treatment were (mean$\pm$SD) 281$\pm$107 and 105$\pm$62 ng/ml for 900 ppm SP respectively, and 774$\pm$674 and 304$\pm$176 ng/ml for 1800 ppm SP, respectively. Weight gain in mice fed SP was not different from mice that received C diet.

Conclusion: Eight weeks of treatment with SP attenuated increases in albuminuria and GS associated with the development of IgAN in gddY mice. If translated to the clinic, these data support SP as a new approach to the treatment of IgAN.

P0349

A MISSPROCESSED FORM OF APOLIPOPROTEIN A-I IS SPECIFICALLY ASSOCIATED TO RECURRENT FOCAL SEGMENTAL GLOMERULOSCLEROSIS.

Conxita Jacobs Cachá[1,2], Natàlia Puig Gay[3], Dominic Helm[4], Mandy Rettel[4], Joana Sellares[1,2], Anna Meseguer[3], Mikhail M. Savitski[4,5], Francesc Moreso[1,2], María José Soler[1,2], Daniel Seron Micas[6,7], Joan López Hellín[6,7]

[1]Vall d'Hebrón Institut de Recerca (VHIR), Nephrology research group, Barcelona, Spain, [2]Hospital Universitari Vall d'Hebrón, Nephrology department, Barcelona, Spain, [3]Vall d'Hebrón Institut de Recerca (VHIR), Renal Pathophysiology Group, Barcelona, Spain, [4]European molecular biology laboratory, Proteomics core facility, Heidelberg, Germany, [5]European molecular biology laboratory, Genome Biology, Heidelberg, Germany, [6]Hospital Universitari Vall d'Hebrón, Biochemistry department, Barcelona, Spain and [7]Vall d'Hebrón Institut de Recerca (VHIR), Biochemistry Research Group, Barcelona, Spain

Background and Aims: Recurrence of idiopathic FSGS, a glomerular disease of unknown aetiology, is a serious complication after kidney transplantation. There are no accurate means to diagnose the relapses or to detect the patients at risk. In an exploratory study we detected Apolipoprotein A-Ib (ApoA-Ib), a high molecular weight form of ApoA-I, specifically in urine of kidney transplanted patients that relapsed of FSGS. The diagnostic performance of ApoA-Ib has been assessed in two independent cohorts obtaining high specificity (94,1 %) and sensitivity (87,5 %) to detect FSGS relapses. It has also a potential to detect patients at risk of relapse as ApoA-Ib predates the recurrence episodes in most of the cases. As urinary ApoA-Ib is strongly associated to primary FSGS we aimed to unravel the nature of the modification present in ApoA-Ib.

Method: The whole *APOA1* gene was sequenced in ApoA-Ib positive and negative patients and the protein structure was studied using 2D electrophoresis followed by mass spectrometry.

Results: No genetic variations in the *APOA1* gene were found in the ApoA-Ib positive patients that could explain the increase in the molecular mass. The mass spectrometry analysis revealed three extra amino acids at the N-Terminal end of ApoA-Ib that were not present in the standard plasmatic form of ApoA-I. These amino acids corresponded to half of the propeptide sequence of the immature form of ApoA-I (proApoA-I). These results suggest that proApoA-I is miss-cleaved producing ApoA-Ib probably due to an altered protease activity in recurrent FSGS patients

Conclusion: ApoA-Ib, found specifically in urine of recurrent FSGS patients, is a misprocessed form of ApoA-I that retains three aminoacids of the six-aminoacid N-terminal propeptide of proApoA-I. The description of ApoA-Ib could be relevant not only to allow the automated analysis of this biomarker in the clinical laboratory but also to shed light into the molecular mechanism of idiopathic FSGS.

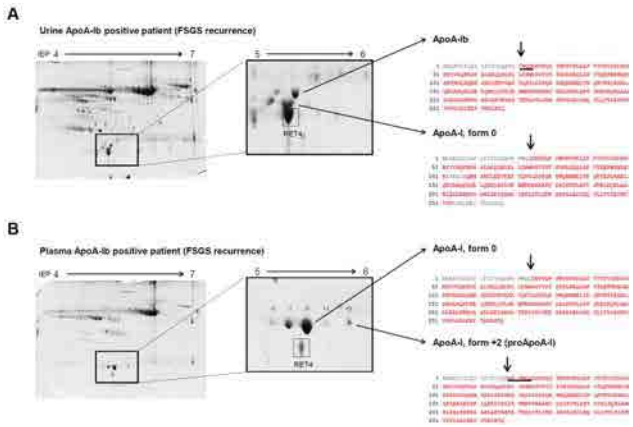


Figure:

P0350 **THE DURATION OF PROTEINURIA REMISSION AND CLINICAL OUTCOMES IN IGA NEPHROPATHY**

Mark Canney[1], Sean Barbour[1], Sophia Zheng[2], Rosanna Coppo[3], Hong Zhang[4], Zhi Hong Liu[5], Keiichi Matsuzaki[6], Yusuke Suzuki[6], Ritsuko Katafuchi[7], Heather Reich[8], Daniel C. Cattran[8]

[1]University of British Columbia, Division of Nephrology, Vancouver, Canada, [2]BC Renal, Vancouver, Canada, [3]Regina Margherita Children's University Hospital, Nephrology Department, Torino, Italy, [4]Peking University, Institute of Nephrology, Beijing, P.R. China, [5]Nanjing University, School of Medicine, Nanjing, P.R. China, [6]Juntendo University, Faculty of Medicine, Tokyo, Japan, [7]National Fukuoka Higashi Medical Center, Fukuoka, Japan and [8]University of Toronto, Division of Nephrology, Toronto, Canada

Background and Aims: A relative reduction in proteinuria has been proposed as a surrogate outcome for therapeutic trials in IgA nephropathy. It is currently unknown how long a reduction in proteinuria needs to be maintained in order to mitigate the long-term risk of disease progression. To address this knowledge gap we sought to quantify the association between duration of proteinuria remission and the risk of disease progression in IgA nephropathy.

Method: In this retrospective multi-ethnic international cohort of adult patients with biopsy-proven IgA nephropathy, we defined proteinuria remission based on three criteria: (i) peak proteinuria on/after biopsy $\geq$1g/day; (ii) an absolute reduction in proteinuria to $<$1g/day; (iii) a $\geq$25% reduction in proteinuria from the peak value. The exposure of interest was the total duration of first remission, treated as a time-varying covariate using longitudinal proteinuria measurements. The primary outcome was the occurrence of end-stage kidney disease or a sustained 50% reduction in estimated glomerular filtration rate (eGFR). The association between duration of remission and the primary outcome was visualized using restricted cubic splines, and quantified using extended Cox proportional hazards regression models.

Results: A total of 1864 patients met criteria for remission, which occurred a median of 8.3 months after biopsy (IQR 3.6-22). They had a median age of 36.8 (IQR 29.4-46.6) years and a median eGFR of 78 (IQR 55-104) mL/min/1.73m^2. Median proteinuria was 1.54 (IQR 1.09-2.4) g/day at the time of biopsy and 0.55 (IQR 0.33-0.76) g/day at the time of entering remission. During a median follow-up of 3.9 years, 274 patients (14.7%) experienced the primary outcome. The relationship between duration of proteinuria remission and the primary outcome was non-linear (Figure). Each 3 months in sustained remission up to 51 months was associated with an additional 9% reduction in the risk of disease progression (hazard ratio 0.91, 95% confidence interval 0.89-0.93). In contrast, each additional 3 months in remission beyond 51 months was associated with a smaller non-significant risk reduction (hazard ratio 0.99, 95% confidence interval 0.96-1.03). These finding were robust to multivariable adjustment and were consistent across subgroups based on the MEST histology score, and whether or not the remission occurred while on renin-angiotensin-aldosterone-system blockade or after immunosuppression treatment. Results were similar when relapse was defined as either a 50% or 100% increase in proteinuria from the nadir value after remission to an absolute value of $\geq$1g/day.

Conclusion: We observed a strong non-linear dose-response relationship between the duration of proteinuria remission and the risk of disease progression in patients with IgA nephropathy. The ability to quantitate the renal survival benefit related to the duration of remission is an important advance for patients and their physicians. Rather than there being a minimum duration of proteinuria remission in IgA nephropathy, our results demonstrate that even short durations in remission, or small increases in remission duration, are both associated with significant reductions in the risk of disease progression. For future therapeutic trials in IgA nephropathy using proteinuria as a surrogate outcome, our findings illustrate the need to consider the duration of proteinuria reduction, in addition to the magnitude of proteinuria reduction, when evaluating the anticipated treatment effect on long-term clinical endpoints.

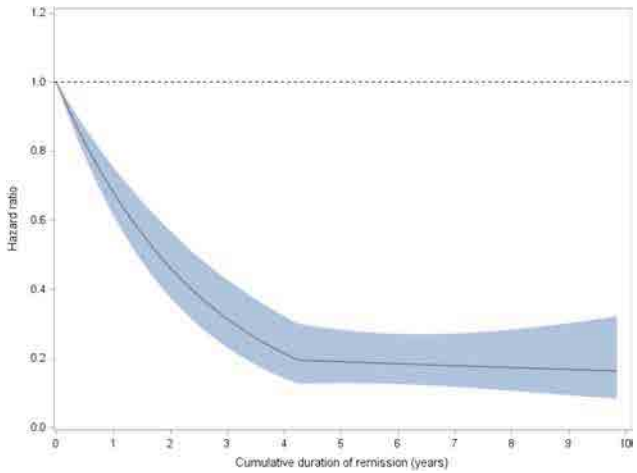


Figure: Smoothed plot of the hazard ratio (grey line) and associated 95% confidence interval (blue shaded area) for the risk of the primary outcome associated with the cumulative duration of proteinuria remission.

P0351 IMPACT OF APOL1 POLYMORPHISM ON LUPUS NEPHRITIS

Carole Burger[1], KARRAS Alexandre[2]

[1]Hôpital Necker, Kidney Transplantation, Paris, France and [2]Hôpital Européen Georges-Pompidou, Nephrology, Paris, France

Background and Aims: African ancestry is associated with more severe kidney involvement and end stage renal disease (ESRD) in lupus nephritis (LN). Two polymorphisms of the apolipoprotein L1 gene (APOL1), defining the risk allels (RA) G1 and G2, particularly frequent among subjects of African ancestry, markedly increase the risk of ESRD and the occurrence of collapsing glomerulopathy (CG) in the general population. The aim of this study was to assess the impact of ApoL1 RA on clinical, biological, and histological presentation of LN, and its prognosis.

Method: Patients of African ancestry with biopsy-proven LN were included between January 2017 and September 2018. Clinical, laboratory and pathology datas were retrospectively collected and ApoL1 genotyping was performed.

Results: Among the 53 included patients, 31 had no RA, 16 were heterozygous with only one RA and 6 had 2 RA (G1/G1 or G2/G2 or G1/G2). The population was divided in 2 groups: low risk polymorphism (LRP) group defined by the presence of 0 or 1 RA, and high risk polymorphism (HRP) group with 2 RA. At presentation, hypertension (OR 25,4 [1,3-510,3]) and acute renal failure (OR: 9,3 [1,3-65,2]), were more frequent in the HRP group when compared to the LRP group. Initial median serum creatinine was respectively 363 µmol/l (IQR 119-594) vs 64 µmol/l (IQR 55-127). After 2-year follow-up, median eGFR was 59mL/min (IQR 41-91) in the HRP group and 117mL/min (IQR 92-124mL/min) in the LRP group. Patients in the HRP group were more likely to have an impaired renal function with an estimated glomerular filtration rate (eGFR) $<$60mL/min compared to patients in the LRP group (OR: 13,5 [2,1-86,5]). Moreover, ESRD-free survival was worse in the HRP group (Hazard ratio: 78,8 [5,3-1124,0]) despite similar chronicity indexes on initial kidney biopsy and comparable therapeutic strategies. As for histological findings, CG was observed in 67% of patient's kidney biopsy in the HRP group whereas it only concerned 12% of patient's kidney biopsy in the LRP group (OR: 14,8 [2,4-84,8]).

Conclusion: The ApoL1 polymorphism strongly affects LN prognosis in patients with African ancestry, resulting in more severe inaugural presentation, higher risk of subsequent severe chronic kidney disease and development of collapsing glomerulopathy for subjects with 2 RA.

P0352 P-SELECTIN BLOCKADE AMELIORATES RENAL HYPOXIA OF LUPUS NEPHRITIS IN MRI/LPR MICE

Xiao Li[1]

[1]*Ruijin Hospital, Shanghai Jiaotong University, Nephrology department, Shanghai, P.R. China*

Background and Aims: Lupus nephritis is one of the most common and severe complications of systemic lupus erythematosus, of which poor prognosis is indicated by aggravated renal hypoxia and tubulointerstitial fibrosis. Cell adhesion molecules play a key role in the progression of lupus nephritis tubulointerstitial lesion, including P-selectin, which mediates the rolling of leukocytes and subsequent adhesion and infiltration and then initiates the inflammatory immune response and ischemia and hypoxia injury. However, the effects and mechanisms of P-selectin in lupus nephritis remain to be investigated, and a noninvasive measurement of lupus nephritis tubulointerstitial hypoxia and fibrosis remains to be explored.

Method: Thirty-four MRL/lpr mice were randomly divided into the following three groups: MRL/lpr, saline, and anti–P-selectin, which consisted of no treatment, treatment with normal saline, and treatment with anti–P-selectin monoclonal antibody (mAb) from 12 to 16 weeks of age, respectively. Ten male C57BL/6 mice of the same age served as normal controls. Twenty-four-hour urinary protein, urinary albumin–creatinine ratio, and periodic acid–Schiff were used to assess kidney damage; Western blot or immunohistochemical staining of the hypoxia probe HypoxyprobeTM-1, hypoxia-inducible factor 1α (HIF-1α), and CD31 were used to evaluate hypoxia in renal tissue; and NADPH oxidase subunit gp91phox and p22phox were used to examine renal oxidative stress. The correlation between kidney injury and blood oxygen level–dependent magnetic resonance imaging (BOLD-MRI) was calculated to assess the clinical value of BOLD-MRI.

Results: P-selectin is upregulated in lupus nephritis. Blocking P-selectin with mAb alleviated renal tubulointerstitial fibrosis, renal hypoxia, and peritubular capillary loss, without alteration of the levels of lupus activity indicators, anti-dsDNA antibody, or complement C3. BOLD-MRI showed that the reduced R2* values in the renal cortex and medulla of lupus mice were increased when treated with anti–P-selectin mAb as compared with those treated with normal saline, which were negatively correlated with HypoxyprobeTM-1 hypoxia probe and the expression of HIF-1α.

Conclusion: Early intervention of lupus nephritis with anti–P-selectin mAb can significantly improve the hypoxic state of the kidney and reduce the severity of tubulointerstitial lesions. BOLD-MRI techniques are noninvasive and can dynamically evaluate the changes in renal lesions and intrarenal oxygenation levels before and after treatment in lupus nephritis.

P0353 **EFFECT OF RITUXIMAB IN PATIENTS WITH RELAPSED OR REFRACTORY PRIMARY MEMBRANOUS NEPHROPATHY**

Arif Akyildiz[1], Omer Uludag[1], Safak Mirioglu[2], Ali Riza Ucar[3], Erol Demir[3], Yasar Kerem Caliskan[3,4], Yasemin Ozluk[5], Aydin Turkmen[3], Mehmet Sukru Sever[3], Halil Yazici[3]

[1]Istanbul Faculty of Medicine, Department of Internal Medicine, Turkey, [2]Cerrahpasa Medical Faculty, Division of Nephrology, Department of Internal Medicine, Turkey, [3]Istanbul Faculty of Medicine, Division of Nephrology, Department of Internal Medicine, Turkey, [4]Saint Louis University School of Medicine, Division of Nephrology and Hypertension, Saint Louis, United States of America and [5]Istanbul Faculty of Medicine, Department of Pathology, Turkey

Background and Aims: Membranous nephropathy (MN) is the most common cause of glomerulonephritis in non-diabetic adults. B-cell dysfunction is an important pathway involved in pathogenesis. We, therefore, investigated effects of rituximab (RTX) on the outcome of patients with relapsed or refractory primary MN.

Method: In this retrospective analysis, 48 patients with primary MN were evaluated. Patients, who had relapsed or refractory biopsy-proven disease, with a nephrotic-range proteinuria despite at least six months of prior immunosuppressive therapy using corticosteroids, calcineurin inhibitors or mycophenolic acid derivatives, which were used according to KDIGO guidelines. All patients received at least 2 doses of 375 mg/m2 of RTX. Proteinuria and serum albumin levels of the patients were recorded at baseline, and 3,6,12,18 and 24 months.

Results: Of 48 patients who participated in this study, 27(56.3%) were male. Mean age was 45.3±17.2 years. Results of serum anti-phospholipase-A2-receptor (PLA2R) were available in 31 patients, 23 of whom (74%) were positive. Proteinuria levels at 3, 6, 12, 18, and 24 months after treatment with RTX showed a significant decrease when compared to baseline ($p<0.05$) (Figure 1): From 7±3.5 g/24h at baseline to 2.6±2.4 g/24h at 12 months. Serum albumin levels at 3, 6, 12, 18, and 24 months after RTX significantly increased compared to baseline values ($p<0.05$) (Figure 2): From 2.97±0.76 g/dl at baseline to 3.88±0.67 g/dl at 12 months.

Conclusion: Treatment with RTXiseffective in patients suffering from relapsed or refractory primary MN.

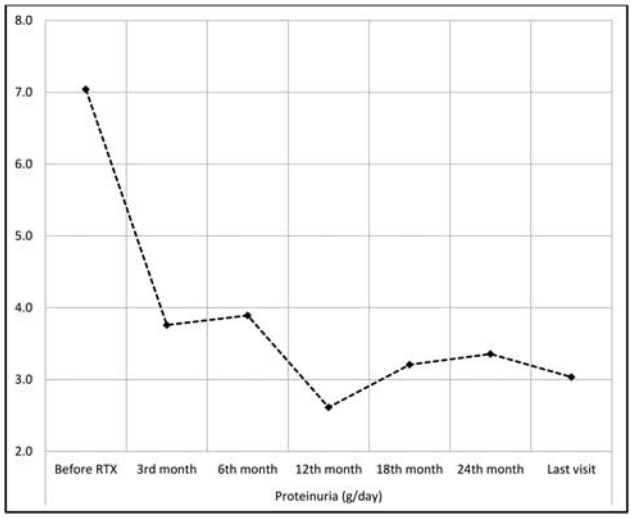


Figure 1. Proteinuria levels throughout the follow-up.

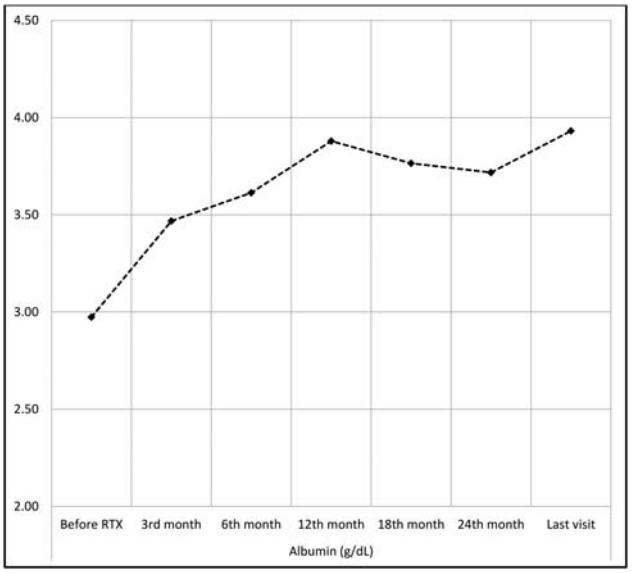


Figure 2. Serum albumin levels throughout the follow-up.

P0354

MATRIX ASSISTED LASER DESORPTION/IONIZATION MASS SPECTROMETRY IN PROTEIN ALTERATIONS ASSOCIATED WITH THE PROGRESSION OF IGA NEPHROPATHY DISCOVERY

Mariia Ivanova[1,2], Olena Dyadyk[2], Dmytro Ivanov[3], Francesca Clerici[1], Andrew Smith[1], Fulvio Magni[1]

[1]University of Milan Bicocca, School of Medicine and Surgery, Monza, Italy, [2]National Medical Academy of Post-Graduate Education Named After P.L. Shupik, Pathology, Kyiv, Ukraine and [3]National Medical Academy of Post-Graduate Education Named After P.L. Shupik, Nephrology and RRT, Kyiv, Ukraine

Background and Aims : IgA nephropathy (IgAN) is one of the most diffuse glomerulonephrites worldwide, but there are still many issues regarding its prognosis and pathogenesis understanding. Although the diagnosis is established by renal biopsy examination, there are still remaining pitfalls in primary origin discrimination, and therefore for prognosis and outcome for the patient.

Method : In this pilot study we performed matrix-assisted laser desorption/ionization (MALDI) mass spectrometry imaging (MSI) with a high spatial resolution (raster sampling of 20 μm) on formalin fixed paraffin embedded renal biopsies obtained from patients with IgAN (n=11) and other mesangioproliferative glomerulonephrites (MesPGN, n=6) attempting to enlighten proteomic alterations that may be associated with the progression of IgAN. The patients in both disease groups were separated according to their CKD stage (CKDI, CKDII, CKDIII and more). After MALDI-MSI analysis, all biopsies were stained with hematoxylin and eosin, scanned and overlaid with molecular image in order to verify the signals' spatial distribution.

Results : Using MALDI-MSI we detected clear differences in the proteomic profiles of IgAN and other MesPGN tissues. Fourteen signals (AUC $\geq$ 0.8) were observed to have an altered intensity among the different CKD stages within the IgAN group. In particular, large increases in the intensity of these signals could be observed at CKD stages II and above. Putatively identified, these signals primarily corresponded to proteins involved in inflammatory and healing pathways and their increased intensity was localised within regions of tissue with large amounts of inflammatory cells or sclerosis (Figure 1), verified by immunohistochemical staining (Figure 2).

Conclusion : The capability of MALDI-MSI to provide highly spatially resolved proteomics analysis of complex renal tissue demonstrates it a useful additional diagnostic and prognostic tool and a promising approach in the search for prognostic or predictive markers in glomerular diseases.

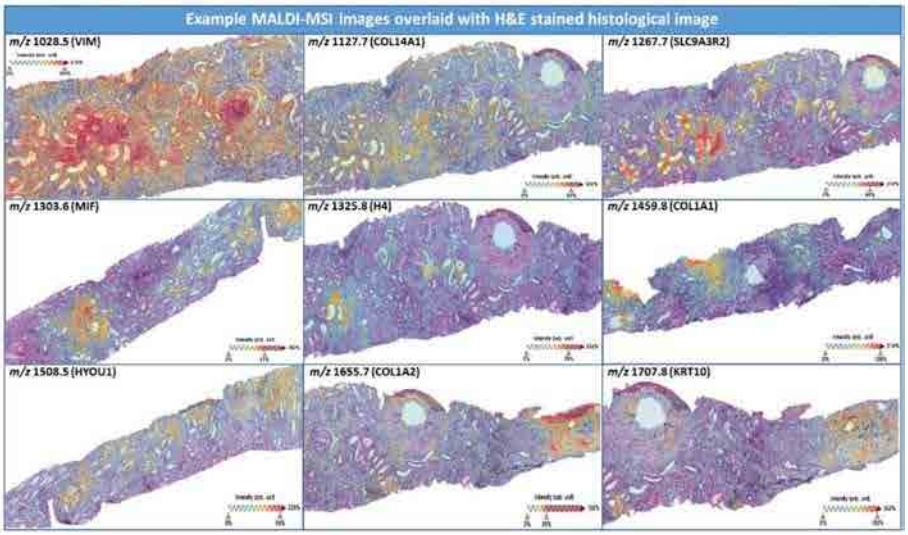


Fig. 1. Example MALDI-MSI images overlaid with hematoxylin and eosin stained biopsies.

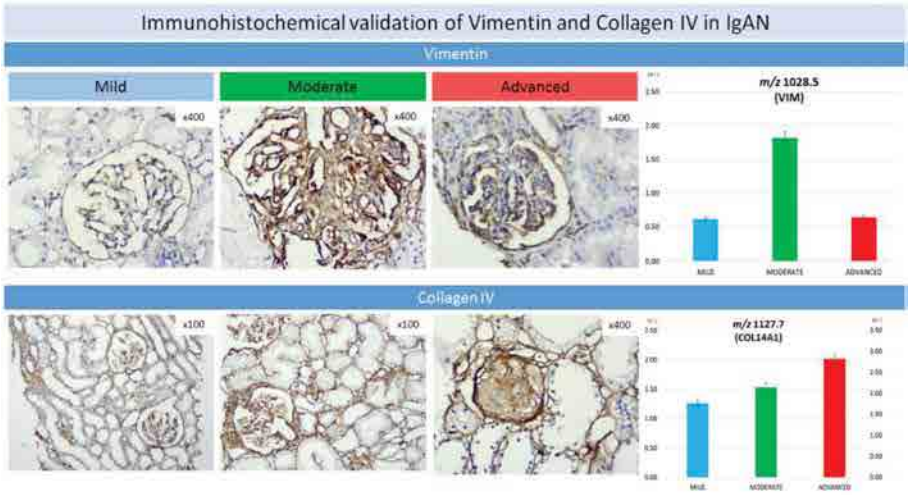


Fig. 2. Immunohistochemical validation of Vimentin and Collagen IV in IgAN patients.

P0355 **FAMILY HISTORY OF COMPLEX TRAITS IN THE CUREGN COHORT: ASSOCIATIONS WITH RENAL FUNCTION, COMORBIDITY BURDEN AND DISEASE PROGRESSION**

Francesca Zanoni[1], Miguel Verbitsky[1], Lucrezia Carlassara[1], Maddalena Marasa[1], Krzysztof Kiryluk[1], Ali Gharavi[1]

[1]*Columbia University Irving Medical Center, Department of Medicine, division of Nephrology, New York, United States of America*

Background and Aims: Family history (FHx) of complex traits may reflect shared genetic/environmental risk. Few studies suggest associations with increased risk of comorbidities and worsening renal function, but this has not been examined in primary glomerulopathies (GNs). Herein, we studied the association of FHx of complex traits with presentation patterns, comorbidities and disease progression in a prospective cohort of patients with primary GN.

Method: The Cure Glomerulopathy Networ (CureGN) is a prospective multi-center observational study of GN patients (N=2474) affected by biopsy-proven Focal Segmental Glomerulosclerosis (FSGS), Minimal Change Disease (MCD), Membranous Nephropathy (MN) and IgA Nephropathy/Vasculitis (IgAN/V). Associations of self-reported FHx of diabetes (DM), coronary artery disease (CAD), cancer (C), clotting disorders (CD), and autoimmune diseases (AD) with eGFR, UPCR at diagnosis, and comorbidities prevalence were studied using linear and logistic regression models adjusted for age, sex, ethnicity, race, BMI and other relevant clinical covariates. Associations between FHx and ESRD/40%eGFR reduction were investigated with multivariate Cox models.

Results: FHx of DM was associated with lower eGFR and higher UPCR at diagnosis in the entire cohort (p=0.006 and p=0.03), lower eGFR in FSGS (p=0.02) and higher UPCR in IgAN/V (p=0.01). Regarding comorbidity burden (Table 1), FHx of DM was associated with higher prevalence of DM, heart failure and infections requiring hospitalization, FHx of C with cancer, FHx of CD with higher prevalence of thrombosis and FHx of AD with inflammatory bowel, celiac diseases, asthma and drug allergies. At the survival analysis adjusted for age, sex, ethnicity, race, BMI, diagnosis group, eGFR and UPCR at diagnosis, DM, hypertension, use of immunosuppressants and RAAS-inhibitors, FHx of DM was associated with higher risk of the composite outcome of ESRD/40%eGFR reduction in the entire cohort (HR 1.39, 95%CI 1.07-1.81, p=0.01), and specifically in FSGS (HR 1.76, 95%CI 1.08-2.85, p=0.02) and in the paediatric subgroup (HR 1.98, 95%CI 1.04-3.80, p=0.04).

Conclusion: FHx of complex traits are associated with higher prevalence of specific comorbidities. FHx of DM identifies patients with lower eGFR at diagnosis, higher prevalence of infections and higher risk of renal disease progression. These findings, which need to be confirmed in other cohorts, suggest that FHx could be an additional useful parameter for risk stratification and management of primary GN.

Table 1: Family history of complex traits and comorbidity prevalence

	Comorbidity		Comorbidity		Comorbidity		Comorbidity	
Family History	**OR(95% CI)**	**p**	**OR(95% CI)**	**p**	**OR(95% CI)**	**p**	**OR(95% CI)**	**p**
FHx DM	**DM**		**Heart failure**		**Infections requiring hospitalization**			
All	1.8(1.1-2.7)	0.009	2(1.1-3.7)	0.03	1.4(1.1-1.9)	0.0028		
MCD	7.2(1.6-3)	0.009	8.7(1.2-40)	0.03	1.4(0.8-2.5)	0.1		
FSGS	0.6(0.2-1.7)	0.3	0.8(0.2-3)	0.8	1.8(1.1-2.9)	0.02		
MN	1.4(0.6-3.2)	0.3	1.8(0.6-5.5)	0.3	0.9(0.5-1.5)	0.6		
IgAN/V	3.8(1.5-9.6)	0.003	4.8(0.8-28)	0.08	1.9(1.1-3.2)	0.01		
FHx C	**Cancer**							
All	3.7(1.5-8.9)	0.003						
MCD	1.9(1.1-40)	0.04						
FSGS	3(0.8-11)	0.08						
MN	1.3(0.2-6.5)	0.7						
IgAN/V	1.5(0.01-40)	0.9						
FHx CD	**Deep Vein Thrombosis**		**Other thrombosis**					
All	2.9(1.6-5.3)	0.0003	3.3(1.7-6.5)	2E-04				
MCD	6.1(1.6-23)	0.007	36(6.7-200)	3E-05				
FSGS	4.8(1.5-15)	0.006	1.8(0.4-7.9)	0.4				
MN	1.5(0.4-5)	0.5	1.8(0.4-8.2)	0.4				
IgAN/V	2.8(0.6-12)	0.2	2.1(0.7-14)	0.1				
FHx AD	**In˘amm. Bowel disease**		**Celiac disease**		**Asthma**		**Drug allergies**	
All	2.3(1.3-4.3)	0.003	4.5(1.1-17)	0.03	1.9(1.4-2.5)	3E-06	1.5(1.2-1.9)	0.0001
MCD	1.2(0.2-6.1)	0.8			2.1(1.1-4)	0.02	1.4(0.8-2.4)	0.2
FSGS	2.8(0.4-18)	0.3			1.4(0.8-2.5)	0.2	2(1.3-3.1)	0.001
MN	2.7(0.9-7.5)	0.05	1.7(0.2-11)	0.5	2.1(1.1-4)	0.02	1.3(0.8-2.1)	0.2
IgAN/V	2.6(1.1-7)	0.04	1.3(1.2-14)	0.03	2.2(1.3-3.8)	0.002	1.6(1.1-2.6)	0.01

adjusted for age, sex, race, ethnicity, BMI, smoking, immunosuppressant use

P0356 **QUANTITATIVE ASSESSMENT OF GALNAC NUMBER IN THE HINGE REGION OF IGA1 IN IGA NEPHROPATHY WITH CRESCENTS FORMING**

Guizhen Yu[1], Yong Zhang[2], Xinfang Xie[1], Bo Meng[2], Wantao Ying[2], Jicheng Lv[1,3], Hong Zhang[1]

[1]Peking University First Hospital, Renal Division, Beijing, P.R. China, [2]Beijing Institute of Lifeomics, Beijing Institute of Lifeomics, Beijing, P.R. China and [3]Peking University First Hospital

Background and Aims: Aberrant IgA1 *O*-linked glycosylation of IgA1 hinge region (HR) has been shown playing an important role in the pathogenesis of IgA nephropathy (IgAN). Serum levels of galactose-deficient IgA1 (Gd-IgA1) was associated with the development and progression in IgAN, however variations in the composition of IgA1 HR glycoforms are unknown. In this study we aim to quantitative assessment of GalNAc number in the hinge region of IgA1 in IgAN with crescents forming using mass spectrometry.

Method: Plasma polymeric IgA1 (pIgA1) was purified from a discovery cohort including crescentic IgAN (n=11) non-crescentic IgAN (n=10) and healthy controls (HC, n=10) and a validation cohort (crescentic IgAN, n=10; non-crescentic IgAN, n=10 and healthy controls, n=11). After denaturation, reduction, alkylation and trypsin digestion, liquid chromatography-high-resolution mass spectrometry (LC-MS) was used to analyse the IgA1 HR glycans. The intensity of the identified IgA1 *O*-glycopeptide was calculated and expressed as the relative abundance for each glycopeptide. The molecular weight (MW) of intact *O*-glycopeptide was calculated as the formula following:

$MW = HR + x\ GalNAc + y\ Gal + z\ NeuAc + H^+$

(x, y and z represent the number of GalNAc, galactose and NeuAc which bind to one HR in IgA1 *O*-linked glycopeptides respectively)

Glycopeptide content ratio = (glycopeptide peak intensity/ total glycopeptide intensity) $\times 100\%$.

Results: In the discovery cohort population, the level of Gd-IgA1 was highest in patients with crescentic IgAN, middle in patients with non-crescentic IgAN and lowest in healthy controls (347.69±57.89 U/ml vs 336.32±38.44 U/ml vs 330.14±33.22 U/ml), albeit that didn't reach the statistical significance. There were significantly difference in GalNAc number of IgA1 HR among patients with IgAN and healthy controls. Overall the numbers of GalNAc bound to one HR was much lower in the patients than healthy controls. As shown in the Figure 1, the proportion of GalNAc 3, defined as *O*-glycans that were bound to one HR at 3 sites, were highest in patients with crescentic IgAN, then the non-crescentic IgAN and lowest in the healthy controls (9.92%±3.37% vs 6.65%±1.53% vs 4.05%±1.24%; p-value for the trend<0.001). Similar results were observed in GalNAc 4 (45.91%±4.75% vs 41.13%±2.95% vs 40.98%±2.95%; P=0.004. However regarding the GalNAc 5 and GalNAc 6, crescentic IgAN was lowest, then non-crescentic IgAN and highest in the healthy control (GalNAc 5: 45.17%±5.46% vs 46.90%±2.78% vs 48.05%±3.02%, P=0.001 GalNAc 6:1.62%±1.60% vs 3.95%±1.92% vs 5.39%±2.38%; P<0.001). These results were consistent in the validation cohort (Figure 1).

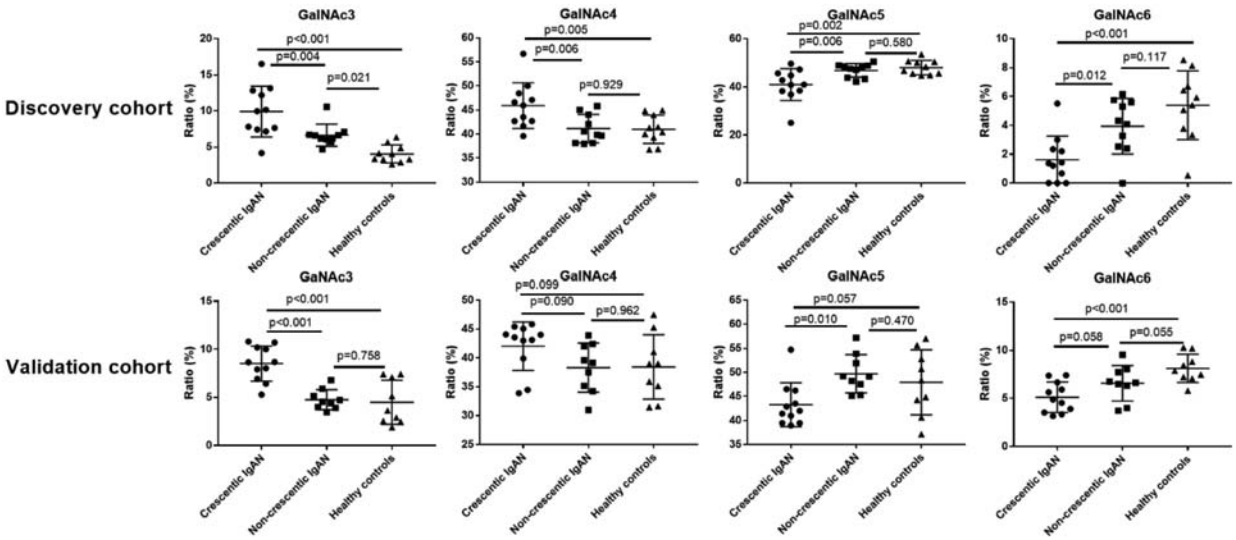


Figure 1: Comparison of *O*-glycans ratios according to the numbers of GalNAc. GalNAc 3, the proportion of GalNAc 3, defined as O-glycans that were bound to one HR at 3 sites.

Conclusion: GalNAc numbers in IgA1 HR was lower in patients with IgAN especially in crescentic IgAN. These results suggest that the *O*-glycans of IgA1 were associated with the severe phenotype in IgA nephropathy.

P0357

VALIDATION OF THE ANCA RENAL RISK SCORE IN A LONDON COHORT: POTENTIAL IMPACT OF TREATMENT ON PREDICTION OUTCOME

PEK GHE TAN[1], Jennifer O'Brien[1], Megan Griffith[1,2], Marie Condon[1], Tom Cairns[1], Jeremy Levy[1], Terry Cook[2], Charles Pusey[1,2], Stephen McAdoo[1,2]

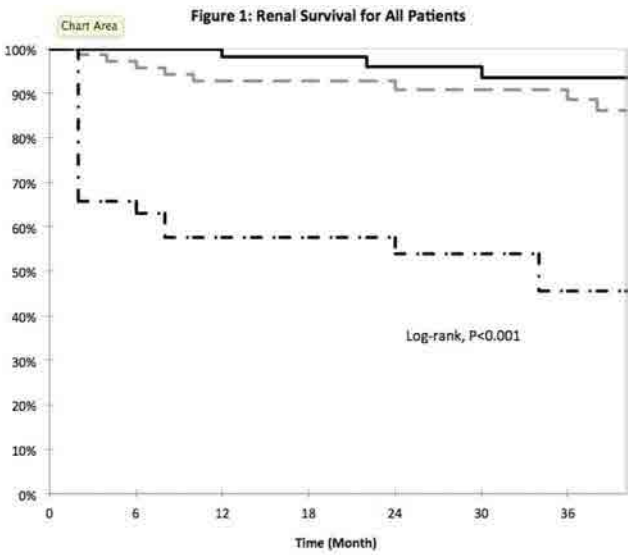
[1]Imperial College Healthcare NHS Trust, Specialist Nephrology Clinic, London, United Kingdom and [2]Imperial College London, Centre for Inflammatory Disease, London, United Kingdom

Background and Aims: A renal risk score was recently developed to predict the risk of progression to end stage kidney disease (ESKD) in patients with ANCA-associated glomerulonephritis (ANCA-GN). The score defines three risk groups, each with distinct renal survival at 36 months: 68% of high-risk patients reaching ESKD, compared to 26% and 0% in the medium- and low-risk groups, respectively. The majority of patients (101/115) used to define the risk score were treated with IV cyclophosphamide and steroids. At our centre, we employ a combined low-dose IV cyclophosphamide, rituximab and oral corticosteroid induction regimen, with or without plasma exchange (PEX) depending on disease severity, for ANCA-GN. A recent cohort study suggested this combination regimen may lead to better renal survival. We thus hypothesized that choice of remission-induction treatment may affect prediction accuracy of the risk tool. We retrospectively test the validity of the ANCA renal risk score in patients with ANCA-GN treated at our centre.

Method: All patients with newly diagnosed, biopsy-proven ANCA-GN from 2006-19 were identified from local renal histopathology database. Patients with relapsing ANCA-GN, EGPA, other coexisting GN, or missing data on induction therapy or eventual renal outcome were excluded. ANCA-negative pauci-immune GN was included. Baseline demographics, ANCA serology, initial therapy and parameters in the ANCA risk score (including % normal glomeruli, % tubular atrophy and interstitial fibrosis (TAIF), and estimated glomerular filtration rate were collected. All patients were stratified using the risk tool and Kaplan Meier survival analysis was applied to examine the ESKD prediction. Subgroup analysis was then performed for patients who received the combination regimen of cyclophosphamide and rituximab.

Results: 178 patients with a median follow up of 44 month were included in the analysis. The median age was 62 years and 82 patients (46%) were female. 94(53%) were MPO-ANCA positive, 66(37%) PR3-ANCA positive, 15 (8%) ANCA-negative, and 3 (2%) were double PR3/MPO-ANCA positive. 148 (83%) patients received the combination regimen, and 45 had concurrent PEX. Total of 37 (21%) patients reached ESKD. 29 (78%) of these, developed ESKD within 36 months of initial diagnosis. Using the risk score, 64(36%), 76(43%) and 38(21%) patients were deemed low-, medium- and high-risk, respectively. Very distinct poor renal survival at 36 months was seen in high-risk group (55% reaching ESKD, $p<0.01$), but was less apparent between low- (95%) and medium-risk (90%)($p=0.052$) (Figure1); In the subgroup of patients treated with combination regimen without concurrent PEX, the high-risk subgroup continues to demonstrate poor renal survival at 36 months (60% ESKD), but renal survival between low- and medium-risk group were comparable (0 and 2% respectively, $p=0.57$) (Figure 2).

Conclusion: In our cohort, the ANCA Renal Risk Score reliably predicted rapid ESKD progression at 36-month in high-risk patients, but was less accurate for distinguishing patients with low-and medium-risk. The subgroup analysis suggested combined cyclophosphamide and rituximab therapy may have modified long-term renal outcome especially in the medium-risk cohort, influencing the accuracy of the prediction tool. Large multi-centre cohorts are required to further evaluate the potential impact of treatment on predicting outcome.



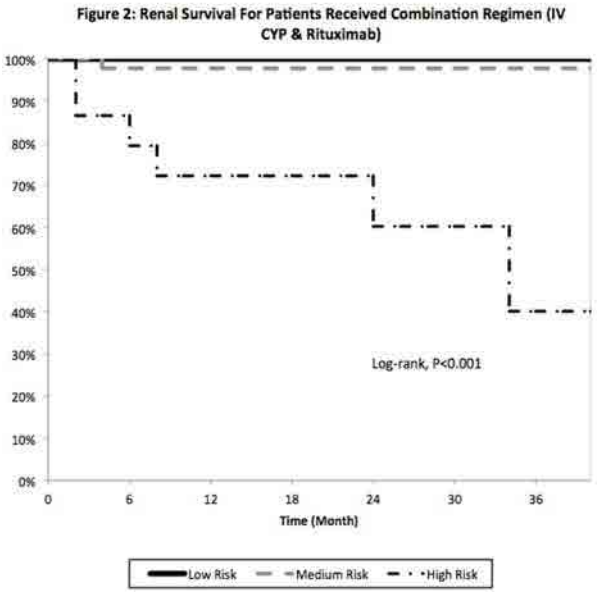


Figure:

P0358 HYDROXYCHLOROQUINE PREVENTS ANTI-GBM GLOMERULONEPHRITIS IN RATS.

Miki Torigoe[1], Yoko Obata[1], Hiro Inoue[1], Kenta Torigoe[1], Akira Kinoshita[2], Takehiko Koji[3], Tomoya Nishino[1]

[1]Nagasaki University Graduate School of Biomedical Sciences, Department of Nephrology, Nagasaki, Japan, [2]Nagasaki University Graduate School of Biomedical Sciences, Department of Human Genetics, Nagasaki, Japan and [3]Nagasaki University Graduate School of Biomedical Sciences, Department of Histology and Cell Biology, Nagasaki, Japan

Background and Aims: Anti-glomerular basement membrane (GBM) glomerulonephritis (GN), characterized by glomerular crescent formation, requires early treatment because of poor prognosis. Hydroxychloroquine (HCQ) is a well-known antimalarial drug. In addition, it has immunomodulatory, anti-inflammatory, and autophagy inhibitory effects and its recognized in the treatment of autoimmune disease such as SLE. However, its effect for anti-GBM GN is unknown. In this study, we investigated the effect of HCQ against anti-GBM GN in rats.

Method: 7 week old male, WKY rats were induced by the administration of anti-GBM serum (50μg/rat). We administered either HCQ (50mg/kg) or vehicle (Phosphate-buffered saline) from day 0 to day 7 after the induction of nephritis. Renal function was assessed by measuring serum creatinine, proteinuria, hematuria. Urine was collected for 24 hours on day 1, 3, 5, and 7. Rats were sacrificed on day 7 after induction of anti-GBM GN. Renal histological changes were assessed by PAS staining, and Masson trichrome stain, and macrophage was assessed by ED-1 stain. Mitogen-Activated Protein Kinase (MAPK) was evaluated by western blotting (WB) and inflammatory cytokines were evaluated by ELISA using urine.

Results: HCQ treatment suppressed renal function decline. Histologically, extracellular and intracellular cells were increased from day 1, fibrinoid necrosis and ED-1 positive cells were observed from day 3. Rats with anti-GBM GN had high levels of interferon-α, interleukin-6, monocyte chemotactic protein-1, and tumor necrosis factor-α. These changes were significantly suppressed by HCQ. In addition, HCQ suppressed phosphorylation of JNK/p38 MAPK.

Conclusion: Our study showed that HCQ could attenuate anti-GBM GN and have an anti-inflammatory effect by inhibiting JNK/p38 MAPK activation. HCQ may have therapeutic potential in anti-GBM GN.

P0359

CROSS-TISSUE AND MURINE-HUMAN COMPARATIVE TRANSCRIPTOME ANALYSES IDENTIFY TARGETABLE GENES FOR HUMAN SYSTEMIC LUPUS ERYTHEMATOUS AND LUPUS NEPHRITIS

Eleni Frangou[1,2], Panagiotis Garantziotis[1], Maria Grigoriou[1], Angelos Banos[1], Nikolaos Panousis[3], Emmanouil Dermitzakis[3], George Bertsias[4], Dimitrios T. Boumpas[1,5,6], Anastasia Filia[1]

[1]Biomedical Research Foundation of the Academy of Athens, Lab of Autoimmunity and Inflammation, Athens, Greece, [2]Limassol General Hospital, Department of Nephrology, Limassol, Cyprus, [3]University of Geneva, Institute of Genetics and Genomics, Geneva, Switzerland, [4]University of Crete, Department of Rheumatology, Clinical Immunology and Allergy, Heraklion, Greece, [5]National and Kapodistrian University of Athens, 4th Department of Internal Medicine, Attikon University Hospital, Athens, Greece and [6]University of Cyprus, medical School, Nicosia, Cyprus

Background and Aims: Systemic Lupus Erythematosus (SLE) is a complex disease associated with non-synchronous multi-tissue dysfunction of varying severity. Involvement of major organs, such as kidneys, contributes significantly to morbidity and mortality. We sought to unravel new pathways to be used as potential biomarkers and therapeutic targets. To this end, we compared the patterns of gene transcription -as determined by the use of RNA-sequencing- across tissues between healthy and lupus-prone mice at different stages of the disease, and explored their implications for human disease and prediction of kidney involvement, in our whole blood RNA sequencing dataset comprised of 120 SLE [55 lupus nephritis (LN), 65 non-LN] patients and 58 healthy individuals (HI).

Method: NZB/W-F1 lupus-prone mice were sacrificed at the pre-puberty, pre-autoimmunity and nephritic stage. Age-matched C57BL/6 mice were used as controls. An "effector" tissue (spleen) and major end-organ tissues (kidneys, brain) were collected. Total RNA was isolated, and mRNA-sequencing was performed. Differential expression and time-series analyses were performed using DESeq2. Differentially expressed genes (DEGs) were hierarchically clustered and functionally interpreted using gProfiler enrichment analysis. Human orthologous genes of mouse common DEGs in each tissue and across all disease stages, were compared to human DEGs. Using machine learning techniques, human orthologs identified in the common DEGs across all stages in the kidneys of lupus-prone vs healthy mice were used to predict kidney involvement in the human dataset, which was split in training and validation sets.

Results: ***Gene signatures:*** the *common cross-tissue signature* was identified by the comparison of DEGs between tissues of lupus-prone vs healthy mice at each stage of the disease. A total 134 genes (including *C4A, LYRM7* and *HDDC3*) were found, suggesting their involvement in a common pathogenic mechanism across "effector" and end-organ tissues. *Tissue-specific signatures* showed enrichment of FCERI mediated NF-kB activation pathway in the spleen, steroid hormone biosynthesis pathway in the kidney and phosphatidylcholine metabolic process in the brain, suggesting distinct pathways implicated in end-organ injury.

Comparative murine-human transcriptome analysis: 76 human orthologs (including *CCL5*, *IFIT* and *HLA* genes) identified in the murine spleen signature were also differentially expressed in SLE patients vs HI, suggesting their involvement in systemic autoimmunity. A total of 68 human orthologs (including *FCGR2A*, *C1R* and *JAK1*) identified in the mouse kidney-signature and 25 human orthologs (including *APOA2*) identified in the mouse brain-signature, were differentially expressed in LN patients vs HI and neuropsychiatric SLE patients vs HI, respectively.

Kidney involvement prediction in human SLE: using a neural network model, 193 human orthologs predicted LN patients vs HI with high accuracy (accuracy=0.86, sensitivity=0.82, specificity=0.91 in the validation set). Using a support vector machine model, 30 human orthologs and age and gender were the best predictors of LN vs non-LN SLE patients (accuracy=0.71, sensitivity=0.73, specificity=0.69 in the validation set).

Conclusion: Murine RNA-sequencing uncovered both shared cross-tissue and tissue-specific gene signatures that could be potentially targeted in SLE. Murine-human comparative transcriptome analysis revealed common gene signatures suggesting that similar biological processes and pathways are disturbed across species, with murine kidney lupus signature predicting kidney involvement in human SLE. Validation in other datasets is ongoing.

P0360 **URINARY PEPTIDOMIC ANALYSIS IN PROLIFERATIVE VERSUS NON-PROLIFERATIVE LUPUS NEPHRITIS : RESULTS OF THE PEPTIDU-LUP STUDY.**

Maxence Tailliar[1], Joost Schanstra[2], Tim Dierckx[3], BREUIL Benjamin[2], Guillaume Hanouna[4], Mickael Bobot[1], Stephane Burtey[1], Bertrand Dussol[1], Laurent Chiche[5], Justyna Siwy[6], Stanislas Faguer[7], Laurent Daniel[8], Eric Daugas[9], Noemie Jourde-Chiche[10]

[1]AP-HM,Centre de Néphrologie et Transplantation Rénale, Hôpital de la Conception, Marseille, France, [2]Université de Toulouse, INESERM U1048, I2MC, Toulouse, France, [3]KU Leuven, Microbiology and Immunology, Laboratory of Clinical and Epidemiological Virology, Leuven, Belgium, [4]4AP-HP, Service de Néphrologie, Hôpital Bichat, Paris, France, [5]Médecine interne, Hôpital Européen, Marseille, France, [6]Mosaiques Diagnostics, GmbH, Hannover, Germany, [7]CHU de Toulouse, Service de Néphrologie, Toulouse, France, [8]AP-HM, Laboratoire d'Ananatomie Pathologique, Hôpital de la Timone, Marseille, France, [9]AP-HP, Service de Néphrologie, Hôpital Bichat, paris, France and [10]AP-HM, Centre de Néphrologie et Transplantation Rénale, Hôpital de la Conception, Marseille, France

Background and Aims: Lupus nephritis (LN) is a frequent manifestation of Systemic Lupus Erythematosus (SLE). The therapeutic strategy relies on the result of kidney biopsy, which differentiates proliferative LN (PLN) from non-proliferative LN (NPLN). The analysis of the urinary peptidome has led to the identification of prognostic biomarkers in chronic kidney disease (CKD, namely the CKD273 classifier), or, as a liquid biopsy, for the diagnosis of glomerulonephritides. We verified whether urinary peptidomics could predict the severity of renal pathological injury and damage in LN.

Method: Urine samples, collected before kidney biopsy, were analyzed by capillary-electrophoresis coupled to mass-spectrometry (CE-MS). Urinary peptide profiles were compared between PLN and NPLN. Predictive values for chronic pathological lesions (glomerulosclerosis and interstitial fibrosis/tubular atrophy (IF/TA)), response to therapy and development of CKD were also assessed. Clinical characteristics, routine laboratory parameters and immunological SLE markers were collected at inclusion and prospectively for at least 24 months.

Results: We collected 100 urinary samples from patients with LN, forming a discovery (n=67) and an independent validation (n=33) cohort. Overall there were 69 patients with PLN (class III or IV +/-V with active lesions) and 31 patients with NPLN (class II or V or chronic lesions). In the discovery cohort, the abundance of 36 urinary peptides differed between PLN and NPLN (Mann-Whitney test). However, these peptides did not resist multiple testing correction. Among them, 17 could be sequenced (fragments of collagen-I, -II, -III, apolipoprotein A-I, Fibrinogen alpha chain and Histone H2B). Of the 17 sequenced peptides, 7 were also part of the CKD273 classifier. A mathematical model combining the 36 peptides classified PLN and NPLN patients from the validation cohort with an AUC of 0.75 and sensitivity and specificity of 0.81 and 0.53, respectively. Positivity of anti-dsDNA antibodies had the best sensitivity (0.96) and sterile pyuria the best specificity (0.68) to differentiate PLN from NPLN, and including the CKD273 score did not improve the accuracy of the predictive models. No urinary peptidomics profile was identified to predict early response to therapy in patients with LN.

Glomerulosclerosis was observed in 63/100 biopsies. In the discovery cohort, the abundance of 38 urinary peptides (including 22 sequenced) differed between patients with vs without glomerulosclerosis (Mann-Whitney test). Again, these peptides did not resist multiple testing correction. Of the 22 sequenced peptides, 7 (different from the peptides associated with PLN) belonged to the CKD273 classifier. A mathematical model combining the 38 peptides classified patients from the validation cohort with an AUC of 0.75 and sensitivity and specificity of 0.82 and 0.54, respectively, for the presence of glomerulosclerosis. Although the quantification of IF/TA was correlated to the pre-existing CKD273 classifier, including the CKD273 score did not improve the prediction of IF/TA when tested in combination with simple clinical parameters. Only 3 patients developed CKD after a mean follow-up of 4 years, therefore contribution of urinary peptidomics for the prediction of CKD in LN could not be evaluated.

Conclusion: Different urinary peptidomics signatures were identified among patients with LN, according to the presence of active proliferative lesions or chronic lesions. However, these panels did not resist multiple testing correction, and did not improve the diagnostic accuracy when combined with clinical or immunological markers. The contribution of urinary peptidomics to predict CKD in patients with LN, or as an early predictor of renal flares, could not be evaluated. Kidney biopsy remains central for the care of patients with LN.

P0361 **THE PREDICTIVE VALUE OF SERUM URIC ACID IN PRIMARY GLOMERULONEPHRITIS PATIENTS: A 5-YEARS RENAL PROGNOSIS**

Mykola Kolesnyk[1], Natalia Stepanova[1], Lyudmyla Snisar[1], Larysa Lebid[1]

[1]*State Institution «Institute of Nephrology of the National Academy of Medical Sciences», Nephrology & Dialysis, Kyiv, Ukraine*

Background and Aims: Primary glomerulonephritis (PGN) is one of the leading causes of end-stage renal disease worldwide. Preservation of renal function is a crucial global goal in the management of patients with chronic kidney disease (CKD) in general and PGN in particular. In addition to classical risk factors, hyperuricemia is regarded to be an independent risk factor for CKD development and progression. However, only a few studies have investigated the impact of hyperuricemia on PGN progression.

Therefore, this study aimed to analyze the association between serum uric acid (SUA) concentration and renal prognosis in PGN patients during a 5-year follow-up.

Method: A total of 344 patients with CKD 1-3 stages were included in this retrospective observational single-center study. Among them, there were 194 (56.4 %) patients with biopsy-proven PGN and 150 (43.6 %) patients with a clinical diagnosis of PGN. All patients were treated according to the KDIGO Practice Clinical Guidelines for Glomerulonephritis.

eGFR (milliliters per minute per 1.73 m^2) was calculated using the CKD-EPI formula and its baseline value was based on the first available eGFR in PGN diagnosed patients. The patients with eGFR< 30 mL//min/1.73 m^2 were excluded from the study at the time of PGN diagnosis. None of the patients was on urate- or lipid-lowering therapy at the time of baseline data.

Hyperuricemia was defined as SUA concentration ≥420 μmol/L (7 mg/dL) for males and ≥360 μmol/L (6 mg/dL) for females. The rate of eGFR fall per year was used to assess CKD progression. It was calculated as the difference between eGFR (mL/min/1.73m2) at baseline and the last values: (Last eGFR – Baseline eGFR) / Follow-up period per year).

For the analysis, the patients were gender-stratified into 3 SUA quartiles according to average SUA levels at baseline: Q1- < 265 μmol/L for men and <220 μmol/L for women, Q2- 265-446 μmol/L for men and 220-369 μmol/L for women, Q3- ≥ 447 μmol/L for men and ≥ 370 for women. The analysis and all graphs were performed using MedCalc (Belgium).

Results: Hyperuricemia was found in 72/206 (35 %) men and 38/138 (27.5 %) women (p = 0.0003). During the average 5-years follow-up period (5.3 [3.8-6.2]), there were 114 (33.1%) patients who eventually progressed to eGFR<15 mL/min/1.73 m2 or started RRT. Among them there were: Q1- 10 (12%) patients, Q2 - 52 (31.5%) patients, Q3 - 52 (54.7%) patients (p< 0.0001).

The highest renal progression level was observed in Q3 patients: -5.5 [-15.4; -1.8] mL/min/1.73 m^2 versus -3.5 [-6.4; -1.7] and -4.6 [-10.6; -2.7] mL/min/1.73 m^2 in Q2 and Q1 patients, respectively. In multivariate logistic regression analysis, SUA level in men (≥ 447 μmol/L) and women (≥ 370) was determined as an independent risk factor for rapid CKD progression (OR: 2.5, 95% CI: 1.47-4.23, P = 0.0007).

Conclusion. Our study showed that a higher SUA level was associated with a significant rapid eGFR decline during a 5-year follow-up. The study findings suggest that hyperuricemia is a potentially modifiable factor for CKD progression.

P0362 ROLE OF REPEATED RENAL BIOPSY IN ANCA VASCULITIS

MAROUA BAAZIZ[1], Eric Thervet[2], Dominique Nochy[2], KARRAS Alexandre[2]

[1]Hospital André Grégoire, Montreuil, France and [2]Hôpital Européen Georges-Pompidou, Paris, France

Background and Aims: Antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is a systemic disease characterized by inflammation of small vessels and presence of ANCA. Pauci-immune necrotizing crescentic glomerulonephritis is a severe renal complication of AAV. Despite immunosuppressive therapy, relapses are frequent during the course of the disease, affecting up to 50% of the patients.

Kidney biopsy is routinely used to diagnose AAV at initial presentation and to predict renal prognosis. Although the activity of renal AAV is not easily evaluated by plasma or urine biomarkers, kidney biopsy is rarely performed when relapse is suspected.

We herein analyze the clinical, laboratory and renal pathology data from patients who underwent repeated kidney biopsies during the course of AAV.

Method: We retrospectively reviewed data from 37 patients who underwent at least 2 kidney biopsies in our centre, between 2002 and 2018. The first renal biopsy (B1) was constantly performed at diagnosis. A follow-up biopsy (B2) was performed for purpose, either for suspicion of refractory disease or confirmation of renal relapse.

Modifications of renal pathology between B1 and B2 were studied, by comparing presence of active and chronic lesions. Active lesions were defined by the presence of cellular crescents and/or fibrinoid necrosis. Chronic lesions were quantified by the percentage of globally sclerotic glomeruli and the percentage of interstitial fibrosis / tubular atrophy (IF/TA).

Results: Median age at diagnosis was 57 years, M/F ratio was 21/16. ANCA specificity was anti-MPO in 65% of cases, anti-PR3 in 32%. The median delay between B1 and B2 was 3,3 [0,9-5,8] years. B2 was done for suspicion of refractory disease (n=8) or of renal relapse (n=29). Causes of B2 were : persistence or reappearance of haematuria in 78% of cases, increase of creatinine in 43%, increase of ANCA titer in 67%.

Systemic AAV activity was more important at B1 vs B2 (median BVAS 18 vs 9), as well as renal dysfunction (median sCreat 200 vs 156 µmol/l).

Active glomerulonephritis was constantly found at B1 but was present in only 35% of B2. Presence of cellular crescents decreased from 71,4 to 29,7% ($p = 0,002$), whereas fibrinoid necrosis decreased from 80,6 to 35,1% ($p = 0.0003$).

Five factors were significantly associated with the presence of active lesions : presence of at least one extra-renal AAV manifestation ($p = 0.0006$), increase of ANCA titer ($p = 0.0022$), CRP>30mg/l ($p = 0.001$), absence of IF/TA ($p=0,02$) and high percentage of normal glomeruli ($p=0,014$) at B1. Interestingly, level of proteinuria and persistence of hematuria were not associated with histological activity at B2 ($p =0,64$ and 0,22 respectively).

In contrast, chronic lesions such as glomerulosclerosis and IF/TA were more severe at B2 compared to B1 ($p <0,0001$ and 0,014 respectively). The worsening of fibrotic lesions was not associated with ANCA specificity (anti-MPO vs -PR3).

Conclusion: This is the largest cohort reporting on repeated renal biopsy in AAV. Despite several clinical and laboratory signs suggesting active renal AAV, B2 revealed no relapse in 2/3 of cases, allowing avoidance of a new immunosuppressive induction treatment. Our results suggest that rebiopsy is crucial when renal relapse is suspected, as proteinuria and hematuria do not predict active disease, suggesting that their persistence could be explained by glomerular scarring.

P0363 ANTIPROLIFERATIVE AGENTS IN ADDITION TO STEROIDS IN IGA NEPHROPATHY: A SINGLE-CENTER COHORT STUDY

Francesco Fontana[1], Emanuela Vicari[2], Giulia Ligabue[2], Silvia Giovanella[2], Gaetano Alfano[1], Marco Leonelli[1], Gianni Cappelli[2]

[1]Policlinico of Modena University Hospital of Modena, Nephrology and Dialysis Unit, Modena, Italy and [2]University of Modena and Reggio Emilia, Nephrology and Dialysis Unit, Modena, Italy

Background and Aims: IgA nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide. The optimal approach to its treatment remains a significant challenge; despite recent evidence suggesting that immunosuppressive (IS) therapy does not offer significant benefits over supportive treatment alone, many nephrologists continue to offer steroids and other IS drugs to patients in order to reduce proteinuria and prevent progressive kidney dysfunction. Anti-proliferative agents have been used in combination with steroids to treat IgAN, but data regarding their efficacy are controversial, especially in Caucasian patients.

Method: We conducted an observational, single center retrospective cohort study to compare the efficacy of different IS regimens in the treatment of IgAN. We included 48 patients (98% Caucasians) with a histological diagnosis of IgAN and without crescentic glomerulonephritis. Patients were divided into three groups according to treatment: steroids alone (ster, n=11), steroids + mycophenolate mophetil (ster+MMF, n=28) and steroids + azathioprine (ster+aza, n=9). Data regarding histological characteristics at diagnosis (MEST-C score, percentage of interstitial fibrosis/tubular atrophy), serum creatinine and proteinuria/creatininuria (P/C) during follow-up, and progression to end stage kidney disease (ESKD) were collected for all patients; adverse events were registered. As primary outcome we considered the complete response at 24 months, defined as a composite outcome of proteinuria/creatininuria < 0.3 and $<20\%$ reduction of eGFR during follow-up. Secondary outcomes were: differences in time-averaged proteinuria (TAP), 50% reduction of P/C from baseline, eGFR<30 ml/min, development of ESKD.

Results: Mean follow-up for our cohort was 53.88 months. Clinical baseline characteristics did not differ significantly among groups, apart for male sex, more expressed in the steroid group (see table 1). Groups were comparable for histological characteristics at diagnosis (table 2). Interestingly, the addition of anti-proliferative agents did not lead to a reduction of total steroid dose (table 3). Time to complete response in the first 24 months, estimated with Kaplan-Meier method with log-rank test, was not different between the three groups (p=0.44, see figure 1). Moreover, we encountered no differences in TAP measured at 6-months periods for the first two years (figure 2). Groups were also comparable in time to 50% reduction in P/C from baseline, time to eGFR<30 ml/min, time to ESKD (figure 3). No significant adverse events were registered, apart from a higher incidence of diarrhea in the ster+MMF (14%) and ster+aza (11%) groups compared to the ster group. At multivariate logistic regression after adjusting for age and sex, only P/C at baseline was predictive of the absence of complete response (figure 4).

	steroids	steroids + MMF	steroids + AZA	p value
n. of patients	11	28	9	
age, yr	39 (35-55)	35 (28,25-46,5)	35 (31-54,5)	0,34
male, nr (%)	11 (100)	16 (57,1)	8 (88,9)	0,01
body mass index	24,9 (22,73-26,40)	25,25 (23,05-27,63)	23,80 (20,85-25,80)	0,33
mean arterial pressure	90 (81,50-97,75)	91,50 (84,00-103,0)	90 (86-102,5)	0,80
serum creatinine, mg/dl	1,450 (0,91-3,59)	1,305 (0,9150-1,665)	1,040 (0,94-2,115)	0,64
estimated GFR, ml/min per 1.73 m2	58,40 (18,70-108,5)	60 (45,03-102)	81,80 (38,5-91,75)	0,78
eGFR < 30 ml/min, nr (%)	3 (27,3)	3 (10,7)	2 (22,2)	0,41
proteinuria / creatininuria	0,9 (0,67-2,3)	1,23 (0,64-2,29)	0,8 (0,3-3,2)	0,72
hematuria, nr (%)	132 (46-233,5)	99 (22-211)	86,5 (27,75-169)	0,93
serum albumin, g/dl	4 (3,7-4,3)	3,9 (3,62-4,1)	4 (3,6-4,45)	0,43
serum cholesterol, mg/dl	211 (163-218)	189 (162,5-222,5)	177 (165-190,5)	0,50

Figure 1. Kaplan-Meier curves for time to complete response in the first 24 months.

	steroids	steroids + MMF	steroids + AZA	p value
M>0, nr (%)	11 (100)	25 (89,3)	9 (100)	0,32
E>0, nr (%)	10 (90,9)	23 (82,1)	8 (88,9)	0,74
S>0, nr (%)	10 (90,9)	28 (100)	8 (88,9)	0,23
T>0, nr (%)	6 (54,5)	18 (64,3)	7 (77,8)	0,56
C>0, nr (%)	1 (9,1)	10 (35,7)	3 (33,3)	0,25
IFTA, %	25 (12,5-45)	26,25 (15-41,88)	25 (17,5-32,5)	0,79

Figure 2. Time averaged proteinuria in 6-months periods for the first 2 years.

		steroids	steroids + MMF	steroids + AZA	p value
steroid					
	months on steroids	10,5 (8,5-12,5)	10 (9-11)	11 (11-12)	0,04
	cumulative dose (g)	4948 (3498-5465)	4968 (4104-5425)	4852 (4270-5347)	0,96
	dose mg/kg	56,85 (44,83-75,70)	69,10 (53,08-76,73)	69,30 (55,40-79,90)	0,51
MMF					
	average months on MMF		14.6		
	average dose (mg/day)		855		
Aza					
	average months on Aza			18.3	
	average dose mg/day			72	

Figure 3. Kaplan-Meier curves for time to 50% reduction in proteinuria from baseline, survival from GFR<30 ml/min, survival from ESKD.

Conclusion: In our study, the combination of MMF or aza plus steroid treatment did not offer any benefit over steroids alone in terms of reduction of proteinuria and reduction of eGFR in IgAN patients. Even if safe in terms of severe complications (only mild to moderate diarrhea was reported in the anti-proliferative groups), currently evidence is lacking to support their use in Caucasian patients. Limitations of our study include its retrospective and single-center design, and the relatively low number of patients.

P0364

A NOVEL INTERPLAY BETWEEN INTESTINAL BACTERIA AND METABOLITES IN IGA NEPHROPATHY IDENTIFIED VIA INTEGRATED MICROBIOME AND METABOLOME APPROACHES

Hongwei Wu[1], Yong Dai[2], Fanna Liu[1], Lianghong Yin[1]

[1]The First Affiliated Hospital of Jinan University, Department of Nephrology and Blood Purification, Guangzhou, P.R. China and [2]The Second Clinical Medical College of Jinan University, Department of Nephrology and Blood Purification, Shenzhou, P.R. China

Background and Aims: Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis. Intestinal bacteria and their metabolites have been implicated in various diseases. Improved understanding of the gut microbiota and its metabolic capabilities will facilitate development of diagnostic, therapeutic, and prognostic methods for IgAN

Method: We identified gut microbiota and metabolite biomarkers of IgAN by analyzing microbiomes and metabolomes of fecal and serum samples of IgAN patients and healthy controls using 16s ribosomal RNA gene sequencing and liquid chromatography-tandem mass spectrometry, respectively, and bioinformatics approaches

Results: We found that relative abundances of *Streptococcus* and *Enterococcus* were higher in IgAN patients, whereas *Bacteroidetes* and *Bacteroides* were lower. The changes in gut microbiota affected metabolism and absorbance of microbiota-associated metabolites of IgAN patients, in particular polyunsaturated fatty acids, free amino acids and oligopeptides, and activated the phenylalanine metabolism pathway. Also, 5-hydroxyeicosatetraenoic acid and 5-hydroxy-6E,8Z,11Z-eicosatrienoic acid were proved to be associated with the classification of segmental glomerular sclerosis but not 24h urine protein and estimated glomerular filtration rate.

Conclusion: Our findings demonstrate an interplay between intestinal bacteria and metabolites in IgAN. The identified metabolites may have diagnostic and therapeutic applications.

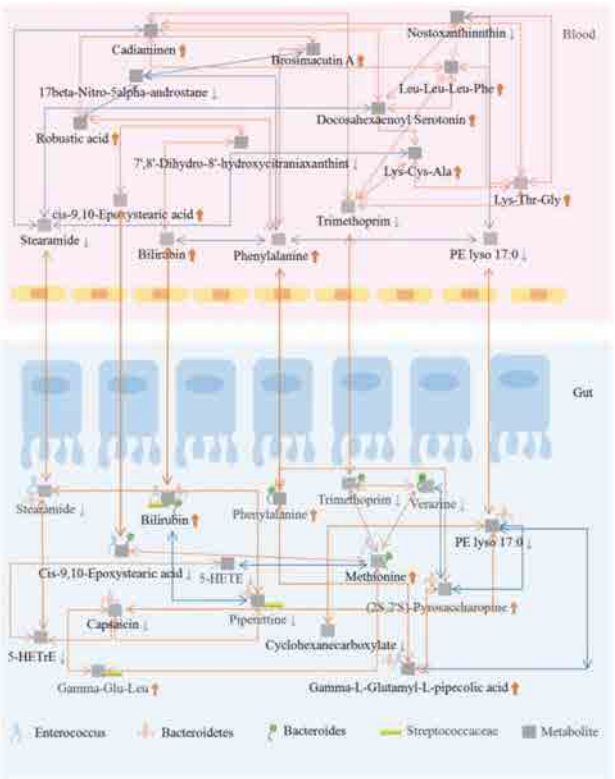


Figure. Fecal microbe-serum metabolite-fecal metabolite network in IgA nephropathy patients.

P0365 INCREASED LIFETIME RISK OF END-STAGE RENAL DISEASE IN FAMILIAL IGA NEPHROLOGY

Jingyuan Xie[1]

[1]*Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Nephrology Department, Shanghai, P.R. China*

Background and Aims: Familial IgA nephropathy (IgAN) has been widely reported around the world. However, it's clinico-histological characteristics and long-term prognosis are not clear.

Method: In this study, 348 familial IgAN cases from167 independent IgAN families were recruited and their clinico-histological characteristics were compared to 1,116 sporadic IgAN patients from the same geographic region. Inheritance patterns, clinical features, and treatment regimens of all recruited patients were recorded and lifetime risk of end-stage renal disease (ESRD) was compared between familial and sporadic cases.

Results: Of all familial IgAN patients, 60 (17%) came from 32 single-generation (SG, defined as all affected individuals are siblings) families, while 286 (82%) came from 134 multiple-generation (MG, affected individuals were present in at least two consecutive generations) families. There're totally 178 transmissions, 79 of which (44%) were paternal transmission and 99 (56%) were maternal transmissions. We observed evidence for incomplete penetrance in 30 (22%) MG families. The lifetime risk of progression to ESRD was significantly higher in familial IgAN patients than sporadic patients after adjusted by gender [HR=1.40, 95%CI: 1.12-1.74, P=0.004], with 5-year younger in median ESRD onset age [median ESRD-free survival of 60 years vs. 65 years in familial and sporadic cases separately]. As expected, compared to the ones without progressive renal failure at disease onset (eGFR$\geq$60ml/min), familial cases with progressive renal failure (eGFR$<$60ml/min) had higher risk of lifetime ESRD [HR=6.32, 95%CI: 3.73-10.72, P$<$0.001]. Interestingly, among familial cases, we found cases from SG families [vs MG families: HR=2.62, 95%CI: 1.59-4.31, P$<$0.001] or with early onset (onset age $<$30yrs) [vs late onset: HR=4.79, 95%CI: 3.16-7.26, P$<$0.001] had higher lifetime risk of ESRD. Furthermore, among sporadic patients, compared to females, males had lower eGFR, higher urine protein, higher Oxford T score and resulted in a higher risk for lifespan ESRD (male vs female, 25% vs 17%, P=0.003) while these gender difference was not seen in familial patients.

Conclusion: In conclusion, familial IgAN cases had poorer renal outcomes and less gender differences compared to sporadic cases. These findings provide evidence that familial disease represent a distinct subtype of more progressive IgAN.

P0366 SAFETY OF STEROID THERAPY IN IGA NEPHROPATHY: THE CLINICAL EXPERIENCE OF 48 NEPHROLOGY UNITS IN ITALY

Ivano Baragetti[1], Francesca Ferrario[2], Federico Alberici[3], Andrea Amendola[4], Maria Carmen Luise[5], C Sarcina[6], Anna Sara Sorrentino[7], Cristiana Rollino[8], Domenico Giannese[9], Elena Mancini[10], Alessandra Pola[3], Mario Cozzolino[11], Claudio Pozzi[12]

[1]Ospedale Bassini, Medicine- Division of Nephrology and Dialysis, Cinisello Balsamo, Italy, [2]Ospedale Bassini, Medicine-Division of Nephrology and Dialysis, Cinisello Balsamo, Italy, [3]ASST Civil Hospital of Brescia, Division of Nephrology and Dialysis, Brescia, Italy, [4]IRCCS MultiMedica, Division of Nephrology and Dialysis, Sesto San Giovanni, Italy, [5]Ospedale Bassini, Division of Nephrology and Dialysis, Cinisello Balsamo, Italy, [6]ASST Santi Paolo e Carlo, Emergency Department, Milano, Italy, [7]Azienda Ospedaliero-Universitaria Careggi, Division of Nephrology and Dialysis, Firenze, Italy, [8]Ospedale San Giovanni Bosco, Division of Nephrology and Dialysis, Torino, Italy, [9]Pisa, Ospedale Cisanello, Division of Nephrology and Dialysis, Pisa, Italy, [10]Policlinico Sant'Orsola-Malpighi, Division of Nephrology and Dialysis, Bologna, Italy, [11]ASST Santi Paolo e Carlo, Division of Nephrology and Dialysis, Milano, Italy and [12]In Salus, Nephrology, Lecco, Italy

Background and Aims: Steroid therapy is efficient in inducing remission of IgA nephropathy (IgAN) and preventing end stage renal disease (ESRD) but there are concerns about their safety. The TESTING trial in particular has been stopped early because of a higher incidence of side effects than conservative treatment thus inducing a conservative therapy with RAAS (renin angiotensin antagonist system) blockers. The aim of this analysis was to evaluate the incidence of adverse events (AE) in a retrospective observational trial on the real clinical practice.

Method: We evaluated 1209 patients (pz) with IgAN coming from 48 Italian centers: 285 pz in RAAS blockers alone, 732 treated for 6 months with steroid and 192 with a combination of steroid and other immunosuppressants (also with RAAS blockers). The analysis was limited to the 6 months of therapy.

Results: The basal characteristics of the 3 groups are shown in the table below.

The figure shows the frequencies of 69 adverse events related with immunosuppression: the most frequent were infections (23, 2.73% of all patients, 34.3% of all AE), impaired glycemic control (11, 0.91% of patients, 16% of all AE), severe hypertension (6, 8.7% of all AE) and leukopenia (9, 0.80% of patients, 13% of all AE). Infections were observed in 16 (2.19%) pz in steroid therapy and 7 (3.65%) pz in steroid+immunosoppressive treatment. Liver toxicity and and gastrointestinal AE were observed almost in pz receiving steroid+ immunosuppressants [1(0.14%) and 2 (1.04%) pz, respectively]. 7 pz in steroid therapy (0.96%) and 2 in steroid+ immunosuppressants experienced an impaired glycemic control. All the 9 cases of leucopenia were registered in pz in steroid+ immunosuppressants (4.69%). A slightly higher incidence of allergies was observed in the RAAS blocker group (20 cases, 0.7%). The higher rates of infections and leucopenia were observed in pz above 70 years of age (6.12%,$p<0.05$), as higher incidence of infections and impaired glycemic control were registered in pz with an eGFR<30 ml/min/1.73 m^2 (4.64 and 1.99%,$p<0.05$). Severe hypertension and leucopenia were observed respectively in 9 and 3 pz with an eGFR <60 ml/min/1.73m^2. No significant relationships were found between AE, proteinuria and sex. Multivariate logistic regression showed an independent association of immunosuppressive treatment and age with any AE [ODDS ratio: 3,35 (CI:2,18-5,14) and 1,02 (CI:1,01-1,04), respectively; $p<0.05$]. Death occurred for sepsis in a 70 years old pz (eGFR=21.7 ml/min/m^2, 24hproteinuria=16.1 g/day) after 3 months of treatment.

Conclusion: the incidence of EA in our observational study is lower than that observed in the TESTING and STOP trials (5.71% vs 14.7% and 40%, respectively). The most frequent AE were almost observed in oldest subjects with impaired renal function on steroid+other immunosuppressants. Though this trial is not randomized nor controlled (RC), it considers a large cohort of pz coming from the real clinical practice of the Italian Nephrology Units and demonstrates that the significantly lower incidence of steroid related AE than that observed in some RC trials doesn't justify the abstention from steroids in IgAN at risk of progression. Much more attention should be paid in elderly pts with severe renal dysfunction with a closer follow-up, dose adjustments and antibiotic prophilaxis.

	RAAS blockers	Steroids	Steroids+ azathioprine	p
Creatininemia (mg/dl) (mean ± SD)	1.41 ±0.80	1.48 ±0.86	1.80 ±1.38	0.0001
eGFR (ml/min) (mean ± SD)	70.50 (±31.05)	69.08 (±31.84)	62.80 (±32.62)	0.0233
Proteinuria (g/24h) (mean ± SD)	1.90 (±2.43)	2.44 (±2.12)	3.16 (±2.66)	0.0001
Males/Females (%)	69/31	72/23	72/28	ns
Age (years) (mean ± SD)	42.74 (±14.94)	41.78 (±14.94)	39.97(±14.73)	0.1364
Arterial hypertension (%)	59	50	42	ns

Figure:

P0367

STATIN THERAPY AS A PROTECTOR FACTOR OF VENOUS THROMBOEMBOLIC EVENTS IN PATIENTS WITH ANCA-GLOMERULONEPHRITIS ?

NICOLAS HENRY[1], GANSEY Renaud[2], DJEMA Assia[3], PICCOLI Giorgina[4], SUBRA Jean François[1], AUGUSTO Jean François[1]

[1]CHU Angers, Service de Néphrologie Dialyse Transplantation, ANGERS, France, [2]CH Laval, Service de Néphrologie Hémodialyse, LAVAL, France, [3]CH Cholet, Service de Néphrologie Hémodialyse, CHOLET, France and [4]CH Le Mans, Service de Néphrologie Hémodialyse, LE MANS, France

Background and Aims: The incidence of venous thromboembolisms (VTE) is greatly increased in patients with anti-neutrophil cytoplasmic antibody (ANCA)- associated vasculitis (AAV). However, its incidence and risk factors in patients with ANCA-glomerulonephritis (ANCA-GN) has been poorly analyzed. Thus, the aim of the present study was to assess the frequency, the risk factors and outcomes of patients with VTE after ANCA-GN diagnosis.

Method: Patients from the Maine-Anjou AAV registry with a biopsy showing pauci-immune glomerulonephritis between 01/01/2000 and 01/01/2019, were included. VTE events, the site and delay from AAV diagnosis were retrieved from patient's medical records.

Results: Among the 165 patients, 133 fulfilled the inclusion criteria and were analyzed. After exclusion of arterio-venous fistulae thrombotic events, VTE episodes were diagnosed in 23/133 (17.3%) at a median delay of 3 months from ANCA-GN diagnosis or relapse. As compared to patients that did not developed VTE, patients with VTE had less frequently PR3 ANCAs (p=0.05), tended to be older (p=0.081), had lower serum albumin at AAV diagnosis (p=0.040) and were less frequently on statin therapy (p=0.028). Univariate cox analysis identified age (HR 1.49 for each 10-year increase, p=0.028), serum albumin at diagnosis (HR 2.21 for each 10g/L decrease, p=0.045), lack of statin therapy (HR 5.26, p=0.008) and rituximab treatment (HR 4.10, p=0.026) to be significantly associated with VTE occurrence. However, after adjustment in the multivariate model, only lack of statin therapy (HR 4.80; p=0.039) was significantly associated with VTE, while serum albumin was borderline (HR 2.20 for each 10 g/L decrease, p=0.067). Patients with VTE developed more frequently end-stage renal disease (p=0.040), but AAV relapse rate and mortality were not significantly different as compared to patients without VTE.

Conclusion: Patients with ANCA-GN are at high risk of VTE, especially within the first months following AAV diagnosis. We identified the lack of statin therapy as an independent risk factors of VTE development in our cohort. Thus, our results suggest that statins may have anti-thrombotic properties in ANCA-GN, which opens new therapeutic perspectives.

Figure: Univariate and multivariate analysis of risk factors associated with occurrence of venous thromboembolic events (excluding arterio-venous fistulae thrombosis).

	Univariate analysis		Multivariate analysis	
	HR (CI)	*P*	HR (CI)	*P*
Age*	1.49 (1.04-2.11)	**0.028**	1.32 (0.92-1.92)	0.134
Hypertension (yes)	2.10 (0.85-5.17)	0.106	-	-
PR3-ANCA (yes)	0.37 (0.11-1.24)	0.107	-	-
Serum albumin at onset**	2.21 (1.02-4.84)	**0.045**	2.20 (0.95-5.10)	0.067
Antiplatelet agents (no)	3.91 (0.91-16.8)	0.066	-	-
Statin therapy (no)	5.26 (1.55-17.8)	**0.008**	4.80 (1.08-21.4)	**0.039**
Rituximab (yes)	4.10 (1.18-14.2)	**0.026**	2.86 (0.61-13.4)	0.184

* per 10 year increment

** per 10 g/L decrease

P0368

THE ADDED IMPACT OF CRESCENTS ON DEVELOPMENT OF END-STAGE KIDNEY DISEASE IN COMBINATION WITH OTHER PATHOLOGICAL FEATURES OF OXFORD CLASSIFICATION IN PATIENTS WITH IGA NEPHROPATHY

Shahrzad Ossareh[1], Neda Nazemzadeh[1], Mojgan Asgari[2], Hanri Afghahi[3]

[1]Iran University of Medical Sciences- Hasheminejad Kidney Center, Medicine-Nephrology, Tehran, Iran, [2]Iran University of Medical Sciences- Hasheminejad Kidney Center, Pathology, Tehran, Iran and [3]Skaraborg Hospital, Nephrology, Skövde, Sweden

Background and Aims: Oxford classification of IgA nephropathy (IgAN) consists of the presence of four key pathologic features: mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental sclerosis (S) and tubular atrophy and interstitial fibrosis (T). The association between MEST score and renal outcome has been evaluated in previous studies. More recently crescents (C) were added to Oxford classification but the additive effect of the crescents on prediction of renal outcome is less well studied. The aim of the study was to assess the added impact of crescents, as an independent variable, on development of end stage kidney disease (ESKD) in combination with other pathological features of Oxford classification, in patients with IgAN.

Method:

One- hundred fifteen patients with IgAN (76% male, mean age: 37±13 years, mean serum creatinine: 4.0±4.3 mg/dl and mean proteinuria: 3.4±2.5 g/24 hours) were followed for 43±29 months. MEST score was defined according to Oxford classification (M0/M1, E0/E1, S0/S1). To increase the power of the study, T was defined as T0<25% and T1≥ 25%. Crescents were defined as C0: absence and C1: at least one crescents in biopsy. Additionally in sensitivity analysis, the risk of ESKD was estimated at different cut-off levels of at least 10%, 20% and 30% crescents. Furthermore the additive effect of the presence of crescents on the other Oxford classification score was studied.

Association between Oxford Classification score and risk of ESKD was examined by time-dependent Cox model to estimate hazard ratio, through univariate and multivariate analyses, adjusted for demographics, laboratory and pathological findings. Kaplan–Meier and the log-rank tests were used to estimate kidney survival.

Results: During follow-up 40 patients (35%) developed ESKD (dialysis or kidney transplantation). Forty- six patients (40%) had at least one crescent and among them 25 (46%) developed ESKD. In sub- analysis in 11 patients with C≥30%, 7 (66%) developed ESKD. Among 57 patients with T1, 34 (60%) developed ESKD. Twenty- seven patients had both T1 and C1 and among them 20 (74%) developed ESKD. In adjusted model, among patients with crescents, only C≥30% (HR: 3.15, 95% CI 1.15-11.00,P=0.027) and the presence of T1+ C1 (HR: 7.18, 95% CI 1.90-27.10,P=0.004) were associated with increased risk of ESKD and the combinations of M1+C1, E1+C1 or S1+C1 were not significantly associated with increased risk of ESKD (P=0.067, P=0.450, P=0.035, respectively). The median kidney survival was 78.0 months (95% CI, 70.5-85.6 months) with T0+C0 and 32.3 months (95% CI, 19.3-45.3 months) with T1+C1.

Conclusion: In this study based on Oxford classification, tubular atrophy and interstitial fibrosis≥25%, and presence of crescents≥ 30%, were independently associated with increased risk of ESKD. This risk was strongly increased in combined presence of at least one crescent and T1≥25% and 74% of such patients developed ESKD within a mean interval of 27 months.

P0369 **MINOR GLOMERULAR ABNORMALITIES ARE ASSOCIATED WITH DETERIORATION OF LONG-TERM KIDNEY FUNCTION AND MITOCHONDRIAL INJURY**

Mooyong Park[1], Byung Chul Yu[1], Su Jung Park[1], Jin Hoon Park[1], Kyung Ho Lee[1], Ahrim Moon[2], Soo Jeong Choi[1], Jin Kuk Kim[1], Seung Duk Hwang[1]

[1]Soonchunhyang University Bucheon Hospital, Division of Nephrology, Department of Internal Medicine, Bucheon, Korea, Rep. of South and [2]Soonchunhyang University Bucheon Hospital, Department of Pathology, Bucheon, Korea, Rep. of South

Background and Aims: Minor glomerular abnormalities (MGAs) are unclassified glomerular lesions indicated by the presence of minor structural abnormalities that are insufficient for a specific pathological diagnosis. The long-term clinical outcomes and pathogenesis have not been examined. We hypothesized that MGAs would be associated with the deterioration of long-term kidney function and increased urinary mitochondrial DNA (mtDNA) copy numbers.

Method: We retrospectively enrolled patients with MGAs, age-/sex-/estimated glomerular filtration rate (eGFR)-matched patients with IgA nephropathy (IgAN), and similarly matched healthy controls (MHCs; $n = 49$ each). We analyzed the time×group interaction effects of the eGFR and compared mean annual eGFR decline rates between the groups. We prospectively enrolled patients with MGAs, age- and sex-matched patients with IgAN, and MHCs ($n = 15$ each) and compared their urinary mtDNA copy numbers.

Results: Compared to the MHC group, the MGA and IgAN groups displayed differences in the time×group effects of eGFR (Figure 1), higher mean annual rates of eGFR decline (Table), and higher urinary mtDNA copy numbers (Figure 2); however, these groups did not significantly differ from each other.

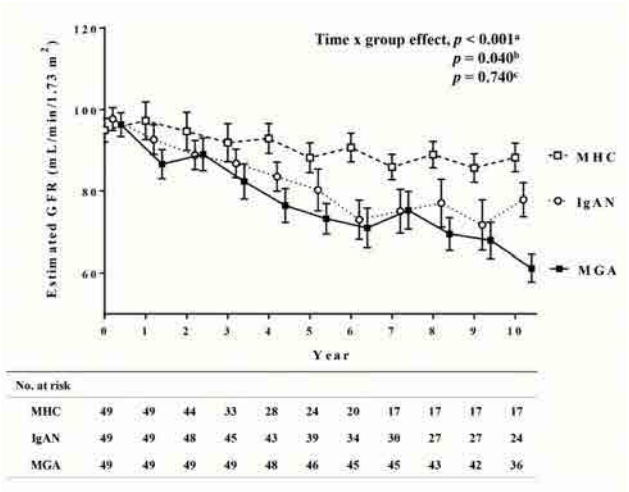


Figure 1. Changes in the estimated glomerular filtration rate (eGFR) in the minor glomerular abnormality (MGA), matched healthy control (MHC), and immunoglobulin A nephropathy (IgAN) groups in the 10 years after kidney biopsy. Time effects were tested using a linear mixed model. [a]MGA and MHC groups; [b]MHC and IgAN groups; [c]MGA and IgAN groups.

(MHC), minor glomerular abnormality (MGA), and immunoglobulin A nephropathy (IgAN) groups. Data were analyzed by the Mann-Whitney test. *$p < 0.001$. *MT-ND1*, mitochondrially encoded NADH dehydrogenase 1; COX3, cytochrome c oxidase subunit III.

Table. C hanges in eGFR in the MGA, MHC, and IgAN groups in the retrospective study.

Variable	MHC Group ($n = 49$)	MGA Group ($n = 49$)	*p* Value[a]	IgAN Group ($n = 49$)	*p* Value[b]
Mean follow-up duration (months)	110.69 ± 20.82	64.40 ± 44.27	**<0.001**	107.80 ± 57.68	**<0.001**
Mean annual rate of eGFR decline (mL/min/1.73 m^2/year)	0.64 ± 1.10	3.89 ± 5.95	**<0.001**	3.09 ± 6.13	0.570

Data are expressed as the mean ± standard deviation. [a]MGA and MHC groups; [b]MGA and IgAN groups. MHC, matched healthy control; MGA, minor glomerular abnormality; IgAN, immunoglobulin A nephropathy; eGFR, estimated glomerular filtration rate.

Conclusion: The results indicate that MGAs are associated with deteriorating long-term kidney function, and mitochondrial injury, despite few additional pathological changes. We suggest that clinicians conduct close long-term follow-up of patients with MGAs.

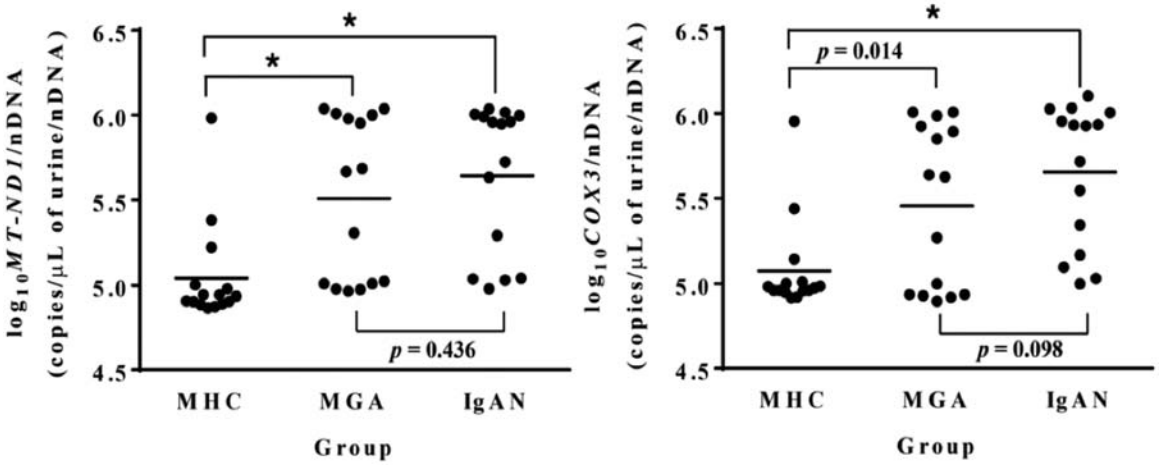


Figure 2. Urinary mitochondrial DNA copy numbers in the matched healthy control

P0370

RELATIONSHIP BETWEEN ATTENUATION OF C3 GLOMERULAR DEPOSITION AND CLINICAL PROGNOSIS IN IGA NEPHROPATHY: REPEAT-BIOPSY BASED OBSERVATION

Mizuho Morooka[1], Takehiko Kawaguchi[1], Akane Miura[1], Kazuyuki Ri[1], Azumi Fukuta[1], Masahiro Hyodo[1], Eri Okada[1,2], Moritoshi Kadomura[1], Hiroshi Kitamura[2], Toshiyuki Imasawa[1]

[1]National Hospital Organization Chibahigashi hospital, Nephrology, Chiba-city, and [2]National Hospital Organization Chibahigashi hospital, Pathology, Chiba-city,

Background and Aims: In IgA nephropathy (IgAN), mesangial IgA deposition activates the complement systems and amplifies the local inflammation, resulting in renal injuries. Although previous studies based on repeat biopsies suggested that the change of MEST-C scores of Oxford classification might be related to the prognosis, there have been few reports about immunofluorescence (IF) changes in repeat biopsies. In this study, we aimed to elucidate the relationship between the changes in the degree of glomerular IgA and C3 depositions and clinical prognosis of IgAN based on repeat biopsy observation.

Method: Fifty-five patients with IgAN who underwent repeat biopsies at our hospital between 2000 and 2019 were analyzed retrospectively. IF staining in each case was graded with a semiquantitative scale from 0 to 3 (0, negative; 1, weak; 2, moderate; 3, strong staining). MEST-C scores of the Oxford classification were also evaluated. When each score of IF staining or MEST-C in second biopsy was less compared with that in the first biopsy, it was regarded as "improved". The primary outcome was the time to achieve complete remission (CR), which is defined as disappearance of both urinary protein (UP) (<0.3 g/gCr) and microhematuria (<5/HPF). The secondary outcome was disappearance of microhematuria, disappearance of UP and the rate of eGFR decline. Multivariate analyses were conducted using Cox proportional hazards regression models or linear regression models, adjusted for age, sex and eGFR at the first biopsy.

Results: Twenty-seven patients (48%) were male. At the first biopsy, median age and eGFR were 38.5 years (Interquartile ratio (IQR) 17-49) and 92 mL/min/1.73 m^2 (IQR 63-108). Median urinary protein creatinine ratio was 0.6 g/gCr (IQR 0.3-1.7) and 45 patients (80%) had microhematuria. Thirty-three patients (59%) were treated by renin angiotensin system inhibitors and forty-three patients (78%) were treated by immunosuppressive therapy. Median period between the two biopsies was 36 months (IQR 25-55). Median IF scores of glomerular IgA and C3 were 2 (IQR 2-3) and 2 (IQR 1-2) in the first biopsies and 2 (IQR 1-2) and 1 (IQR 1-2) in the second biopsies, respectively. During the median 55 months (IQR 17-99) follow up period, disappearance of UP and microhematuria were observed in 47 (84%) and 36 (64%). Thirty-three (59%) patients reached CR. Improvement of the degree of C3 deposition between two biopsies was significantly associated with CR (Hazard ratio (HR) 0.37; 95% confidential interval (CI) 0.17-0.80, p=0.012), while that of IgA deposition had no association (HR 057; CI 0.27-1.19, p=0.125). Improvement of the degree of C3 deposition was also significantly associated with disappearance of microhematuria (HR 0.45; 95%CI 0.24-0.86, p=0.016), but not with disappearance of UP (HR 0.60; 95%CI 0.34-1.2, p=0.15). Multivariate linear regression revealed that the rate of eGFR decline was not related to IF scores. Any of the Oxford classification scores were not associated with these outcomes.

Conclusion: Attenuation of glomerular C3 deposition is associated with CR. This suggest that C3 deposition, rather than IgA deposition, may be related with the clinical prognosis of IgAN.

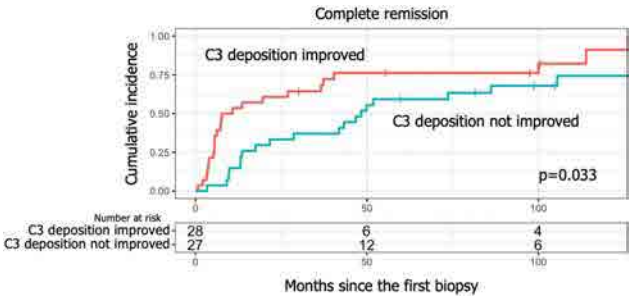


Figure:

P0371

DENTAL CARIES INDUCED BY CNM-POSITIVE STREPTOCOCCUS MUTANS DERIVED FROM IGA NEPHROPATHY PATIETNS IN RATS INDUCED GLOPERULONEPHRITIS LIKE IGA NEPHROPATHY

Yasuyuki Nagasawa[1], Shuhei Naka[2], Kaoruko Wato[3], Ryota Nomura[3], Taro Misaki[4], Seigo Ito[5], Aritoshi Kida[1], Yoshimasa Nanami[1], Yukiko Hasuike[1], Kuragano Takahiro[1], Michiyo Matsumoto-Nakano[2], Kazuhiko Nakano[3]

[1]Hyogo college of Medicine, Department of Internal Medicine, Division of Kidney and Dialysis, Nishinomiya, Japan, [2]Okayama University, Deparment of Pedtric Densistry, Okayama, Japan, [3]Osaka University, Department of Pediatric Densistry, Suita, Japan, [4]Seirei Hamamatsu General Hospital, Division of Nephrology, Hamamatsu, Japan and [5]National Defense Medical College, Department of Nephrology and Endocrinology, Tokorozawa, Japan

Background and Aims: IgA nephropathy (IgAN) is one of most common primary glomerulonephritis, whose pathogenesis had remained unclear. We had reported that *Cnm*-(+)*Streptococcus mutans*, a kinds of major dental caries bacteria. *Cnm*-(+)*S. mutans* had strong collagen binding ability, resulting in high pathogenicity. We reported that the prevalence of *Cnm*-(+)*S. mutans* in IgA nephropathy is significantly higher than that in control (Misaki-T et al, Clin Exp Nephrol 2015; 19:844-50), and that *Cnm*-(+)*S. mutans* in IgA nephropathy was associated with proteinuria (Misaki-T et al, *Sci Rep 2016*). We also reported *C.rectus* and *S. mutans* increased proteinuria synergistically (Misaki-T et al, Nephron, 2018). In this point, there is no direct evidence that *Cnm*-(+)*S. mutans* could induce IgA nephropathy. In this study, we evaluated the renal lesions in rats which had dental caries induced by *Cnm*-(+)*S. mutans* derived from IgA nephropathy patient to confirm the pathogenesis of IgA nephropathy like lesions induced by *Cnm*-(+)*S mutans*.

Method: Cmn-(+)*S. mutans* from saliva of IgA nephropathy patients was orally administrated into 4 weeks old male Sprague-Dawley rats. Addition of sugar to water had been kept during study period to develop dental carits. At week 34 after the infection, blood, urine, and kidney samples were evaluated. Kidney samples were stained by Periodic Acid-Schiff (PAS), IgA, C3. Historical evaluation by electron microscope analysis was also performed.

Results: At week 34, plaque score and dental caries score in infectious rats significantly elevated, compared with control rats ($P<0.001$) (Figure 1). These findings suggested Cmn-(+)*S. mutans* from IgA nephropathy patients induced dental caries in rats. PAS staining revealed the significant mesangial proliferation. At week 34, the prevalence of IgA deposition in infections rats was higher than that in control rats (52.4% vs 4%), and the prevalence of C3 deposition in infectious rats was also higher than that in control rats (42% vs 11%) (Figure 2). Incidence of hematuria was also significantly higher in dental caries group than control. Electron microscopy analysis revealed high dense deposit in mesangial areas.

Conclusion: Cmn-(+)*S. mutans* from saliva of IgA nephropathy patients could induce IgA-dominant infection-associated glomerulonephritis, or IgA nephropathy.

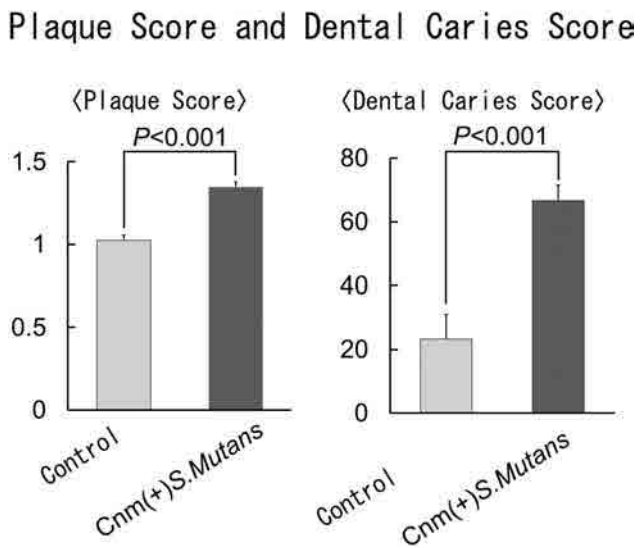


Figure:

P0372

RITUXIMAB IN IDIOPATHIC FOCAL SEGMENTAL GLOMERULOSCLEROSIS OF THE ADULT: A MULTICENTRE RETROSPECTIVE SURVEY OF 31 PATIENTS

Martina Tedesco[1], Isabella Pisani[2], Marco Allinovi[3], Giovanni Casazza[1], Lucia Del Vecchio[4], Marisa Santostefano[5], Francesca Ferrario[6], Ciro Esposito[7], Pasquale Esposito[8], Domenico Santoro[9], Roberta Lazzarin[10], Elisa Delbarba[11], Angelo Ferrantelli[12], Renato A. Sinico[13], Mario Gennaro Cozzolino[1], Maurizio Gallieni[1], Francesco Scolari[14], Calogero Cirami[3], Augusto Vaglio[15], Federico Alberici[14]

[1]University of Milan, Milan, Italy, [2]University Hospital of Parma, Parma, Italy, [3]Careggi University Hospital, Florence, Italy, [4]Alessandro Manzoni Hospital, Lecco, Italy, [5]S. Orsola-Malpighi Hospital, Bologna, Italy, [6]ASST Nord Milano, E. Bassini Hospital, Cinisello Balsamo, Italy, [7]ICS Maugeri SpA SB, University of Pavia, Pavia, Italy, [8]University of Genova, [9]University of Messina, Messina, Italy, [10]Hospital of Castelfranco Veneto, Castelfranco Veneto, Italy, [11]ASST Spedali Civili, Brescia, , [12]Azienda Ospedaliera Civico, Palermo, Italy, [13]University of Milano-Bicocca and ASST Monza, Monza, Italy, [14]University of Brescia, Brescia, Italy and [15]University of Florence, Florence, Italy

Background and Aims: Idiopathic Focal Segmental Glomerulosclerosis (FSGS) is a rare glomerulonephritis often complicated by a chronic relapsing course frequently characterized by dependency or resistance to immunosuppressive treatment. Moreover, about half of the patients with active disease would develop end-stage renal disease within 10 years from the diagnosis, highlighting the need of novel therapeutic approaches. Rituximab (RTX), a chimeric monoclonal antibody against CD20, showed promising results in pediatric steroid-dependent/frequently relapsing FSGS and in post-transplantation recurrence. However, evidence about its role in the FSGS of the adult is still lacking with small case series suggesting conflicting results. In this study we assess the efficacy of RTX in the largest cohort of adults with FSGS currently available in literature.

Methods: Adults with biopsy proven idiopathic FSGS treated with RTX were retrospectively identified among several Italian nephrology units. Response to RTX was evaluated at 3, 6, 12 months and, when available, during the long-term follow-up. A positive response (POR) was defined as: (1) proteinuria <3.5 g/die with a decrease >50% compared to baseline, (2) stable renal function (3) decreased or stable dose of glucocorticoids and other immunosuppressants. Severe Adverse Events (SAEs) have been recorded.

Results: 31 patients have been identified: 18 steroid-dependent, 11 steroid-resistant, and 2 patients with major contraindication to steroid therapy. RTX has been administered at a median of 87 months (IQR 54–96) from the diagnoses using heterogeneous schedules of administration. Overall, the POR rate at 6 months was 52% (steroid-dependent=69%; steroid-resistant=22%). At univariate analyses, POR to RTX at 6 months was associated to the steroid-dependent status (p=0.0347) and a proteinuria at RTX <5 g/die (p=0.0173); a trend towards better response was observed in patients with IgG at RTX <500 mg/dl (p=0.0774). Over the first year of follow-up, the proteinuria and serum albumin significantly improved (respectively, p=0.0021 and p=0.0277 at 12 months), while serum creatinine remained stable (figure). Among treated patients, the median dose of prednisone decreased from 15 mg/die (IQR 12.5–25) at baseline to 10 mg/die (IQR 5–15) at 12 months, while the proportion of patients free from glucocorticoids respectively increased from 42% to 54%. Six patients have been retreated within a year since the first RTX: of these only the 2 patients who have experienced a POR to the first administration obtained a further POR after retreatment. After the 12th month, 11 patients have been followed for a median time of 17 months (IQR 15–33.5): of the 5/11 with a POR at the 12th month, 2/5 maintained a POR without needing further immunosuppression, 2/5 maintained a POR with a pre-emptive RTX based maintenance treatment, 1/5 experienced a relapse successfully managed with RTX needing then a pre-emptive RTX based maintenance therapy able to allow a persistent POR. Overall, 9 SAEs have been recorded with requirement of hospital admission for clinical deterioration being the most frequent.

Conclusion: RTX may be an option in the FSGS of the adult, especially in the steroid-dependent patients and the ones with less severe nephrotic syndrome. In the responders, a RTX based maintenance therapy may be required.

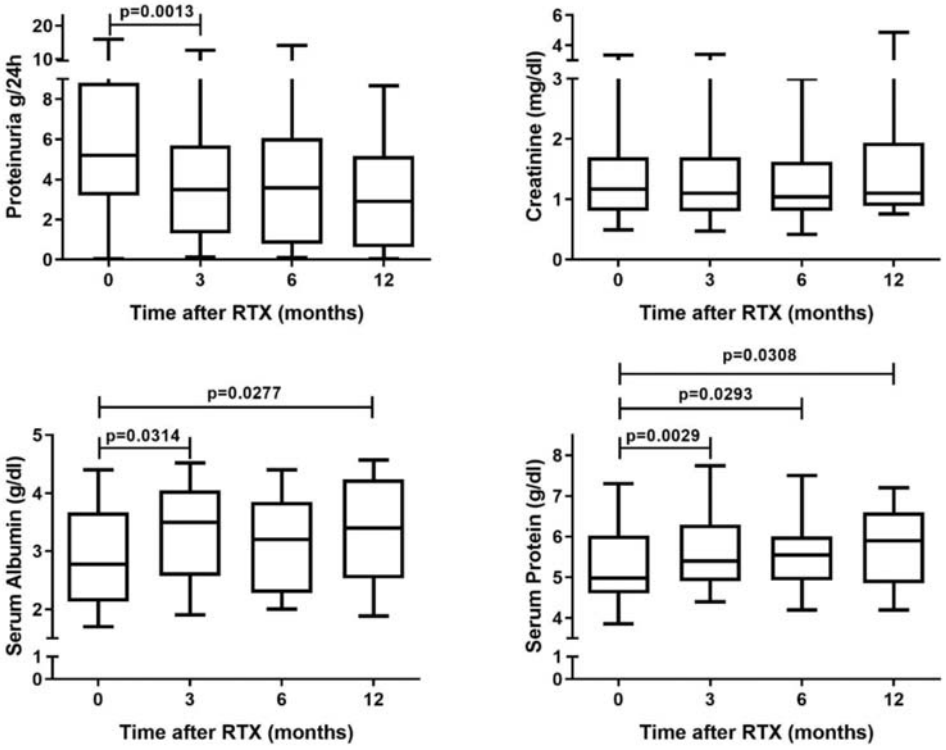


Figure: Changes in serum albumin, serum protein, serum creatinine and 24/h proteinuria over the first year of follow-up after RTX in the overall cohort of 31 patients affected by idiopathic FSGS

P0373 **MEPOLIZUMAB THERAPY FOR EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA) - ONE YEAR FOLLOW-UP STUDY USING ANTI-IL5 AS A STEROID SPARING THERAPEUTIC APPROACH**

Allyson Egan[1], Pasupathy Sivasothy[2], Robin Gore[3], Marcos MartinezDel-Pero[1], Lisa Willcocks[1], Rona Smith[1], Stella Burns[1], Caroline Owen[3], Rachel B. Jones[1], David Jayne[1]

[1]Addenbrooke's Hospital, The Vasculitis and Lupus Centre, University of Cambridge, United Kingdom, [2]Addenbrooke's Hospital,, The Vasculitis and Lupus Centre, University of Cambridge, United Kingdom and [3]Addenbrooke's Hospital, Respiratory medicine, United Kingdom

Background and Aims: EGPA is a small vessel vasculitis characterised by the presence of tissue eosinophilia, necrotising vasculitis and granulomatous inflammation[1]. Typically, a prodromal asthmatic phase, leads to an eosinophilic stage, which can evolve to include the presence of vasculitis with renal manifestations. In the recent randomised, placebo-controlled MIRRA trial for relapsing and refractory EGPA, adjuvant therapy with anti-IL5 mAB Mepolizumab [MEPO] at 300mg s/c monthly, accrued longer times in remission, reduced steroid exposure and reduced relapse rates[2]. The aim of our study was to analyse the response and outcome for EGPA patients who received 100mg s/c of MEPO monthly for a minimum of 52 weeks, with particular focus on the steroid minimisation benefits.

Method: This retrospective, descriptive study analysed 13 patients with EGPA, who received 100mg s/m monthly MEPO therapy under the eosinophilic asthma care-pathway. Time points of assessment included MEPO commencement [M0] and 12 [M12] months.

Results:

Table 1: EGPA patients receiving Mepolizumab therapy for one year [100mg s/c]

Demographics All [n=13]	
Gender ratio M/F	4M:9F
ANCA positive/ negative	ANCA: 3MPO, 1 PR3 positive/ 9 ANCA negative
Age of diagnosis of asthma	35 yrs [IQR 28.5-40]
Age of diagnosis of EGPA	47 yrs [IQR 43.5-53.5]
Median age	51 yrs [IQR 47.5- 60.5]
EGPA disease characteristics N=13 [%]	
Asthma 13 [100]	
Serum eosinophilia or biopsy evidence [N= 12] 12 [100]	
Pulmonary infiltrates, non-fixed 8[61.5]	
Neuropathy, mono/poly 4[30.7]	
Sino-nasal abnormality 12[92.3]	
Glomerulonephritis 3[23]	
Cardiovascular 4[30.7]	
Prior Immunosuppressants N=13 [%]	
Steroids	13[100%]
Cyclophosphamide 6[46%]	
Rituximab	6[46%]
Azathioprine	10[77%]
Mycophenolate mofetil	8[62%]
Methotrexate	4[31%]
Campath 1[7%]	
Response to therapy M0 [%] Post M12 [%]	
Prednisolone dose N= 13	
Mean ±SD 18.925 mg ±11.44 10.575mg ± 5.85	
Eosinophil count $X10^9$/L N=13	
Mean ±SD 0.415mg ±0.25 0.035±0.039	
Asthma Control Questionnaire [ACQ] N=5	
Mean ±SD 2.92 ±1.27 1.31± 0.79	
BVAS N= 13	
Mean ±SD 7.307±6.29 2.2307±1.69	
Creatinine N=9	
Mean ±SD 68.44±15.03 69.11±17.84	
Continuation of anti-IL5 therapy N=13 12/13 [92.3%]	

Continued

Long term plan > 12 months N=13 [%] Current Months Adjuvant therapy 12M		
1 Continue	15	Aza
2 Switched Benralizumab	26	MMF [+], IVIG [-]
3 Continue	18	
4 Switched Benralizumab	14	
5 Discontinued Rituximab	12	MTX
6 Continue	14	
7 Continue	24	MMF Reduced
8 Continue	18	MTX [+]
9 Continue	15	MMF [-]
10 Continue	14	
11 Continue	13	
12 Continue	13	Aza
13 Continue	12	

One patient had MEPO switched to Rituximab to treat both EGPA and new onset rheumatoid arthritis

Conclusion: The relapsing nature of EGPA places a potential dependency of therapy on steroids for asthmatic and vasculitic flares. This underscores the importance of targeted pathway specific biologic therapy to minimise steroid exposure, prevent tissue damage and ensure early response to therapy. This study demonstrates that anti-IL5 serves as a favourable model with steroid minimisation, improvement in asthma control questionnaire, reduction in BVAS and eosinophil counts at the 100mg s/c dosage. ANCA positive serology normalised in all four patients, independent of subtype. Well tolerated, it demonstrated considerable clinical benefit, with 12 patients [92.3%] continuing anti-IL5 therapy beyond 12 months. Adjuvant therapy with conventional immunosuppressants was well tolerated and renal function was preserved.

ADDIN Mendeley Bibliography CSL_BIBLIOGRAPHY 1. J.C.Jenette, *et al* Revised International Chapel Hil Consensus Conference Nomenclature of Vasculitides. **65**, 1–11 (2013).

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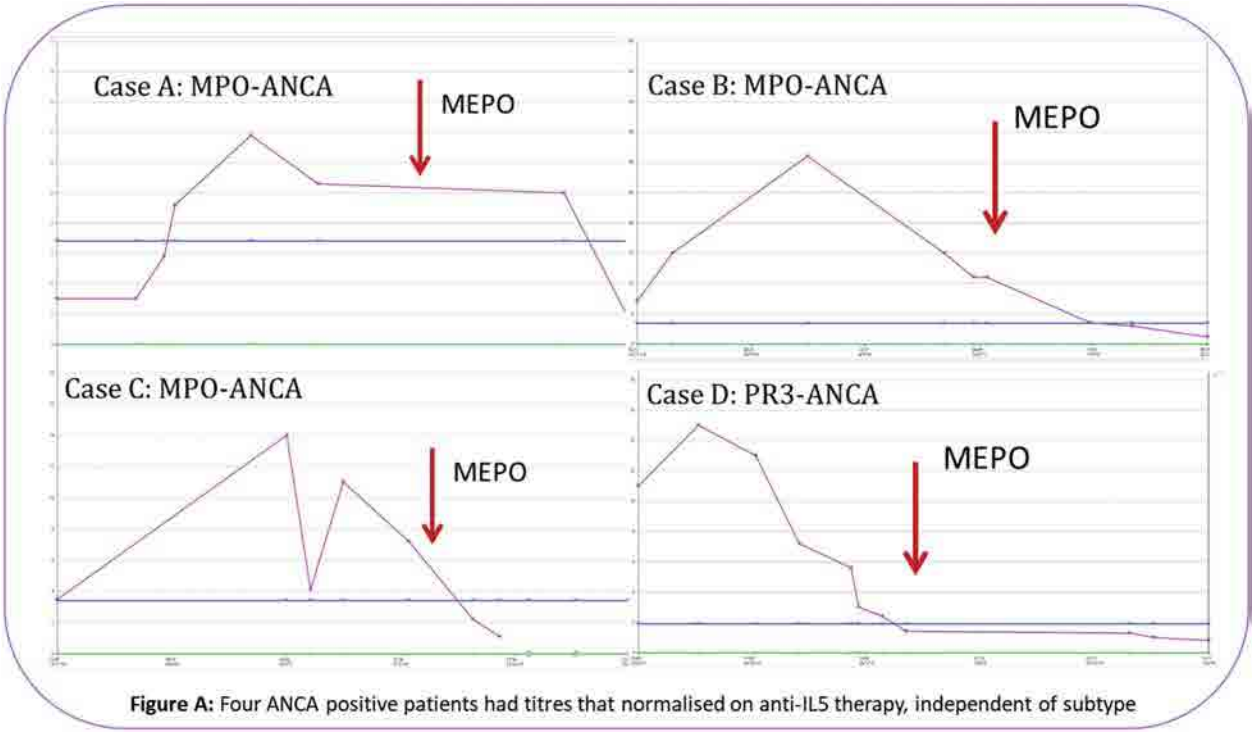


Figure A: Four ANCA positive patients had titres that normalised on anti-IL5 therapy, independent of subtype

Figure:

P0374 **TREATMENT EFFICACY OF BIOSIMILAR RITUXIMAB (TRUXIMA) COMPARED TO THE ORIGINATOR (MABTHERA) IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS**

PEK GHE TAN[1], Jennifer O'Brien[1], Rachna Bedi[1], Megan Griffith[1,2], Marie Condon[1], Tom Cairns[1], Jeremy Levy[1], Charles Pusey[1,2], Stephen McAdoo[1,2]

[1]Imperial College Healthcare NHS Trust, Specialist Nephrology Clinic, London, United Kingdom and [2]Imperial College London, Centre for Inflammatory Disease, London, United Kingdom

Background and Aims: Truxima is a biosimilar version of rituximab. It was licensed & launched in the United Kingdom in April 2017. A biosimilar medicine is made to be highly similar in quality, safety and efficacy to existing licensed "reference" biological medicine and the cost is often significantly lower. A recent systematic review showed comparable long-term efficacy and safety of biosimilar rituximab to the originator drug in treatment of rheumatoid arthritis and non-hodgkin's lymphoma. Fewer data are available in regards to the efficacy of biosimilar rituximab in treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). A retrospective study was thus conducted in our centre to examine the efficacy of Truxima when compared to the reference rituximab (MabThera) in the treatment of patients with AAV.

Method: All patients with new or relapsing AAV who received first ever rituximab therapy between 1/1/2016 and 31/12/2018 were identified via hospital dispensing database. Patients were stratified into Truxima or MabThera treatment group depending on the version of rituximab administered. Primary outcomes that were assessed include: time to B cell depletion (defined as absolute B cell count (ABC) $\leq$10) and repletion (i.e ABC $>$10 and $>$20); time to antimyeloperoxidase(MPO)/antiproteinase 3(PR3)-ANCA negativity; Secondary outcomes assessed include: overall survival, time to major relapse (defined as relapse requiring further course of rituximab for remission induction); adverse events including episodes of neutropenia, hypogammaglobulinemia and major infusion reactions. Subgroup analysis in patients who received concomitant cyclophosphamide and rituximab or other induction therapy was performed to examine if it impacts on the treatment efficacy.

Results: 59 and 60 patients received Truxima and MabThera respectively for treatment of new or relapsing AAV. The baseline characteristic (age, gender, entry estimated Glomerular Filtration Rate, proportion of patients received concomitant cyclophosphamide, ANCA serology and organ involvement) of both group were comparable. All patients achieved clinical remission following induction treatment. Using Kaplan Meier analysis and log rank test, no difference was identified in time to B cell depletion or repletion (Figure 1&2), MPO/PR3-ANCA negativity (Figure 3), overall survival or major relapses requiring further rituximab as induction therapy.

Treatment efficacy of Truxima and MabThera did not differ in subgroup analysis. However we observed that patients who received concurrent cyclophosphamide during induction therapy achieved MPO/PR3-ANCA negativity more rapidly compared to those who did not irrespective of the version of rituximab received. No difference in adverse events such as major infusion reactions was seen in either group upon first rituximab exposure. Two patients in each group developed reactions following repeated dosing of rituximab.

Conclusion: Biosimilar rituximab Truxima appears to have comparable treatment efficacy compared to the reference drug in our cohort of patients with AAV.

P0375 URINARY DICKKOPF-3 PREDICTS RENAL SURVIVAL IN ANCA-ASSOCIATED VASCULITIS

Yunayka Diaz Enamorado[1], Amir Shabaka[1], Francisco Jose Garcia Iñigo[2], Javier Villacorta[1], Clara Maria Cases Corona[1], Patricia Dominguez Torres[1], Gema Maria Fernandez Juarez[1]

[1]Hospital Universitario Fundación Alcorcón, Nephrology, Alcorcón, Spain and [2]Hospital Universitario Fundación Alcorcón, Clinical Analysis, Alcorcón, Spain

Background and Aims: Urinary Dickkopf-related protein-3 (DKK3), a stress-induced renal tubular glycoprotein, has been identified as a novel biomarker for chronic kidney disease patients at risk of kidney disease progression. The aim of our study was to assess urinary DKK3 as a diagnostic biomarker for predicting GFR loss and renal survival in a cohort of patients with ANCA-associated vasculitis

Method: We measured baseline urinary DKK3 levels in a cohort of patients diagnosed with ANCA-associated vasculitis (AAV), and repeated measurements at 1 and 3 months of diagnosis. Urinary DKK3 levels were normalized to urinary creatinine concentrations to account for dilution of the urine. The association between baseline uDKK3/creatinine levels and the rate of GFR loss was measured. The primary composite outcome was defined as an increase of >50% in baseline serum creatinine, initiation of renal replacement therapy or death.

Results: We included 36 AAV patients with a mean age 71.2 ±12.0 years, 55.6% males, with baseline eGFR at diagnosis 22.3 ±14.1 ml/min. There was a correlation between baseline DKK3-creatinine levels and age (r=0.48, p=0.003) and baseline eGFR (r=-0.327, p=0.051). Ten patients (27.8%) reached the primary composite outcome. Patients were then stratified into two groups according to baseline uDKK3 levels. The group of patients with baseline uDKK3-Creatinine >16000 pg/mg were older (76±12.5 vs 66.4 years, p=0.014), presented a lower baseline eGFR (16.2±10.8 vs 28.5±14.5 ml/min, p=0.007) and had higher baseline uCD163 levels (1135.1 [312.4-2537.5] vs 397.2 [146-809.4], p=0.089]). There were no differences in baseline proteinuria, microhematuria or histological class across the groups. After a median follow-up of three years, 44.4% of the patients in the highest DKK3 group reached the primary composite outcome, whereas only 11.1% of those with lower DKK3 levels reached the endpoint at the end of follow-up (p=0.026) . The area under the time-dependent curve for predicting the primary composite outcome according to uDKK3 was 0,677, with a sensibility of 80% and specificity of 61.5% at the cutoff 16056 pg/mg. Additionally, patients who had a >30% increase in uDKK3 levels after one month reached the primary composite outcome more often (40%) than those who remained with a stable or decreasing DKK3 levels (0%, p=0.04). There were no differences in the rate of change in DKK3 and the different treatment regimens.

Conclusion: Elevated urinary DKK3 levels help identify those patients who are at a higher risk of kidney disease progression and dialysis dependency over the next three years in ANCA-associated vasculitis. DKK3 monitoring could be considered in the follow-up of these patients to assess the effect of treatment and predict the long-term response.

P0376 **EFFECTS OF HYPERURICEMIA ON THE PROGNOSIS OF IGA NEPHROPATHY AND ITS SEX DIFFERENCE**

Tae Ryon Oh[1], Hong Sang Choi[1], Chang Seong Kim[1], Seong Kwon Ma[1], Soo Wan Kim[1], Eun Hui Bae[1]

[1]*Chonnam National University Medical School, Department of Intenal Medicine,, Gwangju, Korea, Rep. of South*

Background and Aims: Hyperuricemia is a potential risk factor for immunoglobulin A nephropathy (IgAN) progression, but its sex-specific effects on IgAN progression remain unclear. This study aimed to determine the effect of serum uric acid on IgAN progression and whether its effect varied according to sex.

Method: A total of 4339 patients were retrospectively analyzed at a university medical school. We assessed the effect of serum uric acid on IgAN progression using Kaplan–Meier survival analyses and Cox proportional hazards models. The study's primary end point was IgAN progression that was defined as a 50% decline in the estimated glomerular filtration rate or the initiation of dialysis.

Results: On average, the serum uric acid levels were higher in the men than in the women. In the fully adjusted Cox proportional hazards model that considered all subjects, the risk of IgAN progression increased by about 25.6% for every 1 mg/dL increase in the baseline uric acid level. The serum uric acid level was an independent risk factor for IgAN progression in both sexes, but its effect was more pronounced in the women (hazard ratio [HR], 1.383; confidence interval [CI],1.263 to 1.514; $P<0.001$) than in the men (HR, 1.181; CI, 1.097 to 1.272; $P<0.001$) ($P_{interaction}<0.001$). A sensitivity analysis involving serum uric acid quartiles generated consistent and robust results.

Conclusion: The serum uric acid level was an independent risk factor for IgAN progression, and its effect was more pronounced among the women compared with that among the men.

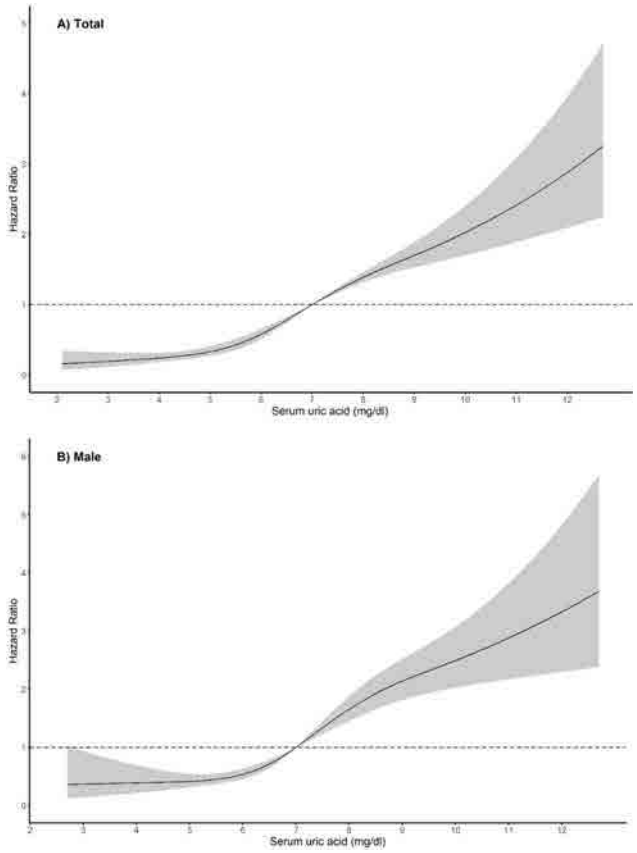


Figure: Restricted cubic spline curve of hazard ratio of serum uric for major adverse renal outcome by sex

Serum uric acid levels and major adverse renal outcome showed a nonlinear relationship in all groups.

P0377

THE RELATIONSHIP BETWEEN SEVERITY OF INTERSTITIAL FIBROSIS AND ANEMIA IN PATIENT WITH PRIMARY GLOMERULONEPHRITIS: THE DATA FROM TSN-GOLD WORKING GROUP

Egemen Cebeci[1], Kenan Turgutalp[2], Savas Ozturk[3], Yasemin Ozluk[4], Sibel Gokcay Bek[5], Abdullah Sumnu[6], Nurhan Seyahi[7], Mahmut Yavuz[8], Serhan Vahit Piskinpasa[9], Omer Faruk Akcay[10], Tamer Sakaci[11], Garip SAHIN[12], Bulent Tokgoz[13], Gulizar Manga Sahin[14], Ilter Bozaci[15], Belda Dursun[16], Savas Sipahi[17], Arzu Ozdemir Kayalar[18], Gultekin Suleymanlar[19], Memnune Sena Ulu[20], Fatma Betul Guzel[21], Sim Kutlay[22], Ergun Parmaksiz[23], Suleyman Koz[24], Ilhan Kurultak[25], Nedim Yılmaz Selcuk[26], Yasar Yildirim[27], Meltem Gursu[28], Caner Cavdar[29], Meryem Timucin[30], Zeki Aydin[31], Deren Oygar[32], Serdar Kahvecioglu[33], Muge Uzerk Kibar[34], Dilek Torun[35], Dilek Guven Taymez[36], Mehmet Kucuk[37], Serap Demir[38], Leyla Koc[39], Siren Sezer[40], Murat Duranay[41], Simge Bardak[42], Luftullah Altintepe[43], Mehmet Koc[44], Alper Azak[45], Ali Riza Odabas[46], Zulfikar Yilmaz[27], Saime Paydas[47]

[1]Haseki Training and Research Hospital, Department fo Nephrology, Istanbul, Turkey, [2]Mersin University, Department of Nephrology, Mersin, Turkey, [3]Haseki Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [4]Istanbul University, Department of Pathology, Istanbul, Turkey, [5]Kocaeli University, Department of Nephrology, Kocaeli, Turkey, [6]Medipol University, Department of Nephrology, Istanbul, Turkey, [7]Istanbul University Cerrahpasa, Department of Nephrology, Istanbul, Turkey, [8]Uludag University, Department of Nephrology, Bursa, Turkey, [9]Ankara Numune Research and Educational Hospital, Department of Nephrology, Ankara, Turkey, [10]Gazi University, Department of Nephrology, Ankara, Turkey, [11]Sisli Etfal Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [12]Eskisehir Osmangazi University, Department of Nephrology, Eskisehir, Turkey, [13]Erciyes University, Department of Nephrology, Kayseri, Turkey, [14]Istanbul Sultan Abdülhamid Han Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [15]Bozyaka Training and Research Hospital, Department of Nephrology, İzmir, Turkey, [16]Pamukkale University, Department of Nephrology, Denizli, Turkey, [17]Sakarya University, Department of Nephrology, Sakarya, Turkey, [18]Bakirkoy Sadi Konuk Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [19]Akdeniz University, Department of Nephrology, Antalya, Turkey, [20]Afyon Kocatepe University, Department of Nephrology, Afyon, Turkey, [21]Kahramanmaras Sutcu Imam University, Department of Nephrology, Kahramanmaraş, Turkey, [22]Ankara University Ibni Sina Hospital, Department of Nephrology, Ankara, Turkey, [23]Kartal Lutfi Kirdar Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [24]Inonu University, Department of Nephrology, Malatya, Turkey, [25]Trakya University, Department of Nephrology, Edirne, Turkey, [26]Necmettin Erbakan University, Meram Medical Faculty, Department of Nephrology, Konya, Turkey, [27]Dicle University, Department of Nephrology, Diyarbakır, Turkey, [28]Bezmialem Vakif University, Department of Nephrology, Istanbul, Turkey, [29]Dokuz Eylül University, Department of Nephrology, Izmir, Turkey, [30]Cumhuriyet University, Department of Nephrology, Sivas, Turkey, [31]Darica Farabi Training and Research Hospital, Department fo Nephrology, Kocaeli, Turkey, [32]Burhan Nalbantoglu Hospital, Department of Nephrology, Lefkosa, Cyprus, [33]Bursa Yuksek Ihtisas Training and Research Hospital, Department of Nephrology, Bursa, Turkey, [34]Hacettepe University, Department of Nephrology, Ankara, Turkey, [35]Baskent University, Adana Teaching and Research Center, Department of Nephrology, Adana, Turkey, [36]Kocaeli Government Hospital, Department of Nephrology, Kocaeli, Turkey, [37]Okmeydani Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [38]Mersin University, Department of Internal Disease, Mersin, Turkey, [39]Istanbul Gaziosmanpasa Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [40]Atilim University Medicana International Hospital, Department of Nephrology, Ankara, Turkey, [41]Ankara Training and Research Hospital, Department of Nephrology, Ankara, Turkey, [42]Batman Government Hospital, Department of Nephrology, Batman, Turkey, [43]Selcuklu University, Department of Nephrology, Konya, Turkey, [44]Marmara University, Department of Nephrology, Istanbul, Turkey, [45]Balikesir Training and Research Hospital, Department ofNephrology, Balikesir, Turkey, [46]Istanbul Medeniyet University, Department of Nephrology, Istanbul, Turkey and [47]Cukurova University, Department of Nephrology, Adana, Turkey

Background and Aims: Anemia is one of the most important complications in chronic renal disease and inadequate erythropoietin production is the most important reason for anemia. Fibrosis of renal interstitium may be associated with inadequate synthesis of erythropoietin and anemia. In our study, we investigated the relationship between the severity of interstitial fibrosis (IF) in patients with primary glomerulonephritis (PGN) and anemia parameters.

Method: A total of 2794 patients who were recorded to the database of the Turkish Society of Nephrology, Glomerular Diseases (TSN-GOLD) Working Group between May 2009 and June 2019 were included in our national multicenter (44 centers) study. Patients aged 16 years or more with documented biopsy were included in the study. Patients were divided into four groups according to IF severity. IF was not detected in the interstitial area, was defined as none, if fibrosis was present in less than 25% of the area, defined as mild, if fibrosis was present in 25-50%, defined as moderate and if more than 50%, defined as severe. Anemia was defined as hemoglobin <12 g/dl in adult female patients and <13 g/dl in adult male patients, according to Clinical Practice Guidelines for anemia of CKD published by The Kidney Disease: Improving Global Outcomes Foundation. The relationship between IF severity and anemia parameters at the time of biopsy was investigated.

Results: In the study, 57% of the patients were male and their mean age was 41.0 ± 14.3 years. The mean eGFR was 82.7 ± 36.9 ml / min / 1.73 m^2 and the hemoglobin level was 13.1 ± 1.9 g/dl. General characteristics of patients with and without anemia are given in Table 1. While 41.1% of patients had no IF, 41.2% had mild, 14.1% had moderate and 3.5% had severe IF. When the patients were divided into four groups according to the severity of IF, the mean hemoglobin and hematocrit levels were significantly different between the groups (Figure 1). Anemia was present in 960 patients (34.4%) (Figure 2). Anemia rate was significantly higher in the patients with IF than patients without IF (36.8% vs 30.9%, p = 0.001). Anemia rate was %25.1 in patients with eGFH≥60 ml/min/1.73m2 and 56% in patients with eGFR<60 ml/min/1.73m^2. Gender, serum albumin, eGFR, proteinuria, presence of diabetes, presence of nephrotic syndrome, and presence of IF were the independent variables in the regression analysis of hemoglobin-related factors (Table 2).

Conclusion: Approximately one-third of PGN patients had anemia at the time of biopsy and the frequency of anemia increases in patients with IF. The presence of IF is an independent risk factor associated with the development of anemia in PGN. The elucidation of the etiopathogenesis of anemia in PGN patients may play an important role in the follow-up and treatment of patients. Studies on IF can play a critical role.

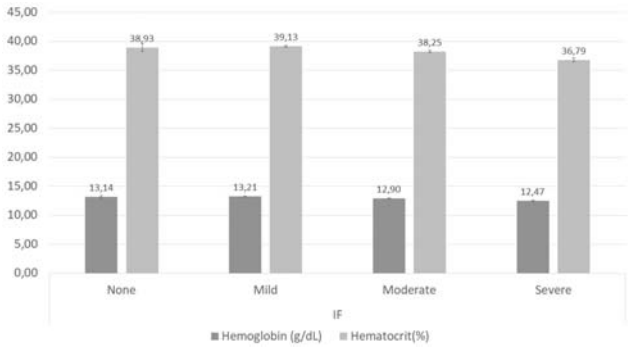


Figure 1. Hemoglobin and hematocrit in four groups according to the severity of interstitial fibrosis

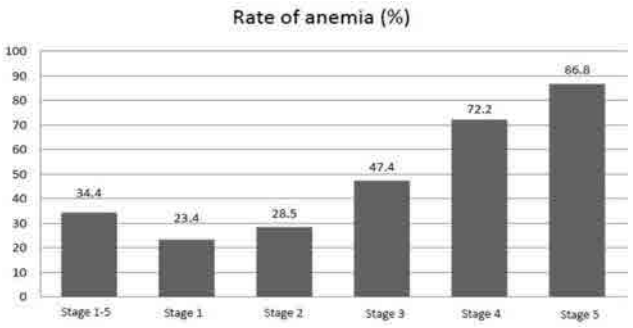


Figure 2. Rates of anemia in patients with different stage of CKD

Table 1. General characteristics of patients with and without anemia

	Patients with anemia (n=960)	Patients without anemia (n=1834)	p value
Age (years)	42.7±15.2	40.0±13.8	<0.001
Gender (male, %)	52.8%	59.1%	0.001
Etiology of PGN			<0.001
Membranous GN	29.5%	31.1%	
IgAN	30.7%	30.6%	
FSGS	23.1%	27.9%	
MPGN	14.3%	6.3%	
Mesangioproliferative GN	1.7%	3.6%	
Others	0.7%	0.5%	
Interstitial Fibrosis			<0.001
None	37.0%	43.3%	
Mild	39.6%	42.1%	
Moderate	18.4%	11.8%	
Severe	5.0%	2.8%	
Interstitial Fibrosis	63.0%	56.7%	<0.001
eGFR (ml/min/1.73 m^2)	67.5±39.9	90.7±32.5	<0.001
Albumin (g/dl)	3.1±0.9	3.4±0.9	<0.001
Proteinuria (mg/day)	3662(IQR 1700-6600)	3299(IQR 1485-6256)	0.524
Hemoglobin (g/dl)	11.0±1.2	14.1±1.3	<0.001
Hematocrit (%)	33.1±3.9	41.8±4.0	<0.001
Total Cholesterol (mg/dl)	247±90	259±99	0.002
Diabetes Mellitus (%)	10.8%	8.9%	0.098
Hypertension (%)	39.9%	30.6%	<0.001

P0378 SERUM URIC ACID IS ASSOCIATED WITH PROGNOSIS OF LUPUS NEPHRITIS IN FEMALE BUT NOT IN MALE

Tae Ryon Oh[1], Hong Sang Choi[1], Chang Seong Kim[1], Soo Wan Kim[1], Eun Hui Bae[1], Seong Kwon Ma[1]

[1]*Chonnam National University Medical School, Department of Intenal Medicine,, Gwangju, Korea, Rep. of South*

Background and Aims: Lupus nephritis (LN) is one of the major complications of systemic lupus erythematosus. Early intervention in lupus nephritis is known to benefit patients' prognosis. Recent studies have found an association between hyperuricemia and lupus nephritis, but the sex-specific role of uric acid in lupus nephritis remains unclear. The purpose of this study is to elucidate the relationship between lupus nephritis and hyperuricemia, and to investigate sex differences.

Method: We retrospectively analyzed 394 patients who diagnosed with LN by renal biopsy. We assessed the effect of serum uric acid on progression of LN using Kaplan–Meier survival analyses and Cox proportional hazards models. The study's primary end point was LN progression that was defined as the initiation of dialysis.

Results: The male had a higher mean of serum uric acid level than female. In the overall patient analysis, every 1 mg / dL increase in baseline uric acid level increased the risk of LN progression by about 16.9%. The serum uric acid level was an independent risk factor for LN progression in female (hazard ratio [HR], 1.177; confidence interval [CI],1.024 to 1.353; $P<0.001$) but not in male (HR, 1.0351; CI, 0.661 to 1.622; $P=0.880$). A sensitivity analysis involving serum uric acid tertile generated consistent and robust results.

Conclusion: The serum uric acid level was an independent risk factor for LN progression in female but no in male.

P0379

BION-1301, A FULLY BLOCKING ANTIBODY TARGETING APRIL FOR THE TREATMENT OF IGA NEPHROPATHY: ASSESSMENT OF SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS IN LONG-TERM NONCLINICAL STUDIES

Joost Kreijtz[1], Peter Van Zandvoort[1], Jos Van de Crommert[1], Maarten Friesen[1], Jeannette Lo[2], Aaron Endsley[3], Veronique Lauriault[4], Thomas Mueller[2], Andrea Van Elsas[1]

[1]Aduro Biotech Europe, Oss, Netherlands, [2]Aduro Biotech Inc, Berkeley, United States of America, [3]Certara, Princeton, United States of America and [4]ToxConsult LLC, San Francisco,

Background and Aims: IgA Nephropathy (IgAN) is a common form of glomerulonephritis and its pathogenesis is thought to consist of sequential pathogenic hits, including the production of auto-antigen galactose-deficient IgA1 (Gd-IgA1) and auto-antibody formation ultimately resulting in immune complex deposition, inflammation and functional deterioration of the kidney. Serum levels of APRIL (A PRoliferation Inducing Ligand, TNFSF13) and levels of Gd-IgA1 are correlated with severity of disease (Zhao et al, 2012). As a ligand for the receptors BCMA and TACI, APRIL is thought to regulate differentiation and proliferation of B cells and plasma cells and IgA class switching. BION-1301 is a humanized antibody neutralizing APRIL. In nonhuman primates, BION-1301 reduced serum levels of IgA, IgM, and IgG with no drug-related toxicity (Dulos J, et al. ASN Annual Meeting. 2018). Here we describe the nonclinical safety assessment of BION-1301, to support its continued clinical development for the treatment of IgA Nephropathy.

Method: A 14-week repeat-dose toxicity and toxicokinetic/pharmacodynamic (TK/PD) study in non-human primates (NHP) was performed by biweekly intravenous bolus (IV) administration of BION-1301 at three different dose levels. To support a potential change in route of administration, a 4-week repeat-dose NHP bridging study was conducted with weekly subcutaneous (SC) administration of BION-1301 at three different dose levels.

Results: In both the 14-week IV study and the 4-week SC study, BION-1301 was evaluated for safety, TK and PD. For TK and PD, BION-1301 levels, uncomplexed APRIL levels and immunoglobulin levels (IgA, IgG, IgM) were quantified in serum. Immunophenotyping was performed on peripheral blood to assess the impact of BION-1301 on the B cell compartment. In both studies BION-1301 was well tolerated with no test-article related findings. 14-week IV dosing as well as 4-week SC dosing of BION-1301 reduced serum APRIL levels as well as serum immunoglobulin levels.

Conclusion: Results of these nonclinical toxicity studies with toxicology, TK and PD endpoints demonstrate that BION-1301 is well tolerated for up to 14 weeks of dosing, corroborates pharmacodynamic proof-of-mechanism and support prolonged dosing and SC administration of BION-1301 in patients with IgA Nephropathy.

P0380

INFECTION PROFILE AND ASSOCIATED RISK FACTORS IN AGGRESSIVE GLOMERULONEPHRITIS TREATED WITH INDUCTION AND MAINTENANCE REGIMENS OF IMMUNOSUPPRESSIVE THERAPY

Alexandra Vornicu[1], Bogdan Obrisca[1], Roxana Jurubita[1], Andreea Gabriella Andronesi[1], Bogdan Marian Sorohan[1], Camelia Achim[1], Diana Zilisteanu[1], ELENA EMANUELA RUSU[1], Gener Ismail[1]

[1]*Fundeni Clinical Institute, Nephrology Department, Bucharest, Romania*

Background and Aims: Infections remain an important contributor to the morbidity and mortality of immunosuppressive (IS) therapy in aggressive glomerulonephritis. We sought to investigate the infection profile and associated risk factors in a compiled cohort of patients with lupus nephritis (LN), cryoglobulinemic vasculitis (CryoVas) and ANCA-associated vasculitis (AAV) treated with induction and maintenance IS regimens.

Method: A total of 162 patients (101 with LN, 24 with CryoVas and 37 with AAV) were retrospectively reviewed for any infection that occurred from initiation of induction therapy. Infections were graded (1-5) according to the Common Terminology Criteria for Adverse Events. Infection site and type of microorganism were also recorded. Univariate and multivariate Cox proportional hazard regression analysis were performed in order to identify independent risk factors for infection.

Results: Eighty-two patients (50.6%) had at least one infection with a total 179 episodes of infection occurring during a median follow-up of 12 months (IQR:4-36.25 months). The majority of patients (64 of 82) had infections during the first 24 months since IS treatment initiation with a 24-month infection-free rate of 55%. The most common site was lung infection (in 32.7% of patients), while 39.5% of patients had bacterial infections (1.8% with Mycobacterium tuberculosis). 36.7% of patients had severe infections (grade 3 or higher) with 4.4% of infection-related deaths (8 patients). The most common induction regimen was cyclophosphamide in addition to corticosteroids (62%), while 43% received either mycophenolate mofetil or azathioprine in addition to corticosteroids as a maintenance regimen. In univariate Cox regression analysis, chronic obstructive pulmonary disease (HR 3.91; 95% CI, 1.76-8.68, p=0.001), pulmonary involvement in the setting of systemic disease (HR 2.35; 95% CI, 1.26-4.37, p=0.007), pulse methylprednisolone (HR 2.7; 95% CI, 1.7-4.31, p=0.001) and high-dose ($\geq$30 mg/day) oral corticosteroids (HR 3.38; 95% CI, 2.11-5.43, p=0.001) were risk factors for infection. In multivariate Cox regression analysis, high-dose oral corticosteroids (HR 2.67; 95% CI, 1.5-4.76, p=0.001) remained an independent predictor of infection risk. Of the risk factors associated with severe infections (grade 3 or higher), in univariate analysis we identified pulmonary involvement in the setting of systemic disease (HR 3.65; 95% CI, 1.72-7.77, p=0.001), pulse methylprednisolone (HR 3.56; 95% CI, 1.7-7.3, p=0.001), high-dose ($\geq$30 mg/day) oral corticosteroids (HR 3.56; 95% CI, 1.77-7.16, p=0.001), estimated GFR (HR 0.98; 95% CI, 0.98-0.99, p=0.01) and AAV (by comparison to CryoVas and LN) (HR 2.81; 95% CI, 1.39-5.66, p=0.004) as risk factors for infection. After multivariate adjustment, pulmonary involvement in the setting of systemic disease (HR 2.38; 95% CI, 1.01-5.73, p=0.05) and high-dose oral corticosteroids (HR 2.44; 95% CI, 1.04-5.72, p=0.04) were identified as independent predictors of infection risk.

Conclusion: Infections occur frequently with current immunosuppressive regimens in aggressive glomerulonephritis. In addition to pulmonary involvement in the setting of systemic disease, a high dose corticosteroid regimen was the most significant risk factor for infection.

P0381

THE UTILITY OF LOW DOSE RITUXIMAB FOR INDUCTION AND MAINTENANCE TREATMENT IN ELDERLY PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: A SINGLE CENTRE EXPERIENCE

El Hakem Metraiah[1], Paula Dospinescu[2], Nicholas Fluck[3], Neil Basu[4], Dana Kidder[1]

[1]Aberdeen Royal Infirmary, Aberdeen Renal Unit, Aberdeen, United Kingdom, [2]Department of Rheumatology, Aberdeen Royal Infirmary, Aberdeen, United Kingdom, [3]NHS Grampian, Aberdeen, United Kingdom and [4]Institution of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom

Background and Aims: Elderly patients with Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) tend to have higher rates of mortality and treatment-related adverse events. Rituximab is now widely used in the treatment of patients with AAV based on the results of remission induction (RITUXVAS and RAVE) and remission maintenance (MAINRITSAN) randomized controlled trials. Elderly patients were relatively under-represented in these trials. In this observational study we aimed to examine the outcome of elderly patients who received Rituximab (either as low dose Rituximab (LDR) or standard dose Rituximab (SDR)) for remission induction and maintenance.

Method: We investigated the outcome of three treatment strategies in elderly (age>65 years) patients who presented with AAV to our Vasculitis clinic from 1 July 2007 to 9 of July 2017. These strategies included: LDR (17 patients), SDR (14 patients) and Cyclophosphamide/Azathioprine (Cyc/A) 26 patients. LDR patients received two dose of 500mg Rituximab fortnightly followed by six monthly 500mg doses for 2 years. SDR patients received 1g Rituximab fortnightly followed by six monthly 1g doses for 2 years. Cyc/A patients received 1.5mg/kg oral Cyclophosphamide for 3 months followed by 18 months of Azathioprine.

Results: Among 57 AAV patients, 56% were females and mean age of 79.6 +/- 4 (LDR), 72.4 +/- 7.2 (SDR), and 71.1 +/- 5 (Cyc/A) (p=0.001). The distribution of MPA and GPA was 11/6 in LDR, 7/7 in SDR and 18/8 in Cyc, respectively. Relapsing GPA was significantly higher in SDR 12/2 compared to LDR 3/14, and Cyc/A 0/26 (p=0.0001). There were no significant differences in serum creatinine, BVAS scores or CRP between groups at initiation of treatment. Patients survival at 24 months was 88% (LDR), 92% (SDR), and 77% (Cyc), p=0.3. The mean corticosteroids dose at 3 months from onset of treatment was significantly lower in the LDR (7.6 +/- 1.7) and SDR (8.6 +/- 3.1) compared with Cyc/A (12.5 +/- 3.6), p=0.001. 1 patients relapsed in the SDR group and 4 patients in the Cyc/A group. Hospitalization for infections were significantly lower in the LDR (3 episodes) compared to Cyc/A (17 episodes), p=0.004. The number of patients with hypogammaglobulinemia was not significantly different between LDR and SDR.

Conclusion: In this single centre observational study, we found that low dose Rituximab for remission induction and maintenance associated with similar patient outcome to SDR. The findings of this study needs to be replicated with longer duration of follow-up.

P0382

"FALSE" POSITIVITY OF SERUM ANTI-PHOSPHOLIPASE A2 RECEPTOR ANTIBODY (ANTI-PLA2R AB) IN PATIENTS WITH NON MEMBRANOUS GLOMERULAR DISEASE

Irene Mok[1], Jason Choo[1]

[1]*Singapore General Hospital, Renal Medicine, Singapore, Singapore*

Background and Aims: Phospholipase A2 receptor (PLA2R) is the major target antigen in primary membranous nephropathy (PMN) and the detection of circulating autoantibodies to PLA2R (Anti-PLA2R Ab) is a major advance in understanding this disease. In this study, we aimed to determine if Anti-PLA2R Ab serves as a specific marker for PMN in our multi-ethnic Southeast Asian cohort.

Method: This was a prospective cohort study of all adults with glomerular disease undergoing biopsy between 1st January 2015 and 30th June 2018. Anti-PLA2R antibody levels were quantitatively determined by IgG ELISA (Euroimmun). Results are expressed as RU/ml. We considered a value of >20RU/ml to represent a positive result, value of <14RU/ml to be negative and values between 14-20 RU/ml to be indeterminate.

Results: Out of the cohort of 192 patients, there were 27 patients with Membranous Nephropathy (MN), with 12 PMN and 15 with secondary MN (SMN). Secondary causes were Hepatitis (1), Malignancy (1), Lupus (13). In our analyses, 10 (83.3%) PMN pts were positive for Anti-PLA2R Ab, with 7(58.3%) strongly positive with titres >200RU/ml and 2(16.7%) negative. For SMN, the majority, 12 out of 14 patients (85.7%) tested negative and the remaining 2 (7.7%) yielded values of indeterminate levels.

Of note, among the 165 patients with non membranous glomerular disease, there were 15 patients (9.1%) with indeterminate Anti-PLA2R Ab levels and 31 patients (18.9%) tested positive for Anti-PLA2R antibody, with levels >20 RU/ml. Of these 31 patients, the majority of the patients had low levels of Anti-PLA2R Ab of <50 RU/ml. However there were 5 patients who had considerably high levels of Anti-PLA2R Ab of >50 RU/ml and their characteristics are tabled below (Table 1)

Conclusion: Consistent with other published studies, positive Anti-PLA2R antibody levels were highly specific for PMN in our multi-ethnic Southeast Asian population and our centre has since been consistently using this test for differentiating between PMN and SMN. What is most striking in our study is that we have found high-titre Anti-PLA2R antibody positivity in non-MN patients, which has not been frequently reported in literature. The unifying feature amongst these patients appear to be the presence of arterial and arteriolar sclerosis which is usually non-specific. Though we would not normally do the Anti-PLA2R antibody test in a patient with low suspicion of MN, our study findings warrants further investigation and may indicate the limited usefulness of Anti-PLA2R antibody levels as a screening tool for glomerulonephritis.

	Age/ Gender	Ethnicity	Anti-PLA2R Ab titre	Proteinuria	Serum Creatinine/ EGFR (MDRD)	Biopsy diagnosis
Patient 1	32/M	Chinese	168.3	0.27	58/ 149.7	Minor glomerular changes and mild to moderate arteriolar sclerosis
Patient 2	48/F	Chinese	69.3	0.54	173/ 29	Mild mesangial proliferation and moderate arterial sclerosis
Patient 3	68/M	Chinese	56.3	0.15	179/ 35	Minor glomerular changes, moderate arteriolar hyalinosis and arterial sclerosis
Patient 4	53/F	Chinese	77.1	0.4	50/ 119	Mesangioproliferative Disease consistent with IgA disease, moderate arterial sclerosis
Patient 5	67/F	Indian	101.1	2.92	142/ 34	Marked arterial and arteriolar nephrosclerosis with underlying diabetic alterations

P0383 A LONG-TERM RETROSPECTIVE OUTCOME ANALYSIS OF ANCA-NEGATIVE PAUCI-IMMUNE GLOMERULONEPHRITIS

Jennifer O'Brien[1], Pek Ghe Tan[1], Charles Pusey[1,2], Stephen McAdoo[1,2]

[1]Imperial College Healthcare NHS Trust, Specialist Nephrology Clinic, London, United Kingdom and [2]Imperial College London, Centre for Inflammatory Disease, London, United Kingdom

Background and Aims: Pauci-immune glomerulonephritis (GN), usually associated with circulating antineutrophil cytoplasm antibodies (ANCA), is one of the most common causes of rapidly progressive glomerulonephritis that results in high incidence of end-stage kidney disease (ESKD). Most of the existing large trials looking at treatment efficacies exclude ANCA-negative patients, and relatively few studies have reported their long-term outcomes. Therefore, we conducted a single-centre retrospective study to examine the long-term overall survival and renal outcome in this cohort of patients.

Method: All cases of newly diagnosed biopsy-proven pauci-immune GN from 2006 - 2019 were identified through a local histopathology database. Patients with negative anti-myeloperoxidase (MPO) and anti-proteinase-3 (PR3) serology were identified (ANCA-negative group) and comparisons made with the cohort of patients with positive serology (MPO/PR3 positive group). Patients with relapsing ANCA-GN, eosinophilic granulomatosis with polyangitis, other co-existing glomerulonephritis or missing data on induction therapy or outcome were excluded.

Baseline demographics, initial serum creatinine (sCr), estimated glomerular filtration rate (eGFR), systemic involvement and histopathology features including percentage normal glomeruli, and interstitial fibrosis/tubular atrophy score of >25% were collected and compared.

Kaplan Meier survival analysis was used to compare overall survival and end-stage kidney disease (ESKD) progression rate between the two groups.

Results: 178 patients were identified with a median follow-up of 44 months. 83 were female (47%) and median age was 62 years. 15 (8%) were ANCA-negative. 163 (92%) were MPO- and/or PR3-ANCA positive.

There were no differences in baseline characteristics such as age, gender and proportion of patients with normal glomeruli <25% on initial histology. However, we observed a significantly higher proportion of patients with renal-limited vasculitis in the ANCA-negative group (67% vs 24% p=0.01) and more severe renal dysfunction at presentation (median sCr 309umol/L vs 204umol/L, p= 0.01). We also demonstrated a higher proportion of patients with an IFTA score of >25% on renal biopsy (53% with >25% IFTA in ANCA-negative cohort vs 27%, p =0.03). The ANCA-negative group were more likely to receive combination immunosuppressive therapy that included plasma exchange (47% vs 23%, p value 0.04).

When considering overall survival there was significantly higher mortality (40% vs 16%, p value 0.009) and rate of progression to ESKD (53% vs 18%, p value 0.001) in the ANCA-negative group as a whole. When we compared patients with renal-limited vasculitis only however, there was no significant difference in either overall survival or rate of progression to ESKD (p=0.85 and 0.84 respectively). We found that ANCA-negative patients with systemic disease did still have significantly higher rates of both progression to ESKD and overall mortality (p=0.002 and p=0.02 respectively).

Conclusion: In our cohort, patients with ANCA-negative pauci-immune GN have poorer renal function and higher IFTA scores on biopsy at presentation perhaps reflecting delayed diagnosis due to a lack of diagnostic serology and the higher proportion of renal-limited disease in this subgroup. Despite intensive immunosuppressive therapy, this study observed overall higher treatment failure rates in ANCA-negative patients, largely in those with systemic disease. This possibly relates to a different underlying disease process. Larger, prospective studies are required to enhance understanding of the disease pathogenesis to allow optimal tailored treatment for these patients.

P0384 **PROTEINURIA SELECTIVITY INDEX MAY PREDICT RITUXIMAB RESPONSE IN MCD AND FSGS**

Marco Allinovi[1], Giorgio Trivioli[1], Gianmarco Lugli[1], Leonardo Caroti[1], Giulia Antognoli[1], Calogero Cirami[1]

[1]*Careggi University Hospital, Nephrology, Dialysis and Transplantation, Florence, Italy*

Background and Aims: Proteinuria selectivity index (PSI) predicts steroid responsiveness in minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS). Rituximab, a monoclonal antibody targeting CD20, has increasingly recognized as a potential therapy of idiopathic podocytopathies, such as MCD and FSGS, although the mechanism of action is still unrecognized and randomized controlled studies are still lacking. Currently, no tools are available to predict responsiveness to RTX. We explored the role of PSI as a potential predictor of RTX responsiveness in MCD and FSGS.

Method: We analysed cases of biopsy-proven MCD and FSGS followed at one single centre, who received RTX therapy. Baseline data, including proteinuria and PSI, were collected. Proteinuria was considered selective with PSI (clearance of urinary IgG/transferrin ratio) <0.20. Complete remission (CR) was resolution of proteinuria and clinical symptoms, while partial remission (PR) was proteinuria decrease (>50%) and substantial improvement of clinical symptoms.

Results: RTX was administered to 14 patients with MCD and 16 patients with FSGS and, of them, PSI was available before treatment for 10 and 14 patients, respectively. Baseline characteristics of the patients are shown in Table 1. Among the 24 cases with available PSI, CR was reported in 12 and PR in 5, while 9 did not respond to RTX. All patients who achieved CR and PR had selective proteinuria at baseline, while all patients with PSI >0.20 did not respond to RTX (Figure 2). Median relapse-free survival was 25.4 months. Among responders, in 10 out of 19 patients (53%) the relapse occurred between 4 and 60 months from initial treatment. No potentially life-threatening adverse events have been observed.

Conclusion: Selective proteinuria before treatment can predict the response to RTX in adult patients with steroid-dependent and refractory forms of MCD and FSGS.

	MCD	FSGS
N° of patients	14	16
Age at onset (mean, years)	37,5	34,8
Gender M/F	10 / 4	6 / 10
At the time of ˚rst rituximab:		
N° of relapses (mean)	3,5	1,8
Response to:	13/14 (93%)	7/16 (44%)
corticosteroids (n°, %)	6/6 (100%)	5/9 (56%)
immunosuppressive drugs (n°)		
Serum creatinine (mean, mg/dL)	0,93	1,73
PSI index (mean)	0,11	0,28
PSI <0.20	10/10 (100%)	5/14 (36%)
24h proteinuria (mean, g)	5,53	8,96
After rituximab therapy:		
CR (n°)	13/14 (93%)	1/16 (6%)
PR (n°)	1/14 (7%)	4/16 (25%)
NR (n°)	0	11/16 (69%)
At last follow-up:		
Lenght of follow-up (mean, months)	33,1	31,0
Serum creatinine (mg/dL)	0,93	4,00
24h proteinuria	0,625	7,65

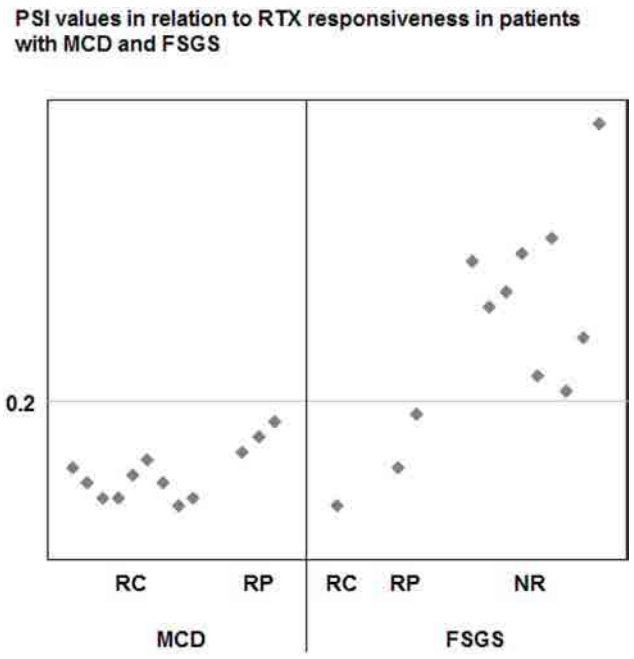


Figure 1:

P0385 CLINICAL DIFFERENCES OF MEMBRANOPROLIFERATIVE GLOMERULONEPHROPATHY (MPGN) ACCORDING TO PRESENCE OF HEPATITIS B VIRUS INFECTION

Hea Eun Kim[1], HO JUN CHIN[1,2]

[1]Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam-si, Korea, Rep. of South and [2]SEOUL NATIONAL UNIVERSITY COLLEGE OF MEDICINE, INTERNAL MEDICINE, SEOUL, Korea, Rep. of South

Background and Aims: Traditional definition of MPGN by morphologic changes on light microscopic examination was reclassified into MPGN caused by immunoglobulin/immune complex injury and C3 glomerulopathy (C3G) with alternative complement pathway abnormality based on immunofluorescence staining. MPGN might be caused by various causes such as malignancy, infection, autoimmune diseases, etc. It was rarely known the clinical characteristics of MPGN according to the possible causes excluding C3G.

Method: We enrolled 20,481 adult patients having native kidney biopsy for diagnosis of nephritis between 1979 and 2018, retrospectively. Among them, there were 553 patients with MPGN whom we reclassified into 18 patients with C3G and 535 MPGN patients. We excluded patients with cancer, autoimmune disease, hepatitis C virus infection, C3G, or combined pathologic diagnosis other than MPGN. Finally, we enrolled 156 patients without hepatitis B surface antigen (HBsAg)[MPGN] and 48 patients with HBsAg [MPGN_HBV]. The final outcomes were incidences of end stage renal disease (ESRD) and death.

Results: Patients with MPGN_HBV are younger than MPGN (45.5 $\pm$ 15.8 years vs 54.6 $\pm$ 15.7 years, p=0.001) and included more males (43 (89.6%) vs 97 (62.2%), p<0.001). The systolic blood pressure was not different between groups but the diastolic blood pressure was higher in MPGN_HBV (85.4 $\pm$ 10.4 mmHg vs 80.7 $\pm$ 13.4 mmHg, p=0.018). The level of urine protein to creatinine ratio was not different between groups but the level of glomerular filtration rate (GFR) was higher in patients with MPGN_HBV compared to patients with MPGN (65.8 $\pm$ 29.0 ml/min/1.73 m^2 vs 57.5 $\pm$ 34.8 ml/min/1.73 m^2, p=0.039). Mortality was observed in 2 patients with MPGN_HBV (4.2 %) and 9 patients with MPGN (5.8%)(p=1.000) during 64.9 months (median). Incident ESRD was notified in 6 patients with MPGN_HBV (13.3 %) and 39 patients with MPGN (26.5 %)(p=0.067) during 47.8 months (median). HBV positivity was not a risk factor to mortality (p=0.847) and was not a risk factor to incident ESRD (p=0.108), either, by Cox's hazard proportional model adjusted with related factors to mortality. The most important risk factor was hemoglobin and GFR at renal biopsy.

Conclusion: The clinical characteristics of MPGN according to presence of HBsAg were different, however, the prognosis was not dependent on HBsAg positivity, which suggested the severity of renal injury was more important than the cause of renal injury.

P0386

OUTCOMES OF PAUCI-IMMUNE CRESCENTIC GLOMERULONEPHRITIS BASED ON THE INTERNATIONAL HISTOPATHOLOGICAL CLASSIFICATION AND RECENTLY PROPOSED RENAL RISK SCORE IN ADULTS: A SINGLE CENTER STUDY

Pallav Gupta[1], Satyendra Dharamdasani[1], Devinder Singh Rana[2], A K Bhalla[2], Ashwani Gupta[2]

[1]*Sir Ganga Ram Hospital, Renal Pathology and Histopathology, New Delhi, India and* [2]*Sir Ganga Ram Hospital, Nephrology, New Delhi, India*

Background and Aims: Pauci-immune crescentic glomerulonephritis is rare form of glomerulonephritis that frequently presents as rapidly progressive renal failure. The histopathological classification proposed by Berden a decade earlier described difference in the outcomes of patients in the focal, crescentic, mixed and sclerotic category with best prognosis for focal and worst for sclerotic group. The newly proposed renal risk score (Brix SR at al.) takes into account both the histopathological parameters (% of normal glomeruli, tubular atrophy and interstitial fibrosis) and clinical parameter (eGFR) which influence outcome in these patients. Present study was undertaken to determine outcomes of pauci-immune crescentic glomerulonephritis based on both of these prognostic systems and also to determine effect of individual risk factors on renal outcome.

Method: 64 patients diagnosed as pauci-immune crescentic glomerulonephritis from January 2013 to December 2018 were retrospectively analyzed. There histopathological slides were reviewed for percentage normal glomeruli, extent of interstitial fibrosis and tubular atrophy and biopsies were also grouped according to histopathological classification into focal, crescentic, mixed and sclerotic categories. The clinical parameters including serum creatinine, eGFR at time of biopsy and follow-up, and status of ANCA positivity were obtained from electronic records. Renal biopsies were scored based on renal risk score depending on the % of normal glomeruli ($>$25%,10-25% and $<$10%), percentage of tubular atrophy and interstitial fibrosis($\leq$25%,$>$25%) and eGFR($>$15ml/min,$\leq$15ml/min) into 3 risk categories.

Results: There were 61 adult patients and 3 pediatric patients. Two patient with insufficient glomeruli ($<$7) on biopsy and 8 patients without follow-up were excluded. A total of 51 adult patients were included of which 28 were male and 23 females. The mean age was 51.2$\pm$15.7 years. The mean serum creatinine at the time of biopsy was 7.05$\pm$4.57 mg/dl and the mean eGFR was 13.6$\pm$12.16 ml/min/1.73m2. There were 33 ANCA positive and 18 ANCA negative(35%) cases. Distribution of patients according to Berden's histopathological classification was focal(4), crescentic(29), mixed(12) and sclerotic(6). The distribution of patients into risk categories based on renal risk score was low(8),medium(23) and high(20). Univariate Cox regression analysis showed that eGFR at biopsy (p 0.024), % IFTA (p 0.001) and % normal glomeruli in biopsy (p 0.023) are predictors of ESRD. Multivariate Cox regression analysis including age, eGFR, % IFTA and % normal glomeruli in biopsy also confirmed IFTA ($p<0.001$) and % normal glomeruli in biopsy (p 0.018) as significant predictors of ESRD. When % normal glomeruli was replaced by Berden's histopathological classed it didn't reach statistical significance to predict ESRD. Kaplan-Meier survival analysis for histological categories showed best renal survival in focal group and worst in sclerotic group (Log-Rank p=0.046). Kaplan-Meier analysis for the renal risk categories showed best survival in low risk group followed by medium and high risk groups respectively (Log-Rank p=0.002). Kaplan-Meier survival analysis was also done for percentage of normal glomeruli, IFTA and renal function.

Conclusion: In our study of Pauci-immune crescentic glomerulonpehritis ANCA was negative in 35% cases. Percentage of normal glomeruli, IFTA and eGFR at time of biopsy were important histopathological and clinical risk factors influencing renal survival in these patients. Results of our study validate that recently proposed renal risk score is a better predictor of survival (p=0.002) as compared to histological classification proposed by Berden (p=0.046).

P0387 PATHOLOGICAL FEATURES AND CLINICAL COURSE OF LATE-ONSET LUPUS NEPHRITIS

Amir Shabaka[1], Beatriz Sanchez Alamo[1], Serena Gatius[2], Clara Maria Cases Corona[1], Elena Valdes[2], Patricia Dominguez Torres[1], Yunayka Diaz Enamorado[1], Gema Maria Fernandez Juarez[1]

[1]Hospital Universitario Fundación Alcorcón, Nephrology, Alcorcón, Spain and [2]Hospital Clinico San Carlos, Nephrology, Madrid, Spain

Background and Aims: It has been described that the early onset of lupus nephritis (LN) at a young age can determine the clinical course and outcome of the disease, being more aggressive with a higher mortality rate. However, no studies have explored the influence of age at onset of the disease in European cohorts of LN patients, neither have they analyzed treatment outcomes depending on age at presentation. Therefore, the aim of our study was to compare the clinical and histological characteristics of patients with late-onset LN compared to those with an onset at a younger age.

Method: We performed a retrospective observational study of biopsy-proven LN diagnosed between 1981 and 2018. Patients were stratified according to their age at presentation of LN, considering an onset with >50 years old as late-onset. Demographic, clinical and serological data at presentation of systemic lupus and LN, during and at the end of follow-up, as well as extrarenal manifestations, histological characteristics of the kidney biopsy, clinical course, received treatment regimens and related adverse effects were registered.

Results: 85 LN patients were included in the study, 10 of whom had late-onset LN (11.7%). Late-onset LN patients presented significantly higher serum C3 and C4 levels at the time of kidney biopsy (92.8 ± 22.4 mg/dl vs 62.5 ± 25.7 mg/dl, p=0.002, and 18.6 ± 5.0 vs. 9.3±5.8 mg/dl, p<0.001 respectively), and had lower eGFR measured by CKD-EPI (58.50±19.79 vs 90.41±30.53,p=0.003), a higher frequency of serositis manifestations (53.45% vs 17.46%, p=0.034), predominantly pleuritis (79.37% vs 51.75% p=0.013). Early-onset LN had predominantly Class IV LN (50% vs 10%, p=0.017), whereas in late-onset LN the most frequent type was Class V LN (50% vs 21.3%, p=0.048). Tubular atrophy was more common in late-onset LN (75% vs 34.9%, p=0.035). The group of patients with late-onset LN achieved complete clinical remission more frequently (87.5% vs 57.1%), but there were no differences in relapses between the groups. No differences were found in treatment regimens among the groups. Late-onset LN patients were more seronegative (100% vs 61.3%, p=0.015) at the end of follow-up. Severe infectious complications related to immunosuppression were significantly higher in late-onset LN patients (62.5% vs 22.2%, p=0.027)

Conclusion: Late-onset LN has a milder complement consumption at presentation compared to early-onset, and Class V LN is its most frequent form of presentation. Complete renal remission is more frequently achieved in late-onset LN compared to those with an early-onset, but present more adverse events associated with immunosuppression, particularly infectious complications.

P0388

ABC-R ANCA STUDY ESTABLISHMENT OF AN ANATOMOPATHOLOGICAL BIOLOGICAL AND CLINICAL PROGNOSTIC SCORE IN THE MANAGEMENT OF ANCA VASCULITIS WITH RENAL IMPAIRMENT

Florine HODIQUE[1], Mathilde NOUVIER[2], Cecile PICARD[3], Maud RABEYRIN[3], Laurent Juillard[4], Frederique DIJOUD[3], Nicole FABIEN[5], Denis Fouque[5], Thomas BARBA[4], Arnaud HOT[1]

[1]Hospital Édouard Herriot, Internal medicine, Lyon, France, [2]Lyon Sud Hospital Center, Nephrology, Pierre-Bénite, France, [3]Groupement Hospitalier Est - HCL, Pathology, Bron, France, [4]Hospital Édouard Herriot, Nephrology, Lyon, France and [5]Lyon Sud Hospital Center, Immunology, Pierre-Bénite, France

Background and Aims: Glomerulonephritis is common in ANCA associated vasculitis (GN-AAV). There is extensive published data on the renal prognosis of these conditions. However, few authors have described predictive factors for end-stage renal disease (ESRD) in patients with GN-AAV. Many authors suggest that renal biopsy should be abandoned in patients whose diagnosis would be established by antibody positivity alone.

The aim of the study was to establish a prognostic score for renal damage during ANCA vasculitis and demonstrate need for prognostic renal biopsy.

Method: One Hundred and eighteen patients referred to 2 french nephrology departments in Lyon between January 2003 and January 2019 were retrospectively analysed. Patients were randomly divided in 2 cohorts at a ratio of 70/30: training and validation cohorts. ESRD was defined as glomerular filtration rate (eGFR) $\leq$ 15mL/min/1.73m2,need of chronic dialysis or renal transplantation.

Results: Of the 118 patients, 38 (32.20%) developed ESRD. We identified 3 criteria associated with development of ESRD in patients with GN-AAV. One point was assigned to each criterion according to a threshold value: eGFR at the time of renal biopsy $\leq$ 15 mL/min; percentage of sclerotic glomeruli $\geq$ 11% and percentage of normal glomeruli $<$ 20%. A new prognostic renal score was established in patients with GN-AAV. It classifies patients into 3 categories at risk of developing ESRD: low ($\leq$ 1 point), moderate (2 points) and high (3 points).

Conclusion: Two of the three criteria of our score are histological. Biopsy remains, when possible, an essential tool for diagnosis and especially to predict renal prognosis of ANCA vasculitis with renal impairment.

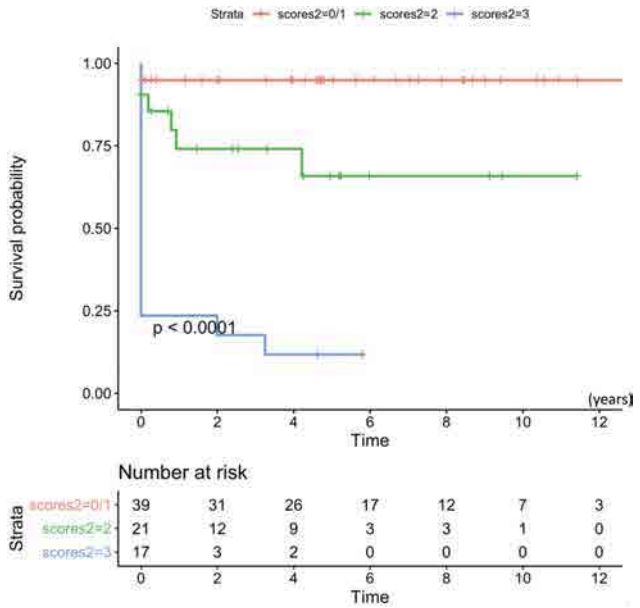


Figure: Kaplan-Meier curves according to ABC-R ANCA score

a) **Renal survival (years) of training cohort (n=77) Low** risk ($\leq$ 1point); moderate risk (2 points) High risk (3 points)

b) **Renal survival (years) of validation cohort (n=41) Low** risk ($\leq$ 1point); moderate risk (2 points) High risk (3 points)

P0389

THE PREVALENCE, CLINICAL AND PATHOLOGICAL CHARACTERISTICS OF PRIMARY FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN TURKISH ADULTS: THE DATA FROM TSN-GOLD (TURKISH SOCIETY OF NEPHROLOGY GLOMERULAR DISEASES) WORKING GROUP

Ilhan Kurultak[1], Ozkan Gungor[2], Savas Ozturk[3], Ahmet Burak Dirim[4], Necmi Eren[5], Ezgi Yenigun[6], Elbis Ahbap Dal[7], Mevlut Tamer Dincer[8], Feyza Bora[9], Suat Akgur[10], Abdullah Sumnu[11], Belda Dursun[12], Savaş Sipahi[13], Hakkı Çetinkaya[14], İdris Sahin[15], Garip SAHIN[16], Mürvet Yılmaz[17], Bulent Vatansever[18], Emre Aydin[19], Memnune Sena Ulu[20], Ali Gundogan[21], Sedat Üstündağ[1], Hayriye Sayarlioglu[22], Gizem Kumru Şahin[23], Omer Celal Elcioglu[24], Zeki Aydin[25], Nedim Yılmaz Selçuk[26], Ceren Onal[27], Meric Oruc[28], Mehmet Kucuk[29], Nimet Aktas[30], Ülver Derici[31], Gultekin Suleymanlar[9]

[1]Trakya University, Faculty of Medicine, Nephrology, Edirne, Turkey, [2]Sutcu Imam University, Faculty of Medicine, Nephrology, Turkey, [3]Haseki Education and Research Hospital, Nephrology, Istanbul, Turkey, [4]Istanbul University, Faculty of Medicine, Nephrology, Istanbul, Turkey, [5]Kocaeli University, Faculty of Medicine, Nephrology, Kocaeli, Turkey, [6]Ankara Numune Education and Research Hospital, Nephrology, Ankara, Turkey, [7]Hamidiye Sisli Etfal Education and Research Hospital, Nephrology, Istanbul, Turkey, [8]Istanbul Cerrahpasa University, Faculty of Medicine, Istanbul, Turkey, [9]Akdeniz University, Faculty of Medicine, Nephrology, Antalya, Turkey, [10]Uludag University, Faculty of Medicine, Nephrology, Bursa, Turkey, [11]Medipol University, Faculty of Medicine, Nephrology, İstanbul, , [12]Pamukkale University, Faculty of Medicine, Nephrology, Denizli, Turkey, [13]Sakarya University, Faculty of Medicine, Nephrology, Sakarya, Turkey, [14]Sultan Abdulhamid Han Education and Research Hospital, Nephrology, Istanbul, Turkey, [15]Inonu University, Faculty of Medicine, Nephrology, Malatya, Turkey, [16]Eskisehir Osmangazi Universitesi, Faculty of Medicine, Nephrology, Eskişehir, Turkey, [17]University of Halth Sciences, Bakırköy Dr. Sadi Konuk Education and Research Hospital, Nephrology, Istanbul, Turkey, [18]Izmir Bozkaya Education and Research Hospital, Nephrology, Izmir, Turkey, [19]Dicle University, Faculty of Medicine, Nephrology, Urfa, Turkey, [20]Afyon University, Faculty of Medicine, Nephrology, Afyon, Turkey, [21]Erciyes University, Faculty of Medicine, Nephrology, Kayseri, Turkey, [22]Ondokuz Mayıs University, Faculty of Medicine, Nephrology, Samsun, Turkey, [23]Ankara University, Faculty of Medicine, Ibni-Sina Hospital, Nephrology, Ankara, Turkey, [24]Bezmialem Vakıf University, Faculty of Medicine, Nephrology, Istanbul, Turkey, [25]Darıca Farabi Education and Research Hospital, Nephrology, Kocaeli, Turkey, [26]Selçuk University, Faculty of Medicine, Nephrology, Konya, Turkey, [27]Hacettepe University, Faculty of Medicine, Nephrology, Ankara, Turkey, [28]Kartal Dr. Lutfi Kırdar Education and Research Hospital, Nephrology, Istanbul, Turkey, [29]Okmeydanı Education and Research Hospital, Nephrology, Istanbul, Turkey, [30]Bursa Yuksek Ihtisas Education and Research Hospital, Nephrology, Bursa, Turkey and [31]Gazi University, Faculty of Medicine, Nephrology, Ankara, Turkey

Background and Aims: Focal segmental glomerulosclerosis (FSGS) is one of the primary glomerulopathies which is the most common cause of end-stage renal disease among all primary glomerular diseases. In adults, nephrotic syndrome develops 10-35% due to FSGS. However, its frequency has been increasing in recent years. This study was aimed to present the data and the prevalence of primary FSGS patients in Turkey.

Method: These data were obtained from the National Multicenter (47 centers) Primary Glomerular Diseases registry system, which was entered into the **T**urkish **S**ociety of **N**ephrology **Glo**meru**l**ar **D**iseases (TSN-GOLD) database between May 2009 and June 2019. The presented data in this study is cross-sectional and includes the recorded data of the patients in the hospitalization period for the kidney biopsy. These demographic, clinic and pathological data of patients were evaluated with using statistically.

Results: Of the 3875 patients enrolled in the Primary Glomerular Diseases database, 850 (21.9%) had FSGS. The mean age of the patients was 47.1 ± 13.7 and 435 (52%) of patients were male. Two hundred and eighty one (33.1%) had hypertension and 93 (11%) had diabetes. Five hundred and four patients (59.3%) were diagnosed as nephrotic syndrome. At the time of diagnosis, the mean systolic blood pressure was 13.8 ± 18.6 mm Hg and the mean diastolic blood pressure was 81.4± 11.4 mm Hg. The laboratory findings at the time of diagnosis on following; serum creatinine 1.2 ± 0.04 mg / dl, albumin 3.3 ± 0.03 g / dl, and 24 hours urinary proteinuria amounts to 4743 ± 181 mg / day. Demographical and clinical data of the patients at the time of diagnosis were presented on Table 1. In pathological examination; the mean number of glomeruli was 16.8 ± 0.3, global sclerotic glomeruli were 3.1 ± 0.1, and segmental sclerotic glomeruli were 2.4 ± 0.1. Summary of Pathological Findings were presented on Table 2

Conclusion: It is very difficult to determine the absolute incidence and prevalence of primary FSGS. Incidence rates have been reported to range from 0.2 to 1.8 / 100,000 per year in the literature. In a United States study, the most common diagnosis in 2501 kidney biopsies was FSGS (35.9%). According to this database, the prevalence of FSGS in primary glomerular diseases in our country is 21.9%.

Table 1: Demographical and Clinical data of the Patients at the Time of Diagnosis

Demographical Characteristics	**n, %**
Male	435, (52%)
Female	425, (48%)
Total, **N**	850 (100%)
Age, *year (mean±SD)*	47.1 ± 13.7
Clinical Characteristics	**Mean±SD**
Weight, *kg*	77,3±16.8
Length, *cm*	167.1±12.4
Body Mass Index, *kg/m2*	27.5±5.6
Systolic Blood Pressure, *mm Hg*	130.8±18.6
Diastolic Blood Pressure, *mm Hg*	81.4±11.4
Laboratory Analysis	**Mean±SD**
Glucose, *(mg/dL)*	96,9±1,1
BUN, *(mg/dL)*	21,1±0,5
Creatinine, *(mg/dL)*	1,2±0,04
Albumin, *(g/dL)*	3,3±0,03
Cholestrol, total *(mg/dL)*	264±4
Triglyceride *(mg/dL)*	218±5
HDL *(mg/dL)*	53±0,9
LDL *(mg/dL)*	166±3
Calcium *(mg/dL)*	8,93±0,03
Hemoglobulin *(g/dL)*	13,2±0,07
Sedimantation Rate *(mm/hour)*	37±1
Proteinuria *(mg/day)*	4743±181

Table 2: Summary of Pathological Findings

	Mean±SD
Glomerulus count, Total	16,8±0,3
Global Sclerotic	3,1±0,1
Segmental Sclerotic	2,4±0,1
Crescentic	0,1±0,03
Thickened Basal Membrane, (%)	21,4
Tubulary Atrophy	**%**
Absent	36,6
Grade 1 (<%25)	47,6
Grade 2 (%25-50)	11,9
Grade 3 (>%50)	3,9
İnterstitial Fibrosis	**%**
Absent	37.5
Grade 1 (<%25)	44,5
Grade 2 (%25-50)	13,9
Grade 3 (>%50)	4,1

P0390

THERAPEUTIC EFFECTS AND SERUM METABOLOMIC VARIATIONS IN FOCAL SEGMENTAL GLOMERULOSCLEROSIS MICE ON TREATMENT WITH HUMAN UMBILICAL MESENCHYMAL STEM CELLS

Cailli Wang[1]

[1]*Nephrology, The First Affiliated Hospital of Baotou Medical College, Baotou, P.R. China*

Background and Aims: Focal segmental glomerulosclerosis (FSGS) mediates the kidney podocyte dysfunction and leads to chronic renal diseases worldwide. Current treatment options are limited, owing to the poor understanding of the metabolic pathologic variations and regeneration of FSGS. Mesenchymal stem cells (MSC) offer the better insights to prevent renal injury and could promote the recovery of renal structure and function through complex mechanisms. Due to the safe, feasible, and therapeutic features, we first designed to investigate the role of human umbilical mesenchymal stem cells (HUMSCs) on FSGS mice and explored the potential serum metabolomic variations.

Method: Nephropathy was induced by adriamycin (ADR) in male Balb/C mice to study FSGS *via* intravenous administration. 2*106 HUMSCs are provided to treat FSGS model for 3 times. Renal function was measured by urine protein, serum urea nitrogen (BUN) and serum creatinine (SCr) in the study. Serum metabolic profiles from three groups of Balb/C mice were analysed using ultra- performance liquid chromatography coupled with a triple quadrupole-linear ion trap mass spectrometer and a novel mass spectrometry (UPLC-MS/MS) data collection technique.

Results: The concentrations of SCr and BUN were apparently decreased after HUMSCs injection for three times compared with the FSGS model and body weight from HUMSCs group was improved significantly. A total of 532 differential metabolites were identified between FSGS group and the normal control group. Bile acid dysregulation and valine/leucine/ isoleucine metabolism pathway, especially, N-acetylvaline and L-valine, were positively associated to ADR-induced FSGS. A panel of identified specific metabolites (pyrrole-2- carboxylic acid, urocanic acid and 6-hydroxynicotinic acid) as well as valine/leucine/isoleucine metabolism pathway rather than bile acid metabolism were related to the renal repair after HUMSCs treatment.

Conclusion: The administration of HUMSCs in FSGS induced ADR provides the promising protection owing to the improvement of metabolomics.

Group	BUN (mmol/L)	SCr (ng/μL)
Negative control	562.65±51.86	21.56±3.08
FSGS	991.48±57.37[a]	34.71±5.79[a]
FSGS+HUMSCs	632.41±32.93[ab]	23.00±3.37[b]

[a]P <0.05 vs. Negative control group; [b]P <0.05 vs. FSGS group.

Figure 1. HUMSCs identification by appearance and immune-phenotype.

Figure 2. The distribution of DiR-HUMSCs *in vivo*.

Figure 3. Kidney pathology using periodic acid-Schiff (PAS) and Masson staining.

Figure 4. Metabolome profiling analysis and Venn diagram for comparisons of numbers from each group.

Figure 5. Metabolic pathway analysis results from FSGS + Saline and FSGS + HUMSCs groups.

Figure S1. The quality control (QC) of serum metabolomics was designed and performed as follows.

Figure S2. Metabolic pathway analysis results from FSGS + Saline and Normal + Saline groups.

Figure S3. Metabolic pathway analysis results from FSGS + HUMSCs and Normal + Saline groups.

P0391 STUDY OF ANTI COMPLEMENT FACTOR H MEDIATED DISEASE AT A TERTIARY CARE CENTRE

Umesh Lingaraj[1]

[1]*Institute of Nephro Urology, Nephrology, Bengaluru, India*

Background and Aims: To study the clinical profile and outcome of patients with anti complement factor H mediated disease at our centre.

Method: We conducted a prospective study over 24 months (August 2016 to July 2018) to assess the clinical profile and outcome of patients with anti complement factor H mediated disease at our tertiary care centre. We had a total of 18 cases during the study period. All patients were followed up to assess their response to therapy.

Results: A total of 28 cases of atypical HUS were seen during the study period of which anti factor H antibody was elevated in 18 (64.2%). All patients presented with hypertension with active urinary sediments and rapidly progressive renal failure. Mean serum creatinine at presentation was 6.8 +/- 1.2 mg/dl and all patients were oliguric at presentation and required haemodialysis. Anti complement factor H antibody was elevated in all patients with a mean of 549 +/- 90 AU/ml. (normal - 0 to 100 AU/ml).Renal biopsy showed thrombotic microangiopathy in 12 patients (66.6%) while features were suggestive of C3 glomerulopathy in 6 patients (33.3%). All patients received induction with plasmapheresis and pulse steroids followed by oral steroids at 1mg / kg with IV cyclophosphamide 500mg/ m 2 monthly for 6 months . This was followed by maintenance immunosuppression with azathioprine +/- oral steroids. 10 patients (55.5%) attained complete remission. Patients with anti complement factor H mediated disease presenting with TMA had better prognosis compared to patients presenting with C3 glomerulopathy. Also patients in the paediatric age group showed good response to treatment

Conclusion: Our study shows that anti complement factor H mediated disease is more common in the paediatric age group with good response to plasmapheresis and immunosuppression in the form of oral steroids and cyclophosphamide. Patients presenting with TMA have better prognosis compared to C3 glomerulopathy

P0392 AHUS ASSOCIATED WITH IGA NEPHROPATHY.

Lucio Manenti[1], Marco Delsante[1], Isabella Pisani[1], Federico Ricco[1], Micaela Gentile[1], Enrico Fiaccadori[1]

[1]*Azienda Ospedaliera-Universitaria di Parma, UOC Nefrologia, Parma, Italy*

Background and Aims: . IgAN is characterized by the presence of intense deposits of C3 accompanying IgA. As documented in several studies this is due to the activation of the complement system by pathological IgA; the mechanism of IgA–mediated complement activation remains poorly understood but is thought to act with different mechanisms such as the stabilization of the C3 convertase, the activation of the lectin pathway through polymeric IgA and eventually inherited partial deficiencies of complement regulatory genes [Maillard N, Wyatt RJ, Julian BA, Kiryluk K, Gharavi A, Fremeaux-Bacchi V, Novak J.J Current Understanding of the Role of Complement in IgA Nephropathy.Am Soc Nephrol 26:, 2015] . Dysregulation of the C3 convertase is a recognized cause of thrombotic microangiopathy (TMA) in atypical hemolytic uremic syndrome (aHUS). The association between aHUS and IgAN has been sporadically described .

In this study we report a series of 6 patients, observed in our department, with biopsy proven IgAN, who developed aHUS during the follow-up. We report a series of aHUS associated IgA nephropathy.

Method: . This report describes 6 patients with aHUS IgAN who were identified among all patients with biopsy proven IgAN observed at the Department of Nephrology, University of Parma, from March 2010 to March 2015. The diagnosis of aHUS was suspected in the presence of renal biopsy with documented typical signs of TMA (glomerular or arteriolar thrombi, onion skin lesions) associated with non-immune microangiopathic haemolytic anemia, increased reticulocyte count, negative Coomb test, thrombocytopenia (platelets <150000/mm3).

Results: Data collected on the 6 patients with IgA nephropathy associated with aHUS are described in Figure 1. All the cases of aHUS-IgAN were characterized by worsening of nephrotic proteinuria and reduced serum C3. Pathogenetic variant of *CFH,* predisposing for aHUS were identified in 2/6 cases; in the remaining patients a predisposing risk aplotype for aHUS was documented. All patients were treatment resistant for IgA nephropathy, had persistent proteinuria and progressed to ESRD.

Conclusion: It is known that most cases of aHUS are associated with the presence of genetic or acquired alterations of the regulation of the complement AP. However overlapping of other triggering conditions was documented in 70% of aHUS cases [Noris M, Caprioli J, Bresin E, et al. Relative Role of Genetic Complement Abnormalities in Sporadic and Familial aHUS and Their Impact on Clinical Phenotype. Clin J Am Soc Nephrol. 2010;5: 1844–1859].

Our case series shows that the presence of genetic factors predisposing to uncontrolled activation of the C3 convertase associated to continuous activation of the same enzyme from pathological IgA, could lead to sC3 consumption, development of aHUS and consequent rapid progression towards ESRD.

In conclusion during the natural history of IgAN, appearance of hemolysis, thrombocytopenia, serum C3 reduction and increasing proteinuria would suggest to search for aHUS, allowing to early treatment with plasmapheresis and/or new available complement targeted inhibitors to prevent renal failure.

Figure 1. Case series of aHUS-IgAN

Case	Sex	Age at biopsy	IF	C3	Urinary protein (g)	Genetics		Outcome
						Risk haplotypes	Mutation aHUS related	
1	F	25	C3 +++/IgA +++	89	11	CFH-H3, SNP in MCP		ESRD
2	M	63	C3 +++/IgA +++	65	16	SNP in C3, CFB		ESRD
3	F	62	C3 +++/IgA ++	59,5	4	CFH-H3	CFH SCR 9	ESRD
4	M	31	C3 +++/IgA +++	63,3	15,3	CFH-H3/H3 MCP-TC		ESRD
5	M	20	NA	38	NA	MCP	CFH SCR 15	ESRD
6	F	17	C3++/IgA +++	64,7	8	ongoing		ESRD

Figure:

P0393 **NEPHROTIC SYNDROME IN POST HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS-20 YEARS' EXPERIENCE IN A SINGLE CENTER**

Myung Ah Ha[1], Chul-Woo Yang[2], Yong-Soo Kim[2], Cheol Whee Park[2]

[1]Bucheon St. Mary's Hospital, Internal Medicine, Bucheon, Korea, Rep. of South and [2]Seoul St. Mary's Hospital, Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Nephrotic syndrome (NS) is an extremely rare complication of hematopoietic stem cell transplantation(HCT) that usually occurs in association with chronic graft-versus-host disease. The etiology and pathogenesis of NS in HCT recipients remain unclear. There are only a few case reports and case series of NS following HCT that have been published.

Method: We reviewed the records of kidney biopsy in Seoul St. Mary's Hospital between January, 2008 and January, 2019, and identified 32 kidney biopsy specimens from patients obtained after HCT. All patients underwent kidney biopsy for proteinuria or increased creatinine. Patient demographic data and laboratory data were collected for analysis. Responses to treatment were categorized as complete remission (CR), partial remission (PR), or non-response. The CR and PR were defined as a reduction of urine protein/creatinine ratio to <0.3g/day and urine protein/creatinine ratio between 0.31g/day and 3.4g/day, respectively.

Results: Of the 32 cases, 21 were male and 11 were female patients. The mean patient age was 43.7(range: 15-68). Average follow-up period was 46.6 months (range: 2-107 months). The mean duration between HCT and renal biopsy was 33.2 months (range: 6–206 months). The underlying diseases resulting in the need for HCT were acute myeloid leukemia, 10 patients; acute lymphoid leukemia, 9 patients; aplastic anemia, 4 patients; myelodysplastic syndrome, 3 patients; multiple myeloma, 3 patients; chronic myeloid leukemia, 1 patient; amyloidosis, 1 patient; and blastic plasmacytoid dendritic cell neoplasm, 1 patient. The most common histopathological finding was membranous glomerulonephritis (N=20). Other glomerular diseases identified were thrombotic microangiopathy, amyloidosis, C1q nephropathy, focal segmental glomerulosclerosis and diabetic nephropathy. During the follow-up period, 25 patients were treated with steroids or cytotoxic agents.18 patients were treated with angiotensin II receptor antagonist. There was no statistically significant difference between the groups in terms of ANOVA of the decrease in proteinuria according to steroids or cytotoxic agents treatment (p = 0.075) and ARB treatment. (p = 0.156)

Conclusion: Based on our result, more case will require discussion of treatment options for NS following HCT.

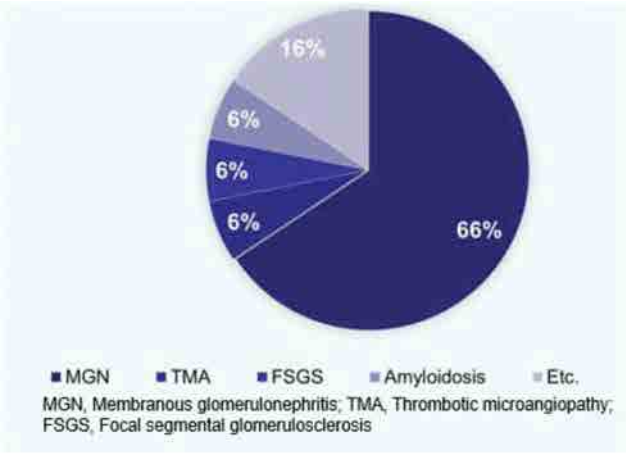


Figure 1. Histopathological Findings of Kidney Biopsy

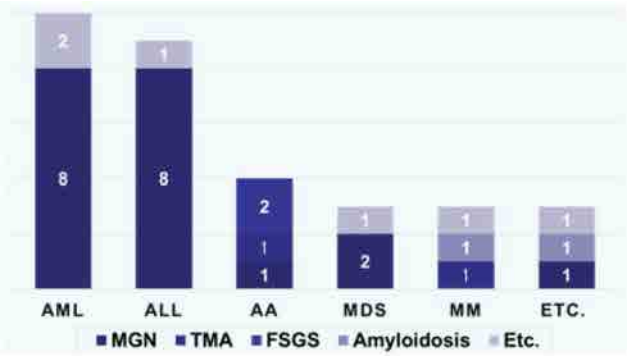


Figure 2. Histopathological Findings of Kidney Biopsy by the Underlying Hematologic diseases

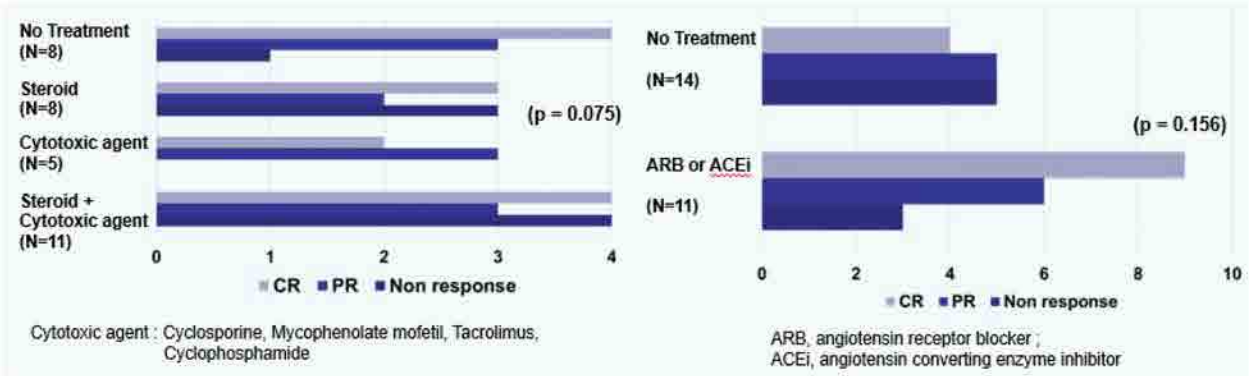


Figure 3. Response of Treatment

P0394 EFFICACY AND SAFETY OF A CHINESE PATENT MEDICINE-SHENYANKANGFU TABLETS FOR PRIMARY GLOMERULONEPHRITIS:A RANDOMISED CONTROLLED TRIAL

Jie Wu[1], Shuwei Duan[1], Hongtao Yang[2], Guang-Yan Cai[3], Xiangmei Chen[1], Yueyi Deng[4], Yani He[5], Zhaohui Ni[6], Yongli Zhan[7], Jingai Fang[8], Wei Li[9], Xusheng Liu[10]

[1]Chinese People's Liberation Army General Hospital, Nephrology, Beijing, P.R. China, [2]First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Nephrology, Tianjin, P.R. China, [3]Chinese People's Liberation Army General Hospital, Nephrology, Beijign, P.R. China, [4]Longhua Hospital Shanghai University of Traditional Chinese Medicine, Nephrology, Shanghai, P.R. China, [5]Daping Hospital, Third Military Medical University, Nephrology, Chongqing, P.R. China, [6]Renji Hospital, Shanghai Jiao Tong University, Nephrology, Shanghai, P.R. China, [7]Guang'anmen Hospital of China Academy of Traditional Chinese Medical Sciences,, Nephrology, Beijing, P.R. China, [8]First Affiliated Hospital of Shanxi Medical University, Nephrology, Datong, P.R. China, [9]Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Nephrology, Jinan, P.R. China and [10]Guangdong Provincial Hospital of Chinese Medicine, Nephrology, Guangzhou, P.R. China

Background and Aims: Chronic kidney disease is a common disease. Most chronic kidney diseases evolve from primary glomerulonephritis. Proteinuria is an independent risk factor for the progression of chronic kidney disease. The general consensus is that therapy administered to decrease proteinuria should include steroids and/or immunosuppressants, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers. However, the side effects of, and adverse reactions to, these agents reduce the benefits to patients. Therefore, additional effective drugs to decrease proteinuria are urgently needed. Shenyankangfu tablets (SYKFT) have been a widely applied Chinese patent medicine for many years to decrease proteinuria. However, there is a lack of research-derived data regarding the clinical use. Therefore, we designed the present trial to compare the efficacy and safety of SYKFT versus losartan potassium for control of proteinuria in patients with primary glomerulonephritis.

Method: This was a multicenter, prospective, double-blind, double-dummy, randomized controlled clinical trial. Primary glomerulonephritis patients aged 18 to 70 years, blood pressure $\leq$140/90 mmHg, estimated glomerular filtration rate $\geq$45 mL/min/1.73 m2, 24-hour proteinuria level of 0.5 to 3.0 g, were recruited in 41 hospitals across 19 provinces in China and were randomly divided into the following groups at a 1:1:1:1:1 ratio: SYKFT group, losartan potassium 50 mg group, losartan potassium 100 mg group, SYKFT plus losartan potassium 50 mg group, and SYKFT plus losartan potassium 100 mg group. All groups were followed up for 48 weeks; follow-up visits were performed, at weeks 0, 4, 8, 12, 24, 36, and 48. The primary efficacy outcome was the post-treatment change in the 24-hour proteinuria level, and the secondary efficacy outcomes was the post-treatment changes in the serum creatinine level, estimated glomerular filtration rate (eGFR), traditional Chinese medicine (TCM) syndrome score, and serum albumin level. The protocol was approved by the Ethics Committee of each participating center. This trial was registered at the clinicaltrials.gov (NCT02063100).

Results: A total of 720 participants were enrolled and 673 patients were included in the analysis. The difference in the urine protein reduction among different groups was statistically significant (Z=20.084, P=0.001). The urine protein reduction in the SYKFT group [-150.000 (-692.500, 153.000) mg/d], more than that in the losartan potassium 50mg alone group [-80.000 (-420.000, 295.250) mg/d, Z=-2.015, P=0.044], was not less than that in the losartan potassium 100mg group [-260.000 (-623.900, 84.000) mg/d, Z=-0.339, P=0.734]. The urine protein reduction in the SYKFT plus losartan potassium 50mg group [-269.150 (-755.000, 159.085) mg/d] was more than that in the losartan potassium 50mg alone group [Z=-2.582, P=0.010]. The urine protein reduction in the SYKFT plus losartan potassium 100mg group [-388.000 (-743.500, -10.000) mg/d] was more than that in the losartan potassium 100mg alone group [Z=-1.999, P=0.046]. The changes in serum creatinine, eGFR, and serum albumin from the baseline were not statistically significant among different groups (P all >0.05). The change in TCM syndrome scores between the patients who took SYKFT and who did not take SYKFT was statistically significant (P=0.003).

Conclusion: SYKFT can decrease the proteinuria of primary glomerulonephritis patients with minor- to moderate-range proteinuria. SYKFT plus losartan potassium therapy can decrease proteinuria to a relatively large extent compared with losartan potassium therapy alone. And SYKFT can also improve the TCM syndrome scores of the patients.

P0395 DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS IN TURKEY

Zeki Aydin[1], Kultigin Turkmen[2], Fatih Dede[3], Emre Yasar[4], Savas Ozturk[5], Mehmet Aydin[6], Erhan Tatar[7], Garip SAHIN[8], Gulizar Manga Sahin[9], Ozgur Akin Oto[10], Abdullah Sumnu[11], Eray Eroglu[12], Mevlut Tamer Dincer[13], Belda Dursun[14], Necmi Eren[15], Mustafa Sevinc[16], Fatma Betul Guzel[17], Serkan Feyyaz Yalin[18], Sim Kutlay[19], Suheyla Apaydin[20], Hacı Bayram Berktas[21], Sinan Kazan[22], Hamad Dheir[23], Feyza Bora[24], Taner Basturk[16], İdris Sahin[21]

[1]Darica Farabi Training and Research Hospital, Nephrology, Kocaeli, Turkey, [2]Necmettin Erbakan University, Meram Medical School, Nephrology, Turkey, [3]Ankara Numune Training and Research Hospital, Nephrology, Ankara, Turkey, [4]Gazi University Medical School, Nephrology, Ankara, Turkey, [5]Haseki Training and Research Hospital, Nephrology, Istanbul, Turkey, [6]Uludag University Medical School, Nephrology, Bursa, Turkey, [7]Bozyaka Training and Research Hospital, Nephrology, Izmir, Turkey, [8]Osmangazi University Medical School, Nephrology, Eskisehir, Turkey, [9]Sultan Abdülhamid Han Training and Research Hospital, Nephrology, Istanbul, Turkey, [10]Istanbul University Medical School, Nephrology, Istanbul, Turkey, [11]Medipol University Medical School, Nephrology, Istanbul, Turkey, [12]Erciyes University Medical School, Nephrology, Kayseri, Turkey, [13]Cerrahpasa University Medical School, Nephrology, Istanbul, Turkey, [14]Pamukkale University Medical School, Nephrology, Denizli, Turkey, [15]Kocaeli University Medical School, Nephrology, Kocaeli, Turkey, [16]Sisli Hamidiye Etfal Training and Research Hospital, Nephrology, Istanbul, Turkey, [17]Sutcu Imam University Medical School, Nephrology, Kahramanmaraş, Turkey, [18]Dr Lutfi Kırdar Kartal Training and Research Hospital, Nephrology, Istanbul, Turkey, [19]Ankara University Medical School, Nephrology, Ankara, Turkey, [20]Bakirkoy Dr Sadi Konuk Training and Research Hospital, Nephrology, Istanbul, Turkey, [21]Inonu University Medical School, Nephrology, Malatya, Turkey, [22]Afyonkarahisar SBU Medical School, Nephrology, Afyonkarahisar, Turkey, [23]Sakarya University Medical School, Nephrology, Sakarya, Turkey and [24]Akdeniz University Medical School, Nephrology, Antalya, Turkey

Background and Aims: Rapidly progressive glomerulonephritis (RPGN) is a clinical condition that develops due to different etiologic causes, characterized by a rapid and progressive decrease in renal function and progresses to end-stage renal failure in weeks to months if not treated. In our study, diagnostic and demographic characteristics of patients diagnosed with RPGN by biopsy, clinical and laboratory findings in our country were investigated.

Method: Data were obtained from national multicenter (47 centers) data entered into the Turkish Society of Nephrology Glomerular Diseases (TSN-GOLD) Working Group database between May 2009 and June 2019. Demographic characteristics such as age, sex, indications for biopsy, diagnosis of the glomerular diseases, comorbidities, laboratory and biopsy findings of all patients were recorded. The data presented is cross-sectional and includes application data for the biopsy period. According to their types, RPGN patients were classified as type 1 (anti-GBM related), type 2 (immunocomplex related) and type 3 (immune-negative; "pauci-immune").

Results: After exclusion of 46 patients with missing data, 200 patients (mean age 47.9 $\pm$ 16.7 years, 44% female) were included in the study which constitutes 5.2% of the total glomerulonephritis database (total number of patients: 3875). Hypertension was present in 62 patients (31.0%) and diabetes was present in 18 patients (9.0%). Renal biopsy was performed in 147 (73.5%) patients due to nephritic syndrome (RPGN included). 80.2% of the patients' biopsies were performed in nephrology clinics and 19.8% of them were performed in radiology clinics. ANCA positivity was found in 121 (60.5%) patients (proteinase 3-ANCA was positive in 55 and myeloperoxidase-ANCA positive in 66 patients). Type 1 RPGN was detected in 11 (5.5%), type 2 RPGN in 42 (21%) and type 3 RPGN in 147 (73.5%) patients. In 21 patients (10.5%), biopsy revealed RPGN with advanced chronic changes (fibrous global sclerotic glomeruli, advanced interstitial fibrosis and tubular atrophy). Mean serum creatinine was 4.2 $\pm$ 3.4 mg/dl, median glomerular filtration rate was 18 (10-37) ml/min and proteinuria 2100 (1229-3526) mg/day according to CKD-EPI formula. The mean number of glomeruli in the biopsies was 18.8 $\pm$ 10.6 and the number of crescentic glomeruli was 9.9 $\pm$ 7.7 (ratio: 52.7%) (Figure). The patients were divided into 3 groups according to their crescentic glomeruli ratios. The proportion of crescentic glomeruli is 10-50% in group 1, 50-80% in group 2, and >80% in group 3. The demographic, laboratory and histopathological characteristics of the groups are given in Figure. It was observed that urea and creatinine increased and calcium and hemoglobin decreased with increasing crescentic glomerular ratio.

Conclusion: Our study provides valuable demographic, clinical, laboratory and histopathological data about RPGN in our country. Our data are generally compatible with the literature. In our study, advanced chronic histopathological findings were prominent in the biopsy of 21 patients. Early biopsy should be performed to confirm the diagnosis of RPGN and to avoid unnecessary intensive immunosuppressive therapy. In addition to the treatments applied, detailed data, including patient and renal survival are needed.

Table - Demographic, laboratory and histopathological characteristics of all patients and patient groups according to crescentic glomeruli ratios. (One Way ANOVA)

Figure:

Parameters **N (%)**	**All Patients** **200(100%)**	**Group 1 Cresent 10-50%** **92 (46%)**	**Group 2 Cresent 50-80%** **74 (37%)**	**Group 3 Cresent >80%** **34 (17%)**	**p**
Demographical data					
Age (years)	**47.9±16.7**	49.0±16.0	48.4±17.4	44.0±17.2	0.332
Body mass index (kg/m2)	**25.7±4.1**	26.4±4.5	24.6±3.7	26.3±3.6	0.101
Systolic blood pressure (mmHg)	**136±21**	136±21	138±23	134±19	0.588
Diastolic blood pressure (mmHg)	**83±12**	82±12	84±11	81±9.6	0.427
Biochemical data					
Glucose (mg/dl)	**102±32**	101±35	105±32	98±24	0.576
Blood urea nitrogen (mg/dl)	**53.5±31.6**	47±29[a]	59±32[b]	58±33[b]	**0.030**
Creatinine (mg/dl)	**4.2±3.4**	3.3±2.86[a]	4.9 ±3.3[b]	5.1±4.2[b]	**0.003**
GFR(CKD-EPI)(ml/min/1.73m^2)*	**18 (10-37)**	26 (12-51)[a]	13 (9-27)[b]	14 (9-29)[b]	**0.001**
Uric acid (mg/dl)	**6.7±1.8**	6.5±1.7	6.8±1.9	6.7±1.9	0.636
Calcium (mg/dl)	**8.7±0.7**	8.9±0.7[a]	8.6 ±0.7[b]	8.4±0.7[b]	**0.009**
Total protein (gr/dl)	**6.4±0.8**	6.4±0.8	6.4±0.9	6.2±0.7	0.404
Albumin (gr/dl)	**3.2±0.7**	3.3±0.7	3.1±0.8	3.1±0.6	0.086
Proteinuria (mg/day)*	**2100 (1229-3526**	1773 (890-3302)	2200 (1650-4000)	2080 (1400-4400)	0.066[+]
Total cholesterol (mg/dl)	**195±57**	204±58[a]	179 ±51	201±61	**0.037**
Triglyceride (mg/dl)	**157±87**	157±74[a]	135 ±51[a]	202±141[b]	**0.002**
HDL cholesterol (mg/dl)	**43±19**	46±18	42 ±21	38±16	0.158
LDL cholesterol (mg/dl)	**118±44**	128±46[a]	106±38[b]	119±42[b]	**0.012**
ALT (U/l)	**19±13**	18±13	20±16	17±9	0.471
ESR (mm/h)	**74±35**	70±33	72±36	87±33	0.086
Hemoglobin (gr/dl)	**10.1±1.9**	10.6±1.9[a]	9.8±1.7[b]	9.4±1.7[b]	**0.003**
Hematocrit (%)	**30.4±5.7**	31.8±5.8[a]	29.7±5.3[b]	28.1±5.7[b]	**0.003**
Histopathological data					
Total glomeruli	**18.8±10.6**	18.4±10.2	19.5±11.6	18.6±10.0	0.773
Global sclerotic glomeruli	**3.4±4.8**	5.1±6.2[a]	2.2 ±2.5[b]	1.1±1.4[c]	**<0.001**
Crescentic glomeruli	**9.9±7.7**	5.6±3.7[a]	12.1±7.8[b]	16.5±8.7[c]	**<0.001**

*Median and interquartile range.

The difference of data with different superscript letters is statistically significant.

SBP; GFR; glomerular filtration rate, HDL; high density lipoprotein, LDL; low density lipoprotein ALT: alanine aminotransferase, ESR: erythrocyte sedimentation rate,

P0396 **THE NEPHRITIC SYNDROME IN JAPAN AND EUROPE**

Maria Weiner[1], Shouichi Fujimoto[2], Yusuke Suzuki[3], Rannveig Skrunes[4,5], Anna Goritschan[6], Matija Crnogorac[7], Colin C. Geddes[8], Kultigin Turkmen[9], Kresimir Galesic[7], Alexander Rosenkranz[6], Shinya Kaname[10], Hitoshi Sugiyama[11], Mårten Segelmark[12,13]

[1]Linköping University, Department of Nephrology and Department of Medical and Health Sciences, Linköping, Sweden, [2]University of Miyazaki, Department of Hemovascular Medicine and Artificial Organs, Miyazaki, Japan, [3]Juntendo University Faculty of Medicine, Department of Nephrology, Tokyo, Japan, [4]University of Bergen, Department of Clinical Medicine, Bergen, Norway, [5]University Hospital Bergen, Department of Medicine, Bergen, Norway, [6]Medical University of Graz, Division of Nephrology, Department of Internal Medicine, Graz, Austria, [7]Dubrava University Hospital, Department of Nephrology and Dialysis, Zagreb, Croatia, [8]Queen Elizabeth University Hospital, Glasgow Renal and Transplant Unit, Glasgow, United Kingdom, [9]Necmettin Erbakan University, Meram School of Medicine, Department of Internal Medicine, Division of Nephrology, Konya, Turkey, [10]Kyorin University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan, [11]Okayama University Graduate School, Department of Human Resource Development of Dialysis Therapy for Kidney Disease, Okayama, Japan, [12]Lund University, Department of Clinical Sciences, Lund, Sweden and [13]Skane University Hospital, Department of Nephrology, Lund, Sweden

Background and Aims: The combination of new onset haematuria, proteinuria and declining GFR, often referred to as *the nephritic syndrome*, constitute a strong indication for renal biopsy. Several different disease entities can underlie these findings, many of them requiring prompt treatment. Epidemiological studies of glomerular diseases are in general hampered by the strong influence of differences in biopsy practices. However, there is reason to believe that such differences are less pronounced in cases of acute/subacute nephritic syndrome. The aim of the present study is to compare the frequencies of diseases causing the nephritic syndrome in Japan and Europe using data from renal biopsy registries.

Method: Data were retrieved from national or regional renal biopsy registries in Japan, Sweden, Norway, Scotland, Austria, Croatia and Turkey from 2007-01-01 to 2018-12-31. Only patients biopsied due to acute or subacute nephritic syndrome, defined as a combination of new onset haematuria, sub-nephrotic proteinuria and reduced GFR, were included. Demographic, clinical and laboratory data were collected from the time of renal biopsy.

Results: A total number of 2789 patients from Japan and 1202 patients from Europe were included. Among the Japanese patients, 46% were women, median age was 67 years (IQR 54-74) and median creatinine concentration at the time of renal biopsy was 198 μmol/L (IQR 109-343). In Europe, 43% were women, median age was 58 years (IQR 42-70) and median creatinine concentration was 210 μmol/L (IQR 127-390). Figures from the different European countries are presented in Table 1. The most common diagnosis in both Japan and Europe was ANCA-associated nephritis (44% in Japan, 34% in Europe), followed by IgA nephritis (8.5% in Japan, 18.6% in Europe) and acute tubulointerstitial nephritis (6.2% in Japan and 7.1% in Europe).

Conclusion: We describe preliminary data from a large multicenter cohort of patients presenting with the nephritic syndrome. This clinical presentation is most often encountered in the 6th and 7th decade of life and the distribution between men and women is fairly equal. The most common underlying cause of the nephritic syndrome in both Japan and Europe is ANCA-associated nephritis.

Table 1. Clinical and demographic data in the participating European countries

	Norway	Sweden	Scotland	Austria	Croatia	Turkey
No. of patients	353	411	94	182	126	36
Age (years)	57 (39-70)	62 (44-72)	63 (53-75)	50 (38-64)	61 (49-70)	42 (31-54)
Female	40.8%	42.5%	55.3%	46.2%	39.7%	38.9%
Creatinine (μmol/L)	192 (120-334)	202 (133-357)	316 (198-453)	138 (90-263)	511 (332-687)	121 (94-188)
Most common diagnoses 1.	ANCA-associated nephritis 32.6%	ANCA-associated nephritis 35.0%	ANCA-associated nephritis 41.5%	ANCA-associated nephritis 25.8%	ANCA-associated nephritis 46.8%	IgA nephritis 36.1%
2.	IgA nephritis 19.3%	IgA nephritis 17.8%	IgA nephritis 18.1%	IgA nephritis 20.3%	Tubulo-interstitial nephritis 13.5%	Acute glomerulo-nephritis 22.2%
3.	Lupus nephritis 7.1%	Tubulo-interstitial nephritis 7.3%	Tubulo-interstitial nephritis 7.4%	Lupus nephritis 19.2%	IgA nephritis 12.7%	Tubulo-interstitial nephritis 11.1%

Data are presented as percentages or as median with interquartile range.

P0397

OUTCOMES OF PROTEINASE 3- AND MYELOPEROXIDASE ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS IN DENMARK 2014-2017

Nicholas Carlson[1,2], Karl-Emil Nelveg-Kristensen[1], Elizabeth Krarup[3], Christian Torp-Pedersen[4], Gunnar Gislason[2,5], Jon Waarst Gregersen[6], Hans Dieperink[7], Per Ivarsen[8], Martin Egfjord[3], Wladimir Szpirt[1]

[1]Rigshospitalet, Department of Nephrology, Copenhagen E, Denmark, [2]The Danish Heart Foundation, The Research Departmemnt, Copenhagen, Denmark, [3]Herlev Hospital, Department of Nephrology, Herlev, Denmark, [4]Nordsjaellands Hospital, Forskningsafdelingen, Hilleroed, Denmark, [5]Gentofte Hospital, Department of Cardiology, Hellerup, Denmark, [6]Aalborg University Hospital, Department of Nephrology, Aalborg, Denmark, [7]Odense University Hospital, Department of nephrology, Odense, Denmark and [8]Aarhus University Hospital, Department of Nephrology, Aarhus N, Denmark

Background and Aims: Anti-neutrophil cytoplasmic antibody associated vasculitis (AAV) defines an uncommon group of autoimmune diseases with antibodies directed against proteinase 3 (PR3) or myeloperoxidase (MPO). Incidence rates of PR3- and MPO-AAV differ geographically, and current evidence based on genetic variations and cluster analyses supports discrimination of associated vasculitis based on PR3- and MPO-positivity. Such discrimination could provide insights of scope for clinical trials with ramifications for improvement of treatment. With the aim of comparing patient characteristics and outcomes between PR3- and MPO-AAV, we report on results from a nationwide retrospective cohort study.

Method: Incident patients positive for PR3- and MPO-anti-neutrophil cytoplasmic antibodies were identified in central laboratories of three of four administrative regions (covering 80% of the population) in Denmark between 1/1-2014 and 31/12-2017. Patient characteristics were identified by cross-referencing of data from multiple national health care registers. Baseline renal function was calculated based on the CKD-EPI equation using plasma creatinine measurements recorded 365 to 7 days prior to index. Incidences of all-cause mortality and end-stage renal disease stratified on baseline eGFR were computed using the Aalen-Johansen estimator. Hazard ratios for specific predictors including strata of baseline eGFR were calculated based on a multiple Cox proportional hazards model adjusted for relevant confounders.

Results: In total 770 patients were included in the study (PR3 n=399 and MPO n=371). Annual incidence rates of PR3- and MPO-AAV were 22.6 and 21.1 per million, respectively. PR3-AAV was associated with greater preponderance for male gender (54.4% vs. 42.3%, p=0.001), lower patient age (61.9 years [IQR 41.6-73.0 years] vs. 64.9 years [IQR 50.0-74.0 years], p=0.016), and greater baseline renal function (eGFR 87 ml/min [IQR 56-101 ml/min] vs. 75 ml/min [IQR 36-92 ml/min] compared with MPO-AAV. Comorbid burden was comparable; 26% of patients had history of hypertension, 15% of patients had a history of ischemic heart disease, and 12% of patients had a history of cancer.

Acute dialysis was initiated in 5.3% and 6.7%, plasmapheresis in 12.8% and 13.7%, and mechanical ventilation in 4.8% and 4.3% of patients with PR3- and MPO-AAV, respectively. Median follow-up was 564 days [234 – 932]. A total of 86 deaths and 25 end-stage renal disease endpoints were recorded during follow-up. Cumulative incidences of all-cause mortality and end-stage renal disease stratified on baseline eGFR are shown in Figure 1.

Adjusted hazard ratios for all-cause death and/or end-stage renal disease showed increased risk associated with PR3-AAV, HR 1.51 (95% CI 1.03 – 2.25, p=0.036), non-European descent, HR 3.63 (95% CI 1.29-10.25, p=0.015) and patient age, HR 1.05 (95% CI 1.03-1.07, p<0.001). In both PR3- and MPO-AAV, only baseline eGFR $\leq$ 20ml/min/1.73m^2 was associated with poorer prognosis (ref.: baseline eGFR >90 ml/min/1.73m^2); MPO-AAV: eGFR 51-90 ml/min/1.73m^2: HR 2.34 (95% CI 0.75 – 7.34, p=0.145), eGFR 21-50 ml/min/1.73m^2: HR 2.11 (95% CI 0.60 – 7.47, p=0.246), and eGFR $\leq$ 20ml/min/1.73m^2: 5.05 (95% CI 1.55 – 16.45, p=0.007); PR3-AAV: eGFR 51-90 ml/min/1.73m^2: HR 1.54 (95%CI 0.53 – 4.46, p=0.427), eGFR 21-50 ml/min/1.73m^2: HR 1.70 (95% CI 0.51 – 5.64, p=0.386), and eGFR $\leq$ 20ml/min/1.73m^2: 8.06 (95% CI 2.83 – 23.0, p=<0.001).

Conclusion: In a nationwide cohort study comparing PR3- and MPO-AAV, PR3-AAV was associated with poorer 24-month outcomes in spite of superior renal function at baseline. Overall, poor prognosis was limited to patients with severe renal insufficiency (eGFR $\leq$20ml/min/1.73m^2) at time of diagnosis in both PR3- and MPO-AAV.

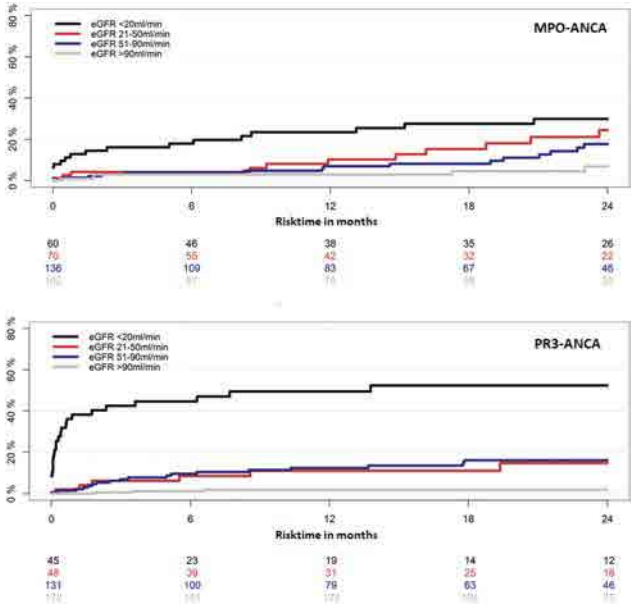


Figure 1: Cumulative incidence of end-stage renal disease and death

P0398 **PREVALENCE OF RED COMPLEX OF PERIODONTAL DISEASE BACTERIA IN TONSILS OF IGA NEPHROPATHY PATIENTS**

Yasuyuki Nagasawa[1], Ryota Nomura[2], Taro Misaki[3], Seigo Ito[4], Shuhei Naka[5], Kaoruko Wato[2], Aritoshi Kida[1], Yoshimasa Nanami[1], Yukiko Hasuike[1], Michiyo Matsumoto-Nakano[5], Kazuhiko Nakano[2]

[1]Hyogo College of medince, Department of Internal Medicine, Division of kidney and Dialysis, Nishinomiya, Japan, [2]Osaka University, Department of Pediatric Dentistry, Suita, Japan, [3]Seirei Hamamatsu General Hospital, Devision of Nephrology, Hamamatsu, Japan, [4]National Difense Medical College, Department of Nephrology and Endocrinology, Tokorozawa, Japan and [5]Okayama University, Department of Pediatric Dentistry, Okayama, Japan

Background and Aims: IgA nephropathy (IgAN) is one of most common primary glomerulonephritis, whose pathogenesis had remained unclear. We had reported that *C.rectus* and *T.denticola*, kinds of major periodontal disease bacteria, in tonsils with IgA nephropathy patients were specific to IgAN patients compared with chronic tonsillitis (Nagasawa-Y et al, Plos One, 2014). We also reported *C.rectus* and *S.mutans* increased proteinuria synergistically (Misaki-T et al, Nephron, 2018). Red complex of bacteria related with periodontal disease consists of *P.gingivalis, T.denticola,* and *Tannerella forsythia,* which has strongest pathogenicity of periodontal disease (Figure 1). But, in this point there were no report of prevalence of red complex of periodontal bacteria in IgA nephropathy. In this study, we evaluated the periodontal disease bacteria including *P.gingivalis, T.denticola,* and *Tannerella forsythia* in tonsils of IgAN patients, and the relationship between these periodontal bacteria clinical features in IgAN patients.

Method: Tonsils were obtained from 23 IgAN patients and 63 chronic tonsillitis patients when the tonsillectomy was operated. mRNAs were extracted from tonsils and the prevalences of *P.gingivalis, T.denticola,* and *Tannerella forsythia* were evaluated by RT-PCR using bacteria specific primers. All patients gave the written informed consent which was approved by Hyogo College of medicine.

Results: Average age was 33+-14 in IgAN patients, and the age in control patients was 27+-7. The average proteinuria in IgAN patietns was 0.9+-1.1g/gcre, and average hematuria was (2+). The prevalence of *T.denticola* was very low in both groups (0%, 1.6% respectively). The prevalence of *P.gingivalis* in IgA patients was significantly higher than that in control patients (33% vs 3.2%, respectively, $P<0.0001$), and the prevalence of *Tannerella forsythia* in IgAN patients was also significantly higher than that in control (28% vs 6.4%, respectively, $P<0.05$) which had not been reported (Figure 2). The types of cilia of *P.gingivalis* (fim A types) were also evaluated. Obviously untypeable of fim A, which is usually minor type, was dominant in IgAN patients.

Conclusion: Prevalence of red complex of periodontal disease bacteria, especially *P.gingivalis, Tannerella forsythia* in IgAN patient was higher than that in control. Red complex of periodontal disease bacteria might have some relationship with pathogenesis of IgAN

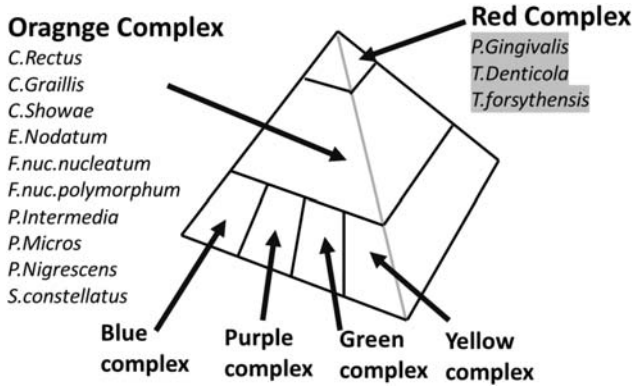


Figure:

P0399 RELAPSE TREATMENT WITH LOW DOSE OF STEROIDS IN STEROID-SENSITIVE MINIMAL CHANGE DISEASE

Marta Álvarez Nadal[1], Irene Martin[1], Daniel Eduardo Villa Hurtado[1], Elizabeth Viera Ramírez[1], Vanessa Lopes[1], Milagros Fernandez Lucas[1], Javier Villacorta[1]

[1]*Hospital Ramon y Cajal, Nephrology, Madrid, Spain*

Background and Aims: Treatment of Minimal change disease (MCD) consists of high dose of steroids (HDS) for several weeks implying significant drug toxicity. On the other hand, renal relapses of steroid-sensitive MCD sometimes respond to lower doses of steroids.

Method: The objective of the study was to analyze weather low dose for steroids (LDS) is effective for treatment MCD relapses among frequently-relapsing steroid-sensitive patients. Since 2019, new relapses of steroid-sensitive patients with MCD within the Nephrology Department of Hospital Ramón y Cajal were treated with LDS. Cumulative dose of steroids, time to remission and time free of relapse were compared between relapse episodes treated with LDS and previous relapses among same patients treated with HDS.

Results: Twenty-six relapses among six steroid-sensitive MCD patients were analyzed. 15 relapses were treated with LDS and compared with 11 previous relapses among same patients treated with HDS. Mean dose of prednisone for initial treatment of the relapse was 0.89 $\pm$ 0.1 mg/kg in patients treated with HDS and 0.45 $\pm$ 0.1 mg/kg in patients treated with LDS. Mean cumulative dose of prednisone among patients treated with LDS and HSD were 1998.1 $\pm$ 1418 mg and 5611.7 $\pm$ 2326 mg, respectively. (p=0.001). Mean cumulative dose of prednisone adjusted by body weight among patients treated with LDS and HSD were 23.43 $\pm$ 14.27 mg/kg and 68.93 $\pm$ 27.05 mg/kg, respectively. (p=0.019). There was no difference in duration of treatment among HDS and LSD groups (163.45 $\pm$ 86.43 vs 138.80 $\pm$ 108.80, respectively; p = 0.525). All patients achieved complete remission after steroid therapy in both LSD and HSD groups. Mean time to remission was 18.7 days among HSD relapses and 18.4 days among the LSD relapses (p = 0.9). Time free of relapse after therapy among HDS and LDS treated relapses was 9.1 $\pm$ 5.3 months and 5.5 $\pm$ 3.5 months, respectively (p = 0.1).

Conclusion: Among steroid-sensitive MCD patients, relapse therapy with low dose of steroids (0.5 mg/kg) seems to be effective and allows minimization of steroid cumulative dose and drug toxicity.

P0400

DECREASED REGULATORY B CELLS AND THEIR ASSOCIATION WITH CLINICAL RESPONSE IN PATIENTS WITH NEW ONSET LUPUS NEPHRITIS

Krishan Lal Gupta[1], Ivedita Girimaji[1], Aruna Rakha[2], Urvashi Kaundal[2], Raja Ramachandran[1], Manish Rathi[2], Aman Sharma[3]

[1]Post Graduate Institute of Medical Education and Research, nEPHROLOGY, Chandigarh, India, [2]Postgraduate Institute of Medical Education and Research, Translational and Regenerative Medicine, Chandigarh, India and [3]Post Graduate Institute of Medical Education and Research, Chandigarh, Internal medicine, CHANDIGARH, India

Background and Aims: Studies in lupus nephritis (LN) have shown impairment in both T regulatory (Treg) number and function. However, the data on B regulatory (Breg) is limited in LN. Our objective was to study Breg and Treg populations in newly diagnosed treatment naïve LN and study their change after initiation of immunosuppression.

Method: Study included 25 patients of newly diagnosed LN of Class III (+V), IV (+V), V and 10 healthy controls (HC). Immunophenotyping was performed for peripheral blood mononuclear cell (PBMCs) samples using fluorochrome labelled monoclonal antibodies for Tregs ($CD3^+CD4^+CD25^{hi}CD127^{lo}FoxP3^+$) and Bregs ($CD19^+CD5^+CD1d^{hi}$ IL-10^+). The cells were expressed as percentage of T and B cells. Each lymphocyte population was analysed at baseline, 2 and 6 months after initiation of immunosuppression which was given as per unit protocol.

Results: Bregs were significantly decreased compared to HC at baseline (p=0.002). With immunosuppression, Bregs showed significant increase at 2 and 6 months (p=0.008) and from baseline to 6 months (p=0.005). Bregs in responders significantly increased from 2 to 6 months (p= 0.017) and from baseline to 6 month (p=0.020), while they did not in non-responders. Tregs did not differ significantly from HC and did not show significant increase at 2 and 6 months, in both responders and non-responders.

Conclusion: Breg population in newly diagnosed LN was significantly reduced and increased significantly with immunosuppression. Bregs had an association with renal remission. This underscores the potential role of Bregs in the pathophysiology of LN and their association with clinical response. This could aid in the design of new immunotherapies for treatment of lupus nephritis.

P0401

RITUXIMAB VESUS CYCLOPHOSPHAMIDE AS FIRST STEROID SPARING AGENT IN CHILDHOOD FREQUENTLY RELAPSING OR STEROID DEPENDENT NEPHROTIC SYNDROME.

Jameela Kari[1], Amr Albanna[2], Khalid Alhassan[3], Osama Safdar[1], Mohamed Shalaby[1], Detlef Bockenhauer[4], Sherif El-Desoky[1]

[1]King Abdulaziz University, Faculty of Medicine, 2Paediatric Nephrology unit, Department of Pediatrics,, Jeddah, Saudi Arabia, [2]King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia, [3]King Saud University, Riyadh, KSA, Pediatrics Department,, Riyadh, Saudi Arabia and [4]University College London, Centre for Nephrology,, London, United Kingdom

Background and Aims: Approximately 50% of children with steroid sensitive nephrotic syndrome (SSNS) will suffer from frequent relapses or steroid dependency, prompting the use of so-called steroid-sparing drugs. In this pilot study, we compare the efficacy and safety of rituximab to oral cyclophosphamide as first-line steroid-sparing medications

Method: A prospective open label randomized study of children with frequent relapsing or steroid-dependant SSNS. Exclusion criteria were steroid-resistant disease, prescription of immunosuppressive agents other than prednisolone or levamisole, evidence of impaired kidney function, leucopenia or active infection. The recruited children were allocated either to the oral cyclophosphamide (3mg/kg/day for 8 weeks) or intravenous rituximab treatment (two doses of 375 mg/m2/dose, 2 weeks apart) and were monitored for relapses and side effects for 12 months

Results: 46 subjects were included from two centers; 27 received cyclophosphamide and 19 received rituximab. One-year relapse-free survival was reached in 17 (58.6%) patients treated with cyclophosphamide compared to 16 (84.2%) with rituximab (adjusted HR: 0.36; 95% CI: 0.09 – 1.45; p=0.151). The mean interval to relapse was 6.9 months in the cyclophosphamide group (N=10) and 6.3 months in the rituximab group (N=3). Both treatments were associated with a significant (p=?) reduction in prescribed dose of oral alternate days steroid from 1.02 to 0.36mg/kg (Cyclophoshamide) and 0.86 to 0.08mg/kg (Rituximab). Importantly, a significantly (P = 0.003) higher percentage of patients achieved complete withdrawal of steroid within 3 months of commencing study treatment in the rituximab (73.7%) versus cyclophosphamide (29.6%) group.

Transient leucopenia was the most frequent adverse effect observed in the cyclophosphamide group (18.5%) and one patient (3.4%) had acute hepatotoxicity beside severe leucopenia and neutropenia on the 7th week of treatment although she showed complete recovery with withdrawal of cyclophosphamide and maintained remission. A minor infusion related reaction was observed in 1 patient (5%) in the rituximab group.

Conclusion: Rituximab is non-inferior to cyclophosphamide and safe as a first-line steroid-sparing agent in children with SSNS. A larger multicenter study is required to assess superiority over cyclophosphamide

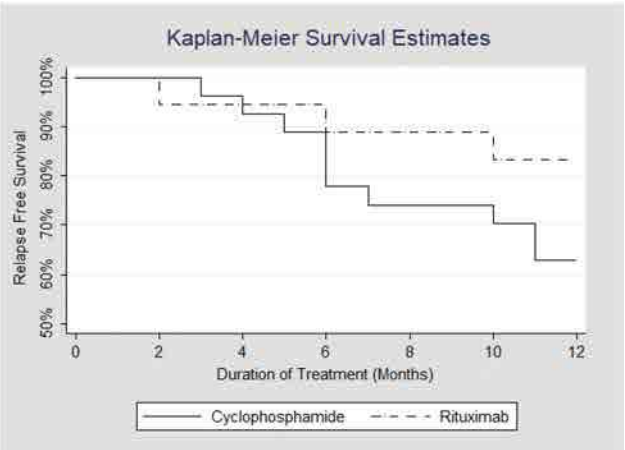


Figure 1: Relapse-free survival during one-year follow-up comparing patients treated with rituximab and cyclophosphamide.

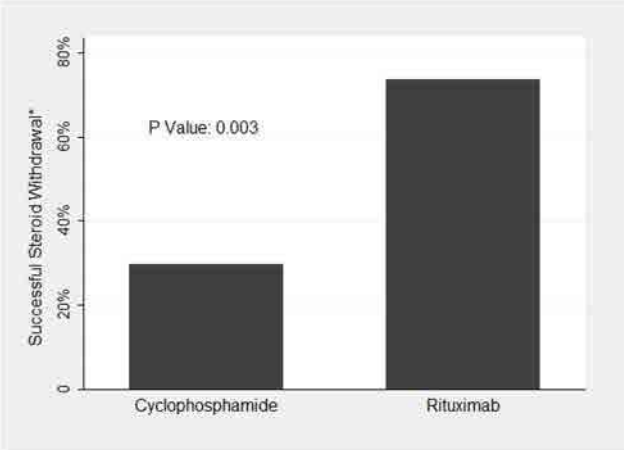


Figure 2: Steroid withdrawal within three months of treatment with rituximab and cyclophosphamide.

Notes: *During the initial three months of treatment.

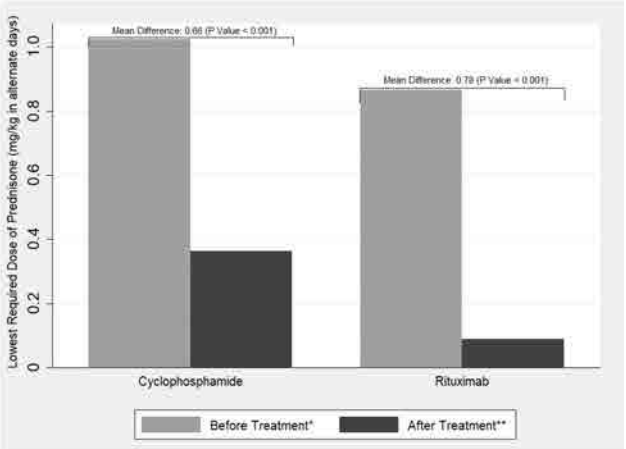


Figure 3: The effect of using rituximab and cyclophosphamide on reducing the steroid dose.

Notes: *During a year of follow-up before the start of treatment; **During a year of follow-up after the start of treatment.

P0402

TACROLIMUS PLUS LOW DOSE PREDNISOLONE THERAPY IS MORE EFFECTIVE IN PLA2R -VE MEMBRANOUS NEPHROPATHY PATIENTS

Akhilesh Kumar Jaiswal[1], Narayan Prasad[2], Vikas Agarwal[3], Mantabya Singh[2]

[1]SGPGIMS, NEPHROLOGY, Lucknow, India, [2]SGPGIMS, Nephrology, Lucknow, India and [3]SGPGIMS, CLINICAL IMMUNOLOGY, Lucknow, India

Background and Aims: Idiopathic Membranous Nephropathy (IMN); an autoimmune concomitant nephrotic syndrome of the adult is mainly associated with PLA2R antibody expressed on podocytes. The lack of exact mechanisms involved in the pathogenesis of IMN is transmitted to its therapeutic management. There is no standard therapy for patients with frequent relapsing or steroid-dependent IMN.

We propose the efficacy of low dose Tacrolimus (Tac) plus prednisolone and associated changes in anti-PLA2R in adult IMN.

Method: Total 101 membranous nephropathy patients were treated with combination of prednisolone 1mg/kg alt-day) and Tac 0.1mg/kg/day (trough 6-10 ng/ml first 6M and 4-6 ng/ml for next 3M) then both taper by 1/3 every month up to 12M. Out of 101 patients; 15 diabetic; 7 lupus; 1HBV and 1 ankylosing spondylitis patients were excluded. Finally; 77 Patients were followed and evaluated for the anti-PLA2R level at baseline; 3M; 6M; 12M and end of follow-up (17-61 ; median 38 months). CR; PR; relapse; and side-effects were recorded.Of the 77 patients; at 3M 60(77.92%; CR-37; PR-23); at 6M 61(79.22%; CR-53; PR-8); at 12M 53(68.86%; CR-47; PR-6) achieved remission. Eight (10.38%) relapsed and 16(20.77%) showed no response at 12M. At end of follow-up; out of 54 responsive patients 37(68.51%; CR-36; PR-1) remained in remission and 17(31.48%) patients relapsed.

Results: Out of 77 patients; 51 (66.3%) were anti-PLA2R positive. Remission rate was significantly low in PLA2R+ve than PLA2R-ve (36/51 vs 24/26; p=0.03) at 3M; (36/51 vs 25/26; p=0.009) at 6M and (31/51 vs 22/26; p=0.03) at 12M. PLA2R level was decreased by 60.38% and 77.56% at 3M and 6M respectively. There were significant correlations between PLA2R level and 24h proteinuria at baseline; 3M and at 6M. During therapy 4 patients develop cutaneous tenia; 1 osteonecrosis of the femur head; 1 corpus tunnel syndrome; 4 onset diabetes; 3 tremor; and 14 patients experienced GI symptoms. The eGFR was decreased significantly (p=0.003) by 26.5% at the end of therapy and was normalized after stopping Tac; and 5 non-responsive patients had doubling of serum creatinine and progressively deteriorated eGFR. To note; 4 females had pregnancy and successful delivery in our cohort of patients.

Conclusion: PLA2R+ve patients showed poor response compare to PLA2R-ve patients. Remission with Tacrolimus and prednisolone therapy is comparable to historical Ponticelli (Pred plus CYP) regimen. Successful pregnency was ovserved on Tac based regimen.

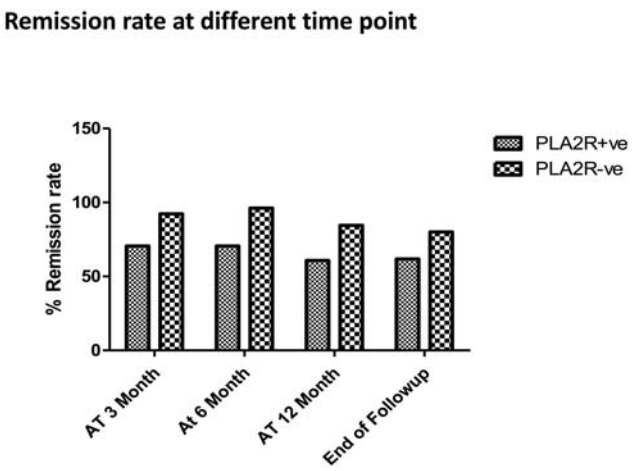


Figure:

P0403

INNATE DEFECTS OF COMPLEMENT ALTERNATIVE PATHWAY AMONG LUPUS PATIENTS WITH AND WITHOUT THROMBOTIC MICROANGIOPATHY

Cai Yue[1], Quexian Cui[1], Xuemei Li[1]

[1]*Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, Department of Nephrology, Beijing, P.R. China*

Background and Aims: Thrombotic microangiopathy (TMA) is a rare and severe complication of systemic lupus erythematosus (SLE). The pathogenesis of TMA among lupus patients is not fully understood yet. The aim of the study was to evaluated innate complement alternative pathway (AP) defects among patients with SLE-TMA.

Method: 15 consecutive lupus patients with clinically or pathologically diagnosed TMA from Peking Union Medical College Hospital through Jan 2017 to Dec 2019 were enrolled. Lupus patients with TMA secondary to antiphospholipid antibodies, ADAMTS13 inhibitor, overlap syndrome, infection, malignant hypertension and medications were excluded. The exonic regions of 13 genes including CFH, CFI, CFB, C3, CFHR1-5, MCP, THBD, DGKE, PLG were analysed with next generation sequencing. Mutations were interpreted according to ACMG 2015 guideline. Patients with atypical hemolytic uremic syndrome (aHUS) (n=2), lupus nephritis (LN) without TMA (n=8), and malignant hypertension (n=6) were set as control.

Results: Six AP mutations rated as VUS or likely pathogenic were detected among 5/15 (33.3%) patients with SLE-TMA, while three were detected among 3/8 (37.5%) of patients with LN, one among 1/6 (16.7%) patients with malignant hypertension, and three among 2/2 (100%) of patients with aHUS. There was no significant difference regarding mutation rate among the groups.

Conclusion: There is no significant difference regarding AP mutations among lupus patients with and without TMA. Mechanisms other than innate AP abnormality may be involved in the pathogenesis of TMA among lupus patients.

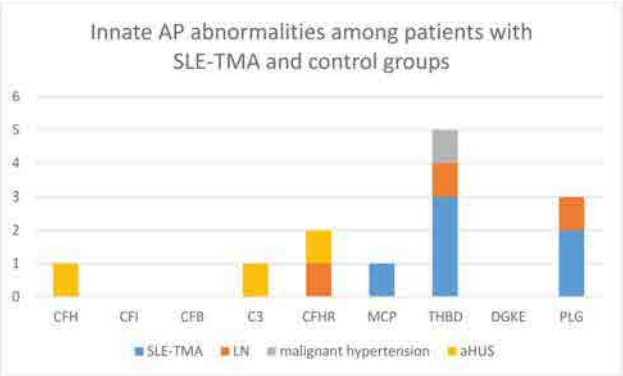


Figure:

P0404

B CELLS FROM PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS FAIL TO REGULATE T CELL INTERFERON GAMMA RELEASE BUT DO REGULATE OTHER ASPECTS OF T CELL ACTIVATION

Srinivas Puli[1], Daniel Appelgren[2], Thomas Hellmark[1], Mårten Segelmark[1,3]

[1]Lund University, Division of Nephrology, Lund, Sweden, [2]Linköping University, Division of Drug Research, Linköping, Sweden and [3]Skånes universitetssjukhus Lund, Nephrology, Lund, Sweden

Background and Aims: Regulatory features of B-cells have gained increased attention in patients with systemic vasculitis, including granulomatosis with polyangiitis (GPA). The aim with this study was to investigate the frequencies and phenotypes of two putative regulatory B (Breg) cell populations and assess the capacity of B-cells from GPA patients to regulate T-cell activation.

Method: 37 GPA patients (22 remission and 15 active) and 31 healthy controls (HC) were included for measurement of $CD19^{+}CD24^{high}CD27^{+}$ (memory) and $CD19^{+}CD24^{high}CD38^{high}$ (transitional) Breg cells, and 11 GPA patients in remission and 12 HC for the functional studies of B-cells. HC were matched for age and gender.

Results: Memory Breg cells were reduced in GPA both during active disease and remission compared with HC, whereas transitional Breg cells did not differ between the groups. Memory Breg cells consisted of less $CD25^{+}$ cells during both active disease and remission but expressed more PD-L1 and CD86 during remission compared with active disease and HC. B-cells from GPA patients regulated T-cell proliferation and IL-17a production but failed to regulate IFN-γ production (Fig 1). The levels of IFN-γ and the IFN-γ regulated cytokine CXCL10 were elevated in patient plasma.

Conclusion: Despite reduced levels and altered phenotypes of memory Breg cells, the capacity of GPA patient B-cells to regulate T-cell proliferation and IL-17a production was unaffected. However, we found a profound inability of patient B-cells to regulate T-cell IFN-γ production. This alteration could be important for the persistent inflammation that continues during remission and results in the chronic relapsing nature of the disease

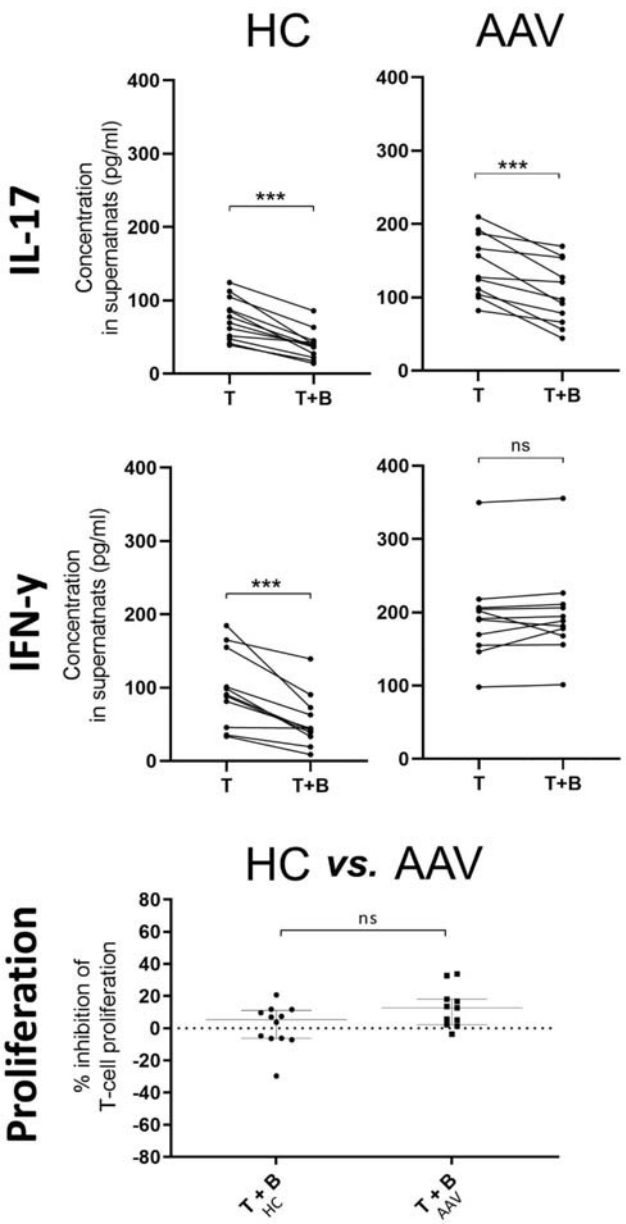


Figure:

P0405 CURRENT STATUS OF NEPHRITIS IN KOREA: EXPERIENCE OF 18 CENTERS DURING LAST 40 YEARS

Su-Ryeong Go[1], HO JUN CHIN[1,2]

[1]Seoul National University Bundang Hospital, INTERNAL MEDICINE, Seongnam-si, Korea, Rep. of South and [2]SEOUL NATIONAL UNIVERSITY COLLEGE OF MEDICINE, INTERNAL MEDICINE, Seoul, Korea, Rep. of South

Background and Aims: Glomerulonephritis (GN) is one of common causes of end-stage renal disease (ESRD) in Korea as well as in the world, however, it is underdiagnosed as a cause of chronic kidney disease. The incidence and prevalence of GNs are different according to periods and countries. We report trends of pathologic diagnosis of nephritis from 18 centers throughout Korea during last 40 years.

Method: We enrolled 21,617 patients having native kidney biopsy for diagnosis of nephritis between 1979 and 2018, retrospectively. We excluded 191 patients diagnosed as cancer or tumor and analyzed the data of 21,426 patients. We defined the primary GN as IgA nephropathy (IGAN), minimal change disease (MCD), membranous nephropathy (MGN), focal segmental glomerulosclerosis (FSGS), membranoproliferative GN (MPGN), and C3 glomerulopathy (C3G). The estimated glomerular filtration rate (GFR) was calculated by original MDRD equation for adults and by height-independent equation for children. The final outcomes were incidences of end stage renal disease (ESRD) and death.

Results: There were 22,203 pathologic diagnoses including 777 patients with two kinds of pathologic diagnosis. The age was 42.1 $\pm$ 17.7 years at renal biopsy. There were 11565 (54.0 %) men and 976 (4.6 %) children <18 years. The frequencies of hypertension and diabetes mellitus were 53.0 % (10994) and 14.0 % (2833), respectively. Mean levels of serum creatinine, GFR, and urine protein to creatinine ratio were 1.62 $\pm$ 1.89 mg/dl, 77.1 $\pm$ 60.4 ml/min/1.73 m^2, and 3.305 $\pm$ 4.164 g/g cr, respectively. The prevalence of GN was 78.45% (17419 diagnoses), followed by tubulointerstitial nephritis (8.84 %), abnormality in glomerular basement membrane (3.43 %), ischemic nephropathies (1.73 %), paraproteinemia related lesions (1.36 %), infection (0.12 %). There were non-specific GN (3.65 %), normal pathology (2.46 %), advanced global sclerosis (1.77 %), inadequate specimen (0.96 %), and miscellaneous lesions (0.12 %), also. The most frequent diagnosis was IGAN (34.17%, 7586 diagnoses), followed by MGN (9.17%), MCD (9.13 %), FSGS (7.65 %), lupus nephritis (LN) (6.30 %), diabetic nephropathy (DMN) (3.99 %), MPGN and C3G (2.79 %), therefore, prevalence of primary GN was 62.90 %. The frequency of IGAN had been increased from 19.9 % at the period of 1979-1989 to 41.4 % at the period of 2005-2009 and then stabilized to 36.0-36.7%. The frequencies of MCD, MGN, and FSGS were not changed since 1990. However, the frequency of MPGN was decreased from 4.7-5.7 % at the period of 1979-1999 to 2.5 % at the period of 2015-2018. The frequency of LN was decreased and that of DMN was increased from 2.5-3.1% during 1990-2009 to 6.3 % during 2015-2018 which might be related to the pathologic classification of DMN, published at 2010 by Tervaert TW et al. The incidences of ESRD and death were 13.3 % (2663/20010 patients) and 2.9 % (608/20884 patients) during follow-up period of 82.6 months (median) for ESRD and 91.5 months (median) for mortality after biopsy. Among patients with primary GN, patients with MCD showed the best prognosis for ESRD, followed by patients with MN, IGAN, FSGS, MPGN, and C3G ($p < 0.001$) by Cox's hazard proportional model adjusted by risk factors related to ESRD. Prognosis for mortality was not different among patients with MCD, MN, IGAN, and FSGS, but, patients with C3G showed the worst prognosis for mortality ($p=0.006$).

Conclusion: IGAN was the most frequent diagnosis followed by MGN and MCD. Compared to Western countries, IGAN and MCD are more prevalent in Korea, while MGN and FSGS are less prevalent. The frequencies of MPGN and LN had been decreased since 2000. The patients with MPGN and C3G showed the worst prognosis.

P0406 **ASSOCIATION OF MICROHEMATURIA WITH OUTCOMES IN ADULT PATIENTS WITH IGA NEPHROPATHY**

Safak Mirioglu[1], Erdem Gurel[1], Merve Guzel-Dirim[1], Asli Kara[1], Yasemin Ozluk[2], Irem Aktar[1], Ahmet Burak Dirim[1], Aylin Ciftkaya[1], Ozgur Akin Oto[1], Yasar Kerem Caliskan[1], Isin Kilicaslan[2], Halil Yazici[1], Aydin Turkmen[1], Mehmet Sukru Sever[1]

[1]Istanbul University Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Nephrology, Istanbul, Turkey and [2]Istanbul University Istanbul Faculty of Medicine, Department of Pathology, Istanbul, Turkey

Background and Aims: Although hematuria is the cardinal symptom of IgA nephropathy (IgAN), its effects on the outcome have not been studied extensively. We, therefore, aimed to analyze the association between microhematuria and clinicopathological features as well as outcome parameters in adult patients with IgAN.

Method: 129 adults with IgAN, diagnosed by kidney biopsy, and followed up for a median duration of 54.5 (IQR: 24.25-92.75) months, were included in this retrospective study. Urinary sediment analyses during the bouts of macrohematuria were not taken into consideration. For the purpose of this analysis, microhematuria was described as ≥5 red blood cells per high-power field (RBCs/hpf) and classified as mild (5-9 RBCs/hpf), moderate (10-19 RBCs/hpf), or severe (≥20 RBCs/hpf). Study outcome (event) was defined as at least a 50% reduction in baseline eGFR or development of stage 5 chronic kidney disease (eGFR <15 ml/min/1.73 m^2). eGFRs of the patients were calculated by using CKD-EPI formula.

Results: Demographic, clinical, laboratory and histopathological features of patients at the time of diagnosis are summarized in the table. Usage of ACEi/ARBs [75/81 (92.5%) vs 45/48 (93.75%), p=0.803], fish oil [30/81 (37%) vs 19/48 (39.5%), p=0.773], azathioprine [16/81 (19.7%) vs 10/48 (20.8%), p=0.882] and mycophenolic acid derivatives [14/81 (17.2%) vs 11/48 (22.9%), p=0.434] were comparable among the patients with and without microhematuria. Corticosteroids were more frequently used in patients with microhematuria [41/81 (50.6%) vs 17/48 (35.4%)], although this difference was not statistically significant (p=0.093). Overall 30 patients (23.2%) reached the study outcome, and there were no differences between patients with (19, 23.4%) and without (11, 22.9%) microhematuria (p=0.944). Kaplan-Meier analysis revealed that event free survival rates were similar across study groups: 77.1% for patients without microhematuria; while 80% for mild, 77.3% for moderate, and 72.7% for severe microhematuria (p=0.436) (Figure). Microhematuria did not predict the study outcome when multivariable Cox regression analyses were performed [HR: 1.847 (95% CI: 0.696-4.904), p=0.218]. Throughout the follow-up, microhematuria disappeared (dropped below 5 RBCs/hpf) in 43 patients (53%), 8 of whom (18.6%) reached the study outcome as compared to 11 patients (28.9%) with persistent microhematuria (p=0.273). Disappearance of microhematuria was not a predictor of study outcome, as well [HR: 0.386 (95% CI: 0.068-2.180), p=0.281].

Conclusion: Microhematuria is not associated with renal outcomes of adult patients with IgAN.

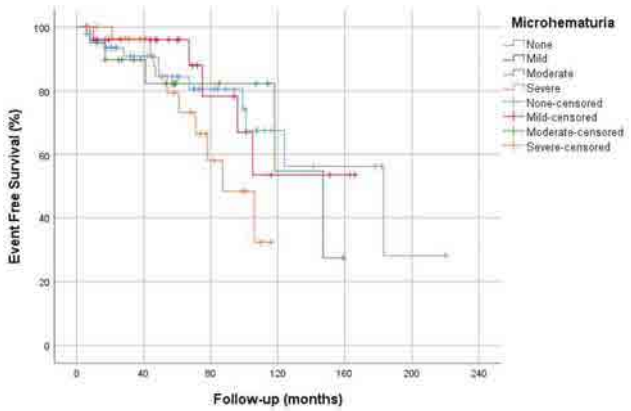


Figure: Kaplan-Meier analysis of event free survival rates across study groups (p=0.436 by log-rank test).

Table. De mographic, clinical, laboratory and histopathological features of patients at the time of diagnosis.

Characteristics	Microhematuria (+) (n=81)	Microhematuria (-) (n=48)	P
Sex, male (%)	38 (46.9%)	27 (56.2%)	0.305
Age, mean±SD (years)	36.2±12.3	38.3±12.8	0.380
Percentage of sclerotic glomeruli, median (IQR)	23.8 (6.4-45.5)	32.2 (12.8-54.5)	0.200
Endocapillary proliferation, n (%)	3 (3.7%)	6 (12.5%)	0.058
Crescents, n (%)	32 (39.5%)	18 (37.5%)	0.821
Moderate to severe interstitial fibrosis, n (%)	9 (11.1%)	6 (12.5%)	0.812
Moderate to severe tubular atrophy, n (%)	12 (14.8%)	10 (20.8%)	0.380
Mean BP median (IQR) (mm±Hg)	100 (90-113.3)	106.6 (93.9-112.5)	0.312
Hemoglobin, mean±SD (g/dl)	12.8±1.8	12.6±2	0.419
eGFR, median (IQR) (ml/min/1.73 m^2)	73.7 (43.5-104.9)	53.4 (44-85.3)	0.098
Serum albumin, median (IQR) (g/dl)	4.1 (3.7-4.4)	4 (3.75-4.3)	0.494
Proteinuria, median (IQR) (g/24h)	1.53 (0.82-2.59)	1.19 (0.6-2.57)	0.311

P0407 **THE INVESTIGATION OF SYNAPTOPODIN EXPRESSION OF PODOCYTES IN GLOMERONEPHRITIS**

Zhigang Zhang[1]

[1]*Fudan University, Pathology, Shanghai, China,*

Background and Aims: Synaptopodin, a proline-rich actin-associated protein, plays an important role in the regulation of podocytes processes structures and dynamics. The mutation or lack of synaptopodin may lead to the changes of podocytes structures and functions and cause the occurrence of proteinuria. But the underlying molecular mechanisms remain primarily elusive.

Method: we used cellular and pathological experiments to observe the expression changes synaptopodin in vivo and vitrio.

Results: The results showed that the reduction expression of synaptopodin and RhoA were found in the podocytes in different nephriris of human renal biopsy as well as in rat adriamycin nephropathy. The cultured cells treated with inflammatory cytokins such as TNF, IL-1 also showed decreased synaptopodin level in podocyte, which led to low RhoA level and disarrange the actin cytoskeleton assembly, result in the abnormal changes of podocyte morphology.

Conclusion: These data preliminarily proved that synaptopodin loss in podocyte injury plays an important role in the regulation of podocyte morphology and function through RhoA signaling pathway, and further researches are required to clarify the more mechanism, which may provide new strategies and methods for the prevention and treatment of glomerular diseases.

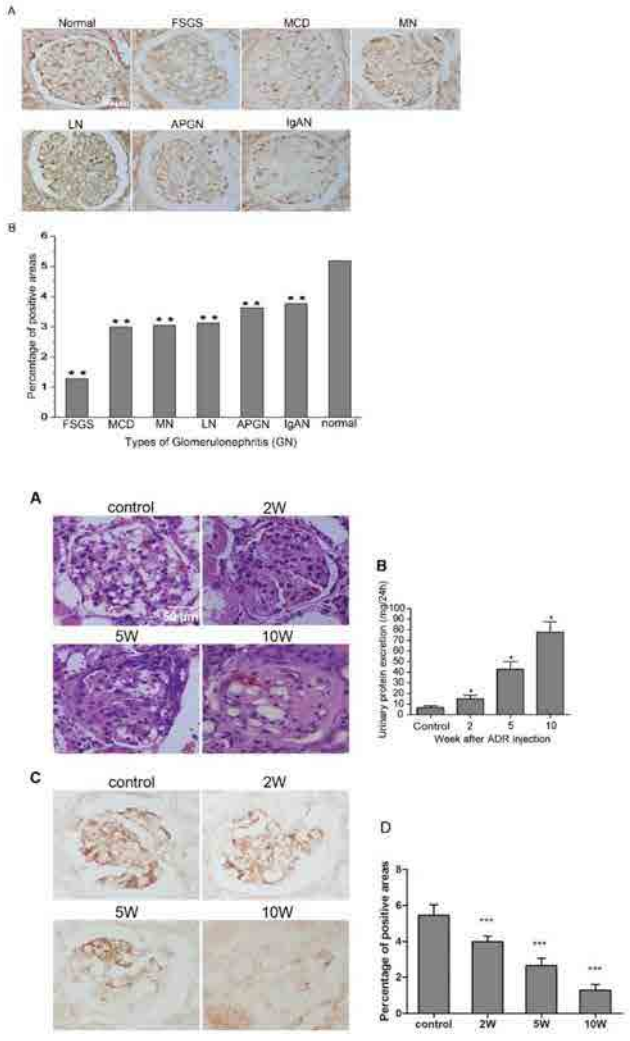


Figure:

P0408

KIDNEY TRANSPLANTATION OUTCOMES IN PATIENTS WITH IGA NEPHROPATHY IN THE MODERN ERA OF IMMUNOSUPPRESSION: A CASE CONTROL STUDY

Sophia Lionaki[1], Ilias Makropoulos[1], Konstantinos Panagiotellis[1], Ioannis Gavalas[1], George Vlahopanos[2], Smaragdi Marinaki[3], George Liapis[3], Ioannis Bokos[2], Ioannis Boletis[1]

[1]Laiko Hospital, National and Kapodistrian University of Athens, Faculty of Medicine, Nephrology &Transplantation Unit, Athens, Greece, [2]Laiko Hospital, Transplantation Unit, Athens, Greece and [3]Laiko Hospital, National and Kapodistrian University of Athens, Faculty of Medicine, Pathology, Athens, Greece

Background and Aims: Advances in immunosuppressants, used for kidney transplantation (KTx) have significantly improved outcomes in this field. We aimed to compare the long-term results of KTx in recipients with IgAN, as cause of end stage kidney disease (ESKD), with those of patients, with non-glomerular causes of renal failure, during the modern era of immunosuppression for KTx.

Method: This is a retrospective, case control study, in which were included patients who received a KTx after 2000. Patients were eligible to be included, if they had IgAN in a native kidney biopsy specimen and follow up longer than 1 year after KTx. IgAN patients were compared to a control-group of patients with non-glomerular primary causes of ESKD matched for age, gender, date of KTx and donor source. Graft biopsies were performed by clinical indication. Patients with ABO incompatible KTx, preemptive KTx, re-KTx, PRA>50%, major surgical complications during the 1st post-KTx month or non-compliance were excluded from the analysis of outcome. Primary outcomes of interest included graft function, patient and graft survival at end of follow up. The rate of IgAN recurrence in the graft and its impact in renal function and survival were also recorded. Computed GFR was calculated using the Modification of Diet in Renal Disease formula.

Results: A total of 102 KTx recipients with biopsy-proven IgAN, were compared to 204 controls with non-glomerular causes of ESKD. The mean age of patients with IgAN was 43.2(±10.15) years and 68(66.7%) were men. The mean time in dialysis was 50.2(±48.7) months and 59(57.8%) of them received a graft from a living donor. The mean cold ischemia time was 17.5(±6.7) hours, while 22(21.6%) of patients experienced delayed graft function. 97.05% of patients received induction therapy with an anti-CD25 inhibitor and 99.3% were maintained with a triple immunosuppressive regimen consisted of a mycophenolate mofetil formulation, a calcineurin inhibitor and glucocorticoids. The mean serum creatinine and eGFR at end of follow up were significantly lower for the IgAN group (p=0.001 and p=0.02 respectfully) with no difference in the frequency of acute rejection. However, graft and patient survival were not different even after controlling for follow up longer than one decade. During a mean follow up time of 120.8(±49.1) months, IgAN recurrence in the graft was documented in 23(22.5%) patients. The mean time to recurrence was 47.8(41.8) months, with a mean serum creatinine 1.83(±0.52) mg/dl and eGFR of 43.45(±18.4) ml/min/1.73m^2 at the end of follow up. Within the IgAN group, although graft function was significantly lower in patients with disease recurrence, compared with that of patients without recurrence (p=0.003), graft loss remained not different between these two subgroups (p=0.49).

Conclusion: In the newer era of immunosuppression, long-term outcomes of KTx in patients with IgAN, as primary disease, appear significantly improved, and although graft function was significantly lower in patients with IgAN at the end of follow up, graft and patient survival was not different, compared to patients with non-glomerular causes of ESKD. Recurrence of IgAN in the graft was documented in 22.5% of patients and was associated with significantly lower eGFR at end of follow up compared to patients without recurrence but it did not impact graft survival in this time period.

P0409

CHARACTERISTICS AND OUTCOME OF ONE HUNDRED EGYPTIAN PATIENTS OF LUPUS NEPHRITIS: A SINGLE TERTIARY CARE CENTER STUDY

Mohammed Saleh[1], Mohammed Kamal Nassar[2], Ehab Awad[3]

[1]Belkas General Hospital, Nephrology Department, Belkas, Egypt, [2]Mansoura University, Mansoura Nephrology and Dialysis Unit (MNDU), Internal Medicine Department, Mansoura, Egypt and [3]Mansoura University, Rheumatology and Immunology Unit, Internal Medicine Department, Mansoura, Egypt

Background and Aims: Renal biopsy is the "gold standard" for diagnosis of lupus nephritis (LN). It is necessary for classification and is the basis for treatment strategy decisions. This study was carried out in order to analyse the results of renal biopsy in LN patients, its effect on treatment and predictors for remission in an Egyptian cohort.

Method: The results of renal biopsies of LN patients undergoing regular follow up in the outpatient clinic of Mansoura Nephrology and Dialysis Unit (MNDU), Mansoura University Hospital, Egypt in the period between October 2017 and September 2019 were reviewed. The histopathological data were analyzed and correlated to the clinical data of the study group.

Results: A total of 100 LN patients with documented renal biopsy were enrolled in this study. The median age of the patients was 29 years. Most of the patients were females (n=89). Serum creatinine at presentation ranged from 0.57 to 13.5 mg/dl (median 1.3 mg/dl). Class IV (diffuse proliferative) LN was the most frequently encountered class, followed by Classes III, V, II and VI respectively, while class I was detected in only one patient. In proliferative classes (III and IV), the total score of activity indices, ranged from 0 to 16 (minimum–maximum). Mesangial hypercellularity was the most frequent encountered active lesions. Total score of chronicity indices ranged from 0 to 10 (minimum-maximum). Interstitial fibrosis was the most frequent chronicity index. Remission was achieved in 73 patients. Patients who achieved remission had lower serum creatinine and lower pathological chronicity score. In a multivariate logistic regression analysis, serum creatinine at presentation was the strongest predictor for renal remission in this cohort and chronicity index was the strongest predictor in proliferative classes (III and IV). Receiver operating characteristic curve (ROC curve) was done to identify the cutoff point of serum creatinine which can indicate the probability of renal recovery in proliferative and non-proliferative classes (n=100) and in proliferative classes only (n=73). A serum creatinine value of 1.65 mg/dl or less identifies the probability of renal recovery with 76% sensitivity and 71% specificity in proliferative and non-proliferative classes . A chronicity index value of 6 or less identifies the probability of renal recovery with 93% sensitivity and 58% specificity.

Conclusion: Renal biopsy is a must in LN to guide treatment and prognosis. In this Egyptian cohort, serum creatinine at presentation and pathological chronicity index score are the strongest predictors of renal response in LN patients.

Table 1: Multivariate analysis logistic regression for remission of proliferative and non proliferative classes (n=100)

	B	S.E.	Sig.	OR	95% CI	
					LL	UL
Serum creatinine	-0.434	0.142	0.002*	0.648	0.49	0.855
24 hours urinary protein	0.000	0.000	0.354	1	1	1
Class (proliferative)	-0.281	0.599	0.639	0.755	0.234	2.442
Constant	2.682	0.714	<0.0001	14.614		

Table 2: Multivariate analysis logistic regression for remission in proliferative classes (n=73)

	B	S.E.	Sig.	OR	95% CI	
					LL	UL
Serum creatinine	-0.156	0.124	0.2	0.856	0.671	1.091
24 hours urinary protein	0.000	0.000	0.68	1	1	1
Activity index	0.001	0.086	0.98	1.001	0.847	1.185
Chronicity index	-0.375	0.145	0.01*	0.687	0.517	0914
Constant	2.729	0.991	0.006	15.316		

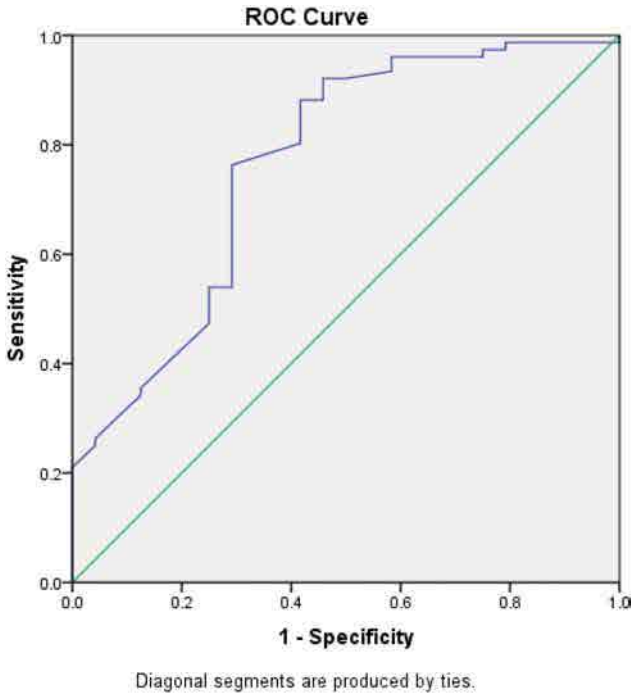


Figure 1: ROC curve for serum creatinine. Area under curve (AUC) 0.766, p<0.0001. A value of 1.65 or less identifies the probability of renal recovery with 76% sensitivity and 71% specificity.

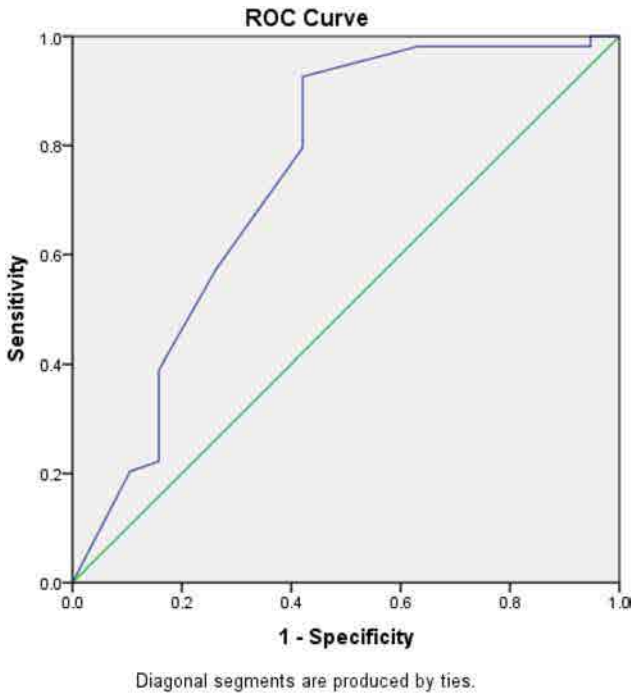


Figure 2: ROC curve for chronicity index. AUC 0.744, p=0.002. A value of 6 or less identifies the probability of renal recovery with 93% sensitivity and 58% specificity

P0410 **SIGNIFICANT BURDEN OF DISEASE DURING MAINTENANCE TREATMENT OF ANCA-ASSOCIATED VASCULITIS (AAV) PATIENTS IN REAL WORLD PRACTICE IN EUROPE**

Peter Rutherford[1], Dieter Götte[1]

[1]*Vifor Pharma, Medical Affairs, Zurich, Switzerland*

Background and Aims: ANCA associated vasculitis (AAV) is a relapsing remitting long term condition and patients are at risk of organ damage from both active AAV and its therapy in particular high dose and/or prolonged glucocorticoids (GC). The remission maintenance phase of AAV is critical for good long term outcomes including renal preservation as well as preventing AAV relapse. This retrospective study aimed to examine the definition of maintenance, therapy and clinical outcomes in patients managed in routine practice.

Method: 1478 AAV patients (France, Germany, Italy, Spain and UK) managed by 493 physicians (61% Nephrologists) who completed induction therapy for organ or life threatening AAV and initiated maintenance therapy between 2014-16 were studied. Data were collected retrospectively at the time maintenance was determined to begin by the physician and then at 6, 12, 18 and 36 months.

Results: 49% had granulomatosis with polyangiitis,; mean age 54.2 years with 56% male. 49% had incident AAV and 51% were studied from the time of a relapse requiring remission induction therapy. 70% received cyclophosphamide and GC and 30% received rituximab and GC as induction treatment with 28% receiving plasma exchange. Physicians defined time of the start of maintenance from induction treatment start with mean of 5.7 months on the basis of fixed time point 40%, starting new drug for maintenance 26%, reaching full remission 26% and no specific criteria 8%. At this time of maintenance start 43% were in full remission vs 50% in partial and 7% refractory. Various maintenance regimes were used, 21% received rituximab (88% 6 monthly and 8% 12 monthly, 4% other) at varying planned doses 34% 1g, 40% 500 mg and 23% 375 mg/m2, 4% other regime. Remission rates varied with patients experiencing disease relapse and many patients experienced adverse events (AE) and infections with prolonged GC use being common. Renal function was relatively unchanged and some patients had worsening eGFR, protein excretion or blood pressure. At the most recent clinical review patients had been followed for a mean of 50.7 months – 6% had died, 38% had relapsed at least once, and 11% required renal replacement therapy. 54% had no vasculitis activity, 26% were ANCA positive without active disease and 19% were still experiencing active disease. 32% were still receiving GCs - 22% of them receiving > 5mg/ day.

Conclusion: Maintenance therapy is variably defined but typically at 6 months from start of remission induction therapy. Achieving full remission and preventing relapse are still clinical problems and many patients require ongoing GC therapy to maintain remission. Infectious complications and adverse events are common and renal disease remains an ongoing clinical problem.

	Maintenance start	6 months	12 months	18 months	36 months
Remission full/partial %	43 / 50	59 / 38	67 / 30	72 / 25	74 / 22
Total relapse / major %		12/49	9 / 45	6/ 44	7 / 32
Receiving GC%	65	61	53	46	39
At least one AE %	66	52	48	43	42
At least one infection %	54	42	32	27	26
eGFR (mean, ml/min)	50.0	56.1	53.3	53.3	53.3
Worsening eGFR %		12	10	10	10
Rising proteinuria %		5	5	4	4
Hypertension (new or worsening) %		23	22	19	18

Figure:

P0411 PREDICTORS OF RENAL AND PATIENT OUTCOME IN PATIENTS WITH IDIOPATHIC MEMBRANOUS NEPHROPATHY: FROM KOGNET DATA

Ji-Young Choi[1], Ji Hye Kim[1], Ga Young Lee[1], Hee Won Noh[1], Soojee Jeon[1], Jeong-Hoon Lim[1], Hee-Yeon Jung[1], Jang-Hee Cho[1], Chan Duck Kim[1], Yong-Lim Kim[1], Sun-Hee Park[1]

[1]School of Medicine, Kyungpook National University, Division of Nephrology, Department of Internal Medicine, Daegu, Korea, Rep. of South

Background and Aims: Idiopathic membranous nephropathy (iMN) is a leading cause of nephrotic syndrome and one of the major causes of end-stage renal disease (ESRD). Various factors can affect renal and patient outcome in patients with iMN. In this study, we analyzed the predictors of renal and patient survival in patients with iMN.

Method: We analyzed 1,776 patients diagnosed with iMN in Korean GlomeruloNEphritis STudy (KoGNET), a retrospective database of patients with renal biopsy from 1979 to 2018 from 18 centers in Korea. Student t-test for continuous variables and Chi-square test for categorical variables were performed for analyses. Cox proportional hazard regression was used to determine risk factors affecting renal and patient survival.

Results: The mean age of patients was 53.0 ± 14.7 years old and 1,075 (60.5%) were male. At the time of renal biopsy, 755 (46.0%) and 266 (16.2%) had hypertension and diabetes, respectively. Serum albumin level was 2.7 ± 0.8 g/dL and 871 (49.0%) had nephrotic range of proteinuria. When analyzed by dividing over 65 and under, the hemoglobin and serum albumin level were lower, more patients showed nephrotic ranged proteinuria, and higher prevalence of comorbidities such as hypertension, diabetes, coronary heart disease and cerebrovascular disease in the group over 65 than in the group under 65. Median duration of follow-up was 88.0 (38.0 – 115.1) months. Complete or partial remission rates were 48.5%, 63.8%, and 68.0% at 6 months, 12months after biopsy, and last follow-up, respectively. In Cox proportional hazard regression, high hemoglobin [HR 0.66 (0.47 – 0.93), p=0.017], high serum albumin level [HR 0.41 (0.18 – 0.94), p=0.034], and high estimated GFR by CKD-EPI equation [HR 0.94 (0.91 – 0.96), p<0.001] at biopsy were good predictors for renal outcome, whereas presence of cerebrovascular disease at biopsy [HR 6.45 (1.16 – 35.71), p=0.033] were poor prognostic factors for ESRD. Age 65 and older [HR 3.26 (1.53 – 6.95), p=0.002] and presence of hypertension at biopsy [HR 2.45 (1.09 – 5.54), p=0.031] were significant risk factors for patient survival in multivariate Cox proportional regression analysis.

Conclusion: High hemoglobin and serum albumin, and good renal function at biopsy were good predictors for renal survival. Older age and hypertension at biopsy were poor prognostic factors for patient survival in iMN patients. Prognostic information of outcomes in this study might be helpful to optimize management in iMN patients.

P0412 **VALUE OF INTERNATIONAL RISK-PREDICTION TOOL IN IGA NEPHROAPTHY : A SINGLE CENTRE STUDY**

Dhawal Arora[1], Durga Kanigicherla[1], Patrick Hamilton[1]

[1]*Manchester royal infirmary, Renal Medicine, Manchester, United Kingdom*

Background and Aims: A new International Risk-Prediction Tool in IgA Nephropathy developed was recently developed to help predict disease progression over a 5-7 year period[1]. We tested use of this Risk-Prediction Calculator in patients diagnosed with IgA Nephropathy to stratify the risk and predict outcomes during follow up.

Method: All adult patients (aged ≥18years) with biopsy proven IgA Nephropathy diagnosed between 2011 and 2016 at Manchester University NHS Foundation Trust were included in the study. Exclusion criteria included patients with secondary causes, prior exposure to immunosuppression, or presentation eGFR of less that 15ml/min. Demographic, clinical phenotypic & renal histological characteristics (MEST score) at baseline were used to calculate the individual risk scores. These risk scores were compared with outcomes seen during subsequent follow up. Primary outcome was a composite of first ESRD or reduction in eGFR to below 50% of value at biopsy. Patients were censored at last follow visit for primary outcome or death. Renal outcomes were analysed using Kaplan Meier survival plots of subgroups based on predicted risk (<16th percentile, 16-50th percentile, 50-84th percentile or >84th percentile).

Results: 121 patients were included in the analyses. 45 other patients were excluded based on exclusion criteria. 84 patients (69%) were males, mean age was 42±16 years, eGFR was 63±34ml/min and uPCR was 151±42mg/mmol. Mean follow up was 51.4±28 months.

87% were on RAS inhibition at or within 6 weeks of kidney biopsy diagnosis. During the follow up period 23 patients (19%) developed the primary outcome. Outcomes were significantly worse in patients with higher risk-prediction scores (Fig 1 log rank p<0.01).

Conclusion: This single centre study confirms that the International IgA Nephropathy Risk-Prediction Model for kidney outcomes can be a valuable tool for prognostication in Primary IgA Nephropathy in routine clinical practice.

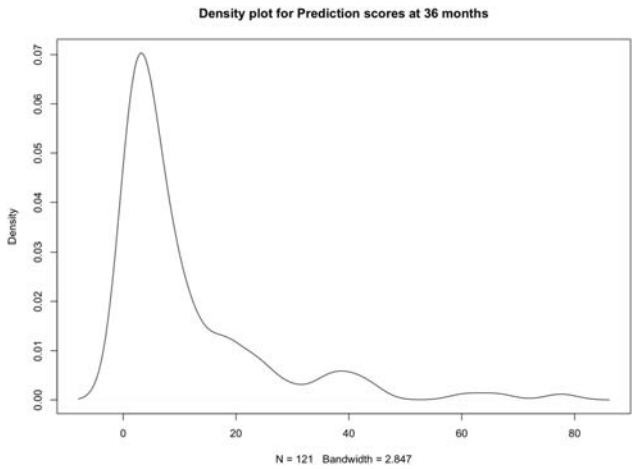


Figure:

P0413

THE ICOS+ TREG/ICOS+ TRESP BALANCE HAS A DECISIVE ROLE REGARDING THE PRESERVATION OF THE REMISSION PHASE IN SLE PATIENTS

Matthias Schaier[1], Claudius Gottschalk[1], Florian Kälble[1], Martin Zeier[1], Andrea Steinborn[2]

[1]University Hospital Heidelberg, Nephrology, Heidelberg, Germany and [2]University Hospital Heidelberg, Department of Obstetrics and Gynaecology, Heidelberg, Germany

Background and Aims: An imbalance between $CD4^+$-regulatory T-cells (Tregs) and $CD4^+$-responder T-cells (Tresps) correlates with active disease flares in Systemic Lupus Erythematosus (SLE) patients. Both cell subsets consist of highly proliferative inducible T-cell co-stimulatory molecule expressing ($ICOS^+$-) and less proliferating $ICOS^-$-Treg/Tresp cells.

Method: In this study we aimed to examine the role of age-dependent differentiation for maintaining the $ICOS^+$-Treg/$ICOS^+$-Tresp or $ICOS^-$-Treg/$ICOS^-$-Tresp balance in SLE remission patients compared to active disease patients and to evaluate the influence of proliferation inhibitor or glucocorticoid therapy concerning the maintenance of these equilibria.

Results: In 83 healthy volunteers, the ratio of $ICOS^+$-Tregs/$ICOS^+$-Tresps increased significantly with age, while that of $ICOS^-$-Tregs/$ICOS^-$-Tresps did not change. In 86 SLE remission patients, medication controlled disease activity was associated with an age-independently increased ratio of both $ICOS^+$-Tregs/$ICOS^+$-Tresps and $ICOS^-$-Tregs/$ICOS^-$-Tresps. In 13 active disease patients this increased $ICOS^+$-Treg/$ICOS^+$-Tresp ratio could not be maintained, due to an age-dependent earlier terminal differentiation of $ICOS^+$-Tregs than of $ICOS^+$-Tresps. The increased ratio of $ICOS^-$-Treg/$ICOS^-$-Tresp was maintained in active disease patients, but it decreased with age. This was attributable to an age-independent aberrant differentiation of $ICOS^-$-Tresps and a resulting loss of age-dependent differentiation of $ICOS^-$-Tregs. Especially the administration of proliferation inhibitors (azathioprine or mycophenolic acid) ensured prolonged differentiation and maintenance of functional $ICOS^+$-Tregs with age. There was a similar but weaker effect of this medication on $ICOS^+$-Tresps, causing a significant decrease of these cells with age. The proliferation capacity was neither affected in $ICOS^+$-Tregs/Tresps nor in $ICOS^-$-Tregs/Tresps. As a result, the ratio of $ICOS^+$-Tregs/$ICOS^+$-Tresps increased significantly with age and kept the patients in remission. In contrast, glucocorticoids increased the differentiation of $ICOS^-$-Tregs especially in younger individuals, but had an adverse effect on their proliferation capacity.

Conclusion: Our data reveal a crucial role of the $ICOS^+$-Treg/$ICOS^+$-Tresp balance for the maintenance of self-tolerance and avoidance of disease flares in SLE. The used immunosuppressive therapy, especially the administration of proliferation inhibitors, has a decisive effect on the preservation of regular differentiation of all Treg/Tresp subsets with age, and most importantly avoids the terminal differentiation and immune senescence of $ICOS^+$-Tregs.

P0414 **URINARY HEPCIDIN AS A BIOMARKER OF NEPHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS**

Marwa Saleh[1], Ahmed Eldeep[1], Adel L Abdelsalam[2], Azza El-baiomy[3], Ehab Awad[2]

[1]Mansoura, nephrology and dialysis unit, internal medicine department, Mansoura, Egypt, [2]rheumatology and immunology unit, internal medicine department and [3], clinical pathology

Background and Aims: Lupus nephritis (LN) is a common complication of systemic lupus erythematosus (SLE) that is associated with poor prognosis. The current available urinary biomarkers are neither sensitive nor specific for diagnosing LN. This study was undertaken to investigate whether urinary hepcidin represents a marker of nephritis in SLE patients.

Method: A cross-sectional study was conducted with 3 study groups compromising 30 patients with biopsy proven LN, 30 patients with non-nephritis SLE and 20 healthy control. Spot urinary samples were collected from all participants and the levels of hepcidin in urine were measured by ELISA, 24 h urinary proteins, urinary and serum creatinine were measured.

Results: Urinary hepcidin was significantly higher in LN patients than in non-nephritis SLE and control (470, 258, 43.0 ng/mg creatinine respectively) ($P < 0.001$) as shown in figure 1. Urinary hepcidin was significantly correlated with serum creatinine (P 0.017) and 24 hours urinary proteins (P 0.003). ROC curve cut-off values of urinary hepcidin were 4.3000, Area under curve (AUC) of hepcidin was 0.553, with sensitivity (SN) of 63.3%, specificity (SP) of 60%, Positive predictive value (PPV) 70.4, negative predictive value (NPV) 52.2 in SLE patients as shown in table 1 and figure 2.

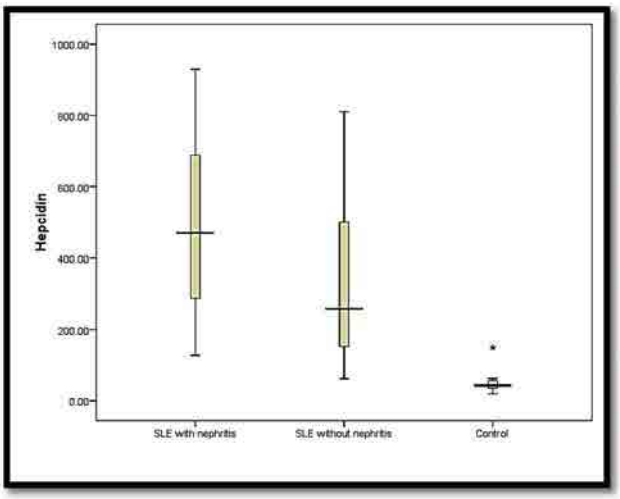


Figure 1: The median value of urinary Hepcidin in SLE patients with nephritis in comparison to non- nephritis and control group.

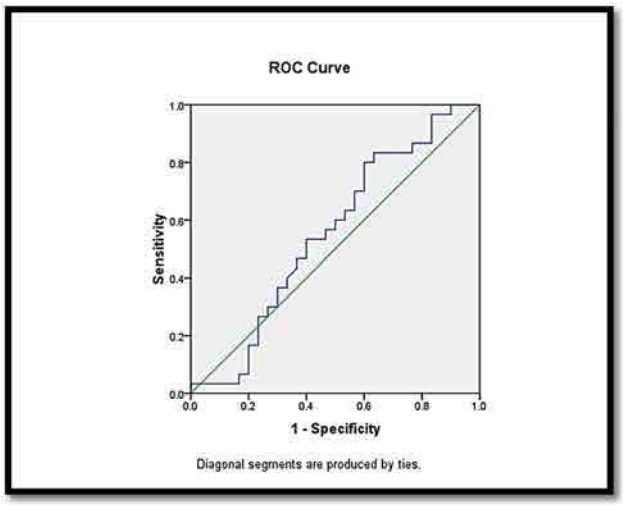


***Figure 2*:** ROC curve for urinary hepcidin in differentiating LN and non-nephritis patients.

Conclusion: Although urinary hepcidin level was significantly higher in LN patients than in non-nephritis SLE and control, it failed to discriminate patients with LN from those without. Further studies are still needed before considering urinary hepcidin as a non-invasive diagnostic marker of LN.

Table 1: Validity of Hepcidin in differentiating LN patients from non- nephritis group.

	AUC (95% CI)	Cut off point	SN	SP	PPV	NPV	Accuracy
hepcidin	0.553 (0.404-0.701)	4.3000	63.3	60.0	70.4	52.2	62.0

Table 2: Correlation between hepcidin and other laboratory results in studied SLE patients.

Urinary Hepcidin		
P-value	**Coefficient**	
0.017*	0.31	**Serum creatinine**
0.028*	-0.28	**Urinary creatinine**
0.003**	0.37	**24 -hour proteinuria**
0.003**	0.38	**Erythrocyte sedimentation rate**
0.31	-0.133	**White blood cells**
0.03*	-0.275	**Lymphocytes**
0.004**	-0.37	**Hemoglobin**
0.27	-0.142	**Platelet**

P0415 **MONOCLONAL GAMMOPATHY-RELATED RENAL DISEASES: NEW CLINICAL AND HISTOLOGICAL PATTERNS.**

Giulia Schiavone[1], Marisa Santostefano[1], Benedetta Fabbrizio[2], Elena Mancini[1]

[1]Ospedale Sant'Orsola - Malpighi, Nephrology, Dialysis and Hypertension, Bologna, Italy and [2]Policlinico Sant'Orsola-Malpighi, Pathology of solid organs and transplants, Bologna, Italy

Background and Aims: In the last few years new clinical-histopathological forms of paraproteinemia associated kidney disease have emerged: light chain proximal tubulopathies, proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID) and C3-glomerulopathy.

It is now widely recognized that the pathogenic role of the monoclonal protein depends on the free light chain chemical-physical features, even in the case of "dangerous small B cell clones".

Thus MGRS (monoclonal gammopathy of renal significance) associated disease is now considered a different entity from monoclonal gammopathy of undetermined significance (MGUS).

Method: We retrospectively evaluated the clinical-histopathological features of the biopsies performed in our Nephrological Unit on patients with MGUS in 2008-2018, in order to re-classify them in accordance with the recent scientific literature.

Results: Nine patients (7 M/2 F; age 46-77 y) were analyzed: five of them suffering from CKD stage 2, four of them with AKI or rapidly progressive CKD, 7 with proteinuria > 1 g/day, 2 with physiological proteinuria. Bone marrow biopsy: 7 patients with MGUS, 2 with smoldering multiple myeloma. Renal biopsy: 4 glomerulopathies (monoclonal fibrillary glomerulonephritis, cryoglobulinaemic (type I) glomerulonephritis, C3 glomerulonephritis, PGNMID), 5 proximal tubulopathies (2 LCPT with Fanconi syndrome, 1 LCPT without cytoplasmic inclusions and with interstitial inflammatory

Table 1 Glomerulopathies

Pz n°	Renal biopsy	Bone marrow plasmacells (%)	VFG, 24 h proteinuria	Monoclonal Ig, FLC κ/λ	Therapy	Monoclonal Ig, FLC κ/λ	Follow-up (months)
1	Proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID)	2	29.4 ml/min 225 mg	No 1.91	Bortezomib+ CYC+Dex	No 1.84 (vs 1.91)	13
4	C3 Glomerulonephritis	10	9.4 ml/min 500 mg	IgG κ 55.2	Bortezomib+Dex	IgG κ 0.89 (vs 55.2)	21
5	Monoclonal fibrillary glomerulonephritis	<10	77.2 ml/min 2848 mg	IgG κ 1.63	No therapy	IgG κ 4.14 (vs 1.63)	119
9	Cryoglobulinaemic (type I) glomerulonephritis	<10	110.8 ml/min 9695 mg	IgM κ 2.05	No therapy	IgM κ 2.05 (vs 2.05)	2

Table 2 Light Chain proximal Tubulopathies

Pz n°	Renal Biopsy	Bone marrow plasmacells (%)	GFR, 24 h proteinuria	Monoclonal Ig, FLC κ/λ	Therapy	Monoclonal Ig, FLC κ/λ	Follow-up (months)
2	Tubulopathy with cytoplasmic inclusions	10	61.6 ml/min 2300 mg	IgA κ 205.81	Alkeran+Prednisone+ Bortezomib	IgA κ 437.7 (vs 205.81)	0
3	Tubulopathy without cytoplasmic inclusions/ATN	20	21.6 ml/min 1488 mg	IgA κ 100	Bortezomib+Talidomide+ Dex+ CYC+Alkeran+ double autologous transplantation	No 2.24 (vs 100)	12
6	Tubulopathy with cytoplasmic inclusions	<10	60 ml/min 2920 mg	IgG κ 141.2	Alkeran+Prednisone+ Bortezomib+Lenalidomide -Dex+ Bendamustina-Bortezomib+ Pomalidomide-Dex+ Carfilzomib	IgG κ 533.14 (vs 141.2)	106
7	Tubulopathy without cytoplasmic inclusions/ATN	10	25.1 ml/min 2120 mg	No 12.49	Bortezomib+Dex	IgG κ 3.9 (vs 12.49)	7
8	Tubulopathy without cytoplasmic inclusions and AIN	<10	65.6 ml/min 224 mg	IgG λ 1.05	Bortezomib+Talidomide+ Dex+ autologous transplantation	No 0.85 (vs 1.05)	7

Figure:

reaction, 2 LCPT with acute tubular necrosis) Table 1, Table 2, Light microscopy and IF of PGNMID.

Conclusion: MGRS is responsible for the pathogenesis of new histopathological renal lesions, based on new pathogenetic pathways. The clinical and histological features of the different disease states are dependent on the structure of FLCs. Our retrospective analysis of MGRS biopsies confirms how difficult and complex the diagnostic challenge of monoclonal renal injury really is.

The differentiation between MGUS and MGRS is based on renal biopsy and demonstration of monoclonality on kidney tissue even if serum/urine immunofixation is negative.

Early biomarkers of the pathogenetic role of monoclonal FLC should be identified both for diagnosis and therapeutical monitoring.

P0416 BODY MASS INDEX IS NOT ASSOCIATED WITH ADVERSE RENAL EVENTS IN BIOPSY-PROVEN PRIMARY GLOMERULONEPHRITIDES

Patricia Dominguez Torres[1], Amir Shabaka[1], Eduardo Gomez Moron[1], Clara Maria Cases Corona[1], Yunayka Diaz Enamorado[1], Gema Maria Fernandez Juarez[1]

[1]*Hospital Universitario Fundación Alcorcón, Nephrology, Alcorcon, Madrid, Spain*

Background and Aims: Obesity is a strong risk factor for the development of chronic kidney disease (CKD) through its close association with hypertension and diabetes. As metabolic demands increase with higher body mass indices, a compensatory glomerular hyperfiltration occurs to meet the increasing burden, consequently increasing intraglomerular pressure that can lead to the development of CKD and may influence the progression of already established kidney damage. The aim of our study was to determine whether there was an association between body mass index (BMI) and kidney disease progression in patients with primary glomerulonephritides (GN).

Method: We performed a single-centre retrospective cohort study in patients with biopsy-proven primary glomerular disease [minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN) and IgA nephropathy (IgAN)] diagnosed between July 1998 and December 2018. We excluded patients with no available data on weight at presentation or height, and those lost to follow-up. Patients were stratified into three groups according to BMI to <25 kg/m^2, between 25-30 kg/m^2 and >30 kg/m^2. Baseline characteristics were compared between the groups, serum creatinine, proteinuria and microscopic hematuria were recorded at presentation, and yearly afterwards until the end of follow-up. We compared among BMI groups the mean yearly change in eGFR, and yearly increase in proteinuria. Renal adverse outcomes were: time to doubling serum creatinine and initiation of renal replacement therapy (RRT). We performed a multivariate survival analysis to evaluate the risk factors associated with a renal composite outcome that included doubling serum creatinine and initiation of RRT.

Results: We included 178 patients that presented with a biopsy-proven primary glomerular disease (18 patients with MCD, 38 had FSGS, 38 MN and 84 IgAN), with a mean age of 50.6 ± 18.0 years, 71.3% were males, mean BMI of 28.2 ± 5.4 kg/m^2. There were no differences in age at presentation, sex or BMI between the four groups of GN. 24.2% of patients had BMI <25 kg/m^2 (Non-obese group), 43.8% had a BMI between 25-30 kg/m^2 (Overweight group) and 32% had BMI >30 kg/m^2 (obese group). Non-obese group had lower baseline systolic and diastolic blood pressure than the overweight group ($p=0.021$ and $p=0.015$) and the obese group ($p=0.001$ and $p<0.001$), but there were no differences in blood pressure between the latter two groups. Patients in the non-obese group were younger ($p=0.001$) than in the other two groups. There were no differences in baseline serum creatinine ($p=0.60$), proteinuria ($p=0.98$) or microscopic hematuria ($p=0.46$) across the three BMI groups. Survival analysis revealed no relation between BMI and the renal composite outcome (log-rank=2.18, $p=0.337$) or death (log-rank=0.117, $p=0.943$). Multivariate survival analysis revealed that the risk factors associated with the renal composite outcome were baseline creatinine ($\chi 2=6.61$, $p=0.010$) and urine albumin-creatinine ratio ($\chi 2=6.48$, $p=0.011$), but there was no association with BMI ($p=0.427$).

Conclusion: BMI at presentation was associated with higher blood pressure, but not with baseline serum creatinine or proteinuria, and was not associated with an increased risk of progression of kidney disease in primary glomerular diseases.

P0417 **THE ABSENCE OF C3 DEPOSIT IN MEMBRANOUS NEPHROPATHY IS ASSOCIATED WITH SPONTANEOUS REMISSION**

Cristina Rabasco[1], Ana Martínez[2], Rosa Ortega[2], Mario Espinosa[1]

[1]University Hospital Reina Sofía., Nephrology, Córdoba, Spain and [2]University Hospital Reina Sofía., Pathological Anatomy, Córdoba, Spain

Background and Aims: Membranous nephropathy (MN) is the most common cause of biopsied nephrotic syndrome in adults. Recently, it has been reported that the pathogenesis of MN may be associated with an activation of the complement system. The pathway of activation is not clearly established. The intensity of C3 deposition could be a good marker of this activation in MN as has been shown in other diseases (IgA nephropathy, crescentic GN). The aim of this study is to evaluate clinical-pathological data in a cohort of patients with MN and the significance of glomerular C3 staining as a possible predictor of renal outcomes.

Method: We analysed patients with idiopathic MN biopsied in our department between January 2000 and December 2019, excluding those who had no material for IF (n = 115). The patients were divided into positive (87 cases) and negative (28 cases) based on glomerular C3 deposition. We assessed the clinical and histological characteristics and the percentage of spontaneous remission (SR) and end-stage renal disease (ESRD).

Results: A total of 115 patients with MN were followed with a median follow-up of 65 (25-161) months. We found no differences in baseline characteristics between both groups, with the exception that patients with C3 deposit had less albumin at the time of biopsy that negative patients [2.4 (2-2.9) vs 2.8 (2.3-3.1) g/dl, P=0.011)].

Patients with C3-negative had a higher percentage of SR than patients with C3-positive (75 vs 24%, P = 0.000) and less need for immunosuppressive treatment (18 vs 56%, P =0.001). At the most recent follow-up, C3-positive group had higher creatinine [1.42 (0.8-1.7) vs 0.97 (0.71-1) mg/dl, P=0.045] and proteinuria [1.64 (0.08-3.2) vs. 0.62 (0.05-0.79) g / 24h, P = 0.039]. Regarding histology, we found no differences in glomerular sclerosis, tubular atrophy and interstitial fibrosis. The renal survival analysis showed no statistically significant differences between both groups (P = 0.091). We analysed a subgroup of patients (n = 23) with antibodies against the phospholipase receptor on blood at the time of the biopsy (13/23 were positive). 84% of this positive group presented C3-positive in the renal biopsy vs 25% of the C3-negative group (P =0.008).

Conclusion: Patients without C3 staining show a higher rate of SR and less need for immunosuppressive treatment than patients with C3-positive.

These results would support the theory that complement activation in this entity can play an important role.

It is possible that these patients with negative C3 deposit represent a MN with evolution to SR and in these patients and that these patients do not need immunosuppressive treatment.

	POSITIVE C3 (n=87)	NEGATIVE C3 (n=28)	Total N=115	p
Age (years)	55 (39-67)	48 (41-66)	55 (40-67)	0.59
Sex male (%)	55(64)	17(61)	72(64)	0.80
Creatinine at biopsy (mg/dl)	1.04 (0.8-1.5)	0.9 (0.8-1.4)	1.0 (0.8-1.5)	0.98
Proteinuria at biopsy (g/24hours)	5.9 (4.7-8.7)	4.1 (3.6-6.7)	5.75 (3.81-8.42)	0.15
Albumin at biopsy (g/dl)	2.4 (2-2.9)	2.8 (2.3-3.1)	2.6 (2.05-3.1)	0.011
Creatinine end follo-up (mg/dl)	1.42 (0.8-1.7)	0.97 (0.71-1)	0.92 (0.78-1.4)	0.05
Proteinuria end follow up (g/24h)	0.74 (0.08-3.2)	0.20 (0.05-0.79)	0.55 (0.05-2.47)	0.006
Spontaneus remision, n (%)	21(24)	20 (74)	41 (37)	0.000
Immunosupressive treatment, n (%)	48(55)	5 (18)	53(47)	0.001
ESRD, n (%)	27 (31)	3(10)	28(26)	0.1

Figure 1. Baseline and clinical characteristics

Figure:

P0418 LUPUS NEPHRITIS: A MONOCENTRIC STUDY

Marwa Omrane[1], Raja Aoudia[1], Mondher Ounissi[1], Soumaya Chargui[1], Mouna Jerbi[2], Hanene Gaied[2], Hafedh Hidri[1], Amel Harzallah[1], Taieb Ben Abdallah[1], Rim Goucha[2]

[1]Charles Nicole Hospital, Internal medicine A, Tunis, Tunisia and [2]Mongi Slim Hospital, Nephrology, La Marsa, Tunisia

Background and Aims: Systemic lupus erythematosus is a multi-visceral autoimmune disease. Renal involvement is one of the most common and serious manifestations of this disease. The histological lesions are highly polymorphic and the renal biopsy remains crucial for the therapeutic management of lupus nephritis (LN). The aim of our investigation was to study the epidemiological, clinical, biological and histological characteristics, outcomes and to evaluate the therapeutic protocols used for lupus nephritis' treatment and to identify predictive factors of renal prognosis in patients with lupus nephritis.

Method: It was a retrospective study including patients over 16 years old with lupus nephritis proved by kidney biopsy and followed up over a period of 17 years in our department.

Results: We collected 155 women and 19 men with a sex ratio F / H of 8.2. The mean age at the time of the discovery of LN was 32.6 years with a maximum between 15 years and 45 years. The most frequent extra-renal manifestations were articular and dermatological manifestations (79%). Renal symptomatology was dominated by proteinuria noted in all patients, associated to a nephrotic syndrome in 68% of patients. At the time of diagnosis of LN, hematuria was present in 69% of patients and renal failure was present in half of cases. Immunologically, antinuclear antibody were positive in 89.1% of cases, anti DNA positive in 73.4% of cases, anti Sm positive in 79.8% of cases and Antiphospholipids were positive in 50% of cases, associated with an antiphospholipid syndrome in 14.9% of cases. We performed 243 renal biopsies with 174 initial and 69 iterative biopsies. The histological lesions were polymorphic dominated by LN class IV (36.6%) isolated or associated with LN class V (17.7%). All patients received a corticosteroid for induction or maintenance treatment. It was associated with immunosuppressive treatment according to different treatment regimens. The median duration of follow-up was 81.2 months. Renal outcome was marked by complete and sustained remission in 36.7% of cases, incomplete remission with chronic kidney disease in 34.5% of cases, chronic renal failure in 28.7% of cases. At univariate analysis, we identified the young age below 35 years at the time of the discovery of LN, the male sex, increased serum creatinine at the time of biopsy, proliferative forms, the presence of histological signs of chronicity and lesions of thrombotic microangiopathy as predictive factors of poor renal outcomes.

Conclusion: Lupus nephritis is one of the most common and serious manifestations of Systemic lupus erythematosus. The generalization of renal biopsy, the use of early codified therapeutic protocols and regular monitoring and evaluation of disease activity according to the appropriate scores can improve management and survival of patients with renal impairment.

P0419 AUTOANTIGEN-SPECIFIC TH17 AND TH22 INFLAME THE KIDNEY IN ANCA-VASCULITIS

Erika Boschmann[1], Tanja Hinkeldein[1], Andreas Kribben[1], Sebastian Dolff[2], Pieter Van Paassen[3], Oliver Witzke[2], Benjamin Wilde[1]

[1]University of Duisburg-Essen, University Hospital Essen, Department of Nephrology, Essen, Germany, [2]University of Duisburg-Essen, University Hospital Essen, Department of Infectious Diseases, Essen, Germany and [3]Maastricht University, Department of Internal Medicine, Maastricht, Netherlands

Background and Aims: Anti-neutrophil-cytoplasmic-antibody (ANCA)-associated-vasculitis (AAV) is an autoimmune small-vessel-vasculitis. T-cells play a pivotal role in pathogenesis as drivers of autoantibody formation and vasculitic damage. However, the involvement of T-cells in renal vasculitis is understood poorly. IL-17C is secreted by epithelial parenchymal cells enhancing the pathogenicity of Th17 cells. Furthermore, IL-17C is a chemotactic factor for Th17 cells. The aim of this study was to assess the role of Th17 cells and IL-17C in the pathogenesis of ANCA-vasculitis in an animal model of AAV.

Method: Wistar-Kyoto-rats were immunized with myeloperoxidase (MPO) in Freunds Adjuvant to induce AAV. Control rats were immunized with Freunds Adjuvant only. Albuminuria was determined weekly and rats were culled after two, four and six weeks. At the time of harvest, renal T-cells were isolated and characterized by flow cytometry. Antigen-specificity was determined by ELiSPOT. Petechial bleedings on the lung surface reflecting pulmonary vasculitis were quantified after harvest. Gene expression in spleen, kidneys and lungs was studied by PCR and is expressed as fold change over controls. IL-17C levels were measured in sera by ELISA.

Results: MPO-rats developed detectable titres of anti-MPO by week two. By week six, all MPO-animals developed renal vasculitis with significant albuminuria and pulmonary vasculitis. Accordingly, MPO animals showed significant crescent formation as compared to the controls (% of affected glomeruli: 11.4 $\pm$10.5% vs. 0.4 $\pm$0.7%, $p<0.005$). The petechial bleeding score on the lung surface was higher in MPO-immunized rats than in controls at week six (68 $\pm$13 vs. 2 $\pm$1, $p<0.05$). From week two on, Th17 and Th22 cells inflamed the kidney as determined by PCR and/or flow cytometry in MPO-rats. The Th17 and Th22 infiltrate was heaviest at week six post-immunization. The intra-renal T-cell response was skewed towards Th17 as compared to the frequency of splenic Th17 cells in MPO-rats (9.1 $\pm$4.3% vs. 1.9 $\pm$0.6%, $p<0.005$). The majority of intra-renal Th17 and Th22 cells was MPO-specific. Control rats did not show renal T-cell infiltration. Renal transcripts for IL-17C were slightly decreased in week 2 (0.88 $\pm$0.1 fold), unchanged in week four (1.0 $\pm$0.2) and slightly increased in week six after immunization (1.7 $\pm$0.7 fold). Pulmonary IL-17C mRNA transcripts were decreased during weeks two and four after disease induction as compared to controls (0.29 $\pm$0.07 fold, 0.98 $\pm$0.2 fold). During week six, pulmonary IL-17C mRNA transcripts were slightly increased over controls (1.9 $\pm$0.4 fold). Serum levels of IL17C were unchanged during weeks two to six after disease induction comparing MPO-immunized rats and controls.

Conclusion: Th17 and Th22 cells are drivers of renal inflammation in ANCA-vasculitis. The role of IL-17C in this cascade needs to be determined.

P0420

PARTIAL PHARMACOGENETIC PODOCYTE DEPLETION IN A HIGH-THROUGHPUT ZEBRAFISH MODEL RESEMBLES HUMAN FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS

Florian Siegerist[1], Kerrin Ursula Ingeborg Hansen[1], Sophie Daniel[1], Maximilian Schindler[1], Antje Blumenthal[1], Weibin Zhou[2], Karlhans Endlich[1], Nicole Endlich[1]

[1]University Medicine Greifswald, Anatomy and Cell Biology, Greifswald, Germany and [2]Icahn School of Medicine at Mount Sinai, Division of Nephrology, Department of Medicine, New York, United States of America

Background and Aims: Although focal and segmental glomerulosclerosis (FSGS) has been in the scientific focus for many years, it is still a massive burden for patients with no causal therapeutic option. In FSGS, glomerular podocytes are injured, parietal epithelial cells (PECs) are activated and engage in the formation of cellular lesions leading to progressive glomerular scarring. Therefore, novel drug-screening assays are needed. Unfortunately, simple cellular *in vitro*-based screening assays are not ideal as glomerular architecture and crosstalk between glomerular cells is insufficiently modelled. Therefore, reliable animal models are still required for drug development, which unfortunately are not ideal for high-throughput applications. To date, due to its size, easy maintenance and breeding, zebrafish larvae are the simplest vertebrate model that are used in high-content screenings. Until today, it was unclear whether zebrafish can be used as a model for human FSGS. We therefore aimed to investigate whether partial podocyte-depletion in larval zebrafish leads to formation of FSGS-like disease and if the model can be used for screening purposes.

Method: We used a transgenic zebrafish model of pharmacogenetic podocyte depletion: In the Tg(nphs2:GAL4), Tg(UAS:Eco.nfsb-mCherry) strain, podocytes express the bacterial nitroreductase under control of the *podocin* promotor and can be dose-dependently ablated upon administration of metronidazole. Proteinuria was quantified using *in vivo* confocal laser scanning microscopy of intravenously administered high-molecular-weight fluorescent dextran. Plastic-embedded larvae where histologically and morphometrically assessed using HE, PAS and Jone's silver staining after metronidazole washout. Glomerular ultrastructure was assessed using transmission electron microscopy of ultrathin sections. Immunofluorescence staining was carried out on kryosections to investigate extracellular matrix deposition (*collagen-1, laminin*), cellular proliferation *(pcna)* as well as parietal cell origin and activation (*pax2a*).

Results: To partially deplete podocytes, larvae where treated with 80 µM metronidazole from 4-6 days post fertilization, so that a subset of podocytes was depleted. In contrast to controls, podocyte-depleted larvae developed severe whole-body edema (Fig. A). Dynamic *in vivo* imaging of intravascular 500 kDa fluorescent dextran revealed massive leakage of the glomerular filtration barrier. Ultrastructural and immunofluorescent evaluation showed broad foot process effacement of remaining podocytes (Fig. D) and massive decrease of the slit diaphragm component *podocin*. Moreover, we found numerous sub-podocyte space pseudocysts (asterisk in Fig. D), microvillous transformation and formation of podocytic tight junctions as well as parietovisceral adhesions of the two layers of Bowman's capsule. Parietal epithelial cells where activated, changed their phenotype towards a cuboidal shape, began to proliferate as demonstrated by *pcna* immunofluorescence and where recruited to cellular lesions on the glomerular tuft as demonstrated by the presence of cuboidal *pax2a*$^+$ cells on the glomerular tuft (arrowheads Fig. B). Moreover, we found significant extracellular matrix deposition by the *pax2a*$^+$ cells as demonstrated by Jone's silver staining and *laminin* immunofluorescence (Fig. C).

Conclusion: Herein we show that upon podocyte-depletion, zebrafish larvae develop important functional and morphological features of human FSGS such as severe proteinuria and edema, podocyte foot process effacement, activation of parietal epithelial cells which contribute to cellular lesions and deposit extracellular matrix on the glomerular tuft. We conclude that this model resembles the human disease in important features and therefore propose its applicability for a high-throughput drug screening assay for FSGS.

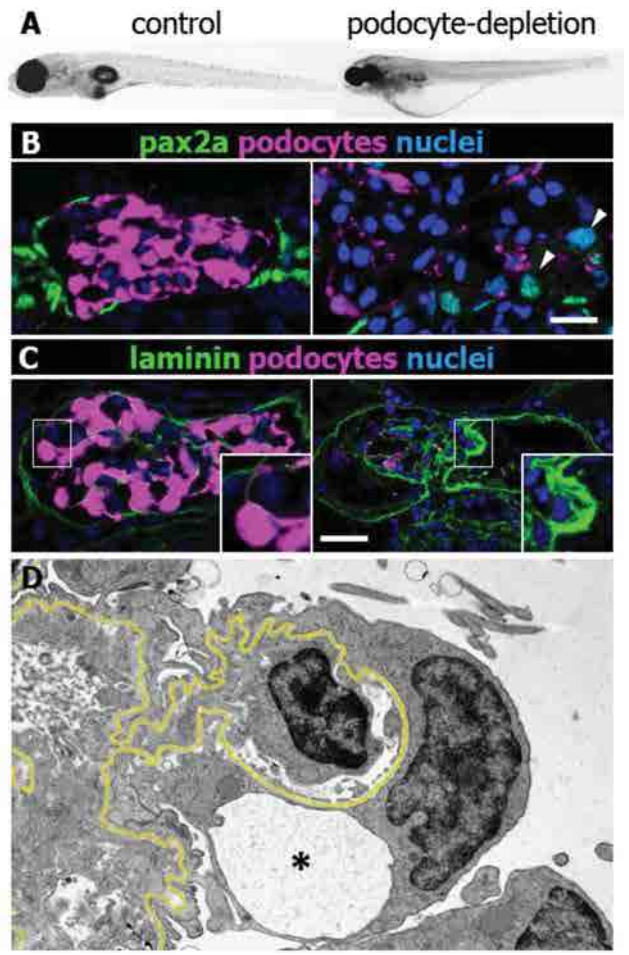


Figure:

P0421

STUDY OF DIFFERENT EXPRESSION PROFILES OF "TRANSIENT RECEPTOR POTENTIAL ION CHANNEL (TRPC) GENE FAMILY" IN PATIENTS UNDERGOING RENAL BIOPSY WITH CLINICAL SUSPECTED GLOMERULONEPHRITIS

Meltem Sezis[1], Yasemin Erac[2], Hale Güler[3], Gökhan Atay[4], Demirci Cenk[5], Mehmet Özkahya[4], Ercan Ok[4], Sait Şen[6], Banu Sarsık Kumbaracı[6], Buket Kosova[7]

[1]Ege University Medical Faculty, Nephrology, Izmir, Turkey, [2]Ege University, Pharmacology, Turkey, [3]Ege University, medical Biology, Turkey, [4]Ege University Medical Faculty, Nephrology, Turkey, [5]Fresenius Medical Care Turkey Izmir, Turkey, [6]Ege University Medical Faculty, Pathology, Turkey and [7]Ege University Medical Faculty, medical Biology, Turkey

Background and Aims: The transient receptor potential ion channels (TRPC) are non-selective Ca^{+2} permeable cation channels and are widely expressed in the tissues of vertebrates. They become active in response to signal transduction pathways associated with phospholipase C stimulation. TRPC6 is expressed in podocytes and is a component of the slit diaphragm. In genetic and acquired glomerular kidney diseases, TRPC6 overactivation causes podocyte damage by pathological Ca^{+2} entry. TRPC1, TRPC2, TRPC4, and TRPC5 interact with a protein called stromal-interacting molecule 1 (STIM 1), which is susceptible to intracellular calcium storage content. As a result of binding with this protein, TRPC channels bind to calcium-releasing zone in endosomes. The aim of the study was to investigate different expression profiles of TRPC family members in renal biopsy specimens in patients with clinically considered glomerulonephritis.

Method: This study was conducted with 108 patients admitted to Ege University Faculty of Medicine Nephrology Clinic who underwent a kidney biopsy with a preliminary diagnosis of glomerulonephritis and 37 patients who underwent a nephrectomy in urology clinic with a diagnosis of primary kidney tumour as a control case. PKD2, NPHS2, TRPC1, TRPC3, TRPC6, STIM-1 and Orai-1 mRNA levels were studied in the biopsy samples.

Results: When we compared the patient and the control group, the gender distribution of both groups was similar. The frequency of diabetes and hypertension was similar. The control group was statistically significantly older and glomerular filtration rates were higher than the patient group. In pathological examination, glomerulonephritis (57.5%) was diagnosed in the majority of patients. The most common etiologic factors were membranous nephropathy 23.1%, IgA nephropathy 13%, Amyloidosis 11.2%, focal segmental glomerulosclerosis 7.1%, proliferative glomerulonephritis 4.6%, minimal change disease 2.8% and membranoproliferative glomerulonephritis was 1.9%. 7.4% of the patients were diagnosed with diabetic nephropathy by renal biopsy.

When we compared the TRPC expression profiles of the patient and the control group, the TRPC1, TRPC6, PKD2, NPHS2, STIM-1 and ORAi-1 mRNA levels of the patient group were statistically significantly higher than those of the control group (Figure). In contrast, TRPC3 mRNA levels were significantly lower in the patient group compared to the control group. When we performed subgroup analysis, the TRPC1, TRPC6 and STIM1 levels of the diabetic group were statistically significantly higher compared to the non-diabetic group of patients. We could not find any difference between TRPC expression profiles between the patients according to pathological diagnosis. Similarly, there was no difference between the amount of proteinuria (nephrotic level versus nephritic level). In correlation analysis, there was a negative correlation with TRPC6 and STIM1 levels with positive C4d staining of glomeruli in renal biopsy. Positive correlation was found between ORAI and glomerular sclerosis rate.

Conclusion: As a result, we found that other than TRPC3 mRNA level, other TRPC and related protein channels mRNA levels were statistically significantly increased in proteinuric kidney patients compared to healthy kidney tissue. We did not find a positive relationship between proteinuria severity and TRPC expression profiles. We found that TRPC6 and STIM1 expression levels were increased in diabetic patients, which supports the knowledge that intracellular calcium pathways were activated in podocyte damage. In our study, there were significantly increased STIM1 and ORAi-1 expression levels in proteinuric patients compared to the control group and their increase was closely related to TRPC6. From this we can conclude that these proteins play an important role in proteinuric kidney damage.

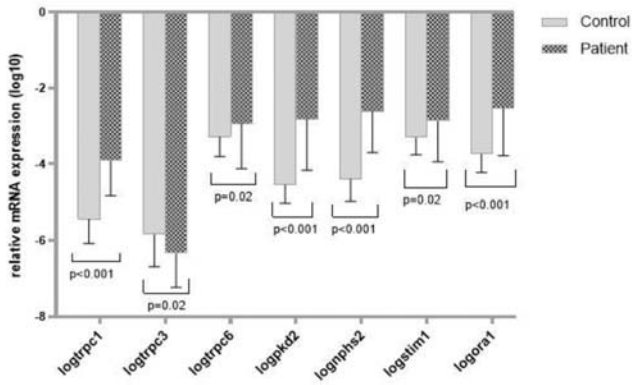


Figure:

P0422 **RED BLOOD CELL DISTRIBUTION WIDTH AND OUTCOME IN SUBJECTS WITH BIOPSY-PROVEN GLOMERULOPATHIES WITHOUT ANEMIA**

Otilia Popa[1], Tudor Popa[1], Ana Stanciu[2], Nicoleta Petre[3], Eugen Mandache[3], Cristina-Stela Capusa[1,4], Gabriel Mircescu[1,4]

[1]Carol Davila University of Medicine and Pharmacy, București, Romania, [2]"Dr. Carol Davila" Teaching Hospital of Nephrology, Hematology Laboratory, București, Romania, [3]"Dr. Carol Davila" Teaching Hospital of Nephrology, Nephropatology, București, Romania and [4]"Dr. Carol Davila" Teaching Hospital of Nephrology, Nephrology and Internal Medicine, București, Romania

Background and Aims: Red blood cell distribution width (RDW) is a marker of anisocytosis and is mainly modified in anemia. However, elevated RDW has recently been reported to predict cardiovascular risk, was correlated with disease activity in inflammatory conditions such as systemic lupus erythematosus, rheumatoid arthritis and, not the least, was associated with increased risk of end stage kidney disease and proteinuria in chronic kidney disease (CKD) subjects. The current study aims to assess if RDW is an independent predictor for renal replacement therapy (RRT) and mortality in subjects with glomerulopathies (GP).

Method: This retrospective, single-center study, included 467 subjects with hemoglobin >12 g/dL at presentation, who were histologically diagnosed with primary and secondary glomerulopathies between 1st Jan. 2008 and 31st Dec. 2017 and who were followed for a mean of 52.8 (95%CI 50.7-55) months, until 31st May 2018. Subjects with inadequate biopsy sample were excluded. Those who deceased until the end of the follow-up were not included in the kidney survival analysis. Predictors of mortality were assessed by logistic regression. Kaplan-Meier method was used to evaluate kidney survival.

Patients were stratified in two groups according to the median RDW value: low RDW group (RDW≤15%; n=342) and high RDW group (RDW>15%; n=125). RRT initiation and all-cause mortality were the primary endpoints of the study.

Results: Subjects with high RDW were older [53 (95%CI 48-56) vs. 45 (95%CI 43-47) years; p=0.03], had more frequent cerebrovascular disease (9.7% vs. 2.7%; p=0.003), congestive heart failure (8.1% vs. 1.8%; p=0.002), connective tissue disease (11.3% vs. 3%; p=0.001) and non-hematologic neoplasia (4.8% vs. 0.9%, p=0.01). Furthermore, they had more severe inflammation as suggested by higher erythrocyte sedimentation rate [54.5 (95%CI 43-60) vs. 35 (95%CI 30-40) mm/hour; p=0.002], fibrinogen [630 (95%CI 562-701) vs. 540 (95%CI 514-585 mg/dL; p=0.02], and C reactive protein [3 (95%CI 2-4) vs. 2 (95%CI 2-3); p=0.03], had lower hemoglobin [13.7 (95%CI 13.4-14) vs. 14.1 (95%CI 13.9-14.4) g/dL); p=0.008], and higher proteinuria [4.2 (95%CI 3.1-5.2) vs. 2.4 (95%CI 2.1-2.8) g/g creatinine; p=0.002]. However, the kidney function between the two groups was similar (56.5 vs. 55 ml/min MDRD; p=0.1).

Secondary GP were more frequent encountered in high RDW group (42.4% vs. 18.1%; p<0.001), especially amyloidosis (19.2% vs. 4.7%; p<0.001) and lupus nephritis (9.6% vs. 3.5%; p=0.01).

During the follow-up period, in high RDW group 26.4% of the subjects died, compared to 11.4% from the other group (p<0.001). In a multivariate logistic regression model, RDW was an independent predictor for mortality [OR 1.5 (95%CI 1.2-15); p=0.007]. Other independent predictors were older age [OR 1.06 (95%CI 1.03-1.08); p<0.001], presence of cerebrovascular disease [OR 3.31 (95%C I1.01-10.8); p=0.04], lower serum albumin [OR 0.48 (95%CI 0.43-0.70), p<0.001] and higher serum creatinine [OR 1.29 (95%CI 1.06-1.57); p<0.001]. There was no difference regarding the frequency of RRT initiation between groups (18% in high RDW group vs. 11% in low RDW group; p=0.07) and the time to kidney death was similar [79.7 (95%CI 72.8-86.6) vs. 87.8 (95%CI 84-91.6) months; log rank p=0.1].

Conclusion: In non-anemic subjects with biopsy-proven glomerular disease, a higher RDW seems associated with a higher risk of mortality, but not with kidney survival. In addition, RDW above 15% might point out to a secondary GP, like amyloidosis and lupus nephritis.

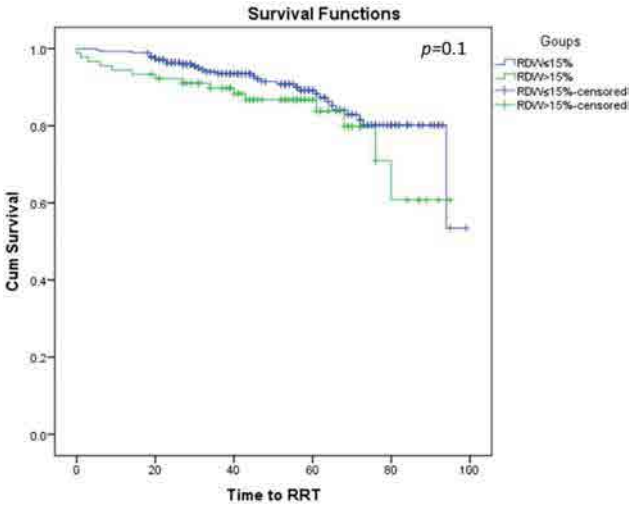


Figure: Kaplan–Meier curve of kidney survival rate in patients with RDW≤15% compared with RDW>15%

P0423 CLINICOPATHOLOGICAL STUDY OF RENAL AMYLOIDOSIS

Anupma Kaul[1]

[1]*Sanjay Gandhi Post graduate institute of Medical sciences, Nephrology, Lucknow, India*

Background and Aims: Amyloidosis constitute a heterogenous group of disorders characterized by extracellular deposition of abnormally folded proteins in different tissues and organs leading to organ dysfunction. An emphasis has been made to classify, grade and score the amyloid deposits in different renal compartments and correlate them with the clinical features, type of amyloid and outcome.

Method: The study included all renal biopsies done in department of nephrology diagnosed as amyloidosis in association with Department of Pathology, SGPGIMS from January 2009 to December 2018 and retrospectively analysed. Besides biochemical parameters ,serum and urine electrophoresis ,immunofixation ,bone biopsy ,FNAC and kidney biopsy was done for the diagnosis.

Results: One hundred forty seven (147) renal biopsies diagnosed as Amyloidosis at the Department of Pathology, SGPGIMS, Lucknow from January 2009 and December 2018 .The mean age was 51.33 ± 14.50 years (Median: 52 year), most common age group affected with Renal Amyloidosis was 50-60 years(6 th decade) in males, while it was one decade younger in females (40-50years). Multiple myeloma as the primary disease was present in 18/147 (12.2%). History of chronic inflammatory disease was found in 65 patients (44%). Tuberculosis was the most common infection while rheumatoid arthritis (18.5%) was found to be the second most commonly associated chronic inflammatory condition. Mean serum creatinine was 2.04 ±1.72 mg/dl. Peripheral neuropathy and bleeding episodes were rarely seen (<5%). Nephrotic range proteinuria was found in 78% Only eight out of eighteen patients with Multiple myeloma showed reversal of A:G ratio. M-band was present in 34 patients . Lambda light chain was found more commonly associated with renal amyloidosis. Out of 71, 27 aspiration cytology smears revealed congophilic deposits which showed apple green birefringence on polarizing microscopy. Bone marrow biopsy was performed in 76, among them 17 patients showed > 10% plasma cells. Histology commonly seen was diffuse mesangio capillary in 77%, followed by advanced amyloidosis (20%). Most of the renal biopsies (84%) showed amyloid deposition in >50% area of glomeruli. Most of the renal biopsies (41.5%) showed mild tubular atrophy. Renal amyloid prognostic score (RAPS) was calculated combining all scores in different renal compartments revealed 74% patients belonged to Grade III. Immuno histochemistry for typing of renal amyloid revealed SAA in 61, two cases were placed in a different group, termed as dual AL+AA positive. one case with positive ALect2 deposits in renal biopsy. Survival analysis showed showed that AL had poor overall survival as compared to AA typePatients with high serum creatinine value (>2.0 mg/dl) had poor survival as compared to the patients with serum creatinine <2.0mg/dl. significant poor survival in patients withcardiomyopathy (p value=0.004) and hypotension (p value=0.026). High burden of plasma cells (> 10%) in bone marrow aspirate also showed significant poor survival.

Conclusion: Final typing of amyloid deposits in kidney biopsy with clinicopathological evaluation revealed AA was the predominant subtype comprising of 50% (n=73) of renal amyloidosis. AL was 33% (n=48) of all cases. The different class of pattern of amyloid deposition correlated well with the grade of amyloid deposition in renal biopsy. Poor survival outcomes are evident with patients with hypotension ,cardiomyopathy, higher grades of amyloid on histology, serum creatinine > 2 mg% and high burden of plasma cells (>10%) in bone marrow aspirate. Thus the number of patients with cardiomyopathy, hypotension and > 10% plasma cells in bone marrow aspirate performed poorly however the study is smalland needs to be validated on a larger cohort.

P0424

CLINICO-PATHOLOGICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH DNAJB9 POSITIVE FIBRILLARY GLOMERULONEPHRITIS

Shaoshan Liang[1], Dandan Liang[1], Feng Xu[1], Mingchao Zhang[1], Fan Yang[1], Ping Li[1], Caihong Zeng[1]

[1]*National Clinical Research Center of Kidney Diseases, Jinling Hospital, Nanjing University School of Medicine, Nanjing, P.R. China*

Background and Aims: To investigate the clinicopathological features and prognosis of DNAJB9 positive fibrillary glomerulonephritis (FGN) in a single center in China.

Method: Cases diagnosed as FGN by renal biopsy from January 2011 to December 2019 in Jinling Hospital were stained with anti-DNAJB9 by immunohistochemistry. The patients with DNAJB9 positive FGN were retrospective analyzed.

Results: DNAJB9 staining of glomerular deposits was seen in 6 cases of FGN. 1 man and 5 women with a median age of 26 years (range, 21 to 49 years) were studied. Underlying autoimmune disease of Sjogren's syndrome and Hashimoto thyroiditis was in 1 case. None of them had dysproteinemia, malignancy, hepatitis C, hepatitis B, cryoglobulinemia, or diabetes. The patients presented with hypertension and edema in 5 cases, renal insufficiency in 1 case, and proteinuria in 6 cases with the median 24-hour urine protein 2.58 g (range, 1.66 to 9.57 g), nephrotic syndrome in 3 cases, and microscopic hematuria in 2 cases. The histologic pattern was mesangial proliferative glomerulonephritis (GN) and membranoproliferative GN. A mean of 9.7% of glomeruli were globally sclerotic. Crescents were present in 1 case (10%). The degree of tubular atrophy and interstitial fibrosis were absent (2 cases) and mild (4 cases), and severe acute tubular injury was in 1 case. All 6 cases showed glomerular positivity for IgG, C3 and C1q, 5 of which were positive for IgM, and 4 of which were positive for IgA. The glomerular deposits stained for polyclonal IgG subclasses and both kappa and lambda light chains in 3 cases. In 1 case, it stained for polyclonal IgG subclasses without kappa or lambda. IgG subclasses were IgG4 dominant in 3 cases and IgG1 dominant in 1 case. In 2 cases, they stained for monoclonal IgG1-kappa and IgG1-lambda. On electron microscopy (EM), the fibrillary deposits were seen infiltrating the mesangium, subendothelial, subepithelial area in all 6 cases, and the lamina densa of the GBMs in 5 cases with diameter of 7-40nm. Combined with observation of DNAJB9 staining, immunofluorescence microscopy and EM, extraglomerular deposits were identified in vessel walls in 5 cases, tubular basement membranes in 3 cases, peritubular capillaries in 3 cases. Congo red positivity was in 4 cases. At a median time of 32.9 months (range, 1 to 68.3 months) after biopsy, 3 cases were stable, 1 case had partial renal function recovery, and 2 cases had partial remission of proteinuria.

Conclusion: DNAJB9 immunohistochemistry is sensitive and specific for FGN. Monoclonal IgG and light chain was observed in young patients. Extraglomerular deposits were common. Prognosis was good in this young patient's series.

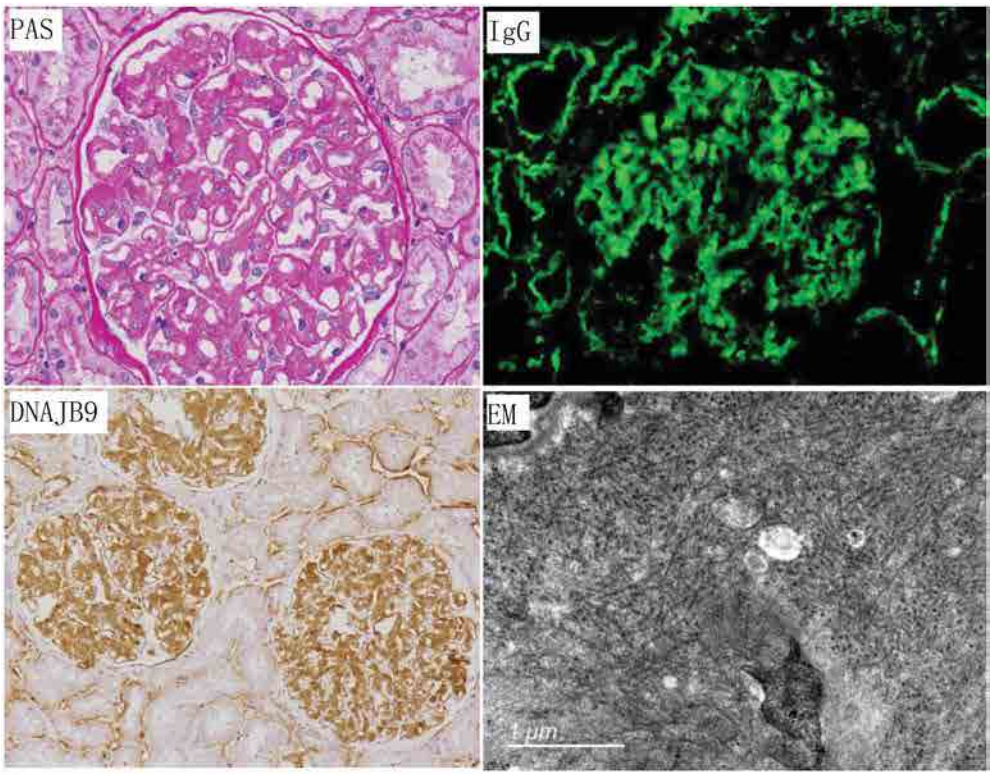


Figure:

P0425 **MEMBRANOUS NEPHROPATHY IN TURKEY: TURKISH SOCIETY OF NEPHROLOGY GLOMERULER DISEASES (TSN-GOLD) DATABASE RESULTS**

Abdulmecit Yildiz[1], Memnune Sena Ulu[2], Aysegul Oruc[1], Ali Riza Ucar[3], Savas Ozturk[4], Selma Alagoz[5], Necmi Eren[6], Ismail Kocyigit[7], Simal Koksal Cevher[8], Ali Burak Haras[9], Abdullah Sumnu[10], Turgay Arinsoy[11], Garip SAHIN[12], Gultekin Suleymanlar[13], Caner Cavdar[14], Gizem Kumru Sahin[15], Ilhan Kurultak[16], Abdulkadir Unsal[17], Gulizar Manga Sahin[18], Sinan Kazan[2], Bulent Vatansever[19], Mehmet Dikec[20], Belda Dursun[21], Hayriye Sayarlioglu[22], Kultigin Turkmen[23], Ayse Serra Artan[24], Nimet Aktas[25], Zulfikar Yilmaz[26], Ahmet Behlül[27], Hamad Dheir[28], Sim Kutlay[15], Nurhan Seyahi[5]

[1]Uludag University, Medical Faculty, Nephrology, Bursa, Turkey, [2]Afyon University, Medical Faculty, Nephrology, Afyon, Turkey, [3]Istanbul University, Istanbul Medical Faculty, Nephrology, Istanbul, Turkey, [4]Haseki Training and Research Hospital, Nephrology, Istanbul, Turkey, [5]Istanbul University, Cerrahpasa Medical Faculty, Nephrology, Istanbul, Turkey, [6]Kocaeli University, Medical Faculty, Nephrology, Kocaeli, Turkey, [7]Erciyes University, Medical Faculty, Nephrology, Kayseri, Turkey, [8]Ankara Numune Training and Research Hospital, Nephrology, Ankara, Turkey, [9]Dr. Lutfi Kirdar Kartal Training and Research Hospital, Nephrology, Istanbul, Turkey, [10]Medipol University, Medical Faculty, Nephrology, Istanbul, Turkey, [11]Gazi University, Medical Faculty, Nephrology, Ankara, Turkey, [12]Eskisehir Osmangazi University, Medical Faculty, Nephrology, Eskisehir, Turkey, [13]Akdeniz University, Medical Faculty, Nephrology, Antalya, Turkey, [14]Dokuz Eylul University, Medical Faculty, Nephrology, Izmir, Turkey, [15]Ankara University, Medical Faculty, İbni Sina Hospital, Nephrology, Ankara, Turkey, [16]Trakya University, Medical Faculty, Nephrology, Edirne, Turkey, [17]Hamidiye Sisli Etfal Training and Research Hospital, Nephrology, Istanbul, Turkey, [18]Sultan Abdulhamit Han Research and Training Hospital, Nephrology, Istanbul, Turkey, [19]Bozyaka Training and Research Hospital, Internal Medicine, Izmir, Turkey, [20]Bakirkoy Sadi Konuk Training and Research Hospital, Nephrology, Istanbul, Turkey, [21]Pamukkale University, Medical Faculty, Nephrology, Denizli, Turkey, [22]Sutcu İmam University, Medical Faculty, Nephrology, Kahramanmaras, Turkey, [23]Necmettin Erbakan University, Meram Medical Faculty, Nephrology, Konya, Turkey, [24]Bezmialem Vakif University, Medical Faculty, Nephrology, Istanbul, Turkey, [25]Bursa Yuksek Ihtisas Training and Research Hospital, Nephrology, Bursa, Turkey, [26]Dicle University, Medical Faculty, Nephrology, Diyarbakir, Turkey, [27]Burhan Nalbantoglu State Hospital, Nephrology, Lefkosa, Cyprus and [28]Sakarya University, Medical Faculty, Nephrology, Sakarya, Turkey

Background and Aims: Membranous nephropathy (MN) is the most common cause of nephrotic syndrome in the adult population. The aim of our study is to determine the demographic and clinical characteristics and biopsy findings of the patients diagnosed with MN in our country.

Method: The study included 991 patients with renal biopsy who were followed in 47 nephrology clinics and enrolled in the database of Turkish Nephrology Primary Glomerular Diseases (TSN-GOLD) Working Group between May 1, 2009, and June 1, 2019. The demographic and clinical characteristics and biopsy findings of all patients included in the study were analyzed.

Results: The mean age of patients included in our study was 46±14.8 years and the gender distribution was (M / F, 582/409). 80.3% (n = 796) of the patients had nephrotic proteinuria at the time of diagnosis. Before the biopsy, the PLAR2 antibody was examined in 137 patients and positive in 71.5% (n = 98) patients. Hypertension was present in 34.6% (n = 343) of the patients. Mean estimated glomerular filtration rate was 93.9±32.8 ml/min/1.73 m^2, albumin level was 2.7 ± 0.2 mg/dL, proteinuria level in urine was 7,1±6,4 gr/day and total cholesterol level was 295±3.7 mg/dL. On light microscopy, baseline membrane thickening was found in 92% (n=907) and interstitial inflammation in 53% (n=524) specimens. In immunofluorescence staining, 3 (+) IgG accumulation was highest in 578 (58.3%) of the specimen.

Conclusion: This multicentre study is the largest study to analyze clinical, laboratory, and biopsy specimens of MN patients at the time of biopsy in our country. The findings are consistent with the literature. Prospective follow-up results of these patients will help us to understand the renal prognosis and treatment response better.

P0426 **HISTOLOGICAL PREDICTORS OF RENAL PROGNOSIS IN LUPUS NEPHRITIS: WHICH COMPARTMENT MAKES THE DIFFERENCE?**

Gabriel Stefan[1,2], Simona Stancu[1,2], Carmen Georgescu[2], Adrian Dorin Zugravu[1,2], Nicoleta Petre[1,2], Gabriel Mircescu[1,2]

[1]Nephrology Hospital Dr. Carol Davila, Nephrology, București, Romania and [2]Carol Davila University of Medicine and Pharmacy, București, Romania

Background and Aims: Lupus nephritis (LN) encompasses a spectrum of glomerular, tubulointerstitial, and vascular lesions; we aimed to evaluate which compartment injury has renal prognostic value.

Method: We retrospectively examined the renal outcome at 31 December 2015 of 66 patients (age 36 [28-52] years; 76% female; eGFR at baseline 60.8 [24.4-78.1] mL/min) who were diagnosed with lupus nephritis by kidney biopsy during 2010-2015. Data regarding the clinical presentation, renal function, histology (presence/absence of lesions - Table 1; ISN/RPS classification) and treatment were retrieved from the electronic patients' files. We used a composite endpoint in the survival analysis (Cox proportional hazard models, CPH): renal replacement therapy initiation, doubling of serum creatinine and death, whichever came first.

Results: Nephrotic syndrome was the most frequent form of presentation (42%), followed by nephritic (24%) and nephrotic-nephritic (15%). Most of the patients received immunosuppression treatment (97%, 70% cyclophosphamide regimen). Twenty-five patients (38%) reached the composite endpoint. They were older, male more often, had higher mean arterial pressure (MAP), lower serum albumin, decreased eGFR and higher proteinuria. Moreover, they were in class IV LN and had glomerulosclerosis more frequently. Median renal survival for the entire cohort was 4.4 (95%CI, 2.3-6.5) years. In the multivariatle CPH for the histological predictors, only ISN/RPS classification and tubular atrophy were associated with renal survival (**Table 1**). In a CPH that included clinical, histological and treatment variables, only lower eGFR (0.97 (95%CI, 0.95-0.99)), MAP (1.03 (95%CI, 1.00-1.06)) and tubular atrophy (4.52 (95%CI, 1.50-13.55)) remained as independent predictors of renal survival.

Conclusion: Tubular atrophy seems to be an important prognostic sign in LN; therefore, greater importance should be given to the tubulointerstitial compartment evaluation.

Table 1. CPH for the histological predictors

	Univariate HR (95%CI)	p	Multivariate* HR (95%CI)	p
Glomerular lesions	2.24 (1.01-4.93)	0.04	0.86 (0.28-2.57)	0.7
Glomerulosclerosis	1.28 (0.56-2.91)	0.5	1.33 (0.50-3.51)	0.5
Endothelial proliferation	1.14 (0.52-2.53)	0.7	0.80 (0.30-2.15)	0.6
Extracapillary proliferation	1.25 (0.46-3.36)	0.6	1.13 (0.37-3.44)	0.8
Subendothelial deposits	1.08 (0.45-2.63)	0.8	1.20 (0.35-4.03)	0.7
Fibrinoid necrosis				
Tubulo-interstitial lesions	2.46 (0.97-6.23)	0.05	-	0.007
Tubular atrophy	1.22 (0.52-2.86)	0.6	4.52 (1.50-13.55)	0.5
Interstitial fibrosis			0.71 (0.25-2.04)	
Vascular lesions	1.70 (0.70-4.11)	0.2	2.04 (0.64-6.44)	0.2
Lupus nephritis	0.01 (0.00-1.90)	0.1	0.01 (0.00-1.90)	0.01
class versus VI	0.07 (0.00-0.81)	0.9	0.02 (0.00-0.46)	0.9
II	0.33 (0.07-1.50)	0.8	0.05 (0.00-0.37)	0.001
III	0.13 (0.02-0.77)	0.1	0.02 (0.00-0.19)	0.05
IV		0.02		0.001
V				

P0427 **IGA GLOMERULONEPHRITIS WITH MASSIVE PROTEINURIA-CASE SERIES WITH CLINICAL AND PATHOHISTOLOGICAL REVIEW**

Miroslav Tisljar[1], Luka Toric[1], Dino Kasumović[1], Matija Crnogorac[1], Ivica Horvatić[1], Nikola Zagorec[1], Danica Galesic Ljubanovic[3], Kresimir Galesic[1]

[1]University hospital Dubrava, Nephrology and Dialysis, Zagreb, Croatia and [3]University hospital Dubrava, Department for Nephropathology and Electron microscopy, Zagreb, Croatia

Background and Aims: IgA nephropathy (IgAN) is the most common glomerulonephritis worldwide. The classic manifestation of IgAN is episodic hematuria and proteinuria. Nephrotic syndrome (NS) is not common in IgAN. It is reported to occur in 5-10% of patients with IgAN. Clinical presentation with massive proteinuria is exceptional.

Method: We retrospectively analyzed patients with pathohistologically proven IgAN who initially presented with 24h proteinuria greater than 10 gr. Here we presented their clinical, biochemical and pathohistological (electron microscopy-EM, was provided in all cases) characteristics with clinical outcomes. Data were taken from Renal biopsy Registry of Department of Nephrology Dubrava University hospital.

Results: All together 12 patients (10 M, 2 F) average age 53 (range 25-81) years were included. This represents 3,2% of all IgAN patients in our Renal biopsy Registry (presently there are more than 2100 patients in total, 366 with IgAN). Arterial hypertension had 10 out of 12 patients and three patients had diabetes mellitus type 2. Other significant comorbidities included lung adenocarcinoma in one patient, history of preeclampsia, mitral valve replacement surgery and liver cirrhosis, each in one patient. Average serum creatinine level at presentation was 223,9 (90-549) μmol/L and average 24h proteinuria was 14,6 (10,2-32) gr. All patients had haematuria. Renal insufficiency was found in 7 patients and additionally in two patients rapidoprogressive clinical pattern was recognized. Oxford classification was applied for all patients. In all except one, mesangial hypercellularity (M1) was found, endocapillary proliferation (E1) in 4 and cellular crescents in 5 patients (C1 in 4, C2 in 1 patient). The average percentage of globally sclerosing glomeruli was 32% (10-85%) and IFTA was 33% (10-60%), respectively. On EM diffuse podocyte foot processes effacement was documented only in two patients. In patients with diabetes mellitus there were not signs of diabetic nephropathy (i.e. thickened GBM on EM). Two patients who presented with purpuric rash and arthritis were considered to have IgA vasculitis (Henoch Schoenlein purpura). Considering treatment, glucocorticosteroids and RAAS blockators (apart from those who were dialysis dependent) were introduced. Five patients were also treated with cyclophosphamide. Average time of follow-up was 53 months (2-156). Regarding clinical outcomes, 4 patients achieved remission (2 partial and 2 complete). One of those experienced clinical relaps and underwent kidney rebiosy. In one patient stationary course and in another one progression of renal insufficiency were noted. Both patients diagnosed as IgA vasculitis were dialysis depended at presentation and during follow-up period unfortunately died. Two more patients died latter on as a consequence of a non-renal disorders. One more patient who developed ESRD was transplanted but afterwards he rejected the graft. One patient was lost from follow-up.

Conclusion: Proteinuria is well known independent progression risk factor in IgAN. In presented study we showed that almost one third of IgAN patients who manifested with massive proteinuria ended up in ESRD in relatively short follow-up period.

P0428

CYTOMEGALOVIRUS INFECTION IN PATIENTS WITH GLOMERÜLER DISEASE TREATED WITH CYCLOPHOSPHAMIDE: A SINGLE-CENTER EXPERIENCE

Gizem Kumru Şahin[1], Şahin Eyüpoğlu[1], Rezzan Eren Sadioğlu[1], Güle Çınar[2], Kenan Ateş[1], Şehsuvar Ertürk[1], Gökhan Nergizoğlu[1], Şule Şengül[1], Sim Kutlay[1], Kenan Keven[1]

[1]Ankara University Faculty of Medicine, Nephrology, Ankara, Turkey and [2]Ankara University Faculty of Medicine, Infectious Diseases and Clinical Microbiology, Ankara, Turkey

Background and Aims: Cytomegalovirus (CMV) infection is an important complication in immunocompomised patients. Although approach to CMV infection is well-defined in stem cell and solid organ transplant recipients, less is known about the frequency and risk factors of CMV disease in patients with glomerulonephritis (GN). As few studies have shown that cyclophosphamide (CYC) treatment is a risk factor for CMV infection in GN patients, we aimed to describe the frequency and risk factors of CMV infection in GN patients treated with CYC.

Method: 268 patients diagnosed GN between January 2017 and November 2019 in Ankara University İbni Sina Hospital, Nephrology Department. We recruited 43 GN patients who were treated with CYC and screened all patients for viral DNA monthly. CMV infection defined by CMV DNA detected >500 copies/µl. Patients developed CMV and no-CMV infection were compared for age, sex, glomerular pathology, renal function and clinical status before and after treatment.

Results:CMV infection was detected in 10 (23,3%) patients at 2±1 (min:1 max:3) months of CYC treatment (Table-1). 7 patients were treated for CMV infection with parenteral ganciclovir, while the other 3 patients with low CMV DNA level (509, 538 and 540 copies/ml) and no disease symptoms were monitored without antiviral treatment. Patients with CMV infection had higher serum creatinine (4,2±3,2 vs. 1,9±1,8 mg/dl, p=0,006), lower estimated glomerular filtration rate (29±11 vs. 65±8 (ml/min/1.73 m^2, p=0.016), lower low-density lipoprotein (144±71 vs. 221±83 mg/dl, p=0,012) at diagnosis compared with no-CMV infection patients (Table-2). Also more patients were diagnosed with rapidly proggressive GN (80,0% vs. 27.3%, p=0,007), and secondary GN was the most common GN diagnosis (80,0% vs. 27.3%, p=0.007) in CMV infection group.

Conclusion:CMV infection is a common complication in GN patients treated with CYC. Routine monitoring and prophylaxis should be considered for the patients who have risk factors for CMV infection.

Table-1. ClinicalCharacteristicsandOutcomes in Patientswith CMV Infection

	CMV Infection (n:10, 23,3%)
Diagnosis time after CYC onset, months (mean±SD)	2±1 (min:1 max:3)
CMV DNAemia (PCR, copies/µl) (mean±SE)	7849±3785 (min:509 max:34601)
CMV disease n,(%)	5, (50,0)
Laboratory values on CMV diagnosis	2,9±1,9
Serum creatinine (mg/dl) (mean±SD)	45±18
eGFR (CKD-EPI)) (ml/min/1.73 m^2) (mean±SE)	2,4±0,4
Serum albumin (g/dl) (mean±SD)	2,9±1,9
Serum CRP(mg/dl) (mean±SD)	3451±1770
24-h proteinuria (mg/d) (mean±SD)	
CMV treatment n,(%)	7, (70,0)

Table-2. Demographic and Clinical Data of Glomerulonephritis Patients, According to CMV Status

	CMV Infection (n:10, 23,3%)	**No CMV Infection (n:33, 76,7%)**	**P-value**	**All patiens (n:43)**
Age (years) (mean±SD)	57±19	49±14	0,183	51±15
Female gender n,(%)	4, (40,0)	11, (33,3)	0,719	15, (34,9)
Laboratory values at GN diagnosis				
Serum creatinine (mg/dl)	4,2±3,2	1,9±1,8	0,006	2,5±2,4
(mean±SD)	29±11	65±8	0,016	57±6
eGFR (CKD-EPI) (ml/min/1.73 m^2)				
(mean±SE)	2,8±0,6	2,7±0,7	0,684	2,7±0,7
Serum albumin (g/dl) (mean±SD)	144±71	221±83	0,012	202±86
Serum LDL (mg/dl) (mean±SD)	6934±6799	8889±7461	0,464	8434±7282
24-h proteinuria (mg/d) (mean±SD)				
Clinical presentation on GN diagnosis				
Nephrotic syndrome n,(%)	3, (30,0)	21, (63,6)	0,079	24, (55,8)
RPGN n,(%)	8, (80,0)	9, (27,3)	0,007	17, (39,5)
Dialysis treatment n,(%)	3, (30,0)	2, (6,1)	0,073	5, (11,6)
Crescents on biopsy n,(%) (n=39)	5, (71,4)	9, (28,1)	0,075	14, (35,9)
Type of glomerular disease			0,007	
Primary GN n,(%)	2, (20,0)	24, (72,7)		26, (60,5)
Secondary GN n,(%)	8, (80,0)	9, (27,3)		17, (39,5)
Total CYC dose (g) (mean±SE)	4,5±1,7	6,7±1,0	0,291	6,2±0,9
Remission n,(%)	6, (60,0)	22, (66,7)	0,719	28, (65,1)
Maintenance treatment n,(%) (n=38)	7, (70,0)	22, (78,6)	0,673	29, (76,3)

P0429 OUTCOMES OF LUPUS NEPHRITIS OVER AN ERA OF EVOLVING IMMUNOSUPPRESSION

Jason McMinn[1], Colin C. Geddes[2], Emily McQuarrie[2]

[1]Forth Valley Royal Hospital, Larbert, United Kingdom and [2]Queen Elizabeth University Hospital, Glasgow, United Kingdom

Background and Aims: The reported incidence of lupus nephritis (LN) is approximately 6.1 cases per million population per year in Scotland based on Scottish Renal Registry biopsy data. Despite immunosuppressive treatment, approximately 10-30% of patients will progress to established renal failure (ERF) within 15 years. In December 2007, our unit moved from a protocol of Cyclophosphamide/ steroid induction with Azathioprine/ Prednisolone maintenance to Mycophenolate/ steroid induction and maintenance. We undertook this study to compare remission rates before and after this change.

Method: A retrospective electronic patient record analysis was performed for all patients in our centre with a documented native renal biopsy showing a histopathological diagnosis of LN, between 1 July 1993 and 31 December 2017. Repeat biopsies were excluded. Baseline demographics, histopathological class and first and second line induction and maintenance therapies were recorded. Endpoints analysed were; partial and complete response (as defined in KDIGO Clinical Practice Guideline for Glomerulonephritis 2012), time to achieve this response, relapse, progression to ERF and death.

Results: 120 patients who underwent a biopsy during the 24.5-year period received a diagnosis of lupus nephritis. 82.5% of patients were Caucasian. Median duration of follow-up was 72 months. 15% of patients died and 5% developed ERF within the follow-up period, representing one death per 56 patient years and one incident case of ERF per 168 patient years.

There were 40 patients in the pre-December 2007 group and 80 in the post-December 2007 group. Those in the earlier group were younger, with a mean age of 35.4 years versus 44.8 years in the later group (p=0.002). 23% had class V in the earlier group compared to 15% in the later group (p=0.31). Proportions of female patients were 80% and 75% in the early and late groups respectively (p=0.54). Median creatinine was 106μmol/L in the pre-December 2007 group and 89.5 μmol/L in the post-December 2007 group (p=0.96).

Patients in the pre- and post- December 2007 groups had comparable rates of complete response, at 72% and 71% respectively. However, those diagnosed before December 2007 were slower to respond, with a median time to achieve complete response of 10.5 months, compared to 6 months in those diagnosed after 1 December 2007 (p=0.007).

Conclusion: Following a change in our immunosuppressive induction regimen from Cyclophosphamide/ steroids to Mycophenolate/ steroids, our response rates have remained similar, however speed of attaining remission has improved.

P0430 **EFFECT OF CORTICOSTEROIDS THERAPY FOR PATIENTS OF IGA NEPHROPATHY WITH CRESCENTS**

Mengjun Liang[1], Aihua Li[1], Zongpei Jiang[1]
[1]*The Six Affiliated Hospital, Sun Yat-sen University, Department of Nephrology, Guangzhou, P.R. China*

Background and Aims: Patients with IgA nephropathy (IgAN) presented proteinuria≥1g/d and eGFR≥50ml/min/1.73m^2 after supportive treatment had been advised 6-month course of corticosteroids therapy. Update of Oxford classification of IgAN had recommended crescents be added to the MEST score for they were predictive of outcome. Whether we should take some more positive therapy for crescents?

Method: We conducted a single-center, retrospective cohort study enrolling 46 patients from 2017.01 to 2018.06, diagnosed with IgAN by renal biopsy. Eligible patients had proteinuria of 0.5∼3.5g/d, eGFR≥30ml/min/1.73m^2 and crescent proportion <50%. Patients were divided into two groups, one for classical steroid treatment (intravenous methylprednisolone 0.25g/d for 3 days at the beginning of months 1, 3 and 5, plus oral prednisone 0.5 mg/kg/d for 6 months, called 1-3-5 Group) and the other assigned an optimized steroid therapy (intravenous methylprednisolone 0.25g/d for 3 days at the beginning of months 1, 2 and 3, plus oral prednisone 0.5 mg/kg/d for 6 months, called 1-2-3 Group). The primary endpoint was remission of proteinuria, secondary endpoint was deterioration in renal function.

Results: There were 23 patients in each group and no significant differences in age, gentle, baseline proteinuria and eGFR between the two groups, except for the proportion of crescents (for Oxford C1 and C2: 52.5% and 13% in 1-3-5 Group vs. 95.7% and 4.3% in 1-2-3 Group respectively, p=0.001). After 6 months therapy, proteinuria in 1-3-5 Group was 0.5(0.2,0.8)g/d (vs. 1.2(0.8,2.6)g/d at baseline, p <0.001) and that in 1-2-3 Group was 0.3(0.2,0.6)g/d (vs. 1.5(0.7,2.6)g/d at baseline, p <0.001). 78.3% of patients in 1-3-5 Group had got remission of proteinuria, while 95.7% in 1-2-3 Group (p=0.187). The 6th month eGFR in 1-3-5 Group was 80.7(59.8,116.2)ml/min/1.73m^2 (vs. 77.5(54.8,104.6)ml/min/1.73m^2 at baseline, p=0.212), while that in 1-2-3 Group was 97.8(68.6,130.9)ml/min/1.73m^2 (vs. 79.5(52.9,108.7)ml/min/1.73m^2 at baseline, p=0.002). The slope of eGFR in 1-3-5 Group was 0.7(-1.7,3.3)ml/min/1.73m^2/month, while that in 1-2-3 Group was 3(1.2,5.4)ml/min/1.73m^2/month, p=0.027. For side effects, two patients in 1-2-3 Group had met bronchitis during the 2nd and 3rh therapy-month respectively; in 1-3-5 Group, one patient had got glaucoma during the 2nd therapy-month and the other had happened steroid-induced diabetes mellitus during the 3rd therapy-month.

Conclusion: Our preliminary results had indicated that optimized steroid therapy had equal effect on reducing proteinuria but more significant advantage to protect against renal function deterioration in IgAN with crescents. 1-2-3 month-steroid pulse therapy had not increase the morbidity of irreversible or severe side effects.

Table1. Clinical features of patients in the two groups

Variable	1-2-3 Group (n =23)	1-3-5 Group (n =23)	P-Value
Age(years)	29.3±9.3	33.9±10.8	0.126
Male/Female(n)	13/10	11/12	0.555
Proteinuria quantification (g/d)	1.5(0.7,2.6)	1.2(0.8,2.6)	0.733
Serum creatinine(μmol/L)	102.1±37.8	98.5±33.1	0.734
eGFR(ml/min/1.73㎡)	79.5(52.9,108.7)	77.5(54.8,104.5)	0.956
Crescent(%)	10.5(7.1,14.2)	5(0,14.2)	0.019
Oxford C(n[%])			0.001
C1	22(95.7)	12(52.5)	
C2	1(4.3)	3(13)	
Lee grade(n[%])			0.461
III	13(56.5)	12(57.1)	
IV	7(30.4)	5(23.8)	
V	1(4.3)	2(9.5)	

Abbreviations: eGFR, Estimated glomerular filtration rate; Oxford C, Crescentic lesions; C1, Crescent in at least 1 glomerulus; C2, Crescent in at least 25% of glomeruli.

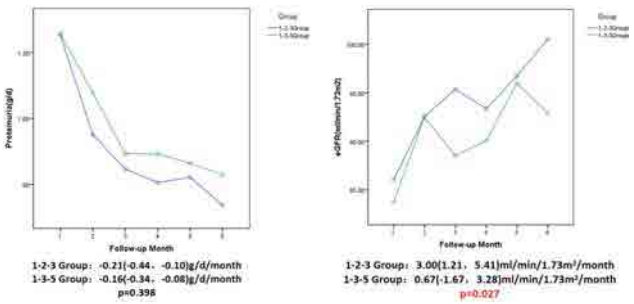


Figure1. Slope of proteinuria and eGFR of patients in the two groups during therapy

P0431

TRENDS OF PRIMARY GLOMERULAR DISEASE IN TURKEY FROM 2009 TO 2017: A REGIONAL REGISTRY REPORT FROM TSN-GOLD WORKING GROUP

Cuma Bulent Gul[1], Mehmet Kucuk[2], Savas Ozturk[3], Erol Demir[4], Necmi Eren[5], Abdullah Sumnu[6], Nurhan Seyahi[7], Mustafa Gullulu[8], Fatih Dede[9], Ülver Derici[10], Yener Koc[11], Garip SAHIN[12], Oktay Oymak[13], Gulizar Manga Sahin[14], Erhan Tatar[15], Belda Dursun[16], Hamad Dheir[17], Süheyla Apaydin[18], Gultekin Suleymanlar[19], Memnune Sena Ulu[20], Orcun Altunoren[21], Sim Kutlay[22], Meral Mese[23], İdris Sahin[24], Sedat Ustundag[25], Kultigin Turkmen[26], Mehmet Emin Yilmaz[27], Rumeyza Turan Kazancioglu[28], Ozcan Uzun[29], Ferhan Candan[30], Zeki Aydin[31], Deren Oygar[32], Nimet Aktas[1], Yunus Erdem[33], Saime Paydas[34], Dilek Guven Taymez[35], Basak Can[36], Ahmet Kıykım[37], Leyla Koc[38], Siren Sezer[39], Murat Duranay[40], Simge Bardak[41], Luftullah Altintepe[42], Burcu Kaya[43], Alper Azak[44], Sabahat Alisir Ecder[45], Caner Cavdar[46], Nedim Yılmaz Selcuk[26]

[1]Bursa Yuksek Ihtisas Training and Research Hospital, Nephrology, Bursa, Turkey, [2]Okmeydanı Training and Research Hospital, Nephrology, Istanbul, Turkey, [3]Haseki Training and Resarch Hospital, Nephrology, Turkey, [4]Istanbul University Medical School, Nephrology, [5]Kocaeli Derince Training and Research Hospital, Nephrology, [6]Medipol Mega University Hospital, Nephrology, istanbul, Turkey, [7]Cerrahpasa University Medical School, Nephrology , [8]Uludag University Medical Faculty Hospital, Nephrology, Bursa, Turkey, [9]Ankara Numune Training and Research Hospital, Nephrology, ankara, Turkey, [10]Gazi University Medical Faculty, Nephrology, Ankara, Turkey, [11]Sisli Hamidiye Training and Research Hospital, Nephrology, Turkey, [12]Osmangazi University, Nephrology, eskisehir, Turkey, [13]Erciyes University, Nephrology, Kayseri, Turkey, [14]Health Science University, Nephrolgy, İstanbul, Turkey, [15]Bozyaka Training and Research Hospital, Nephrology, Izmir, Turkey, [16]Pamukkale University, Nephrology, Denizli, , [17]Sakarya Training and Research Hospital, Nephrology, Turkey, [18]Dr. Sadi Konuk training and reseasrch hospital, Istanbul, Turkey, [19]Akdeniz University Hospital, Nephrology, Antalya, Turkey, [20]Afyon Kocatepe University Medical School, nephrology, Afyonkarahisar, Turkey, [21]Kahramanmaraş Sütçü İmam University, Nephrology, Kahramanmaras, Turkey, [22]Ibn Sina University Hospital, Nephrology, Ankara, Turkey, [23]Kartal Training and Research Hospital, Nephrology, Turkey, [24]Inonu University Medical School, Nephrology, Turkey, [25]Trakya University Medical School, Nephrology, Turkey, [26]Necmettin Erbakan University Meram Medical School, Nephrology, Turkey, [27]Dicle University Medical School, Nephrology, Turkey, [28]Bezmialem University Medical School, Nephrology, Turkey, [29]Dokuz Eylul University Medical school, Nephrology, Turkey, [30]Cumhuriyet University Medical School, Nephrology, Turkey, [31]Darıca Farabi Training and Research Hospital, Nephrology, Turkey, [32]Lefkosa Burhan Nalbantoglu Hospital, Nephrology, [33]Hacettepe University Medical School, Nephrology, Turkey, [34]Cukurova University Medical school, Nephrology, [35]Kocaeli State Hospital, Nephrology , [36]Ok Meydanı Traing and Research Hospital, Nephrology, [37]Mersin University Medical School, Nephrology, [38]Taksim Traing and Research Hospital, Nephrology, [39]Baskent University Medical School, Nephrology, [40]Ankara Traing and Research Hospital, Nephrology, [41]Batman State Hospital, Nephrology, [42]Selçuk University Selcuklu Medical School, Nephrology, [43]Marmara University Medical School, Nephrology, Turkey, [44]Balıkesir Traing and Research Hospital, Nephrology, [45]Medeniyet University Goztepe Traing and Research Hospital, Nephrology and [46]Dokuz Eylul University Medical School, Nephrology

Background and Aims: Several glomerular disease registries in Europe, and they shared their data; however, there was a lack of current data on trends of primary glomerulopathy in Turkey. Glomerular disease patterns can change geographical areas and populations decade by decade. Our aim is to present Turkey's primary glomerular disease pattern from 2009 to 2017.

Method: 3878 native kidney biopsy records were assessed in the Turkish Society of Nephrology Glomerulopathy (TSN-GOLD) Working Group Registry. Secondary disease (lupus, etc.) and transplant biopsies do not enroll in the registry. These records divided into four periods, before 2009, 2009 to 2013, 2013 to 2017, and 2017 to current.

Results: A total of 3858 patients (M = 2173, K = 1685) were examined. There was no difference in the distribution of number of patients according to periods (Q1 = 968, Q2 = 960, Q3 = 968, Q4 = 962). Nephrotic syndrome was the most common biopsy indication in all quarters (58.6%, 53%, 44.1%, 51.6%, respectively). Glomerulopathy types; Membranous GN (29.9%, n = 290) was the first in Q1 and IgA nephropathy (17.7%, n = 172) was the second. IgA nephropathy (28.5%, n = 274) was the most common glomerulopathy in Q2, while Membranous GN (25.5%, n = 245) was the second most common. IgA nephropathy (29.9%, n = 285) was the most common glomerulopathy in Q3, followed by FSGS (22.9%, n = 222) and Membranous GN. In Q4, FSGS (26.8, n = 258) was the most common glomerulopathy, followed by IgA nephropathy (26.7%, n = 257) and Membranous GN (24.5%, n = 236) (Figure 1).

Conclusion: While biopsy indications did not change over the years, the incidence of FSGS and IgA nephropathy gradually increased.

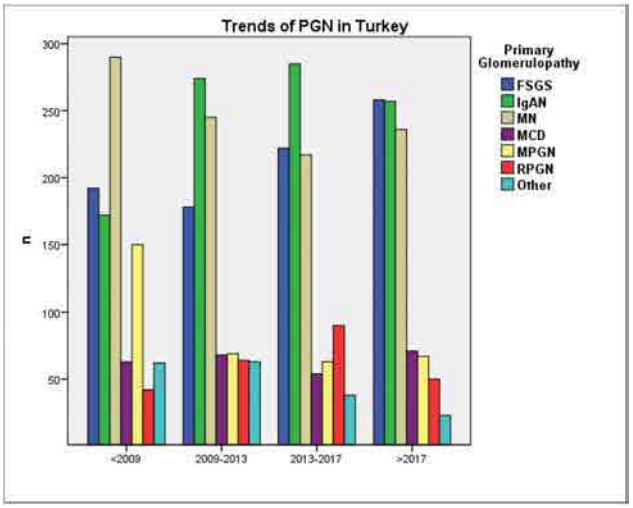


Figure legend: Trends of primary glomerulopathy in Turkey from 2009 to 2017. The data from the Turkish Society of Nephrology, Glomerular Disease Working Group Registry (TSN-GOLD). FSGS: Focal segmental glomerulosclerosis, IgAN; immunoglobulin A nephropathy, MN; membranous glomerulonephritis, MCN; minimal change disease, MPGN; membranoproliferative glomerulonephritis, RPGN; rapidly progressive glomerulonephritis.

P0432 GAMMA DELTA T-CELLS PHENOTYPIC PROFILE IN PATIENTS WITH IGA-NEPHROPATHY

Darya Nizheharodava[1,2], Kirill Komissarov[1,3], V. Pilotovich[4], Maryna Zafranskaya[1,2]

[1]Belarusian Medical Academy of Postgraduate Education, Immunology and Biomedical Technology Department of Scientific and Research Labour, Minsk, Belarus, [2]International Sakharov Environmental Institute of Belarusian State University, Immunology Department, Minsk, Belarus, [3]Minsk Scientific Practical Center of Surgery, Transplantation and Hematology, Nephrology, dialysis and kidney transplantation department, Minsk, Belarus and [4]Belarusian Medical Academy of Postgraduate Education, Urology and Nephrology Department, Minsk, Belarus

Background and Aims: γδT-lymphocytes are enigmatic minor nonconventional peripheral blood cells population responded to non-peptidic antigens and displayed functional diversity, from effector action to immunoregulation, depending on pathological conditions. Although γδT-lymphocytes are known to play a key role in chronic inflammation, their phenotype and functions in patients with chronic kidney diseases (CKD) are relatively unknown. The aim of this study was to investigate a surface phenotype of γδT-lymphocytes in patients with IgA-nephropathy (IgAN) compared to systemic lupus erythematosus (SLE) and chronic glomerulonephritis (CG) due to focal-segmental glomerulosclerosis and minimal change disease patients.

Method: The peripheral blood was obtained from 23 CKD patients (13 IgAN, 5 SLE and 5 GN patients) aged of 32.0 (26.7 ÷ 36.0) y.o., male/female ratio as 12/11. The number of γδT-lymphocytes was determined using monoclonal antibodies γδTCR-PC5, CD3-PC7 as well as phenotypic profile – with CD45RO-ECD and CD27-PE, CD314-PE (NKG2D), CD8-FITC, CD56-PC7 and CD16-ECD and TLR4-FITC using flow cytometry analysis (Cytoflex, «Beckman Coulter», USA). Statistical analysis was done using Statistica 8.0.

Results: The increased number of γδT-cells in peripheral blood of IgAN patients (4.85 (4.13÷8.87)%) compared to SLE patients (3.31 (2.88÷3.48)%; p=0.001) and CG patients (1.14 (0.94÷3.15)%; p=0.03) was established. More than half of γδT-cells in IgAN patients expressed central memory phenotype ($\gamma\delta TCR^+CD45RO^+$: 50.2 (31.6÷61.3)%; $\gamma\delta TCR^+CD27^+$: 58.7 (55.5÷61.8)%) enhancing phosphoantigen-dependent activation, survival, proliferation, and secretion of pro-inflammatory cytokines. Terminally differentiated effector memory $\gamma\delta TCR^+CD45RO^-CD27^-$ phenotype of γδT-cells was dominated in GC patients ($\gamma\delta TCR^+CD45RO^+$: 25.7 (24.0÷27.5)%; $\gamma\delta TCR^+CD27^+$: 43.3 (30.4÷56.2)%; p=0.05) regarded as "exhausted senescent" T cells with poor proliferation and severe functional abnormalities. The cytotoxic properties of γδT-cells in IgAN patients are characterized with significantly higher expression of killer recognition receptor NKG2D ($\gamma\delta TCR^+CD314^+$: 91.7 (51.7÷93.0)%) as well as true effector cytotoxic $CD56^+$ marker ($\gamma\delta TCR^+CD56^+$: 44.4 (27.2÷58.6)%) but not CD16 or CD8 antigens compared the both SLE and CG (p=0.05). Moreover, the number of $\gamma\delta TCR^+CD314^+$ and $\gamma\delta TCR^+CD56^+$ as well as $\gamma\delta TCR^+CD45RO^+$ inversely correlated with glomerular filtration rate (R=-0.6, p=0.05). The increase of pattern recognition receptor TLR4 expression on γδT-cells was reported in all groups of CKD patients suggested the activated state of γδT-cells and their important role in the control of infection.

Conclusion: In IgAN patients the phenotypic profile of γδT-lymphocytes is characterized as central memory $\gamma\delta TCR^+CD45RO^+CD27^+$ cells with increased cytotoxic potential ($CD314^{high}CD56^{high}CD16^{low}CD8^{low}$) what is functionally differed from ones in SLE and GC patients. The inverse correlation of γδT-cells phenotype profile with glomerular filtration rate suggests their pathological role and possible contribution to the initiation of autoimmune inflammation in IgAN patients.

P0433 AGE-RELATED DIFFERENCES IN THE SPECTRUM OF BIOPSY-PROVEN GLOMERULONEPHRITIS

Cristina-Stela Capusa[1,2], Nicolae Pana[1], Otilia Popa[1], Laura Chiotan[1], Eugen Mandache[2], Mariana Lipan[2], Daniela Dumitru[2], Gabriel Mircescu[1,2]

[1]"Carol Davila" University of Medicine and Pharmacy, Nephrology, Bucharest, Romania and [2]"Dr. Carol Davila" Teaching Hospital of Nephrology, Nephrology, Bucharest, Romania

Background and Aims: The proportion of geriatric population is increasing globally and age-related changes, as kidney ageing and decline in immunocompetence, might interfere with frequency of various glomerulopathies (GP). Thus, it is conceivable that the spectrum of biopsy-proven GP varies across different age categories. Accordingly, we aimed to describe age-related variation in clinical presentation and the in prevalence of GP diagnosed by kidney biopsy (KB) in adults.

Method: This retrospective study enrolled 1254 subjects selected from the KB database of a large tertiary academic Nephrology center (which provides specialized care for the south-eastern part of our country), over a ten-year span (01.01.2008-31.12.2017). Inclusion criteria were age >18 years, native kidney biopsy, availability of data from light, immunofluorescence, and electron microscopy, and a histologic diagnosis of GP. Repeated biopsies and inadequate tissue samples were excluded. Demographic (age, gender), clinical and laboratory data at the time of biopsy were extracted from medical records for all the selected subjects.

To investigate the possible influence of age on the spectrum of biopsy-proven GP, the cohort was divided into 4 categories: young adults (18 to 30 years, n=156), adults (31 to 64 years, n=868), elderly (65 to 74 years, n=176) and very elderly (≥75 years, n=54), and the collected data were compared by non-parametric methods (Mann-Whitney, Chi^2 and Fisher exact tests).

Results: The nephrotic syndrome was the most common presentation form in all age groups but had a higher prevalence in very elderly (62%) and elderly (55%) as compared to adults (37%, p=0.01) and young adults (41%, p<0.001). In the groups below age of 65, the chronic nephritic syndrome was the second most common indication for KB (31% and 28%, respectively), followed by chronic renal failure in adults (13%) and acute nephritic syndrome in young adults (10%).

Lupus nephritis (LN) and IgA nephropathy (IgAN) were the most commonly diagnosed GP in young adults (22% each), followed by minimal change disease (MCD, 14%), membranous nephropathy (MN, 8%), focal and segmental glomerulosclerosis (FSGS, 8%), and thin basement membrane disease (6%). In adults, the most common GP were: IgAN (23%), MN (15%), diabetic nephropathy (DN, 11%) and MCD (10 %).

Conversely, in both the elderly and the very elderly, the most common biopsy-proven GP was MN (26% each). Elderly had renal amyloidosis as the second most prevalent histological diagnosis (17%), followed by DN (11%), and by IgAN and MCD (≈10% each). Crescentic glomerulonephritis (CGN) occurred in 7.5% of the elderly, but it was the second pathology (17%) in subjects aged 75+ years, followed by MCD (15%) and DN (13%). IgAN and amyloidosis were identified in about 5% of this group.

It appears that the prevalence of both clinical presentation and histologically diagnosed GP showed some similarities between the first two and, respectively, last two age categories.

Conclusion: Biopsy-proven GP have different frequencies depending on the patient's age, with some pathologies predominantly found at older ages (such as membranous nephropathy, amyloidosis and crescentic GN) or, on the contrary, typical for young adults (lupus nephritis and IgAN). These differences account for the distinct clinical presentations at the time of KB.

P0434

COST-EFFECTIVENESS OF MAINTANCE THERAPY WITH AZATHIOPRIME VERSUS RITUXIMAB (TAILORED OR FIXED-SCHEDULE) IN ADULTS WITH GENERALIZED ANCA VASCULITIS IN COLOMBIA

Kateir Mariel Contreras[1], Viviana Orozco Ortiz[2], Eduardo José Puche[1], Paola Karina Garcia[1], Camilo Alberto Gonzalez[1], Martha Patricia Rodriguez[1], Diego Rosselli[4]

[1]Pontificia Universidad Javeriana, Nephrology, Bogotá, Colombia, [2]Pontificia Universidad Javeriana, Nephrology, Bogotá, Colombia and [4]Pontificia Universidad Javeriana, Clinical Epidemiology and Biostatistic, Bogotá, Colombia

Background and Aims: Azathioprine has been for decades the drug of choice for maintenance therapy in patients with generalized ANCA vasculitis in remission. However, recent studies show that rituximab, a high-cost biological agent, which can be administrated in two different schedules, might be more effective, so it is necessary to know the cost- effectiveness.

Our goal was to compare the cost-effectiveness of the 3 maintenance schemes: standard therapy with azathioprine; fixed-dose rituximab and rituximab tailored according to CD19 lymphocyte level and ANCA titres, from the perspective of the Colombian healthcare system.

Method: We designed a 5-year annual cycle Markov model with the following stages: remission, minor relapse, mayor relapse and death. Transition probabilities were obtained from a systematic review of the literature (Scopus and Pubmed). Following national guidelines for economic studies, costs (in 2018, 1 euro = 3489 Colombian pesos) were estimated based on national drug registries, and official tariff manuals for procedures and other resources. Main outcome was quality-adjusted life years (QALY), using lupus nephropathy as a proxy; values were obtained from Tufts CEA Registry and validated by local expert panel through a modified Delphi technique. Cost-effectiveness threshold was three-times per capita GDP (16.872 euros). Discount rate was 5%. Univariate and probabilistic sensitivity analyses were performed.

Results: Overall discounted 5-years costs were € 1149 for azathioprine; € 4025 for tailored rituximab and € 5221 for fixed rituximab. QALY gains were 2.94, 3.63 and 3.64, respectively. Both tailored and fixed rituximab were cost-effective (cost per QALY gained: € 4168 and € 5817 respectively), but tailored dosing was preferable due to its lower cost. Sensitivity analyses did not modify these results significantly.

Conclusion: To our knowledge this is the first economic evaluation that compare azathioprine with tailored and fixed rituximab regimens as a vasculitis maintenance treatment in adults with ANCA generalized. Due to its lower effectiveness azathioprine should not be the first line of treatment. Tailored rituximab should be a better option than fixed schedule due to its lower cost with similar effectiveness.

P0435 PREDICTORS OF RENAL SURVIVAL IN ELDERLY NEPHROTIC SYNDROME

Tasnim Ben ayed[1,2,3], Imen Gorsane[1,2,3], Raja Trabelsi[1,2], Mondher Ounissi[1,2], Taieb Ben Abdallah[1,2,3]

[1]Charles Nicolle Hospital, Department of Medicine A, Tunis, Tunisia, [2]Faculty of Medecine, El manar university, Tunis, Tunisia and [3]Charles Nicolle Hospital, Laboratory of Research in Immunology of Renal Transplantation and Immunopathology (LR03SP01), Tunis, Tunisia

Background and Aims: With increasing longevity, the numbers of elderly patients presenting with renal diseases including glomerular disease are increasing. Nephrotic syndrome (NS) is a common presentation of glomerular disease in the elderly. We performed this study to assess predictors of renal survival in this population.

Method: A retrospective study including one hundred and six patients aged 65 years or more hospitalized for NS in the Internal Medicine department A of Charles Nicolle hospital at Tunis, between January the 1st, 1975 and December the 31st, 2016.

A multivariate study was carried out, the dependent variable being the evolution towards end-stage renal disease (ESRD).

Results: We studied 106 patients with an average age of 70 ± 4.5years [65-83 years] with a sex ratio (M/F) of 1.7. Twenty-three percent of patients were diabetic. The median proteinuria was 4.6 [3-19.5 g/l], the mean albumin level was 20 ± 5.6g/l and the mean protidemia was 50 ± 6.9 g/l. Nephrotic syndrome was impure in 89.6 % of patients with high blood pressure in 70.5 % of cases, hematuria ≥2 + in 34.7% of cases and renal failure in 88.4 % of cases. The renal biopsy was performed in 41 patients. The most common glomerular lesions were Membranous nephropathy (29 %) followed by amyloidosis (27 %). NS was secondary in 63.2 % of cases mainly to amyloidosis (35.8 %) and diabetes (19.8 %). Idiopathic nephropaty was dominated by membranous nephropathy (11.3 %) and primitive membranoproliferative glomerulonephritis (MPGN) (6.6 %). At the end of follow-up, 35 % of patients achieved complete or partial remission and 58.5 % progressed to ESRD. The multivariate study found as independent risk factors of progression to ESRD uremia ≥ 17 mmol/l (ORa =33.2 [1.3 - 837.7]; $p<0.05$), phosphoremia ≥ 1.6 mmol/l (ORa=22.1 [1.8-266.5]; $p<0.05$), potassium concentration ≥ 4.3mmol/l (ORa=24.7 [2.4,251.5]; $p<0.01$), extra-renal signs (ORa=38,9 [2.4 - 634.3]; p: 0.01), secondary nephropathy (ORa=74 [3.1 - 1788.2]; $p<0.01$) and MPGN (ORa=48[1.4 - 1675.5]; $p<0.05$). The protective factors were hemoglobinemia ≥ 9.3g/dl (ORa=0.007 [0 - 0.2]; $p<0.01$), kidneys well differentiated on ultrasound (ORa=0.032 [0.003 - 0.4]; $p<0.01$) and treatment with two diuretics (ORa=0.03 [0.003 - 0.4]; $p<0.01$).

Conclusion: Elderly NS was characterized by a poor prognosis, in particular secondary to delayed and non-uniform treatment strategies, hence the need for rising physician awarness about this decease and consultation on a standardized treatment strategies.

P0436 REFRACTORY IGA NEPHROPATHY. A MULTICYTOKINE NORMALIZED LEVELS THERAPY FOR T CELLS IMBALANCE

MIGUEL URIOL[1], Aina Obrador Mulet[1], Ana Tugores[1], Vanessa Daza[2], Ana Gomez[3], Joan Gasco[1]

[1]Son Espases University Hospital, Nephrology, Palma, Spain, [2]Son Espases University Hospital, Immunology, Palma, Spain and [3]Son Espases University Hospital, Pharmacy, Palma, Spain

Background and Aims: Interleukine-17(IL-17) is a pro-inflammatory cytokine which influences in glomerulonephritis (GN) in animal models. IgA nephropathy (IgAN) is a primary GN with auto-inflammatory and autoimmune features. Imbalances in Th1/Th17 and Treg/Th17 have been associated with the pathogenesis of the IgAN. We evaluated the effect of sequential treatment with a selective vitamin D receptor activator and with an IL-17 blocker in patients with refractory IgA GN (r-IgAN).

Method: Five patients with r-IgAN (previously treated with steroids, mycophenolate, tacrolimus and a renin-angiotensin-aldosterone system inhibitor) were treated initially with paricalcitol and six months later with secukinumab (IL-17A blocker) with the objective to improve anti-inflammatory and subsequentially inhibit pro-inflammatory milieu, respectively. We evaluate the evolution of the proteinuria, haematuria, plasma creatinine and *urinary* N-acetyl-beta-D-glucosaminidase: u-NAG, as a measure of lysosomal activity during the first month of treatment (induction phase) and at month 3 after treatment. We also evaluate the evolution of the evolution of the Th1/Th17 and Treg/Th17 ratio in whole blood. We evaluated the changes at month (M) 0, 1 and 3.

Results: Five males were included. Age: 43±11 years. Proteinuria (24h-collected) decreased along the study from 3.5, 2.1 to 1.6g ($P<0.01$) at M0, M1 and M3 respectively. Four (80%) patients who presented haematuria at month 0 disappeared at month 3. Creatinine did not show changes over time (1.84, 1.88 and 1.95 mg/dl for M0, M1 and M3, P=0.44). uNAG increased after induction phase from 7.2 to 9.8(P= 0.01) and finally decreased to 8.3 at month 3(P=1, respect to month1). Uric acid decreased but not significantly from 8.0, 7.1 and 7.6g/dl at any time point. The ratio Th1/Th17 and Treg/TH17 changed from the month 0 to month 3, from 1.8 to 2.6 (P =0.25) and 0.23 to 0.32 (P=0.16), respectively.

Conclusion: Sequential treatment was associated with a reduction in proteinuria and haematuria was well controlled.

The changes in u-NAG suggest and intensive initial effect on the lysosomal activity since no changes in renal function was observed.

The theoretical benefit of the Th1/Th17 and Treg/Th17 ratio represents a new modality of treatment that need to be rigorously evaluated for its clinical implication in r-IgAN patients.

P0437 **IS RENAL BIOPSY NEEDED FOR THE DIAGNOSIS OF NEPHROPATHIES OR IT IS SUFFICIENT WITH A CLINICAL DIAGNOSIS?**

Leonardo Calle Garcia[1], Astrid Rodriguez Gomez[1], Manuel Heras Benito[2], Giomar Urzola Rodriguez[1], Maria Jose Fernandez-Reyes Luis[1]

[1]Complejo Asistencial de Segovia, Nephrology, SEGOVIA, Spain and [2]Hspital Universitario de Salamanca, Nephrology

Background and Aims:

Percutaneous renal biopsy (PRB) guided by ultrasound is the gold standard for the diagnosis of nephropathies and glomerulopathies. Sometimes, comorbidity and relative contraindications for PRB could condition us to consider clinical diagnosis as sufficient to treat renal pathology. This is a continuous challenge for the nephrologist due to the prognostic and therapeutic diversity of the different types of nephropathies. Therefore, we wonder if in most cases it is still necessary to perform PRB, or clinical diagnosis would be enough in a significant number of them. We decided to assess our PRB series over 15 years, comparing clinical and biopsy diagnosis, and learning about the complications associated with the technique.

Method:

Cross-sectional analysis of the 262 PRB conducted between January 2003 and December 2018. In our department, before performing the PRB, doctors always make a clinical report with different diagnostic possibilities that facilitates the pathologist's work. For this study the first diagnostic option, being the most clinically compatible with the patient, was always taken. We also collected socio-demographic data, clinical data (hypertension and diabetes mellitus), pre and post-biopsy diagnosis, and complications associated with the technique. For the statistical analysis, the SPSS 15 program was used to calculate frequencies, and the Kappa coefficient for diagnostic concordance.

Results:

262 PRB were performed, of which 149 (56.9%) were performed in men and 113 (43.1%) in women. Average age: 58.6 $\pm$ 19.2 years. 173 patients were hypertensive (66%) and 50 had DM (19.1%). Renal pathologies by age are similar to the data reported by Spanish Society. The table shows the concordance measured by the kappa coefficient in the pre and post-PRB diagnosis of the most frequent nephropathies. There were 15 PRB with complications (5.8%): 12 minors (4.6%, haematuria and hematoma); and 3 major: 2 haemorrhages (0.8%) and 1 nephrectomy (0.4%). 33 PRB (12.6%) were inconclusive due to insufficient material.

Conclusion:

From the data obtained, a high mismatch was observed in very common nephropathies in our environment, such as IgA nephropath and pauci-immune focal and segmental necrotizing glomerulonephritis. In contrast, PRB showed more cases of diabetic nephropathy and tubulointerstitial nephropathy. In the case of the pathologies due to nephrotic syndrome (table) we find a high discordance. This may be due to the fact that in all of those cases there was an initial nephrotic syndrome, and our clinical diagnosis was partly based on the frequency of glomerulopathies in the adult. In conclusion, the different concordances between pre and post-biopsy diagnoses show us that clinical diagnosis is not enough to obtain a final diagnosis. In most cases PRB is necessary for the definitive diagnosis. In addition, after the introduction of the ultrasound, complications have decreased, especially when the biopsy is performed by the nephrologist.

Table: Pre and post biopsy diagnosis concordance (Kappa coefficient)

	CLINICAL DIAGNOSIS (pre biopsy)	FINAL DIAGNOSIS (post biopsy)	Kappa Coefficient (all cases)
IgA nephropathy	64	35	0.57
Pauci-immune glomerulonephritis	36	24	0.55
Membranoproliferative glomerulonephritis	23	16	0.475
Diabetic nephropathy	14	27	0.502
Acute Tubulointerstitial nephropathy	10	13	0.046
Chronic Tubulointerstitial nephropathy	8	10	0.080
Membranous nephropathy	49	26	0.341
Minimal change disease	8	19	0.265
Amyloidosis	9	9	0.195
Focal segmental glomerulosclerosis	7	10	0.089

P0438

PREDICTORS OF TREATMENT RESPONSE AND LONG-TERM OUTCOME IN PATIENTS WITH PAUCI-IMMUNE GLOMERULONEPHRITIS AND SEVERE RENAL DYSFUNCTION AT DIAGNOSIS

Sophia Lionaki[1], Smaragdi Marinaki[1], Petros Kalogeropoulos[1], George Liapis[2], Harikleia Gakiopoulou[2], Helen Kapsia[1], Athanasios Tzioufas[3], Ioannis Boletis[1]

[1]Laiko Hospital, National & Kapodistrian University of Athens, Faculty of Medicine,, Nephrology Department & Transplantation Unit, Athens, Greece, [2]Laiko Hospital, National & Kapodistrian University of Athens, Faculty of Medicine, Greece, Pathology Department, Athens, Greece and [3]National & Kapodistrian University of Athens, Faculty of Medicine, Greece, Department of Pathophysiology, Athens, Greece

Background and Aims: Severe kidney involvement represents a frequent clinical scenario for patients with pauci-immune (PI) vasculitis. We aimed to explore the factors, which are associated with prognosis, in short and long term, following administration of appropriate immunosuppressive therapy.

Method: Patients were included if they had biopsy proven PI glomerulonephritis (GN) with estimated GFR<20 ml/min/1.73 m^2 or dialysis requirement at presentation, received standard immunosuppression and were followed for a minimum period of one year. We recorded clinical, laboratory and histopathological parameters at diagnosis, at 3 months, at 1 year and at the end of follow up. Outcomes of interest included response to treatment, end stage kidney disease (ESKD), and death. Treatment response was defined by the ability to come off dialysis with an eGFR>20 ml/min/1.73 m^2 with no signs of vasculitis. Histopathological evaluation included arteriosclerosis, % of normal glomeruli, activity index, chronicity index.

Results: A total of 83 patients, with a mean age of 59.6 (15.05) years were included. There were, 45 males (54.2%). After 3 months, 59 patients (71.1%) had responded to immunosuppressive therapy, 16 (19.3%) were dialysis depended, 5(6.02%) died and 2 were lost in follow up. By the end of the 1st year, 59 patients (71.1%) achieved remission, 16(19.3%) ended up in ESKD and 6(7.4%) died. Factors which were associated with treatment response included MPO-ANCA positivity [odds ratio OR:3.9, 95%CI (1.13-13.37) p=0.03], eGFR>10ml/min/1.73m^2 at presentation [OR:2.5, 95% CI(0.86-7.30), p=0.009], normal glomeruli >10% [OR:3.8, 95%CI (1.24-12.1), p=0.02], and chronicity index more than 6 [OR:6.2, 95% CI(1.77-22.4), p=0.004]. Risk factors associated with ESKD included non-response to immunosuppressive therapy [Relative Risk RR:0.05, 95%CI (0.01-0.2) p<0.0001)], normal glomeruli<10% in the diagnostic biopsy [RR: 2.9, 95% CI (1.38-6.32), p=0.005] and age>75 years [RR:3.2, 95% CI (0.9-10.6) p=0.055]. Two of the 6 deaths were disease related.

Conclusion: A significant proportion of patients with PI-GN, who presented with severe renal dysfunction, responded to immunosuppressive therapy and recovered renal function approximately 3 months after initiation of therapy. The most important risk factors for ESKD were age>75 years, <10% normal glomeruli in the diagnostic kidney biopsy and non-response to immunosuppressive therapy.

P0439 THE RELATIONSHIP BETWEEN SOCIO-ECONOMIC STATUS AND RENAL VASCULITIS IN SCOTLAND

Oshorenua Aiyegbusi[1], Marina Frleta-Gilchrist[1], Malcolm MacKinnon[1], Jamie Traynor[1], Kate Stevens[1], Colin C. Geddes[1], Emily McQuarrie[1]

[1]*Queen Elizabeth University Hospital, Greater Glasgow and Clyde, Renal and Transplant Unit, Glasgow, United Kingdom*

Background and Aims: Individuals living in areas of multiple socioeconomic deprivation have reduced life expectancy and experience health inequalities. Chronic kidney disease is more common in areas of social deprivation and these patients are more likely to develop end stage kidney disease. Vasculitis is a rare but significant cause of kidney disease. The impact of socioeconomic status on disease activity or outcomes in patients with ANCA Associated Vasculitis (AAV) is yet to be fully explored. The aim of this study was to establish whether there is an association between the incidence of biopsy-proven renal vasculitis and socioeconomic status, as measured by the Scottish Index of Multiple Deprivation (SIMD).

Method: Using the Scottish renal biopsy registry, we identified all adult native renal biopsies performed across Scotland between 2014 and 2018 with a diagnosis of AAV. Patient's postcode and SIMD (2016) rank were recorded. Patients were separated into quintiles of SIMD rank. Baseline demographics were recorded. We derived the denominator population from the 2016 SIMD census. Data were calculated per million population (PMP) served.

Results: 339 biopsy proven cases of AAV were identified. 6 cases were excluded as postcode was unavailable. Overall, mean age was 65.9 (±13.0) years and 45% of patients were male. At time of diagnosis, mean estimated glomerular filtration rate (eGFR) was 61.7 (±25.7) ml/min/1.73m^2 and median urinary protein creatinine ratio (uPCR) was 134mg/mmol (IQR 64-21). Microscopic Polyangiits n=205(65%) was more common than Granulomatosis with Polyangiits n=128(35%). The incidences of kidney biopsy proven AAV were similar across all quintiles of deprivation. In the most deprived 20% of population, incidence rate of kidney biopsy proven AAV was 11.2 per million person-years vs 13.0 per million person-years in least deprived 20% of population. Patients in areas of greatest relative deprivation were younger (64.0 (±12.3) vs. 68.1 (±12.7) years) and had slightly less proteinuria at diagnosis (99mg/mmol (IQR 35-211) vs. 138mg/mmol (IQR 78-281)) when compared to patients living in least deprived areas. However, there was no difference in level of renal function at diagnosis (33.8 (±29.6) ml/min/1.73m^2 vs 31.5 (±23.2) ml/min/1.73m^2).

Conclusion: Our complete national dataset shows that there is no significant difference in incidence of renal AAV across the spectrum of socioeconomic deprivation. The analysis of renal function at presentation suggests no evidence of an association between deprivation and delay in diagnosis in a healthcare system free at the point of access.

P0440 **EPIDEMIOLOGICAL AND CLINICAL CHARACTERSTICS OF IGA NEPHROPATHY PATIENTS IN TURKEY: TSN-GOLD WORKING GROUP.**

Necmi Eren[1], Meltem Gursu[2], Egemen Cebeci[3], Aydin Turkmen[4], Hasan Haci Yeter[5], Nurhan Seyahi[6], Serhan Vahit Piskinpasa[7], Alpaslan Ersoy[8], Taner Basturk[9], Gulizar Manga Sahin[10], Fatma Sibel Kocak Yucel[11], Ahmed Bilal Genç[12], Garip SAHIN[13], Memnune Sena Ulu[14], Merve Soyhan[15], Kultigin Turkmen[16], Sumeyra Ozberk[17], Omer Elcioğlu[2], Orcun Altunoren[18], İdris Sahin[19], Sim Kutlay[20], Sedat Üstündağ[21], Betul Kalender[22], Fatih Dede[23], Bulent Altun[24]

[1]Kocaeli University, Faculty of Medicine, Division of Nephrology, Kocaeli, Turkey, [2]Bezmialem Vakif University, Faculty of Medicine, Division of Nephrology, Istanbul, Turkey, [3]Haseki Training and Research Hospital, Division of Nephrology, Istanbul, Turkey, [4]Istanbul University, Istanbul Medical Faculty, Division of Nephrology, Istanbul, Turkey, [5]Gazi University, Faculty of Medicine, Division of Nephrology, Ankara, Turkey, [6]Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Division of Nephrology, Istanbul, Turkey, [7]Ankara Numune Training and Research Hospital, Nephrology, Ankara, Turkey, [8]Uludağ University Faculty of Medicine, Division of Nephrology, Bursa, Turkey, [9]Şişli Etfal Training and Research Hospital, Division of Nephrology, Istanbul, Turkey, [10]Sultan Abdülhamid Han, Training and Research Hospital, Division of Nephrology, Istanbul, Turkey, [11]Bakirkoy Training and Research Hospital, Division of Nephrology, Istanbul, Turkey, [12]Sakarya University, Faculty of Medicine, Division of Nephrology, Adapazari, Turkey, [13]Eskişehir Osmangazi University, Faculty of Medicine, Division of Nephrology, Eskisehir, Turkey, [14]Afyon Saglik Bilimleri University, Faculty of Medicine, Division of Nephrology, Afyonkarahisar, Turkey, [15]Bozyaka Training and Research Hospital, Division of Nephrology, Izmir, Turkey, [16]Necmettin Erbakan Üniversity, Meram Medical Faculty, Division of Nephrology, Konya, Turkey, [17]Erciyes University, Faculty of Medicine, Division of Nephrology, Kayseri, Turkey, [18]Kahramanmaras Sutcu Imam University, Faculty of Medicine, Division of Nephrology, Kahramanmaras, Turkey, [19]Inonü University, Faculty of Medicine, Division of Nephrology, Malatya, Turkey, [20]Ankara University, Faculty of Medicine, Division of Nephrology, Ankara, Turkey, [21]Trakya University, Faculty of Medicine, Division of Nephrology, Edirne, Turkey, [22]Kocaeli University, Faculty of Medicine, Division Of Nephrology, Kocaeli, Turkey, [23]Ankara Numune Training and Research Hospital, Division of Nephrology , Ankara, Turkey and [24]Hacettepe University, Faculty of Medicine, Division of Nephrology, Ankara, Turkey

Background and Aims: According to the data of the Turkish Society of Nephrology-Glomerular Diseases Working Group (TSN-GOLD Working Group), IgA nephropathy is the most common primary glomerular disease in Turkey. The purpose of this study was to investigate the epidemiological and clinical data of IgA nephropathy patients in Turkey.

Method: 4399 patients with primary glomerular diseases from 47 centers who were followed up between May 2009 and May 2019 were included in the study conducted by TSN-GOLD Working Group. 524 patients were excluded due to lack of pathological data. Among the remaining patients, demographic, clinical and laboratory data of 994 patients with IgA nephropathy were analyzed.

Results: The median age of the patients was 37 (28-47) years, and 37.3% of them were female. The laboratory and clinical data at the time of diagnosis is presented in Figure-1, and biopsy indications are described in Figure-2. The median number of glomeruli was 16 (IQR: 3.5-4.3), sclerotic glomeruli was 2 (IQR: 1-5), and segmental sclerotic glomeruli was 1 (IQR: 1-2). Exudative changes, subendothelial and subepithelial deposition were present in 566 patients (56.9%), 46 patients (4.6%) and in 38 patients (3.8%), respectively. 662 (66.1%) and 611 of the patients (61.4%) had tubular atrophy and interstitial fibrosis in varying degrees, respectively. 672 (%67.6) and 416 patients (%41.9) had interstitial inflammation and vascular changes, respectively. In immunofluorescence staining, 18%, 30.1%, 4.4%, 68% of the patients had IgG, IgM, C1q and C3 positivity, respectively. Crescentic glomeruli were detected in 227 patients (3.3 ± 3.1 glomeruli). Patients with crescentic glomeruli had significantly higher proteinuria and lower eGFR than the patients without [2203 mg/day (15-26078) vs 1807 mg/day (15-29112); p=0.001; 55.3 ml/min/1.73 m^2 (3.72-141.9) vs 72 ml/min/1.73 m^2 (3.84-150.81); p<0.001, respectively]. Oxford classification was applied to 544 patients. Endocapillary hypercellularity (E1), mesengial hypercellularity (M1), tubular atrophy and interstitial fibrosis (T1 and T2), segmental sclerosis (S1) were present in 126 (13%), 425 (42.8%), 306 (30.8%) and 325 patients (%32.7), respectively. Proteinuria levels were higher in patients with endocapillary hypertrophy, mesengial hypercellularity, tubular atrophy-interstitial fibrosis and segmental sclerosis. eGFR levels were lower in patients with endocapillary hypertrophy, tubular atrophy-interstitial fibrosis and segmental sclerosis (Figure-3).

Conclusion: In this study we found that, the most common presentation of IgA nephropathy patients in our country was asymptomatic urinary abnormalities followed by nephritic and nephrotic syndrome. Higher proteinuria and lower eGFR values in patients with crescentic glomeruli, support the adoption of crescentic lesions in the new Oxford classification (MEST-C) to predict more precise outcome of IgA nephropathy patients. The high number of patients to whom the Oxford classification was applied provided us with the opportunity to examine the clinical reflections of pathological features. Evaluation of the follow-up data of the patients will give us the possibility to reveal the effect of initial clinical and pathological features on clinical findings and renal outcome.

	Number of patients (n)	%
Hypertension	321	32.3
RAAS usage rate	314	31.6
Microscopic hematuria	633	63.7%
Blood pressure (systolic/ diastolic, mmHg)	130/80	
	Median	**IQR**
Urea (mg/dl)	41	29-61
BUN (mg/dl)	20	14-29
Creatinine (mg/dl)	1.2	0.9-1.8
eGFR (mL/min/1.73 m^2)	68.15	41.5-101.1
Protein (g/dL)	6.9	6.3-7.3
Albumin (g/dL)	3.9	3.5-4.3
Proteinuria (mg/day)	2000	1000-3402
Uric acid (mg/dL)	6.5	5.2-7.9
Glucose (mg/dL)	91	84-99
Triglycende (mg/dL)	153	107-218
Total cholesterol (mg/dL)	204	173-244
HDL cholesterol (mg/dL)	43	35-52
LDL cholesterol (mg/dL)	126	100-158
Hemoglobin (g/dL)	13.2	11.8-14.6
Hematocrit (%)	39	35-43
Sedimentation (mm/hour)	23	12-39

Data are presented as mean±SD or median (interquartile range) unless otherwise indicated

Figure 1: Laboratory and clinical data at the time of diagnosis

	Number of patients	%
Nephrotic syndrome	191	19.2
Nephritic syndrome	321	32.3
Mixt nephrotic syndrome	56	5.6
Asymptomatic urinary abnormalities	328	33.0
Hematuria and pyuria	26	2.6
Non- nephrotic proteinuria	139	14.0
Non- nephrotic proteinuria and hematuria	152	15.3
Non- nephrotic proteinuria, hematuria and casts	9	0.9
Other	98	10.8

Figure 2: The biopsy indications and findings of the patients

	E0 (n=415)	E1 (n=129)		P
Proteinuria (mg/day)	1850 (1070-3400)	2370 (1521-3993)	-	0.008
eGFR (ml/min/1.73 m^2)	69.85 (3.8-144.8)	59.5 (3.7-140.5)		0.003
	M0 (n=123)	**M1 (n=425)**		
Proteinuria (mg/day)	1582 (973-2868)	2100 (1211-3720)	-	0.002
eGFR (ml/min/1.73 m^2)	77.1 (5.7-143.9)	65.8 (3.7-144.8)		0.168
	S0 (n=220)	**S1 (n=325)**		
Proteinuria (mg/day)	1725 (890-3400)	2262 (1300-3720)	-	0.001
eGFR (ml/min/1.73 m^2)	80.7 (3.7-144.8)	61.3 (3.8-143.9)		<0.001
	T0 (n=245)	**T1 (n=250)**	**T2 (n=56)**	**p**
Proteinuria (mg/day)	1580 (905-2915)	2188 (1290-3700)	3479 (2000-6228)	<0.001*
eGFR (ml/min/1.73 m^2)	89.1 (5.5-144.8)	57.7 (3.8-140.3)	32.8 (3.7-119.9)	<0.001**

*: T0-T1: p<0.001; T0-T2: p<0.001; T1-T2: p=0.002

**: T0-T1: p<0.001; T0-T2: p<0.001; T1-T2: p<0.001

Figure 3: Proteinuria levels of patients in different groups according to Oxford classification.

P0441

CONCOMITANT MEDICATIONS OR IMMUNE CHECHKPOINT INHIBITOR, WHO IS THE CAUSE OF ACUTE TUBULOINTERSTITIAL NEPHRITIS IN IMMUNOTHERAPY?

PAULA ANTON PAMPOLS[1], Laura Martinez Valenzuela[1], Juliana Draibe[1], Ana Coloma[1], Xavier Fulladosa[1], Joan Torras[1]

[1]*Hospital Universitari de Bellvitge, Nephrology, Hospitalet de LLobregat, Spain*

Background and Aims: During the last decades, the incidence of drug-associated acute tubulointerstitial nephritis (ATIN) has markedly increased. In the recent years, immune checkpoint inhibitors (ICI) have shown promising results in the treatment of malignancies such as melanoma or lung cancer. Immune mediated adverse events are frequent during the use of these drugs as a result of their mechanism of action. The most common kidney lesion in ICI-treated patients who present acute kidney injury (AKI) is ATIN. It is well established that classical drug-induced ATIN is an allergic drug hypersensitivity reaction mediated by T lymphocytes that occurs 7-10 days after exposure. On the contrary, the pathomechanism of ICI-related ATIN remains controversial. Together with the hypothesis that ATIN is a hypersensitivity reaction against ICI itself, other authors propose that loss of inhibition of T cells may facilitate hypersensitivity reactions to previously tolerated drugs or kidney antigens.

Method: We reviewed 3 cases of ICI-associated ATIN diagnosed in our nephrology unit with known concomitant medications associated to ATIN. The main demographical, clinical and analytical variables such as gender, age, type of malignancy and oncological treatment were recorded.

Results: Patient 1: A 70 year-old man was diagnosed with a non-small-cell lung carcinoma in June 2018. He was treated with carboplatin, paclitaxel and nivolumab (first cycle 21st June 2018), and underwent lobectomy. NSAIDs were prescribed on September 2018 after surgery. Creatinine was normal at baseline. On September 2018 (110 days after nivolumab initiation and 7 days after NSAIDs prescription) he was admitted to the nephrology unit due to AKI, and the kidney biopsy revealed ATIN. ICI and NSAIDs were discontinued. He was treated with steroids with partial renal recovery.

Patient 2: An 82 year-old man was diagnosed with a locally advanced nasal melanoma. He was treated with pembrolizumab. He was referred to the emergency room 73 days after pembrolizumab initiation presenting acute renal failure. Immunological tests were negative and ultrasonography was normal. No other ATIN-related drugs were identified. The final diagnostic was ATIN confirmed by kidney biopsy and the patient was treated with steroids. ICI was discontinued and the recovery of the kidney function was partial. Six months later he was diagnosed with septic arthritis on his right wrist due to *Pseudomonas aeruginosa.* 7 days after ciprofloxacin prescription he presented AKI. The diagnosis was a flare of interstitial nephritis, thus oral steroids were re-initiated. Kidney function partially recovered.

Patient 3: A 63-year-old woman was diagnosed of renal cancer diagnosed in 2014. She was initially treated with Sunitinib, but it was discontinued due to hypothyroidism. She initiated second-line treatment with Nivolumab 7 months before referral to our nephrology unit. Baseline creatinine was normal. 5 days before referral, she took 3 pills of ibuprofen 600mg during three days due to knee pain. The final diagnostic according to kidney biopsy was ATIN. ICI and NSAIDs were discontinued and she was treated with steroids. Kidney function was totally recovered.

Conclusion: ICI associated ATIN present scarce temporal association with the initiation of ICI. High prevalence of use of other ATIN-related drugs has been noticed among these patients. Herein, we report 3 cases of ATIN in the setting of the treatment with ICI. The temporal association of the first episode with other drugs rather than ICI, and the relapse after the rechallenge with a drug classically associated with ATIN suggests that it might be caused by these drugs rather than by ICI itself, that actually may facilitate the drug hypersensitivity reaction. Research in the pathomechanisms of ATIN in ICI patients is required in order to anticipate, prevent and treat this adverse effect.

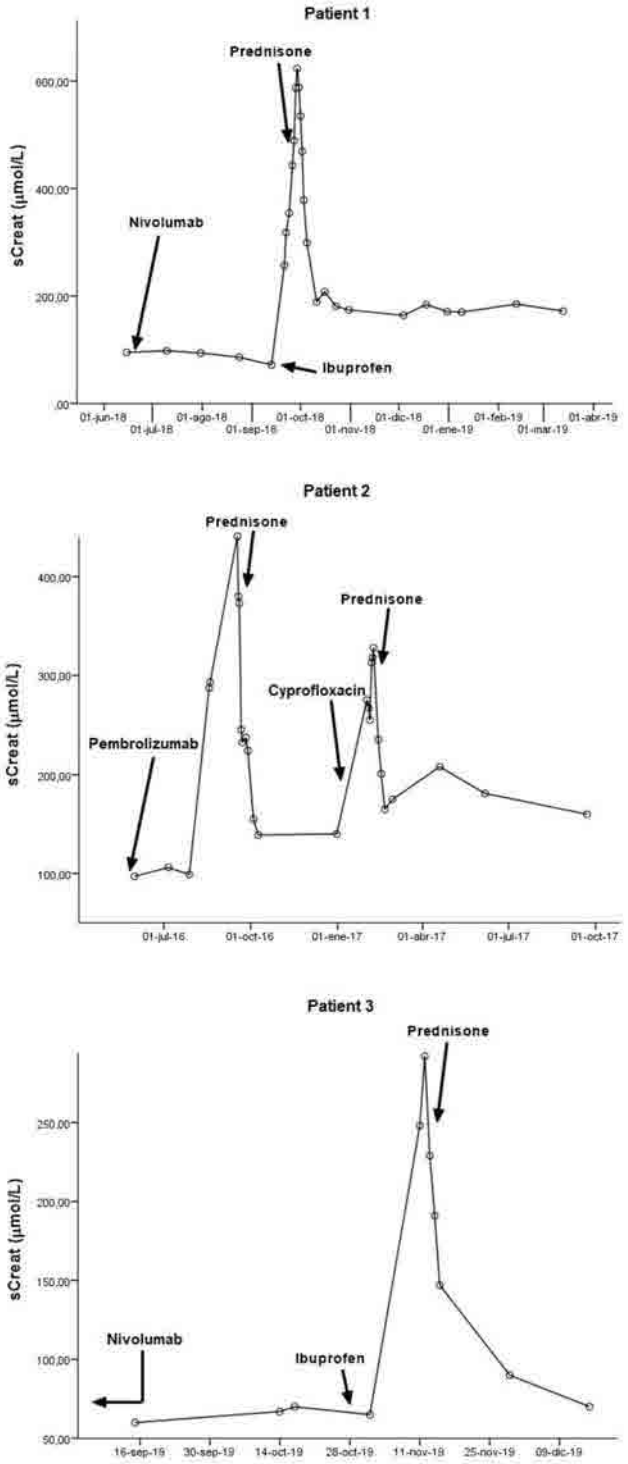


Figure:

P0442 RELATED FACTORS IN THE DEVELOPMENT OF LUPUS NEPHRITIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Andres Ribas[1], Isabel Galcerán[1], Sara Outón[1], Tarek Salman[2], Clara Barrios[1], Adriana S. Ochoa[1], Anna Buxeda[1], Laia Sans[1], Julio Pascual[1], Eva Rodriguez[1]

[1]Hospital del Mar, Nephrology, Barcelona, Spain and [2]Hospital del Mar, Reumathology, Barcelona, Spain

Background and Aims: Lupus Nephritis (LN) is a severe complication of Systemic Lupus Erytemathosus (SLE). This is the main reason why identifying predisposing factors to differentiate patients at risk of developing LN is so important.

Method: Retrospective study of patients with SLE diagnosed between years 2008-2018 in our center. Demographic, clinical and analytical data have been collected.

Results: We included 171 patients, 48 (28%) with diagnose of LN. Age at diagnose of SLE was 39,51 ± 15,40 years, being more frequent in women 151 (87,5%). Time of follow-up since SLE diagnose until development of LN was of 3 ± 5, 3 years. Respectful to the LN classification we found: 4 (8%) class I LN, 6 (12.5%) class II LN, 15 (31.2%) class III LN, 19 (39.5%) class IV LN and 4 (8%) class V LN. At diagnose of SLE, the following variables, where related to developing LN: CH50 [HR: 1,039; CI (95%): 1,004-1,064; p=0,024], C3 [HR: 1,029; CI (95%): 1,016-1,042; p<0,001, titer of Anti- DNACrithidia [HR: 4,364; CI(95%): 1,26-15,064; p=0,02], AntiSM [HR: 4,634, CI (95%) 1,76-12,17, p=0,002], ACA IgG [HR: 7,5; CI (95%): 2,3 -24,449; p=0,001] and Lupus anticoagulant [HR: 4,97; CI (95%): 1,591-15,533; p=0,006]. Treatment with hidroxicloroquine is a protective factor against developing LN [HR: 0,17; CI (95%): 0,063-0,511; p=0.001]. At diagnose of LN, complement factors and titer of anti-DNA crithidia show a positive correlation when compared to the initial determinations: C3 [r= 0,605 (p<0,001]); C1q [r= 0,861 (p=0,006)]; CH50 [r= 0,981 (p<0,001), anti- DNACrithidia [r= 0,529 (p<0,001)], anti-Sm [r=0.8,)p=0.001)].

Conclusion: Consumption of complement factors, high titers of anti-DNAcrithidia, Anti-SM, ACA IgG and Lupus anticoagulant are related to a future LN development at SLE diagnose. Moreover, we see an increase of their titer once we diagnose LN. Otherwise, treatment with hidroxicloroquine seems to be a protective factor.

P0443 **ONE YEAR AFTER PROTEINURIA IN LUPUS NEPHRITIS: EURO LUPUS VS MYCOPHENOLATE, A SINGLE-CENTER EXPERIENCE**

Alessandra Calderaro[1], Valeria Cernaro[1], Raffaele Cordiano[1], Federica giada Vienna[1], Alfredo Laudani[1], Rossella Siligato[2], Guido Gembillo[1], MICHELA AMATRUDA[3], GIULIA LA BARBERA[3], Giovanni Conti[3], Domenico Santoro[1]

[1]Azienda Ospedaliera Universitaria Di Messina G. Martino - Facolta' Di Medicina E Chirurgia, D.A.I Medicina Clinica e sperimentale, U.O.C. Nefrologia e dialisi, Messina, Italy, [2]Azienda Ospedaliera Universitaria Di Messina G. Martino - Facolta' Di Medicina E Chirurgia, D.A.I Medicina Interna, U.O.C. Nefrologia e dialisi, Messina, Italy and [3]Azienda Ospedaliera Universitaria Di Messina G. Martino - Facolta' Di Medicina E Chirurgia, D.A.I. Materno Infantile, U.O.S.D Nefrologia e reumatologia pediatrica con dialisi, Messina, Italy

Background and Aims: Lupus nephritis (LN) develops in about 50% of patients affected by Systemic Lupus Erythematosus (SLE) and it is associated with higher morbidity and mortality risk. Approximately 10 % of LN patients is expected to reach end stage renal disease (ESRD). Proteinuria at 1 year has been demonstrated as the best predictor factor of long-term renal outcome. We compared the effects of two different induction therapies (Euro Lupus protocol [EL] vs Mycophenolate [MMF]) in terms of eGFR, proteinuria, serum albumin and complement activation in LN patients related to our centre.

Method: We retrospectively reviewed the records of 34 adult patients with LN from 2011 to 2019. Patients were divided in two groups according to therapeutic strategy chosen: EL (n=21 patients, group 1) and MMF (n=13, group 2). Data with normal distribution are expressed as average ± standard deviation, while data with non normal distribution are referred to as median and interquartile range [IQR]. Basal values of eGFR, proteinuria, albumin and complement were compared to 1 year values with Student t-test for normal variables or with Wilcoxon test for non normal variables.

Results: The mean age of the patients was 41.27±17.43 years, there was a predominance of female (85,3%) LN was diagnosed at 32±16 years old. According to LN classification, 88.2% of them was affected by III, IV, V and mixed LN class Basal values of eGFR (estimated with CKD-EPI method) were similar between groups 1 and 2 (86.12±52.86 vs 73.75±30.35, P=0.4890) as well as proteinuria (2.00 [0.48-4.57] vs 0.71 [0.28-1.39] g/24h, P=0.3284). After one year of follow up, eGFR did not show significant differences between two groups, while proteinuria was significantly lower in group 1 (2.)). 00 [0.48-4.57] vs 0.44 [0.19-0.91] g/24h, P=0.0034) than in group 2 (0.71 [0.28-1.39] vs 0.15 [0.08-0.77] g/24h, P=0.4687) (fig.1). Moreover, we recorded in group 1 higher values of albumin after one year of follow up (3.20 [2.52-3.94] vs 4.33 [3.99-4.57] g/dl, P=0.0195) (fig.2) and C3 consumption (35.00 [1.00-81.25] vs 89.00 [2.00-112.50] mg/dl, P=0.0067) (fig.3), while group 2 did not show any statistically significant differences.

Conclusion: In patients affected by LN, EL protocol demonstrated to be more effective than MMF in reducing one year after proteinuria, thus improving albumin and C3 serum titer.

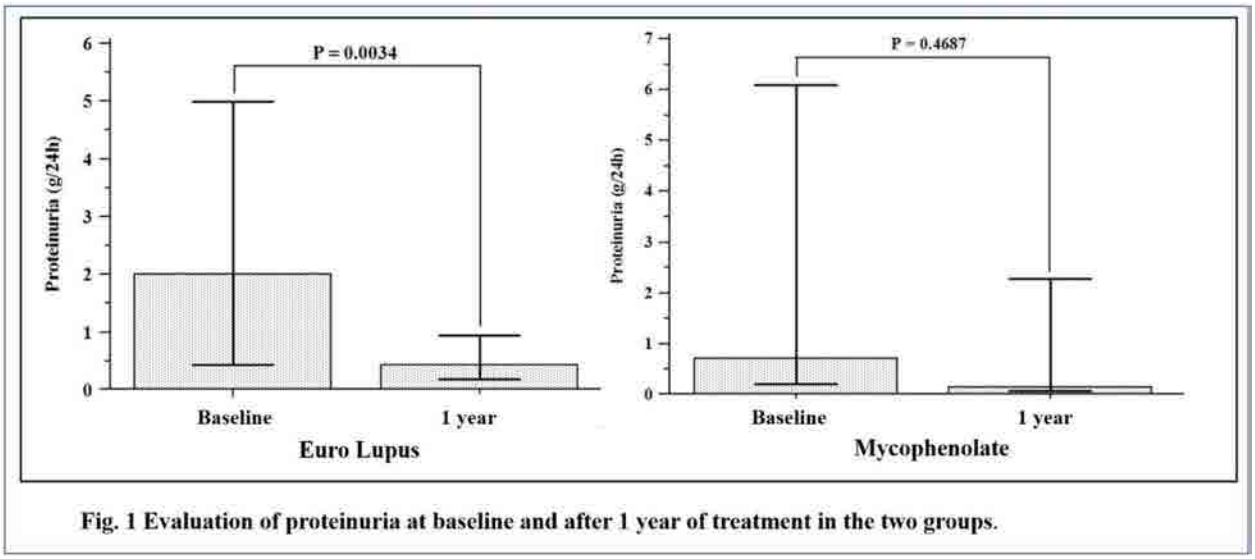


Fig. 1 Evaluation of proteinuria at baseline and after 1 year of treatment in the two groups.

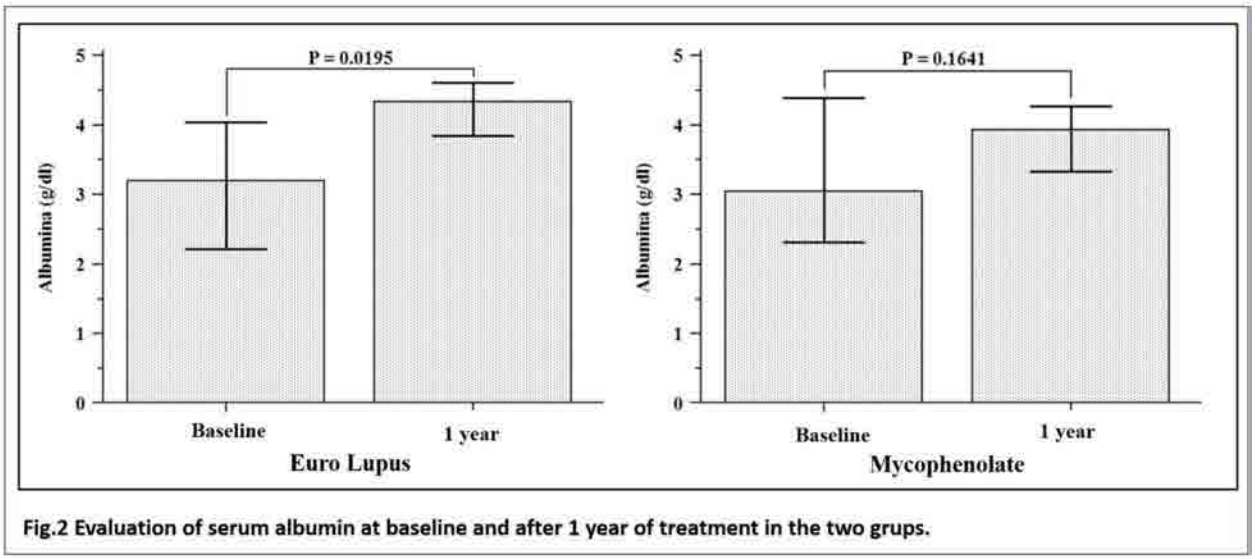


Fig.2 Evaluation of serum albumin at baseline and after 1 year of treatment in the two grups.

Figure:

P0444 SEASONALITY HAS NO ASSOCIATION WITH TIMING OF DIAGNOSIS OF RENAL ANCA ASSOCIATED VASCULITIS

Marina Frleta-Gilchrist[1], Oshorenua Aiyegbusi[1], Malcolm MacKinnon[1], Jamie Traynor[1], Emily McQuarrie[1], Kate Stevens[1], Colin C. Geddes[1]

[1]*Queen Elizabeth University Hospital, Renal and Transplant Unit, Glasgow, United Kingdom*

Background and Aims: Seasonal variation of ANCA associated vasculitis (AAV) and a possible link to extrinsic infective triggers is predominantly based on single centre epidemiological data. Despite frequent confounding factors including difficulty in identifying the precise time of disease onset, seasonality may be associated with the type of vasculitis and may impact the incidence of renal involvement. Therefore, the aim of this study was to explore if there is an association between seasonality, severity and incidence of biopsy-proven renal vasculitis in the Scottish population.

Method: Using the Scottish renal biopsy registry, we identified all adult native renal biopsies performed across Scotland between 2014 and 2018 with a diagnosis of AAV, including microscopic polyangiitis (MPA) and granulomatosis with polyangitis (GPA). Demographic data including ANCA antibody status, histological diagnosis, estimated glomerular filtration rate (eGFR) and proteinuria at presentation were recorded. Seasons were defined as autumn (September – November), winter (December-February), spring (March – May) and summer (June - August). Statistical analysis was performed using multivariate ANOVA analysis and Student's t-test in parametric data.

Results: 339 cases of biopsy proven AAV were identified and included in the analysis. In this cohort, 53% were female with mean patient age of 65.6 years (± 13). Mean estimated glomerular filtration rate (eGFR) at the time of diagnosis of AAV was 32 (± 27.2) mL/min/1.73m^2 and median urinary protein creatinine ratio (uPCR) was 146mg/mmol (IQR 79.8 – 271.3). Diagnosis of MPA n=209(62%) was more common than GPA n=130(38%) and patients with MPA were significantly younger at presentation (63.5 ± 13.6 'vs' 67 ± 12.7 years, p = 0.017). Otherwise, these groups did not differ in mean eGFR (MPA 29.6 ± 25.7 'vs' GPA 34.8 ± 27.6 mL/min/1.73m^2) or median uPCR (MPA 147, IQR 78.6 – 286.5 'vs' GPA 139, IQR 80.5 – 261 mg/mmol) at onset.

We observed a mean of 3.5 (± 1) new cases of MPA and 2.1 (± 0.7) new cases of GPA per month, with no significant difference observed in month-to-month comparison. Seasonal analysis showed mean occurrence of 11.4 (± 4.5) cases of MPA in autumn, 11.2 (± 4.9) in winter, 10.6 (± 1.5) in spring and 8.6 (± 1.9) in summer months. In GPA, mean 6.6 (±2.7) cases occurred each autumn, 5.4 (± 3) in winter, 7.2 (± 2.9) in spring and 6.4 (± 0.9) in summer months. Overall, no significant differences in monthly or seasonal incidence across 5 years of monitoring were detected. Similarly, we observed no difference in renal function at presentation during different seasons for MPA (mean eGFR range 21.8 – 37.6 mL/min/1.73m^2, uPCR median range 112 – 167.5 mg/mmol) or GPA (mean eGFR range 32-37 mL/min/1.73m^2; uPCR median range 110 – 244 mg/mmol).

Conclusion: Our data suggest that there is no seasonal variation in the incidence of AAV diagnosed on kidney biopsy in patients living in Scotland. Additionally, patients present with similar levels of kidney function regardless of season. Thus traditional holiday periods i.e. Easter/Christmas do not seem to lead to a delay in diagnosis. This is the first study to consider seasonality in a complete national cohort and suggests that seasonal extrinsic factors do not play a major role in the pathogenesis leading to AAV onset.

P0445 **PREVALENCE AND PREDICTORS OF GLYCOSURIA IN PRIMARY GLOMERULOPATHIES**

Carolina Ormonde[1], Ivo Laranjinha[2], Augusta Gaspar[2], Margarida Gonçalves[2], Célia Gil[2], Jorge Dickson[2], Domingos Machado[2]

[1]Hospital do Divino Espírito Santo, Nephrology, Ponta Delgada, Portugal and [2]Centro Hospitalar Lisboa Ocidental, Hospital de Santa Cruz, Nephrology, Lisboa, Portugal

Background and Aims: Albuminuria is a marker of glomerular lesion, however some studies have suggested that proximal tubule (endocytosis of albumin) is also essential to determine the amount of albumin excreted in the urine. It has been hypothesized that patients with glomerulopathies and concomitant tubular damage might present higher levels of albuminuria. Glycosuria is a marker of proximal tubular dysfunction and may be used as an easy and useful marker of tubular lesion in glomerular diseases. The aim of this transversal study was to evaluate the prevalence of glycosuria in primary glomerulopathies (GP) and identify its predictors.

Method: We included all patients diagnosed in the last 10 years in our centre with primary GP confirmed by renal biopsy. Clinical, laboratory and biopsy results were collected from patients' charts. Patients were divided in two groups according to their glycosuric status at the diagnosis. Exclusion criteria: patients with diabetes and glucose intolerance, use of SGLT2 inhibitors, transplant kidney patients and secondary GP.

Results: We studied 110 patients – 39 (35.5%) IgA Nephropathy (IgAN), 27 (24.5%) Membranous Nephropathy (MN), 26 (23.6%) Focal Segmental Glomerulosclerosis (FSGS) and 18 (16.4%) Minimal Change Disease (MCD). Demographic data were not different between patients with and without glycosuria. Global prevalence of glycosuria was 9.1% (n=10) – patients with MN had higher prevalence of glycosuria (n=4, 17.4%), followed by FSGS (n=3, 15.5%), MCD (n=1, 5.9%) and IgAN (n=2, 5.4%). We found that patients with glycosuria had higher serum creatinine (3.9±5.1 vs 1.7±1.3 mg/dL, p=0.001), higher albuminuria (7.1±6.3 vs 3.2±3.4 g/g, p=0.002), lower serum albumin (2.3±0.7 vs 3.2±1.1 g/dL, p=0.022) and lower hemoglobin (12.0±2.5 vs 13.4±2.0 g/dL, p=0.050). Nevertheless, we did not find differences between glycosuric and non-glycosuric patients in percentage of glomerular sclerosis (%GS) or interstitial fibrosis and tubular atrophy (IFTA). In a multivariate analysis, glycosuria was positively associated with MN diagnosis, serum creatinine and albuminuria, but not with hematuria, %GS and IFTA.

Conclusion: Glycosuria is not frequent in primary GP. MN is the primary GP that most frequently presents glycosuria. Glycosuria is associated with higher albuminuria and lower serum albumin levels, corroborating the hypothesis that albuminuria as an offender to the tubules will affect the amount of albumin excreted in the urine. We also found that patients with glycosuria presented a more severe renal dysfunction (higher creatinine) at the GP diagnosis.

P0446 OUTCOMES OF CYCLOPHOSPHAMIDE FOR ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES-ASSOCIATED VASCULITIS: DIFFERENT PROTOCOLS, SINGLE-CENTER EXPERIENCE AND LITERATURE REVIEW

José Agapito Fonseca[1], Inês Duarte[1], Joana Gameiro[1], Cristina Outerelo[1], Estela Nogueira[1], Sofia Jorge[1], José António Lopes[1]

[1]*Hospital Santa Maria - Centro Hospitalar Universitário Lisboa Norte, E.P.E., Nephrology and Renal Transplantation, Lisboa, Portugal*

Background and Aims: Cyclophosphamide (CYC), associated with corticosteroids has been considered the mainstay of treatment for severe antineutrophil cytoplasmic antibody–associated vasculitis (AAV) for decades. This protocol is effective in 70-90% of patients resulting in drastic improvement in both renal and patient survival. Nevertheless, cyclophosphamide is associated with significant rates of adverse events, namely severe infections and malignancies. The authors present the single-center experience of the use of CYC for AAV treatment regarding clinical presentation, immunosuppression protocol, outcomes and adverse events, as well as a comparison with the main RCTs and studies using CYC for induction of remission of AAV.

Method: Retrospective analysis of clinical records of patients with AAV diagnosis (*de novo* or relapse) treated with CYC in the ward of the Nephrology Department of Centro Hospitalar Universitário Lisboa Norte between January 2006 and December 2019.

Results: Thirty patients with AAV diagnosis treated with CYC for induction of remission were identified. Average age was 69.4 ± 11.5 years. On admission, serum creatinine (SCr) was 5.03 mg/dL ± 2.24 mg/dL (eGFR 13.3 mL/min/1.73 m^2 ± 11.1 mL/min/1.73 m^2). Twenty patients (67%) required renal replacement therapy at admission and 12 (40%) had alveolar hemorrhage. The average Birmingham Vasculitis Activity Score (BVAS) was 27.5 ± 11.5. Immunosuppressive regimens varied considerably, as they were left to the clinician's consideration. Intravenous methylprednisolone pulses were performed in 29 (96.7%) patients, with total dose ranging from 1000 mg to 5000 mg. Cyclophosphamide was also prescribed at clinician's choice, with only one patient receiving oral CYC and 29 patients receiving from 1 to 11 pulses in different doses. Plasma exchange was performed in 12 (40%) patients due to alveolar hemorrhage and/or rapidly progressive renal insufficiency. After induction of remission, twenty patients received maintenance therapy.

On a 12-month follow-up, 9 (30%) patients were on renal replacement therapy and, in the remaining patients, mean SCr was 2.23 ± 0.98 mg/dL (eGFR 33.4 mL/min/1.73 m^2 ± 19.8 mL/min/1.73m^2). Fifteen (50%) patients experienced severe infection at 6 months, 3 (10.7%) patients developed malignancies and 7 (23.3%) patients died on a 12-month follow-up.

Conclusion: Our cohort of patients treated with CYC is unlike the population that underwent clinical trials. In our cohort, SCr at presentation was considerably higher, being only comparable to MEPEX and the control arm of RITUXVAS. The BVAS score of our patients was also significantly superior than all other studies. Furthermore, most clinical trials do not include patients with alveolar hemorrhage, present in 40% of the patients in our study, nor RRT requirement, present in 67% of our patients. The higher rate of severe infections and mortality registered in our cohort reflects the severity of the disease at presentation, but also highlights the importance of modifying immunosuppression to the population and the need for future regimens which can reduce the rate of adverse effects.

P0448

CHARACTERISTICS OF PRIMARY GLOMERULAR DISEASE PATIENTS WITH HEMATURIA IN TURKEY: THE DATA FROM TSN-GOLD WORKING GROUP

Abdullah Sumnu[1], Kultigin Turkmen[2], Egemen Cebeci[3], Aydin Turkmen[4], Necmi Eren[5], Nurhan Seyahi[6], Aysegul Oruc[7], Fatih Dede[8], Ülver Derici[9], Taner Basturk[10], Garip SAHIN[11], Murat Sipahioglu[12], Gulizar Manga Sahin[13], Erhan Tatar[14], Belda Dursun[15], Savas Sipahi[16], Mürvet Yılmaz[17], Gultekin Suleymanlar[18], Memnune Sena Ulu[19], Ozkan Gungor[20], Sim Kutlay[21], Zerrin Bicik Bahçebaşı[22], İdris Sahin[23], Ilhan Kurultak[24], Can Sevinc[25], Zulfikar Yilmaz[26], Rumeyza Turan Kazancioglu[27], Caner Cavdar[28], Ferhan Candan[29], Zeki Aydin[30], Deren Oygar[31], Cuma Bulent Gul[32], Bulent Altun[33], Saime Paydas[34], Sami Uzun[3], Zulal Istemihan[35], Metin Ergul[5], Mevlut Tamer Dincer[6], Mustafa Gullulu[7], Serhan Vahit Piskinpasa[8], Omer Faruk Akcay[9], Abdulkadir Unsal[10], Sumeyra Koyuncu[12], Mahmut Gok[13], Savas Ozturk[3]

[1]Medipol University, Medical Faculty, Nephrology, Istanbul, Turkey, [2]Necmettin Erbakan University, Meram Medical Faculty, Nephrology, Konya, Turkey, [3]Haseki Training and Research Hospital, Nephrology, Istanbul, Turkey, [4]Istanbul University, Istanbul Medical Faculty, Nephrology, Istanbul, Turkey, [5]Kocaeli University, Medical Faculty, Nephrology, Kocaeli, Turkey, [6]Istanbul University, Cerrahpasa Medical Faculty, Nephrology, Istanbul, Turkey, [7]Uludag University, Medical Faculty, Nephrology, Bursa, Turkey, [8]Ankara Numune Training and Research Hospital, Nephrology, Ankara, Turkey, [9]Gazi University, Medical Faculty, Nephrology, Ankara, Turkey, [10]Hamidiye Sisli Etfal Training and Research Hospital, Nephrology, Istanbul, Turkey, [11]Eskisehir Osmangazi University, Medical Faculty, Nephrology, Eskisehir, Turkey, [12]Erciyes University, Medical Faculty, Nephrology, Kayseri, Turkey, [13]Sultan Abdulhamit Han Research and Training Hospital, Nephrology, Istanbul, Turkey, [14]Bozyaka Training and Research Hospital, Nephrology, Izmır, Turkey, [15]Pamukkale University, Medical Faculty, Nephrology, Denizli, Turkey, [16]Sakarya University, Medical Faculty, Nephrology, Sakarya, Turkey, [17]Bakirkoy Sadi Konuk Training and Research Hospital, Nephrology, Istanbul, Turkey, [18]Akdeniz University, Medical Faculty, Nephrology, Antalya, Turkey, [19]Afyon University, Medical Faculty, Nephrology, Afyon, Turkey, [20]Sutcu İmam University, Medical Faculty, Nephrology, Kahramanmaras, Turkey, [21]Ankara University, Medical Faculty, İbni Sina Hospital, Nephrology, Ankara, Turkey, [22]Dr. Lutfi Kirdar Kartal Training and Research Hospital, Nephrology, Istanbul, Turkey, [23]Inonu University, Medical Faculty, Nephrology, Malatya, Turkey, [24]Trakya University, Medical Faculty, Nephrology, Edirne, Turkey, [25]Ataturk University, Medical Faculty, Nephrology, Erzurum, Turkey, [26]Dicle University, Medical Faculty, Nephrology, Diyarbakir, Turkey, [27]Bezmialem Vakif University, Medical Faculty, Nephrology, Istanbul, Turkey, [28]Dokuz Eylul University, Medical Faculty, Nephrology, Izmir, Turkey, [29]Cumhuriyet University, Medical Faculty, Nephrology, Sivas, Turkey, [30]Darica Farabi Training and Research Hospital, Nephrology, Kocaeli, Turkey, [31]Burhan Nalbantoglu State Hospital, Nephrology, Lefkosa, Cyprus, [32]Bursa Yuksek Ihtisas Training and Research Hospital, Nephrology, Bursa, Turkey, [33]Hacettepe University, Medical Faculty, Nephrology, Ankara, Turkey, [34]Cukurova University, Medical Faculty, Nephrology, Adana, Turkey and [35]Istanbul University, Istanbul Medical Faculty, Internal Medicine, Istanbul, Turkey

Background and Aims: Hematuria is one of the most common laboratory findings in nephrology practice. In different regions of the world, the etiologic causes differ. To date, there is no enough data regarding the clinical and histopathologic characteristics of primary glomerular diseases (PGD) patients with hematuria in our country.

Method: Data were obtained from national multicenter (47 centers) data entered into the Turkish Society of Nephrology Glomerular Diseases (TSN-GOLD) database between May 2009 and June 2019. The data of all PGD patients over the age of 16 years who were diagnosed with renal biopsy and had hematuria data were included in the study. The biopsy samples were processed using a light microscopy and immunofluorescence examination. Demographic characteristics such as age, sex, indications for biopsy, primary glomerular diseases, comorbidities, laboratory and biopsy findings of all patients were also recorded. Hematuria was defined as the presence of at least 5 red blood cells/hpf.

Results: Data of 3394 patients were included to the study after the exclusion of patients with secondary glomerulonephritis and patients with missing biopsy findings. While 1699 (50.1%) patients had hematuria, 1695 (49.9%) patients did not have hematuria. Demographic, laboratory, and histopathological characteristics of patients with and without hematuria are given in Table. Patients with hematuria had statistically higher systolic blood pressure (SBP), serum blood urea nitrogen, creatinine, albumin, levels and urine pyuria, however, these patients had statistically lower age, body mass index, presence of hypertension and diabetes, eGFR, 24-hour proteinuria, serum total, HDL and LDL-cholesterol and C3 levels when compared with patients without hematuria. Figure depicted the etiologic causes of patients with and without hematuria. According to histopathological findings, number of global sclerotic glomeruli, cellular and fibrocellular crescents, the levels of mesangial proliferation, endocapillary proliferation, exudative changes in glomeruli, severe tubular atrophy, interstitial inflammation, subendothelial deposition, moderate and severe IgA and C3 deposition were found to be significantly higher and the levels of basal membrane thickening, interstitial fibrosis, subepithelial deposition, severe IgG staining were found to be significantly lower in patients with hematuria.

Conclusion: This is the first multicenter national report regarding the demographic and histopathologic data of PGD patients with or without hematuria. Hematuria, a feature of nephritic syndrome, was found at a higher than expected in the PGDs presenting with nephrotic syndrome in our national database.

Table. De mographic and laboratory characteristics of the patients with or without hematuria

Parameters	Hematuria positive n: 1699 (50.1%)	Hematuria negative n: 1695 (49.9%)
Age (years)*	40.7±14.8	42.5±14.8
Gender (Male, %)	56.5	57.0
Hypertension (%)*	30.7	34.6
Diabetes Mellitus (%)*	7.0	11.1
Systolic blood pressure (mmHg)*	131±21	129±19
Diastolic blood pressure (mmHg)	81±12	81±12
Blood Urea Nitrogen (mg/dL)*	26±22	21±16
Creatinine (mg/dl)*	1.73±1.78	1.25±1.21
CKD-EPI (ml/min/1.73 m^2)*	72.2±46.0	86.3±48.1
Albumin (gr/dl)*	3.36±0.92	3.17±0.97
Proteinuria (mg/d) *	4247±4886	5416±5396
Uric acid (mg/dl)	6.3±1.9	6.2±1.8
Total cholesterol (mg/dL)*	243±94	273±110
LDL cholesterol (mg/dL) *	153±76	175±92
Triglyceride (mg/dL)*	193±127	225±138
Hemoglobin (gr/dl)*	13±2	13±2
Presence of pyuria (Leukocyte>5/hpf) (%)*	27.7	10.3
Low C3 level (%) *	8	4
Low C4 level (%)	3	2.3

*statistically significant

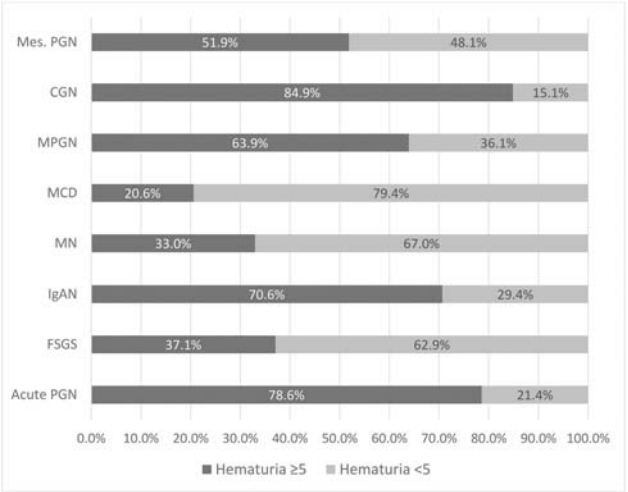


Figure. The etiologic causes of PGN patients with and without hematuria

Mes.PGN: mesangioproliferative GN; CGN: crescentic GN; Acute PGN: acute proliferative GN

P0449

SERUM PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) IN NON-DIABETIC ASIANS WITH NEPHROTIC SYNDROME

Cynthia Lim[1], Irene Mok[1], Hui Zhuan Tan[1], Esther WL Teng[1], Xiu Ping Chue[2], Wei Mian Ang[2], Yok Mooi Chin[1], Marjorie Foo[1], Jason Choo[1]

[1]Singapore General Hospitla, Renal Medicine, Singapore, Singapore and [2]Singapore General Hospital, Research Efficiency Enhancement Program, Division of Medicine, Singapore, Singapore

Background and Aims: Nephrotic syndrome is associated with hypercholesterolemia, while its treatment, often involving high-dose glucocorticosteroids, may cause hyperglycemia. Proprotein convertase subtilisin /kexin type 9 (PCSK9) regulates plasma cholesterol and is associated with post-transplant diabetes. Although a potential therapeutic target in nephrotic syndrome, the relationships between PCSK9 and lipid parameters are not well established. We aimed to characterize serum PCSK9 and metabolic parameters among individuals with nephrotic syndrome.

Method: Single-center prospective cohort study of non-diabetic adults newly-diagnosed with nephrotic syndrome and subsequently treated with immunosuppressant. Fasting serum PCSK9 was measured using ELISA at diagnosis. Clinical history, blood pressure, body mass index (BMI), waist-to-hip ratio (WHR) and biochemistry (fasting glucose and lipid, HbA1c and fasting serum PCSK9) were obtained at diagnosis and at 3 months during immunosuppression therapy. Spearman's correlation was used to evaluate for associations between PCSK9 and glycemic and lipid parameters.

Results: Among 15 adults with nephrotic syndrome, the majority was female (60%) and Chinese (80%). Median age was 40 (IQR 26, 51) years. The most frequent diagnoses were minimal change disease or focal segmental nephrosclerosis (n=7) and lupus nephritis (n=5); the minority had IgA nephropathy, membranous nephropathy or vasculitis. At diagnosis, median eGFR was 97.9 (59.5, 120.9) ml/min/1.73 m2, UPCR 7.6 (6.1, 10.4) g/g, LDL-cholesterol 4.6 (3.1, 6.7) mmol/L and fasting serum PCSK9 317.6 (276.8, 470.1) ng/ml. PCSK9 correlated positively with hypertriglyceridemia (r=0.55, p=0.03) at baseline.

Most patients (n=14, 93%) were treated with prednisolone (monotherapy or in combination with other immunosuppressant) and 1 received tacrolimus monotherapy. At 3 months, the majority (n= 11, 73%) had achieved clinical remission.

Fasting serum PCSK9 was higher at 3 months [median 430.6 (283.1, 496.0) ng/ml] compared to baseline, although the difference was not statistically significant. At 3 months, PCSK9 correlated positively with age (r=0.58, p=0.03), LDL-cholesterol (r=0.90, p=0.04) and change in BMI (r=0.72, p=0.01).

Conclusion: PCSK9 is associated with metabolic parameters at diagnosis and during the treatment course in patients with nephrotic syndrome treated with immunosuppressant.

P0450

END-STAGE RENAL DISEASE PREDICTION IN ANCA-ASSOCIATED GLOMERULONEPHRITIS AT BASELINE: UTILITY OF DIFFERENT APPROACHES IN CLINICAL PRACTICE

Nikolay Bulanov[1], Ekaterina Stolyarevich[2], Anastasiia Zykova[1,3], Elizaveta Safonova[3], Ekaterina Karovaikina[1], Mayra Bulanova[4], Pavel Novikov[1], Sergey Moiseev[1,3]

[1]Sechenov First Moscow State Medical University, Tareev Clinic of Internal Diseases, Moscow, Russia, [2]A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Department of Nephrology, Moscow, Russia, [3]Moscow State University, Chair of Internal Medicine, Moscow, Russia and [4]Vladimir Regional Clinical Hospital, Department of Nephrology, Vladimir, Russia

Background and Aims: Despite significant progress in treatment of ANCA-associated vasculitis (AAV), at least 20% of patients with renal involvement develop end-stage renal disease (ESRD). Histopathologic classification by Berden et al, which addresses only glomerular pathology, has been used to predict renal outcome in ANCA-assoicted glomerulonephritis (ANCA-GN) since 2010.[1] In 2018 Brix et al proposed ANCA renal risk score (ARRS), which combines assessment of morphological (percentage of normal glomeruli, tubular atrophy and interstitial fibrosis) and clinical parameters (estimated glomerular filtration rate) to predict probability of ESRD.[2] The aim of our study was to compare clinical utility of these two methods.

Methods: In our retrospective study we enrolled 57 patients with ANCA-associated vasculitis, diagnosed according to Chapel Hill Consensus Conference (2012) definition and/or American College of Rheumatology (1990) criteria, with histologically proven renal involvement. There were 14 (24.6%) males and 43 (75.4%) females, median age at AAV onset was 48 (33; 57) years. Fifty-one (89.5%) patients were ANCA-positive. Eight (14.0%) patients were diagnosed with renal-limited AAV. Median Birmingham vasculitis activity score (BVAS v.3) at onset was 16 (13; 19). In each case ANCA-GN class was established according to Berden classification: focal (>50% normal glomeruli); crescentic (>50% cellular crescents); mixed (<50% normal, <50% crescentic, and <50% globally sclerotic glomeruli) or sclerotic (>50% globally sclerotic glomeruli). ARRS at onset was also retrospectively assessed and all patients were divided into three groups depending on the risk of ESRD: low risk (0 points), intermediate risk (2 to 7 points), or high risk (8 to 11 points). Thirteen patients (22.8%) developed ESRD after a median of 12 (6.5; 28) months. Renal survival rates were assessed by Kaplan-Meier method and compared by log-rank test.

Results: Among the 57 patients seven (12.3%) had focal, 10 (17.5%) – crescentic, 24 (43.2%) – mixed, and 16 (28.1%) – sclerotic ANCA-GN class according to Berden et al classification. 1- and 3-year renal survival rates were the highest (100% and 100% respectively) in focal, and the lowest in sclerotic class (67% and 50.2% respectively). 1- and 3- year renal survival was similar in crescentic (80% and 80% respectively) and mixed (80.6% and 80.6% respectively) classes (Fig. 1A). The differences were not statistically significant (Log-rank (Mantel-Cox) p = 0.17). Then we retrospectively re-evaluated all cases according to ARSS: 12 cases were classified as low-risk, 27 – as medium risk, 18 – as high risk. One-year and three-year survival rates were 100% and 100% in low-risk group, 86.1% and 74.2% in medium risk group, 50.6% and 50.6% in high risk group (Figure 1B). The differences were statistically significant (Log-rank (Mantel-Cox) p=0.003).

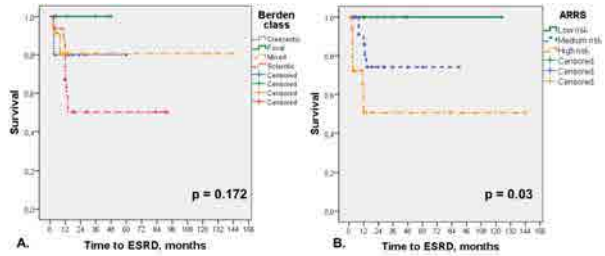


Figure 1. Kaplan-Meier curves showing renal survival in different ANCA-GN classes according to Berden et al classification (A), and different risk groups according to ARRS (B)

Conclusion: In our limited group of patients ANCA renal risk score classification provided better and more clear stratification of patients in terms of ESRD prediction than Berden classification. ARRS is a simple and valuable tool for assessment of renal survival prognosis which can contribute to personalized approach to the management of AAV.

P0451

TEN-YEAR OUTCOME DIFFERENCES IN LUPUS NEPHRITIS PATIENTS TREATED WITH CYCLOPHOSHAMIDE AND MYCOPHENOLATE- BASED TREATMENT REGIMEN

Narayan Prasad[1,2], Jithu Kurian[2], Vikas Agarwal[4], Dharmendra Bhadauria[2], Amit Gupta[2]

[1]Lucknow, Nephrology, lucknow, India, [2]SGPGIMS, Nephrology, lucknow, India and [4]SGPGIMS, Clinical Immunology, lucknow, India

Background and Aims: Lupus nephritis (LN) poses a considerable impact on the morbidity and mortality of SLE patients. Long term comparative outcome data with cyclophosphamide (CYP) and mycophenolate mofetil (MMF) based regimen from the Indian subcontinent is sparse.

We assessed the renal and patient survival of these patients for the types of induction CYP or MMF and the two maintenance therapies – MMF or Azathioprine. We determined the predictors of death and dialysis dependency in the study population.

Method: In this retrospective study, we analysed outcomes of 100 LN patients, total 67 (26 class III, 25 class IV, 6 class III+V, and 10 class IV+V)) treated with CYP (euro lupus-40 and NIH- Dharmendra Bhadauria 27), and 33 with MMF based regimen with the steroid between July 2008 to June 2018. The class distribution of the patients in the two groups was similar. The data were archived regarding demography, clinical, histopathological features, and the treatment given of all 100 biopsy-proven LN patients. Outcomes between two regimens CYP and MMF in terms of remission, dialysis dependency, and patient survival were compared. The renal survival and patient survival at the end of follow-up between two groups were also analysed.

Results: The clinical characteristics were similar in both groups, except the activity index was high in CYP patients (6.13 $\pm$4.48 Vs. 4.61 $\pm$ 2.80); however, the chronicity index was similar. The overall remission was 70% at the end of induction. The CR, PR, and NR in the CYP group was 46.2%, 23.9 %, 29.9% respectively; however, in the MMF group was 57.6%, 12.1%, and 30.3%, respectively. More patients died in CYP (14.9%) than those in MMF (9.1 %) patients. The 1-, 2-, 3-, 4-, 5- and 10-years patient survival in the CYP induction was 89.5%, 86.2%, 86.2%,83.8%, 83.8% and 83.8% however in MMF was 93.9%, 93.9%, 89%, 89%, 89% and 89% respectively. The most common cause of death was sepsis 9/13(69.2%), followed by uremia. The high serum creatinine, low Hb, male, thrombocytopenia, microscopic haematuria, leukocyturia, nephrotic proteinuria, lack of remission in 12 months, dialysis, doubling of creatinine on follow-up were significant predictors of mortality. The 1-, 2- 3-, 4-, 5- and 10- years renal survival (event death-censored, but dialysis dependency) in CP group was 98.5%, 96.7%, 94.7%, 92.4%, 92.4% and 84 % respectively however in the MMF was 96.8 %, 96.8%, 91.9%, 91.9%, 91.9%, and 78.8% respectively. (Figure 1)At the end of the study, dialysis dependency in the MMF group and CYP group was 7.5% and 12.1 %, respectively (NS). In the maintenance therapy, 3/56(5.3%) had to double of creatinine in MMF, and 7/34 (20.5%) in the AZA group (p=0.03).

Conclusion: Long term outcomes in terms of patient and renal survival of LN patients treated with CP and MMF based induction is similar. Serum creatinine doubling was more with MMF than AZA based maintenance. The majority of death occurred during induction, and sepsis was the most common cause of death.

P0452 GLYCOSURIA IN MEMBRANOUS NEPHROPATHY: AN UNDERESTIMATED MARKER?

Carolina Ormonde[1], Ivo Laranjinha[2], Augusta Gaspar[2], Margarida Gonçalves[2], Célia Gil[2], Jorge Dickson[2], Domingos Machado[2]

[1]Hospital do Divino Espírito Santo, Nephrology, Ponta Delgada, Portugal and [2]Centro Hospitalar Lisboa Ocidental, Hospital de Santa Cruz, Nephrology, Lisboa, Portugal

Background and Aims: Membranous nephropathy (MN) is one of the most common causes of nephrotic syndrome in adults. Some studies have suggested that glycosuria is present in the most severe cases of MN and this finding may be associated with tubular injury caused by the overload of filtered proteins. The aim of this study was to evaluate the association between glycosuria in MN and severity and prognosis of the disease.

Method: We conducted a 36-month retrospective cohort study with all patients diagnosed in the last 10 years in our centre with primary MN confirmed by renal biopsy. Data collection was made from patients' charts. Patients were divided in two groups according to their glycosuric status at the diagnosis. Exclusion criteria: patients with diabetes and glucose intolerance, use of SGLT2 inhibitors, transplant kidney patients and secondary MN.

Results: We studied 27 patients with primary MN. Four patients (14.8%) presented glycosuria at the time of diagnosis. Glycosuric and non-glycosuric groups had comparable demographic data. We found that glycosuric patients had higher baseline albuminuria (10.7±8.6 vs 4.6±4.1 g/g, p=0.029) and lower estimated glomerular filtration rate (eGFR) (39.2±24.6 vs 75.2±30.7 ml/min/1.73m2, p=0.037). We also found that patients with glycosuria had higher interstitial fibrosis and tubular atrophy (IFTA) (33.8%±21.4 vs 10.7%±17.1, p=0.035) but no differences in the percentage of glomerular sclerosis. There were no differences between groups in serum albumin, haemoglobin or therapy. At the end of the follow-up period there was no difference in eGFR decline rate (ml/min/year), 3-year eGFR, 3-year albuminuria and 3-year chronic kidney disease stage 5D incidence.

Conclusion: Prevalence of glycosuria in primary MN is approximately 15%. Its presence at the time of diagnosis was associated with more severe clinical and histological markers: lower eGFR, higher albuminuria and higher IFTA. However, we did not find association between glycosuric status at diagnosis and disease progression. Prospective, bigger and longer studies are needed to evaluate these questions.

P0453

BIOSIMILAR RITUXIMAB AND BRAND RITUXIMAB: RELAPSES AND PROTEINURIA IN THE GLOMERULAR PRYMARY DISEASES

Roxana Bury[1], Irene Agraz[1], Maria Jose Soler Romeo[1], Clara Garcia Carro[1], Eugenia Espinel[1], Daniel Seron Micas[1], Bruno Montoro[2], Carlota Varon[2]

[1]Hospital vall d'hebron, Nephrology, Barcelona, Spain and [2]Hospital vall d'hebron, Pharmacology, Barcelona, Spain

Background and Aims:

Biosimilar drugs need to prove similar effectiveness to the brand name drug, in order to have their authorization from regulatory agencies. Rituximab initially developed as a treatment for non-Hodgkin lymphoma, is used as a therapeutic alternative to several autoimmune diseases, including primary glomerular diseases.

The objective of this study is to observe if there were differences in terms of effects measured in proteinuria and relapse episodes between rituximab brand versus biosimilar in primary glomerular diseases

Method:

This is a retrospective descriptive study that included patients receiving rituximab brand or biosimilar for the first time between March 2018 to March 2019, collecting information from the reported medical records with primary glomerulopathy were included. The collected laboratory data included creatinine, proteinuria, leukocyte and lymphocyte count before (0-60 days before) and after (0-60 days after) administration of rituximab.

Results:

A total of 19 patients with primary glomerulopathy were included. Six patients (59-years-old (26-74); 50% female) with baseline 6.52±2.00x10^9/L leucocyte count, 2.28±1.10x10^9/L lymphocyte count, 1.63±1.04 mg/dL creatinine and 6.84±3.36g/24h proteinuria, were treated with biosimilar-rituximab. Thirteen patients (58-years-old (25-81); 30% female) with baseline 9.80±4.62x10^9/L leucocyte count, 1.92±1.13 x10^9/L lymphocyte count, 1.61±0.85 mg/dL creatinine and 5.81±4.55 g/24h proteinuria, were treated with brand-rituximab. After the rituximab administration, these values were 6.13±1.94x10^9/L leucocyte count, 1.30±0.59x10^9/L lymphocyte count, 1.16±1.19 mg/dL creatinine, 3.29±0.58g/24h and proteinuria for the biosimilar group; and 8.77±3.78x10^9/L leucocyte count, 1.67±1.13x10^9/L lymphocyte count, 1.56±1.19 mg/dL creatinine and 3.36±2.20g/24h proteinuria for the brand group. After rituximab administration CD19+ lymphocytes become negative in both groups (5/5 for the biosimilar group; 6/6 for the brand group). There were 2 total remissions, 1 partial remission and 3 without response with the biosimilar and 1 total remission, 5 partial remissions and 7 without response with the rituximab brand. Biosimilar was well tolerated in 6/6 patients and Rituximab brand infection did not develop was well tolerated in 11/13 patients and 4/13 patients showed an episode of infection. No statistically significant results were observed for the response to treatment between both groups.

Conclusion:

The biosimilar shows a similar profile in terms of proteinuria and remissions against rituximab mark in the reported follow-up period, however our study is limited since it has a small sample, so a larger study is necessary to demonstrate these results with statistical significance

P0454 MORPHODENSITOMETRIC FEATURES OF PERIPHERAL BLOOD LYMPHOCYTES IN PATIENTS WITH PRIMARY GLOMERULONEPHRITIS

Vitalii Kaminskyi[1]

[1]*Ivano-Frankivsk National Medical University, Department of Internal Medicine №1, Clinical Immunology and Allergology named after Academician Ye.M. Neiko, Ivano-Frankivsk, Ukraine*

Background and Aims: Lymphocytes play an important role in the development of glomerulonephritis (GN). Their subpopulations are activated under the influence of certain cytokines that act on the activation factors of transcription of these cells, leading to the corresponding regulation of gene expression. However, in addition, in the regulatory processes of lymphocyte functions, epigenetic modifications of the degree of nuclear chromatin compaction are important. The morphological manifestation of the latter may be the state of the optical density of the nuclei and the range of its variability due to the ratio of chromatin condensation/decondensation. The study of the features of potentially reversible changes in chromatin structure in somatic cells becomes actual. One of the convenient objects for studying the epigenetic mechanisms of the genome functioning regulation are interphase nuclei of peripheral blood lymphocytes. Morphodensitometric study permits to establish compensatory changes at the cellular level and to evaluate the functional state of the hereditary apparatus. The aim of the research was to study the morphodensitometric features of genome status of peripheral blood lymphocytes in patients with primary GN.

Method: We examined 119 patients (76 men and 43 women) with primary GN. The average age of patients was (39.65 ± 14.16) years. The patients underwent a renal biopsy to verify the morphological form of the disease. For comparison, a survey of 30 healthy individuals was conducted. Chromatin of nuclei and its changes were studied using an image analyzer based on the programm Image Tool for Windows (v. 3.0). The advantage of this method is the possibility of a combined assessment of morphometric (area, perimeter), spectrometric (optical and integral density) data with the analysis of the microanatomy of isolated chromatin blocks and the chromatin function at the same time. The study of the morphodensitometric characteristics of peripheral blood lymphocytes is an informative and accessible method for assessing the general state of the function and structure of the hereditary apparatus of the organism.

Results: The sexual characteristics of the morphometric and optical parameters of lymphocytes nuclei of patients were established. So, in all patients and especially women, a decrease in the perimeter of lymphocytes nuclei was registered in 1.25 and 1.31 times, respectively ($p < 0.05$). The area of these cells nuclei also naturally decreased in 1.22 times in all patients (in 1.08 and 1.34 times in men and women, respectively) compared to the control ($p < 0.05$). A significant decrease in the area of lymphocytes nuclei with an unchanged density of chromatin packing in these nuclei limits the space inside the nucleus for the interaction of individual chromosome loci in this space. Such limitations can be a serious obstacle to the normal functioning of the genome and its repairing processes. Meanwhile, differences in the optical density parameter of lymphocytes nuclei in both groups were defined. The minimum and maximum optical density were higher in the group of patients, and the range of optical density variability showed wider borders of functional heterogeneity of cells compared to the control.

Conclusion: Comparative analysis of morphodensitometric features of peripheral blood lymphocytes in patients with primary GN detected the changes in the ratio of chromatin condensation/decondensation and normal structure of nuclei, that may indicate functional disorders of the genotype due to exo- and endogenous factors.

P0455 CLINICAL PROFILE OF C3 GLOMERULOPATHY AT A TERTIARY CARE CENTRE

Umesh Lingaraj[1]

[1]*Institute of Nephro Urology, Nephrology, Bengaluru, India*

Background and Aims:

To study the clinico-pathological profile of patients with C3 glomerulonephritis at a tertiary care entre.

Method:

A prospective observational study of all cases of C3 glomerulonephritis was done between August 2016 and December 2017. C3 glomerulonephritis was defined by predominant glomerular C3 fragment deposition with electron-dense deposits on EM

Results:

Total of the 1190 patients under went biopsy during the study period. C3 glomerulonephritis was present in 32 cases (2.68%). The mean age was 35±2 years. Out of the 32 patients, 18 were male (56.25%) and 14 were female (43.75%). Hypertension was present in 30 out of 32 patients (93.7%) while diabetes was present in 7 patients (21.8%). Most common presentation was with RPGN (72%). 100% patients had active urinary sediments. The mean serum creatinine at admission was 5.15mg/dl while it was 3.18mg/dl at discharge. The mean serum C3 was 83.8 mg/dl with 18 patients (56.25%) having low serum C3 levels in our study. All patients had normal serum C4 levels with mean being 29.34 mg/dl. Anti CFH antibody titres were measured in 6 patients of with it was elevated in 2 patients (33.3%). On LM, 14 out of 32 had crescentic GN (43.75%), 12 had diffuse exudative pattern (37.5%), 4 had diffuse mesangioproliferative pattern (12.5%), 3 had MPGN pattern (9.37%), 3 had focal exudative pattern (9.37%), 1 patient had glomerular TMA (3.15%) and 1had chronic sclerosing pattern (3.15%). On IF, all patients had dominant C3 staining. Also 3 (9.37%) patients had IgG staining of 1+ intensity. EM study was done in two patients and was suggestive of DDD in one patient (3.15%). All patients were managed with pulse steroids followed by oral steroids. IV Cyclophosphamide was used monthly for 6 doses in 14 patients (43.7%) while oral cyclophosphamide was used in 2 patients (6.25%). Plasmapharesis was done in 11 patients (34.37%) and 11 patients required haemodialysis (34.37%)

Conclusion:

C3 glomerulonephritis has emerged as a new entity in the recent past with significant percentage of our patients presenting with RPGN. Hypertension was present in most patients. On light microscopy, the most common presentation was crescentic glomerulonephritis, One third of our patients had advanced renal failure requiring haemodialysis. Plasmapharesis was done in one third of patients.

P0456 LONG TERM PATIENT SURVIVAL AND RELAPSE RATE IN ANCA ASSOCIATED PATIENTS WITH RENAL INVOLVMENET - DATA FROM CROATIAN REFERRAL CENTER

Matija Crnogorac[1], Ana Brechelmacher[1], Ivica Horvatić[1], Patricia Kacinari[1], Miroslav Tišljar[1], Luka Toric[1], Petar Senjug[2], Nikola Zagorec[1], Danica Galešić Ljubanović[2], Kresimir Galesic[1]

[1]Dubrava University hospital, Department of nephrology and dialysis, Zagreb, Croatia and [2]Dubrava University hospital, Department of clinical pathology, Zagreb, Croatia

Background and Aims: The aim of the research was to evaluate patient and renal as well as relapse free survival in ANCA associated vasculitis (AAV) patients in our center. Despite the advances in understanding pathogenesis of AAVs and advances in treatment, the outcomes of AAV patient differ in various centers.

Method: This study included 106 consecutive AAV patients with renal involvement in the period from 2007-2017. We performed renal biopsy on patients using automatic 16 Gauge needle. Light, immunofluorescent and electronic microscopy were performed. All the patients were treated with cyclophosphamide and steroids in induction treatment with adjuvant PLEX and dialysis depending on renal function and lung manifestations.

Primary outcomes were combined outcome progression to end-stage renal disease, defined as persistent (more than three months) need for renal replacement therapy or permanent reduction of EGFR to <15ml/minute (according to CKD EPI formula) and/or death (ESRDD), death (D) and ESRD alone, and disease relapse. Kaplan Meyer survival analysis and multivariate Cox proportional hazard regression analysis were used to explore difference between phenotypes and finding significant predictors regarding outcomes.

Out of 106 patients (55,6% female, median age 61; IQR 51-70) there were 66 (61,1%) microscopic poliangitiis (MPA), 20 (18,5%) granulomatosis with angitiis and 20 (18,5%) with renal limited vasculitis (RLV),There were 14 (13%) PR3-ANCA positive patients, 57 (52,8%) MPO ANCA positive, 5 (4,6%) PR3-ANCA+MPO-ANCA positive and 32 (29,6%) ANCA negative patients. Histologically (Berden classification) 43 (39,8%) patients had crescentic, 19 (17,6%) focal, 34 (31,5%) mixed and 12 (11,1%) sclerotic class. Follow up time ranged from 1 to 127 months. Median follow up time was 21 months (IQR = 7-44). Median time to diagnosis was 3 months (IQR 2,0-6,0).

Results: During follow up 21 (19,8%) patients died, 26 (24,5%) patients reached ESRD and 10 (9,4%) patients relapsed. There was no significant difference in outcomes between clinical, serological or histological phenotypes. In multivariant analysis independent predictors for death were age (HR = 1,059, 95% CI =1,001-1,120; p = 0,046), anemia (HR = 0,952, 95% CI =0,908-0,998; p = 0,040) and BVAS (HR = 1,093, 95% CI =1,030-1,159; p = 0,003), for ESRD. the need for acute dialysis (HR = 4,674, 95% CI =1,996-10,946; p = < 0,001), and interstitial fibrosis and tubular atrophy (IFTA) percentage over 50% (HR = 2,652, 95% CI =1,157-6,081; p = 0,021). and for relapse rate younger age (HR = 0,924, 95% CI = 0,870-0,981; p =0,010), lower serum creatinine levels (HR = 0,996, 95% CI = 0,992-1,000; p = 0,033), and the need for acute dialysis (HR = 59,545, 95% CI =3,467-1022,665; p = 0,005). Event free survival after 12, 24, 36 and 60 months was for death 83,9, 81,2, 79 and 74,7%, for ESRD 80,6, 77,9, 76,1 and 71% and for relapse 95,3, 88,4, 88,4 and 85%.

Conclusion: Timely diagnosis and treatment can ensure better outcomes in AAV patients. Though there is an overlap in predictive factors between different cohorts, there are still distinctive differences especially between cohorts from clinical trials and those from observational studies. Our study is among few to show significance of anemia as clinical predictor and IFTA percentage as pathohistological predictor.

P0457 MALE LUPUS NEPHRITES: WHAT ABOUT RISK FACTORS FOR RENAL FAILURE ? EXPERIENCE OF ONE DEPARTMENT

Kharroubi Melek[1], Raja Trabelsi[1], Mondher Ounissi[1], Soumaya Chargui[1], Mouna Jerbi[2], Hanen Gaid[2], Hafedh Hedri[1], Amel Harzallah[1], Taib Ben abdallah[1], Rim Goucha[2]

[1]Charles Nicolle Hospital, Nephrology, Tunis, Tunisia and [2]Mongi SLim Hospital, Nephrology, La Marsa, Tunisia

Background and Aims: The occurrence of renal involvement during the clinical course of systemic lupus erythematous (SLE) is generally considered to be the most important factor influencing the prognosis in terms of morbidity and mortality. The factors influencing prognosis in lupus nephritis (LN) are variable in literature. The aim of our study was to analyze the clinicopathological correlations, and risk factors associated with renal failure in male patients with LN.

Method: We retrospectively studied all male patients with kidney biopsy-proven lupus nephritis (LN) treated in our department during the period between 1979 and 2016. Looking for predictive factors related to renal prognosis, we analyzed clinical, biological and histological data by multivariate analysis using the comparison of the survival rates by the log-rank test.

Results: We collected 41 native renal biopsies showing LN. Patients were aged 32.17 years (17-65 years) at the time of diagnosis of LN. Diagnosis of SLE was made according to the criteria of the American College of Rheumatology. The most common clinical presentation was nephrotic syndrome (61%), and the most frequent pathological finding in sediment was proteinuria (85%). At the time of diagnosis, 17% of patients had hypertension and 39 % of patients had an eGFR under than 60 ml/min/1.73 m^2. LN was of class I, II, III, IV and V in 7.5%, 12.5%, 27.5%, 47.5% and 41.5% of the cases, respectively. Fourteen patients developed end-stage renal failure. The presence of hematuria, renal failure at the time of diagnosis, nephrotic syndrome, low complement, proliferative glomerulonephritis (class IV), high activity index score of LN and thrombotic microangiopathy were significantly associated with poor renal prognosis with (p=0.0053), (p=0.0002), (p=0.0186), (p=0.0287), (p=0.0005), (p=0.058), (p=0.0117), respectively.

Conclusion: Renal failure at the time of diagnosis and active proliferative lesions should be diagnosed and treated as soon as possible because they influence the renal prognosis in lupus man.

P0458

ADVERSE EVENTS AND INFECTIONS, POTENTIALLY RELATED TO GLUCOCORTICOIDS, REMAIN COMMON DURING MAINTENANCE TREATMENT OF ANCA ASSOCIATED VASCULITIS AND ADD TO CLINICAL AND HEALTHCARE RESOURCE USE BURDEN IN EUROPEAN PATIENTS

Peter Rutherford[1], Dieter Götte[1]

[1]*Vifor Pharma, Medical Affairs, Zurich, Switzerland*

Background and Aims: ANCA associated vasculitis (AAV) treatment aims to quickly control vasculitis activity and then prevent relapse during the maintenance phase of this long term condition. Patients are at risk from disease and treatment related complications with high dose and/or long term glucocorticoid use being a major concern. This retrospective study examined adverse events, infections and healthcare resource use in patients managed in routine practice.

Method: 1478 AAV patients (France, Germany, Italy, Spain and UK) managed by 493 physicians (61% Nephrologists) who completed induction therapy for new or relapsing organ or life threatening AAV and initiated maintenance therapy between 2014-16 were studied. Data were collected at the time maintenance was determined to begin by the physician and then at 6, 12, 18 and 36 months. 51% had microscopic polyangiitis, mean age 54.2 years with 56% male. BVAS was not used routinely but 56% had moderate systemic disease and 44% severe systemic disease at the time of start of induction remission treatment.

Results: 78% patients had comorbidity (48% hypertension, 20% dylipidaemia, 17% type 2 diabetes mellitus, 14% depression, 13% COPD/asthma and 9% had BMI $>$ 35) at induction treatment start. Maintenance was defined by physicians as starting approximately 6 months into treatment. AEs potentially linked to GCs were common (values are %, bp = hypertension, DM = diabetes mellitus) during the maintenance phase and many patients remained on long term glucocortioids. Infections were also common, in particular upper (URTI) and lower respiratory tract (LRTI) infection and urinary tract infections (UTI). Hospitilisations still occurred during maintenance period, in particular these are due to infections. Maintenance treatment varied and was changed over follow up (in 13-19% patients at each time point) and in a proportion of patients the change in treatment was precipitated by an adverse event or infection (6 months 21%, 12 months 22%, 18 months 23%, 38 months 26%).

Conclusion: Comorbidity is common in AAV patients and needs to be considered carefully when making treatment decisions. Patients receiving maintenance therapy frequently experience potentially GC related AEs and infections are also common. Healthcare resource use continues in the maintenance phase and this is on the background of comorbidity, less then complete remission rates and high use of long term steroids. New approaches are required to reduce clinical and healthcare system burdens during the maintenance treatment phase of AAV.

	Maintenance start	6 months	12 months	18 months	36 months
Remission full/partial	43 / 50	59 / 38	67 / 30	72 / 25	74 / 22
Receiving GC	65	61	53	46	39
New/worsening bp	32	23	22	19	18
New/worsening DM	21	10	7	6	5
Osteoporosis	4	4	9	9	9
Cardiac Failure	4	4	3	2	2
URTI	20	17	12	10	10
UTI	19	14	12	9	9
LRTI	19	11	9	5	6
Hospitalized		14	8	6	7
Number of total days		2076	1094	695	1069
Cause - Infection		61	61	58	49
Vasculitis		12	4	11	12
Other		27	35	32	39

Figure:

P0459 **ADULT MINIMAL CHANGE DISEASE IN TURKEY: THE RESULTS OF TURKISH SOCIETY OF NEPHROLOGY GLOMERULAR DISEASES WORKING GROUP**

Mürvet Yılmaz[1], Murat Sipahioğlu[2], Erkan Dervişoğlu[3], Nihal Aydemir[4], Sami Uzun[5], Zulal Istemihan[6], Oktay Unsal[7], Erhan Tatar[8], Hacı Bayram Berktas[9], Arzu Ozdemir Kayalar[10], Abdullah Sumnu[11], Gizem Kumru Şahin[12], Hakkı Çetinkaya[13], Sinan Kazan[14], Ismail Kocyigit[2], Cenk Gokalp[15], Nuri Baris Hasbal[16], Ayse Serra Ucar[17], Ruya Ozelsancak[18], Dilek Guven Taymez[19], Serap Yadigar[20], Selma Alagoz[21], Bilal Burçak Aslan[22], Selcuk Yaylaci[23], Zeki Aydin[24], Jabrayil Jabrayilov[25], Kenan Turgutalp[26], Belda Dursun[27], Garip SAHIN[28]

[1]Health Sciences University, Nephrology, İstanbul, Turkey, [2]Erciyes University, Nephrology, Turkey, [3]Kocaeli University, Nephrology, Turkey, [4]Hitit University, Nephrology, Turkey, [5]Haseki Training and Research Hospital, Nephrology, Turkey, [6]Istanbul University, Nephrology, Turkey, [7]Uludag University, Nephrology, Turkey, [8]Bozyaka Training and Research Hospital, Nephrology, Turkey, [9]Inonu University, Nephrology, Turkey, [10]Bakirkoy Dr. Sadi Konuk Training and research Hospital, Nephrology, Turkey, [11]Medipol University, Nephrology, Turkey, [12]Ankara University, Nephrology, Turkey, [13]Sultan Abdulhamit Han Training and Research Hospital, Nephrology, Turkey, [14]Afyon University, Nephrology, Turkey, [15]Trakya University, Nephrology, Turkey, [16]Sisli Etfal Training and Research Hospital, Nephrology, Turkey, [17]Bezmi-alem University, Nephrology, Turkey, [18]Baskent University, Nephrology, Turkey, [19]Kocaeli Hospital, Nephrology, Turkey, [20]Kartal Training and Research Hospital, Nephrology, Turkey, [21]Bagcilar Training and Research Hospital, Nephrology, Turkey, [22]Bursa Yüksek İhtisas, Nephrology, Turkey, [23]Sakatya University, Nephrology, Turkey, [24]Darica Farabi Training and Research Hospital, Nephrology, [25]Hacettepe University, Nephrology, Turkey, [26]Mersin University, Nephrology, Turkey, [27]Pamukkale University, Nephrology, Turkey and [28]Osmangazi University, Nephrology, Turkey

Background and Aims: Minimal change disease (MCD) is the most common cause of the nephrotic syndrome (NS) in children. Although there are many data regarding the course, response to treatment, and outcomes in pediatric patients, only a few series have examined these issues in adults. The aim of the study was to delineate the demographic and clinical properties of MCD of adult population in our country.

Method: All over the country, a total of 47 centers entered data between May 2009 and May 2019 to the database created by of Turkish Society of Nephrology Glomerular Diseases (TSN-GOLD) Working Group. Demographic and clinical characteristics and biopsy findings recorded to the database were analyzed.

Results: In total, 258 patients were compatible with the pathological diagnosis of MCD. Mean age was 36.16±15.44 years and 53.88% were male. At diagnosis, 66.7% patients presented with pretibial edema,15.9% with hypertension. Microscopic hematuria occured in 18.2% patients. Only 24 patients (9.3%) presented with a decrease in renal function (serum creatinine greater than 1.3 mg/dl). The mean daily proteinuria was 6.3 g, and serum albumin was 2.6 mg/dl. The most frequent indication for biopsy was NS (86.4%). On kidney biopsy, the mean number of glomeruli was 18.08±11.11. Mezangial proliferation and mezangial IgM were present in 27.5% and 22.5%, respectively. Only in 3.5% of the included patients, electron microscopic studies were performed.

Conclusion: This study describes the characteristics of a cohort of adult patients with MCD. MCD in adults may sometimes present concurrently with hematuria, hypertension, and acute kidney injury.

P0460

ASSOCIATION BETWEEN CAUSATIVE MICROORGANISMS OF INFECTIVE ENDOCARDITIS AND CLINICAL SPECTRUM OF RENAL LESIONS

Alexandra Pisaruk[1], Nikita Povalyaev[1], Maria Sorokina[2], Elvira Domonova[3], Elizaveta Kotova[1], Nargiz Safarova[4], Yulia Karaulova[1], Alexandr Balatsky[4], Marina Efremovtseva[1], Zhanna Kobalava[1]

[1]Peoples Friendship University of Russia (PFUR), Institute of Medicine,, Moscow, Russia, [2]National Medical Research Center of Pediatric Hematology, Oncology and Immunology named after Dmitry Rogachev, Cellular Hemostasis and Thrombosis Lab, Moscow, Russia, [3]Central Research Institute of Epidemiology, Department of Molecular Diagnostics and Epidemiology, Moscow, Russia and [4]M.V. Lomonosov Moscow State University, Medical Research and Education Center, Moscow, Russia

Background and Aims: The relation between microorganisms and renal lesions in IE has bilateral nature: urinary tract infections may be source of systemic invasion that will cause IE, IE causative microorganisms may cause inflammatory changes in glomeruli or be disseminated in renal parenchyma gematogenously with the formation of the abscesses in case of fragmentation or migration of the vegetations. IE-associated GN - is an immune-mediated GN caused by bacterial infection. More commonly GN presented in cases of streptococcal and staphylococcal IE. For renal embolism is typical association with staphylococcal infection, and there are documented cases of renal infarctions in IE caused by S. pneumonia, and C. burnetti. The effect of microorganisms on other clinical manifestations of kidney damage in IE has not been studied.

Method: The study included 209 patients with verified IE. All patients were performed bacteriological and 81(38,8%) parallel one-moment biomolecular (PCR or PCR with follow-up sequenition) tests. In case of death or cardiac surgery, affected valves (n=15) were tested with the same technique. To asses renal function we calculated glomerular filtration rate with CKD-EPI formula. AKI, AKD and CKD were diagnosed in accordance with present guidelines [KDIGO, 2012].

Results: Renal involvement into the pathological process trended higher in patients with Gr- (p=0,016) and few causative microorganisms (p=0,039). There are significant differences in incidence of different renal syndromes in patients with MRSA, Gr- and few causative microorganisms - these patients more often had acute nephritic syndrome (respectively p=0,036; p=0,005; p=0,003) (tab. 1). Impairment in the renal function was significantly associated with MRSA (p=0,012), Gr- (p=0,01) and few causative microorganisms (p=0,003). In addition long-lasting renal impairment was observed: patients with MRSA had median time of worsening of the renal function 9 days (IQR 4-14), with Gram-negative microorganisms median time was 9 days (IQR 5-12), with polyflora 10 days (IQR 7-14). But there were no significant differences in median time of renal function worsening in patients with other causative microorganisms. Incidence of AKI and AKD depending on causative organism did not significantly differ.

Conclusion: Kidney lesions in IE significantly associated with Gr- microorganisms, MRSA and with the presence of 2 or more causative microorganisms. Clinical spectrum of renal lesions is diverse: from the changes in the urine sediment to longstanding kidney dysfunction.

Table 1. Incidence of renal syndromes depending on the causative agent of IE (n=160).

Causative microorganism	Urinary syndrome (n=105)	Acute nephritic syndrome (n=40)	Nephrotic syndrome (n=15)	χ2
Gr+ microorganisms (n=140), n(%)	75(71,4)	31(77,5)	7(46,7)	8,9*
Staphylococcus (n=96), n(%)	46(43,8)	23(57,5)	6(40,0)	
S. aureus (n=72), n(%)	34(32,4)	18(45,0)	5(33,3)	
MSSA (n=51), n(%)	28(26,7)	9(22,5)	3(20,0)	
MRSA (n=16), n(%)	4(3,8)	7(17,5)	2(13,3)	8,5*
CoNS (n=25), n(%)	12(11,4)	7(17,5)	2(13,3)	
Streptococcus (n=11), n(%)	6(5,7)	3(7,5)	0(0,0)	
Enterococcus (n=37), n(%)	23(21,9)	9(22,5)	0(0,0)	7,0
Gr- microorganisms (n=40), n(%)	17(16,2)	14(35,0)	5(33,3)	12,9**
Fungi (n=8), n(%)	2(1,9)	3(7,5)	1(6,7)	
Few causative microorganisms (n=58), n(%)	25(23,8)	20(50,0)	5(33,3)	14,1**

*p <0,05, **p<0,01, ***p <0,001 – significance of the differences between the groups.

Figure:

P0461 BASELINE SERUM C3 LEVELS IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS AND ITS CLINICAL IMPLICATION.

Maria Maldonado[1], Juan Santacruz[1], Sara Afonso[2], Teresa Olea[1], Lina León[1], Carlos Santos[1], Cristina Vega[1], Begoña Rivas[1], Rafael Selgas[1]

[1]University Hospital La Paz, Madrid, Spain and [2]University Hospital 12 de Octubre, Madrid, Spain

Background and Aims:

The evolution of renal disease and its global impairment in patients diagnosed with ANCA-associated vasculitis (AAV) has been related to baseline C3 serum levels in several studies.

The objective of this study is to evaluate in patients diagnosed with AAV and renal impairment the association between baseline serum C3 levels and the clinical outcomes.

Method:

Our cohort included 56 patients diagnosed with AAV diagnosed from January 1986 to January 2018 in Hospital La Paz. According to C3 serum level measurements, patients were divided into low and normal concentration groups at onset. Histological, clinical and laboratory data were compared between groups.

Results:

Among the 56 AAV cases, 58.9% were women and 96.5% Caucasian with an age mean and SD of 61.08 ± 15.11 years. Mean follow-up was 10.03 ± 7.02 years. MPO ANCAs were found in 69.8% of the patients and PR3 ANCAs in 22.64%. AAV diagnosis was earlier in PR3 AVV (47.59 ± 13.62 years) compared to MPO AVV (65.66 ± 11.53 years) (p=0.001). At diagnosis, baseline serum C3 was measured in 53 patients (94.6%) being lower in MPO AAV (112.79 ± 33.98) vs PR3 AAV (132.41 ± 20.69) (p=0.023). Low C3 was way more frequent in patients with higher percentage of glomeruli showing >50% of sclerosis (100% vs 32.5%) (p=0.007). Staphylococcus aureus nasal carriers were more frequent in patients with low C3 (27.2% vs 3.1%, p=0.045). 15 patients (27.77%) died during follow-up and patient survival median was 21.75 years (IC 95%: 15.41-28.08). 17 patients (31.48%) reached end-stage renal disease (ESRD) during follow-up and renal survival median was 20.1 years (IC 95%: 19.27-21.05).

There were no statistical differences in the levels of baseline serum C3 according to sex, relapses, extrarenal manifestations, treatment, malignancy, cardiovascular events and time to ESRD or death.

Conclusion:

Baseline serum C3 was lower in MPO AV, in Staphylococcus aureus nasal carriers and higher severity histological damage (glomerular sclerosis >50%). Despite previous evidence, in our cohort, time to ESRD and time to death seemed not to be affected.

P0462 HEMODIALYSIS PREDICTORS IN ANCA-ASSOCIATED VASCULITIS AND ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE

Maria Do Mar Menezes[1], Filipa Cardoso[1], Miguel Bigotte Vieira[1], Helena Viana[1], Mário Góis[1], Fernando Nolasco[1]

[1]*Hospital Curry Cabral, Nephrology Department, Lisboa, Portugal*

Background and Aims: Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) and anti-glomerular basement membrane (GBM) disease are autoimmune diseases frequently associated with poor renal outcomes namely hemodialysis. Therefore, the aim of this study was to identify predictors of renal replacement therapy (RRT) at six months in patients with ANCA-associated vasculitis and/or anti-glomerular basement membrane disease.

Method: We performed a single center observational, retrospective study in 40 patients with ANCA-associated vasculitis and/or anti-GBM disease diagnosed between January 2013 and June 2019.

Clinical, analytical and histological variables were included as well as therapeutic regimens and outcomes. The primary endpoint was renal replacement therapy (RRT) at six months.

Continuous variables were presented as means or medians, according to normality and categorical variables presented as frequencies. The comparison between subgroups of patients was performed using the Wilcoxon, Fisher exact test or t-test, chi-square test, according to normality. Univariate logistic regression model was fitted to identify variables associated with renal replacement therapy. STATA 14.2 statistical package was used and $p < 0.05$ was considered statistically significant.

Results: We identified 40 patients, with a mean age of 69 years-old, 18 (45%) were male, 37 (95%) Caucasian. Twenty-seven (68%) had hypertension and 3 (8%) diabetes. The majority (33, 83%) presented with constitutional symptoms. Pulmonary manifestations were seen in 12 (30%) and gastrointestinal in 5 patients (12%). The other symptoms were rare. The mean systolic blood pressure was 140 mmHg and mean diastolic blood pressure 73 mmHg. The mean hemoglobin in hospital stay was 9,4g/dL, albumin 3.0 mg/dL, erythrocyte sedimentation rate 77mm/h, C3 1,11 UQ, C4 0,30 UQ, proteinuria 1,42 gr/24h, hematuria 279 erythrocytes, serum creatinine 3,4 mg/dL, eGFR 14 ml/min/m2, uric acid 7.1 mg/dL. The average ANCA MPO titles were 382 UQ/L, PR3 751UQ/L and GBM 883UQ/L. During hospital stay 11 patients (28%) needed dialysis.

Renal biopsy showed interstitial fibrosis and tubular atrophy grade 0 in 5 patients (13%), grade 1 in 13(33%), grade 2 in 8 (20%) and grade 3 in 14 (35%). The majority had no vessel involvement 24 (60%). Acute tubular necrosis was absent in 13 (33%) patients, grade 1 in 9 (23%) and grade 2 in 18 (45%). Inflammatory infiltrate was present in 25 patients (63%).

Regarding treatment, 38 (95%) of patients received pulse methylprednisolone and all prednisolone. Rituximab was administered to 15 (38%) patients and Cyclophosphamide to 14 (35%). Eighteen (45%) received azathioprine and 3 (8%) mycophenolate mofetil. Plasmapheresis was performed in 14 patients (35%). The average time from beginning of symptoms to treatment initiation was 119 days.

The mean follow-up was 1094 days.

At discharge the mean serum creatinine was 2,5 mg/dL, eGFR 23ml/min/m^2 and none of the patients died.

At six months, mean serum creatinine was 1.6 mg/dL, eGFR 31ml/min/m2 but 15 (38%) patients were dialysis-dependent. Two relapses occurred and 17 (43%) had infections during this period. Five (13%) patients died.

At 12 months, mean serum creatinine was 2.0 mg/dL, eGFR 29 ml/min/m2 and (9) 23% patients were dialysis dependent. Six (30%) patients had infections and 5 (13%) died. In the end of follow up 13 (33%) patients had died.

On univariate analysis, hemoglobin (OR 0.59 [0.36-0.95], p = 0.031), uric acid (OR 1.85 [1.12-3.05], p = 0.027), hematuria (OR 1.00 [1.00-1.00], p = 0.013), hemodialysis performed during 1st hospital stay (OR 22.9 [2.3-217.9], p = 0.006) and plasmapheresis (OR 12.0 [2.4-61.0], p = 0.003) were associated with RRT at six months.

Conclusion: RRT in AAV and anti-GBM disease has decreased over the last decades with the use of immunosuppressive therapies. Clinical presentation and plasmapheresis seem the major predictors for RRT.

P0463 **KIDNEY INVOLVEMENT IN PARAPROTEINEMIC DISEASES - ANALYSIS OF THE SINGLE CENTER REGISTER OF KIDNEY BIOPSIES**

Nikola Zagorec[1], Ana Šavuk[1], Ivica Horvatić[1,2], Dino Kasumović[1], Ana Brechelmacher[1], Miroslav Tišljar[1], Petar Šenjug[3], Danica Galešić Ljubanović[2,3], Kresimir Galesic[1,2]

[1]Dubrava University Hospital, Department of Nephrology and Dialysis, Zagreb, Croatia, [2]University of Zagreb, School of Medicine, Zagreb, Croatia and [3]Dubrava University Hospital, Department of Pathology, Unit for Nephropathology and Electron Microscopy, Zagreb, Croatia

Background and Aims: Kidneys are often damaged in paraproteinemic conditions. Paraproteins are monoclonal immunoglobulins or immunoglobulin fractions that are produced by a clonal population of B- or plasma cell lineage and can cause a variety of histological patterns of kidney injury, such as light chain (AL) amyloidosis or light chain cast nephropathy (LCCN). Monoclonal gammopathy of renal significance (MGRS) represents a group of disorders in which a monoclonal immunoglobulin secreted by B- or plasma cell clone causes renal damage. By definition, these disorders do not meet diagnostic criteria for overt, symptomatic multiple myeloma or a lymphoproliferative disorder, but in contrast to monoclonal gammopathy of undetermined significance (MGUS) there is evidence of end-organ damage that can warrant therapy.

Method: All patients with paraproteinemic kidney disease were identified by retrospective review of the Hospital Register of kidney biopsies done at Department of Nephrology and Dialysis, in Dubrava University Hospital, Zagreb, from 2009 until 2018. Every kidney biopsy was analyzed by light, immunofluorescent and electron microscopy. Laboratory findings, including serum protein electrophoresis, serum free light chain level and immunofixation of serum proteins, were done for every patient. Clinical and histologic features of patients and features of underlying hematological conditions were analyzed.

Results: We identified 47 patients (3,28% of all biopsies that were done in that period) with kidney disease with clear hematological background. The mean patients' age at the time of the biopsy was 63 years and 27 of them were females. Two patients had signs of direct infiltration of kidneys with malignant lymphomic cells (non-Hodgkin lymphoma) and were excluded from the analysis. Clinical presentation of the patients at the time of biopsy were: proteinuria in 85% of patients, full nephrotic syndrome in 55%, azotemia in 66% of patients (80% had acute kidney injury of unclear etiology) and hematuria in 12,7%. Most common histologic patterns of kidney injury were AL amyloidosis (45%) and LCCN (30%) but additionally 7 different histological patterns were found: light chain depostion disease, light chain proxymal tubulopathy, fibrillary and imunotactoid glomerulopathy, proliferative glomerulonephritis with monoclonal immunoglobulin deposition, crioglobulinemic glomerulopathy type I and tubulointerstitial damage caused by immunoglobulin deposition. Figure 1 shows main features of patients with AL amyloidosis and cast LCCN.

Conclusion: Kidney disease can be initial presentation of an underlying paraproteinemia and, as our data showed, can clinicaly present with acute kidney injury, nephrotic or subnephrotic range proteinuria or full nephrotic syndrome. Variety of histologic patterns of kidney injury were described and AL amyloidosis and LCCN were the most common histological findings. Detailed hematologic workup should follow kidney biopsy in order to determine the exact nature and extension of the disease and therefore the most appropriate therapy.

Figure 1. Clinical features of the patients with AL amyloidosis and light chain cast nephropathy (LCCN) with underlying paraproteinemic conditions.

Histologic pattern	No. of patients	Proteinuria No. (%)	Nephrotic syndrome No. (%)	Acute kidney injury No. (%)	Multiple myeloma No. (%)	MGRS No. (%)
AL amyloidosis	21	21 (100)	14 (66,6)	9 (43)	6 (29)	15 (71)
LCCN	14	10 (71)	7 (50)	10 (71)	10 (71)	4 (29)

P0464 **HEALTH ADN ECONOMIC BURDEN OF THROMBOTIC MICROANGIOPATHY. A NEED FOR A MULTIDISCIPLINARY TEAM**

MIGUEL URIOL[1], Aina Obrador Mulet[2,], Ana Escriva[3], Ana Tugores[2,], Albert Perez[4], Antonio Mas[5], José Luis Garcia[1], Joan Gasco[1]

[1]Son Espases University Hospital, Nephrology, Palma, Spain, [3]Son Espases University Hospital, Pharmacy, [4]Son Espases University Hospital, Haematology and [5]Son Espases University Hospital, Neurorradiology

Background and Aims: Thrombotic microangiopathy (TMA) is a life-threatening and rare disease associated with a higher risk of dead and chronic renal replacement therapy (CRRT). Eculizumab is highly effective but also expensive. We evaluate the direct economic burden of the TMA, the cost of CRRT, Eculizumab, and the impact of a multidisciplinary team (MDT) after two years of its implementation.

Method: It is a retrospective study, conducted in a 3rd level hospital. We evaluate the risk of i) dead and ii) CRRT need. The number of patients no treated under futility consideration. The cost (euros) for hospitalization at the floor and intensive care unit admission, CRRT and Eculizumab at the pre-MDT implementation (from January 2008 to May 2016) in comparison with the post-MDT period (from May 2018 to Dec 2018). Clinical outcomes: i) risk of death and ii) risk of CRRT need. To determine the cost per patient-year, we calculated the total number of days of hospitalization, the entire months on dialysis or in kidney transplant program (KTx) and the milligrams of Eculizumab used at any period. The total amount divided by the whole years of observation and finally and by the mean number of patients per year diagnosed at any period. The number of patients-year we determined considering the incidence density (ID: cases/1,000,000 person-year). Patients with ADAMTS-13 deficiency were excluded.

Results: Forty-two patients were included. ID increased from 2.3 cases/1,000,000 person-years (n=20) to 11.7 cases/1,000,000 person-year (n=22). Comparing with the pre-MDT period, the number of patients who died increased from 3(15%) to 7(32%), P=0.20; while the risk for CRRT decreased from 9(45%) to 0, P<0.01 [relative risk (95%CI) for no CRRT requirements: 0.55 (0.37 to 0.81)]. One (5%) and three (14%) patients died under futility consideration at the pre- and post-MDT period, respectively (P=0.60). From all the patients who died, only one was in acute dialysis program while 7 showed neurologic damage. The mean cost per patient-year changed from 319,931 to 150,878 euros from the pre- to post-MDT period.

Conclusion: The implementation of an MDT shows a change in the natural history of the disease, where neurological damage emerges as a risk factor associated with mortality instead of CRRT needs.

TMA patients represent a remarkable economic burden, representing an essential challenge for the health system sustainability that could be improved by an MDT.

P0465 NEPHROTIC SYNDROME IN ELDERLY PATIENTS

Tasnim Ben ayed[1,2,3], Imen Gorsane[1,2,3], Raja Trabelsi[1,2], Mondher Ounissi[1,2], Taieb Ben Abdallah[1,2,3]

[1]Charles Nicolle Hospital, Medecine A, Tunis, Tunisia, [2]Faculty of Medecine, El manar university, Tunis, Tunisia and [3]Charles Nicolle Hospital, Laboratory of Research in Immunology of Renal Transplantation and Immunopathology (LR03SP01), Tunis, Tunisia

Background and Aims: Nephrotic syndrome (NS) is one of the manifestations of acute or chronic glomerular nephropathy in the elderly. Our study objective was to determine the particularities of NS in the elderly.

Method: This is a retrospective study, carried out in the Internal Medicine department A of Charles Nicolle hospital at Tunis, between January the 1st, 1975 and December the 31st, 2016. This study included subjects aged 65 years old or over hospitalized for NS.

Results: We studied 115 patients with an average age of 71 ± 5 years [65-83 years] with a sex ratio (M/F) of 1.7. Twenty-three percent of patients were diabetic. The median proteinuria was 4.7 g/l [3-19.5 g/l], the mean albumin level was 20 ± 6g/l and the mean protidemia was 50.6 ± 6.9 g/l. Nephrotic syndrome was impure in 89.5 % of patients with high blood pressure in 54 % of cases, hematuria ≥2 + in 30% of cases and renal failure in 82.7 % of cases. Renal biopsy was performed in 45 patients. The most common glomerular lesions were Membranous nephropathy (29 %) followed by amyloidosis (24.5 %). NS was secondary in 65.2 % of cases mainly to amyloidosis (35.6 %) and diabetes (19 %). Idiopathic nephropaty was dominated by membranous nephropathy (9.5 %) and primitive primitive (MPGN) (4.3 %). The treatment was symptomatic for 84.4% of patients. Corticosteroids and/or immunosuppressive treatment have been used for 15.6% of patients. At the end of follow-up, 35.3 % of patients achieved complete or partial remission and 56.6 % progressed to ESRD.

Conclusion: Elderly NS was characterized by a poor prognosis due to delayed cosultation and non-uniform treatment strategies. Multicentric study in order to identify different action axes could improve the prognosis of this disease. Multicentric study in order to identify different action axes could improve the prognosis of this disease.

P0466 LUPUS NEPHRITIS IN SOUTH MOROCCO OVER 6 YEARS

Ramia BENHAMOU[1], Allibou Sara[1], Mariem Yahioui[2], Meriem Chettati[3], Wafaa Fadili[1], Lamia Essaadouni[2], Inass Laouad [4]

[1]Mohammed VI University Hospital Center of Marrakesh, Cadi Ayyad University, Nephrology, Marrakesh, Morocco, [2]Mohammed VI University Hospital Center of Marrakesh, Intern medecine, Marrakesh, Morocco and [3]University Hospital Center of Marrakesh, Nephrology, Marrakesh, Morocco

Background and Aims: Lupus nephritis is one of the most serious manifestation of systemic lupus. The study aimed at assessing the epidemiology and clinical features of systemic lupus erythematosus with lupus nephritis (LN) in south Morocco.

Method: A retrospective study was conducted in the Marrakesh-Tensift region by charts review from 2014 to 2019 (included). Patients with a SLE diagnosed with lupus nephritis over 6 years according to ACR/EULAR criteria were included.

Results: In total, 146 patients met inclusion criteria: 133 were women (94%) and mean age at diagnosis was 31,195 $\pm$ 13.5 years. Five percent of all patients had a least one parent with autoimmune disease, and 4,1% with lupus. The main manifestations were musculoskeletal (89%) and mucocutaneous with acute or subacute lesions (68,5%), alopecia (50%), ulcers (3,4%) and discoid lupus (10,27%). Cardiac manifestations in 19,2% and neurological features in 17,9% and psychiatric features in 13,7%. At the moment of diagnosis antinuclear antibodies were positive in 89% (threshold >1/80), and associated to anti-DNA in 91 patients (62,3%), anti-SSA (21,2%), and anti-Sm (34,9%). APL syndrome was diagnosed in 8,2%. Kidney biopsy showed predominantly class IV in 54% and classe I-II in 28%. The average annual standardized incidence of LN between 2014 and 2019 was 2,4 cases per 1,000,000 inhabitants (95% confidence interval [CI]: 5.0–6.0). The prevalence was 21 cases per 1,000,000 inhabitants in 2018 (95% CI: 70–79).

Conclusion: Lupus nephritis in the multi-ethnic population of south moroccan is characterized by high incidence and high rates of diffuse proliferative nephritis.

P0467 **THE DIRECT USE OF ORAL ANTI-COAGULANTS IN MEMBRANOUS NEPHROPATHY**

Maximilian Wills[1], Sanjana Gupta[1], Alice Gage[1], Neil Ashman[1], Suzanne Forbes[1]
[1]*The Royal London Hospital, United Kingdom*

Background and Aims: Barts Health has a dedicated membranous nephropathy (MN) service with 15-20 incident cases per year. Nephrotic syndrome secondary to MN in particular is associated with arterial and venous thrombosis. There is little evidence to guide optimum pharmacological prophylaxis. In those considered high risk, options include warfarin, heparin or aspirin. The advent of direct oral anti-coagulants (DOACs) offers an alternative, though evidence of efficacy is isolated to case studies.

All patients with an albumin <25g/L are offered anticoagulation. We describe our use of DOACs in a large single centre MN cohort.

Method: Retrospective data MN patients between 2015-2019 was analysed. This included: demographics; frequency, type and timing of thromboembolic and bleeding events; biochemical data at initiation and cessation of agent.

Results: Total number of patients: 26

DOAC treatment courses: 30

Exposure to drug (patient days): 9899

Malignancy was excluded in all cases, with the exception of 1 case of MN secondary to cancer.

There were 3 thromboembolic events in 3 patients; all events occurred on rivaroxaban and in PLA2Rab positive MN.

Thrombotic events were all arterial, with no venous events, 2 cerebral artery infarcts and 1 lower limb arterial thrombosis. These patient's mean initial presentation PLA2Rab titres were 164 Kunits/L (75-248) and all were nephrotic at the time of the thromboembolic event. Events were 29, 128 and 340 days post DOAC initiation. 2 of these patients had a venous thrombosis prior to DOAC initiation. Event rate: 0.11 per patient year

Safety data also demonstrated 3 bleeds in this patient cohort - all were minor as per ISTH criteria. 2 epistaxes and 1 associated with rectal prolapse, all without a haemoglobin drop.

Conclusion: Our experience is that DOACs are safe and effective in patients with MN and offer a viable anti-coagulant alternative.

Table 1: Cohort demographics

Gender, n (%)	19 (65) Male / 7 (35) Female
Mean age (range) years	54.9 (26-76)
Mean eGFR (range) ml/min/1.73m^2	63.5 (17-124)
Median albumin (interquartile range) g/L	23.5 (20-28)
Phospholipase A2 receptor antibody (PLA2Rab) positivity, n (%):	
PLA2Rab seropositive	20 (76)
PLA2Rab seronegative, immunohistochemistry positive	2 (8)
PLA2Rab seronegative, immunohistochemistry negative	2 (8)
PLA2Rab seronegative, immunohistochemistry unknown	2 (8)
Median DOAC initiation PLA2Rab titre, Kunits/L (interquartile range)	141 (75-993)
DOAC %	Rivaroxaban 80% Apixaban 20%
Mean treatment course duration, days (range)	330 (46-964)

P0468 RENAL OUTCOME AND MORTALITY OF GLOMERULONEPHRITIS IN A THAI TERTIARY CARE CENTER

Chitimaporn Janphram[1], Chagriya Kitiyakara[2]

[1]Ramathibodi Hospital, Medicine Ramathibodi hospital (Nephrology unit), Bangkok, Thailand and [2]Ramathibodi Hospital, Bangkok, Thailand

Background and Aims: Glomerulonephritis (GN) is a common cause of End-stage renal disease (ESRD) in Asia and around the world. Most studies from renal registries have focused on the prevalence or clinical characteristics of patients with GN. Only a few registry-based data have focused on mortality and ESRD risks of different types of GN. There is limited data from low to middle income countries or from Southeast Asia. The objectives of this study were to evaluate the mortality and ESRD rates among patients with different types of GN referred for a kidney biopsy at a Thai tertiary care hospital.

Method: In this retrospective study, the data of patients (n=1,025) referred for a kidney biopsy at Ramathibodi Hospital from 1 January 2011 to 31 December 2017 were reviewed. Patients were classified in to 11 different types of GN. Patient death and cause of death data was obtained from National Census office. ESRD data was obtained from the Thailand Nephrology Society ESRD registry which includes all patients on renal replacement therapies for greater than 3 months.

Results: Patients with inadequate specimen (n=66) or non-glomerular diseases (n=95) were excluded. Data from 864 patients with GN was analyzed. The age at kidney biopsy was 43.9 ± 16.8 years, median eGFR (CKD-EPI) was 42 (IQR 13-83) mL/min/1.73m^2. The male:female ratio was 0.6. The prevalence of GN were: Lupus nephritis (26.8%), IgA nephropathy (18.2%), focal segmental glomerulosclerosis (FSGS 12.6 %), membranous nephropathy (11.9 %), diabetic nephropathy (10.8%), minimal change disease (9.7%), hypertensive nephrosclerosis (4.3%), pauci-immune complex glomerulonephritis (2.3%), membranoproliferative glomerulonephritis (MPGN 1.6%) and multiple myeloma (1.4%)

Median time follow up was 42 (IQR 23-62) months. Overall mortality was 13 %. Lupus nephritis accounted for highest proportion of all deaths (25%), followed by diabetic nephropathy (19.1%), FSGS (9%). Listed causes of deaths were: sepsis 22% and chronic kidney disease 8%. Mortality rates by disease were: multiple myeloma (50%), diabetic nephropathy (28.7%), MPGN (21.4%), pauci-immune complex GN (20%), hypertensive nephrosclerosis (15.8%), lupus nephritis (14.6%), membranous nephropathy (8.7%), FSGS (8.2%), minimal change disease (5.8%), IgA nephropathy (4.4%)

The incidence of ESRD was 14 %. LN accounted for the highest proportion (29%) of all ESRD, followed by IgA nephropathy (14%), and membranous nephropathy (13%). The rates of ESRD by disease were: multiple myeloma (33.3%), lupus nephritis (15%), membranous nephropathy (14.5%), minimal change disease (14.3%), MPGN (14.2%), IgA nephropathy (10.1%), FSGS (10.1%), diabetic nephropathy (7.4%), pauci-immune complex glomerulonephritis (5%), hypertensive nephroclerosis (2.6%).

Conclusion: Lupus nephritis is the most common GN and accounted for the highest proportion of all deaths and ESRD in this Thai cohort. IgA nephropathy is the most common primary GN and an important cause of ESRD, but the mortality rate is low compared to other GN. Membranous nephropathy has comparable prevalence to FSGS, but is a more important contributor to ESRD. Diabetic nephropathy has higher rate of mortality than ESRD. Multiple myleloma has the highest rate of both death and ESRD.

P0469 **VALIDATING THE DIAGNOSTIC ACCURACY OF MEMBRANOUS NEPHROPATHY IN THE HEALTH IMPROVEMENT NETWORK (THIN) DATABASE**

Roseanna Wheatley[1], Patrick Hamilton[2], Kieran Blaikie[3], Anirudh Rao[4], Durga Kanigicherla[1], Paul Brenchley[2]

[1]Manchester University NHS Foundation Trust, Manchester Institute of Nephrology and Transplantation, Manchester, United Kingdom, [2]University of Manchester, Wellcome Centre for Cell-Matrix Research, Manchester, United Kingdom, [3]University of Manchester, Centre for Biostatistics, Manchester, United Kingdom and [4]Royal Liverpool and Broadgreen University Hospitals, Renal Department, Liverpool, United Kingdom

Background and Aims: Membranous nephropathy (MN) is among the most common causes of nephrotic syndrome in adults worldwide. Despite this, there is currently no robust data on the epidemiology of MN in the UK population. The Health Improvement Network (THIN) is an electronic medical record database that holds longitudinal anonymised patient records for over 17 million patients and has shown to be generalisable to the UK regarding demographics and crude prevalence's of major conditions. To our knowledge, accuracy of the read codes for glomerular disease is yet to be validated. This will be the first study into MN validating the diagnostic accuracy using the THIN database.

Method: THIN database was interrogated for patients with MN using read codes. Two cohorts were considered: *Definite cohort*, defined as read codes expected to correspond to a diagnosis of MN, and *Probable cohort*, defined as read codes that could correspond to a diagnosis of MN. In order to confirm the diagnosis of MN, a short questionnaire was sent to the GP practice of a randomly selected cohort of patients asking if the diagnosis of MN was correct, and that the diagnosis had been confirmed by a specialist renal centre, with or without a renal biopsy.

Results: 267 patients with a record of MN were identified from the THIN database. 235 of the patients had *Definite cohort* read codes, with a mean age at diagnosis of 57 years. There were 155 (66.2%) male and 79 (33.8%) female patients. 32 patients were identified in the *Probable cohort*. GP questionnaires were sent to 71 randomly selected patients with 61 responses (85.9% response rate). This represented 23% (n=53) of the total *Definite cohort* and 25% (n=8) of the total *Probable cohort*. Of the 61 returned questionnaires, an MN diagnosis was confirmed in 96% (n=51) of patients with a definite read code and 25% (n=2) with a probable read code. Amongst the confirmed MN diagnoses in the *Definite cohort*, 88% (n=45) of the patients had primary MN.

Conclusion: The THIN database is a valid data resource for studying MN in patients with a read code from the *Definite cohort* list. Read codes from the *Probable cohort* list cannot be used unless confirmed on a case by case basis such as through the GP. The results of this study will feed into a larger project with an aim to describe accurately the epidemiology of MN in the UK population, and report the incidence and prevalence of specific secondary associations of MN. Once these factors are fully understood, diagnostic and care pathways for MN can be developed.

P0470

IS GLYCOSURIA A MARKER OF TUBULO-INTERSTITITAL FIBROSIS AND PROGNOSIS IN PRIMARY GLOMERULOPATHIES?

Carolina Ormonde[1], Ivo Laranjinha[2], Augusta Gaspar[2], Margarida Gonçalves[2], Célia Gil[2], Jorge Dickson[2], Domingos Machado[2]

[1]Hospital do Divino Espírito Santo, Nephrology, Ponta Delgada, Portugal and [2]Centro Hospitalar Lisboa Ocidental, Hospital de Santa Cruz, Nephrology, Lisboa, Portugal

Background and Aims: Multiple studies have shown that tubular damage is common in glomerular diseases and that it correlates better with chronic kidney disease (CKD) progression than glomerular lesion itself. The link between glomerular and tubular damage is not entirely established. Glycosuria can be found in (proximal) tubular dysfunction and may be used as a marker of tubular lesion and CKD progression. The aim of this study was to evaluate the association between glycosuria (at the diagnosis) and known histological prognostic markers (glomerular sclerosis (%GS) and interstitial fibrosis/tubular atrophy (IFTA)) and CKD progression, in patients with primary glomerulopathies (GP).

Method: We conducted a 36-month retrospective cohort study with 110 patients with primary GP confirmed by renal biopsy in the last 10 years in our centre – 39 (35.5%) IgA Nephropathy, 27 (24.5%) Membranous Nephropathy, 26 (23.6%) Focal Segmental Glomerulosclerosis and 18 (16.4%) Minimal Change Disease. Patients were divided in two groups according to their glycosuric status at the time of the diagnosis. Data was collected from patients' charts. Exclusion criteria: patients with diabetes or glucose intolerance, use of SGLT2 inhibitors, secondary GP and transplant kidney patients.

Results: The global prevalence of glycosuria was 9.1% (n=10). Glycosuric patients had, at baseline, higher serum creatinine (3.9±5.1 vs 1.7±1.3mg/dL, p=0.001), higher baseline albuminuria (7.1±6.3 vs 3.2±3.4 g/g, p=0.002) and lower serum albumin (2.3±0.7 vs 3.2±1.1 g/dL, p=0.022). Both groups had similar proportion of patients that underwent immunosuppressive therapy. At the end of the follow-up, in glycosuric patients, only albuminuria was higher (3.3±0.6 vs 0.7±0.8 g/g, $p<0.0001$); the eGFR decline rate (ml/min/year), 3-year eGFR and 3-year CKD stage 5D incidence were not statistically different. Glomerular sclerosis (%GS) and interstitial fibrosis and tubular atrophy (IFTA) were not different between groups. These results were confirmed by multivariate analysis.

Conclusion: Patients with primary GP with glycosuria at diagnosis had higher baseline creatinine and albuminuria. Even though a worse clinical presentation, glycosuria was not associated with well-known prognostic factors (%GS and IFTA) or CKD progression. We can hypothesize that patients with primary GP with glycosuria have severe diseases at diagnosis, but the lesions may have greater reversibility. Prospective and longer studies are needed to confirm these results.

P0471

DIALYSIS TREATMENT AT THE TIME OF DIAGNOSIS PREDICTS OUTCOMES IN ANCA ASSOCIATED VASCULITIS PATIENTS - DATA FROM CROATIAN REFERRAL CENTER

Matija Crnogorac[1], Ana Brechelmacher[1], Ivica Horvatić[1], Patricia Kacinari[1], Miroslav Tišljar[1], Luka Toric[1], Ivan Durlen[1], Klara Juric[1], Petar Senjug[2], Danica Galešić Ljubanović[2], Kresimir Galesic[1]

[1]Dubrava University hospital, Department of nephrology and dialysis, Zagreb, Croatia and [2]Dubrava University hospital, Department of clinical pathology, Zagreb, Croatia

Background and Aims: Dialysis dependence and ESRD are known complications of ANCA associated vasculitis (AAV) with renal involvement. What is not so often discussed is the role of dialysis treatment at the time of diagnosis and how it affects patient outcomes as well as characteristics of such patients. We present data showing the importance of dialysis treatment at the time of diagnosis as the predictor of clinical outcomes.

Method: This study included 106 consecutive AAV patients with renal involvement in the period from 2007-2017. We performed renal biopsy on patients using automatic 16 Gauge needle. Light, immunofluorescent and electronic microscopy were performed.

Primary outcomes were combined outcome progression to end-stage renal disease, defined as persistent (more than three months) need for renal replacement therapy or permanent reduction of EGFR to <15ml/minute (according to CKD EPI formula) and/or death (ESRDD), death (D) and ESRD alone, and disease relapse. Kaplan Meyer survival analysis and multivariate Cox proportional hazard regression analysis were used to explore difference between phenotypes and finding significant predictors regarding outcomes.

Results: Out of 106 patients (55,6% female, median age 61; IQR 51-70) there were 66 (61,1%) microscopic poliangitiis (MPA), 20 (18,5%) granulomatosis with angitiis and 20 (18,5%) with renal limited vasculitis (RLV). Out of those 14 (13%) were PR3-ANCA positive patients, 57 (52,8%) MPO ANCA positive, 5 (4,6%) PR3-ANCA+MPO-ANCA positive and 32 (29,6%) ANCA negative patients. Average serum creatinine (SCr) levels was 316,5 μmol/l (IQR 207,0-548,5), 24-hour proteinuria median was 1,7g/24h (IQR 0,8-2,8). According to the Berden classification 43 (39,8%) patients had crescentic, 19 (17,6%) focal, 34 (31,5%) mixed and 12 (11,1%) sclerotic class. Follow up time ranged from 1 to 127 months. Median follow up time was 21 months (IQR = 7-44). Median time to diagnosis was 3 months (IQR 2,0-6,0). Patients requiring dialysis treatment at the time of diagnosis were more often MPO – (p=0,04), had more severe anemia (p=0,001), higher CRP (p=0,003), and more pronounced hypoalbuminemia (serums albumin <30g/l; p=0,006).Such patients were older than those not requiring dialysis (p=0,055) na had shorter time to diagnosis (p=0,001). Clinically such patient s presented more often with RPGN (p<0,001) which is in a way expected thus having higher SCr levels (p=<0,001). Histologically dialysis treated patients predominantly had crescentic class, while non-dialysis group had focal class (p<0,001). Of note dialysis group had more acute tubular damage (p=0,007). Interestingly enough there was slightly more positive C3 deposition in dialysis group (p=0,09). In univariate analysis the need for acute dialysis at the time of diagnosis of AAV was significant predictor for combined ESRDD, D, ESRD and relapse rate. In multivariate analysis the need for acute dialysis at the time of diagnosis of AAV remained significant predictor for ESRD (HR = 4,674, 95% CI =1,996-10,946; p = < 0,001) and relapse rate (HR = 59,545, 95% CI =3,467-1022,665; p = 0,005).

Conclusion: The need for dialysis at the time of AAV diagnosis is a strong predictor for ESRD and relapse rate. It is also interesting to further study differences between patients needing dialysis at the time of diagnosis and those who don't need it.

P0472 RENAL OUTCOMES OF IDIOPATHIC MEMBRANOUS NEPHROPATHY IN ELDERLY

Nessrine Breik[1], Mouna Jerbi[2,3], Raja Aoudia[1,3], Soumaya Chargui[1,3], Hanen Guaied[2,3], Imen Gorsane[1,3], Rim Goucha[2,3], Taieb Benabdallah[1]

[1]Charles Nicolle Hospital, Department of Nephrology, Dialysis and Transplantation, Tunis, Tunisia, [2]Mongi Slim Hospital, Department of Nephrology, La Marsa, Tunisia and [3]Charles Nicolle Hospital, Research Laboratory of Kidney Diseases (LR00SP01), Tunis, Tunisia

Background and Aims: Idiopathic membranous nephropathy (IMN) is increasingly seen in older patients but little is known about its treatment and outcomes at long term follow up. The objective of this work is to study the renal survival of IMN in elderly as well as prognostic factors.

Method: We conducted a retrospective descriptive study in the nephrology department at Charles Nicolle hospital over a period of 44 years. All older patients ($\geq$65 years) with histologically proven MN were included in this study. Data collected included demographic, clinical and biological parameters in each patient. Data were entered and analyzed using SPSS software. Chi-squared test with a level of significance of 0.05 was used for the qualitative variables.

Results: Twenty-eight patients were collected. The mean age was 67.03 years (65-78 years) with a male predominance (sex ratio: 2.3) and low socio-economic level in 82.5% of cases. Sixteen patients were smokers (57.14%), 5 ethyl patients (17.8%), diabetes was present in 3 patients (10.7%) and hypertension in 11 patients (39.28%). The clinico-biological picture was dominated by high systolic blood pressure in 21 cases (75%), anasarca in 7 cases (25%), proteinuria in all cases and hematuria in 20 cases (71.14%). Biology revealed nephrotic syndrome (NS) in all cases, hypercholesterolemia in 23 cases (82.14%), high serum creatinine in 14 cases (50%) with an average creatinine level of 127,95 µmol/l, anemia in 17 cases (60.7%) and anti-neutrophil cytoplasmic antibodies were positive in one case. MN was confirmed by a kidney biopsy in all cases. Symptomatic treatment was indicated in all patients. Immunosuppressive therapy was started early in 12 patients (40%) because of the severe NS and the deterioration of renal function. Eight patients (26.6%) received corticosteroids alone, three patients received corticosteroid with mycofenolate mofetil and one patient received corticosteroid with ciclosporin. Fourteen patients received only symptomatic treatment. We noted complete remission in 6 patients (21.42%) and end renal stage disease in 5 patients (17.85%). Our study showed that treatment with angiotensin receptors blockers was associated with better renal survival with a statistically significant difference, ($p = 0.011$). A reduced kidney function at presentation, tubule-interstitial disease and interstitial fibrosis and tubular atrophy were associated with poor survival with a statistically significant result ($p = 0.012$) (p=0,011) respectively.

Conclusion: IMN is the most common cause of nephrotic syndrome in elderly patients and it has the same risk for progression as in younger individuals. Decrements in glomerular filtration rate, increased risk for comorbidities, vascular disease and change in pharmacokinetics justify special attention to treatment decisions in elderly individuals with IMN.

P0473 LONGITUDINAL CHANGES OF IGA1 O-GLYCOFORM IN IGA NEPHROPATHY

YUKAKO OHYAMA[1], Hisateru Yamaguchi[2], Kazuki Nakajima[3], Daijo Inaguma[1], Midori Hasegawa[1], Naotake Tsuboi[1], Matthew B Renfrow[4], Jan Novak[4], Yukio Yuzawa[1], Kazuo Takahashi[1,5]

[1]Fujita Health University School of Medicine, Nephrology, Toyoake, Japan, [2]Fujita Health University School of Medicine, Institute for Comprehensive Medical Science, Toyoake, Japan, [3]Fujita Health University School of Medicine, Center for research promotion and support, Toyoake, Japan, [4]University of Alabama at Birmingham, Biochemistry and Molecular Genetics and Microbiology, Birmingham, Alabama, United States of America and [5]Fujita Health University School of Medicine, Biomedical Molecular Sciences, Toyoake, Japan

Background and Aims:

Elevation of circulatory IgA1 with galactose-deficient (Gd) hinge-region (HR) *O*-glycans (Gd-IgA1) has been detected in most IgA nephropathy (IgAN) patients based on lectin ELISA. However, new approaches are needed for molecular-level characterization of IgA1 HR glycoform(s) in IgAN. We established a high-throughput method for analysis of IgA1 HR *O*-glycoforms using liquid chromatography-high-resolution mass spectrometry (LC-HRMS). To identify IgAN-associated IgA1 HR *O*-glycoforms and to assess their changes after therapy (with or without corticosteroids (CS)), we profiled IgA1 HR glycopeptides from sera collected at two time points (before and after therapy) from Japanese IgAN patients.

Method:

Of the 10 Japanese IgAN patients recruited, 4 received CS treatment (CS group) and 6 have not (non-CS group). Japanese healthy volunteers (HC, n=10) were recruited as controls. Serum IgA1 was purified by affinity chromatography from HC and IgAN patients before and after therapy. After neuraminidase treatment and trypsin digestion, IgA1 HR glycosylation heterogeneity was analyzed by LC-HRMS. The relative abundance (RA, %) for each glycopeptide was calculated as percentage to the total IgA1 HR glycopeptide. The amount of each glycopeptide was then calculated by multiplying serum IgA concentration (mg/dL) by RA.

Results:

Approximately 60% of IgA1 HR *O*-glycoforms in IgAN patients and HC were Gd *O*-glycoforms; these glycoforms contained one to three Gd-glycan(s), designated as 1 Gd-glycoform, 2 Gd-glycoform and 3 Gd-glycoform, respectively. In IgAN patients, the RA of non Gd-IgA1 glycoforms was elevated (P=0.002) and correlated with proteinuria (g/gCr) at renal biopsy (P=0.039, R=0.657). The amounts of non Gd- and 1Gd-glycoforms were higher in IgAN patients compared to HC (each P<0.001). After several years of follow up (2.77 years (1.44-3.85)), the RA of non Gd-glycoforms decreased in CS group of IgAN patients (P=0.039) whereas it remained unchanged in the non-CS group (P=0.488). The amount of non Gd-glycoforms exhibited similar trends, *i.e.,* decreased in CS group (P=0.068) whereas it remained unchanged in the non-CS group (P=0.943).

Conclusion:

This study profiled serum IgA1 for IgAN-associated IgA1 HR *O*-glycoforms at the molecular level and assessed their changes in response to CS *vs.* non-CS therapy. IgA1 HR *O*-glycoforms altered by treatment may serve as a biomarker(s) for monitoring patients' responses to therapy.

P0474 UTILITY OF NATIVE KIDNEY BIOPSY IN OLDER ADULTS: SAFETY AND DIAGNOSES

Hui Zhuan Tan[1], Cynthia Lim[1], Marjorie Foo[1], Chieh Suai Tan[1], Jason Choo[1]

[1]*Singapore General Hospital, Renal Medicine, Singapore, Singapore*

Background and Aims: Population aging is an increasing phenomenon worldwide and consequently more are developing kidney diseases which may necessitate diagnostic kidney biopsy. However, older patients may be at increased risk for complications such as bleeding. We aimed to examine the utility and safety of native kidney biopsies among our older adults.

Method: This was a single-centre retrospective study of older adults ($\geq$60 years) who had native kidney biopsies at the Singapore General Hospital between June 2011 and March 2015. Demographic data, co-morbid illnesses, clinical presentation at kidney biopsy, as well as laboratory results before and after kidney biopsy, were retrieved from electronic medical records. Patient outcomes were recorded until their last visit or death before 30th March 2017. End stage renal disease (ESRD) was defined as estimated glomerular filtration rate (eGFR) $<$15 ml/min/1.73 m^2 or need for renal replacement therapy persisting $>$3 months. All post biopsy bleeding events were documented, with major bleeding defined as the need for transfusion and/or intervention; or if bleeding was either a direct or contributory cause of death.

Results: Older adults accounted for 153 of 545 (28.1%) native renal biopsies performed. The indications for biopsy in older adults included microscopic hematuria with proteinuria (51.0%), nephrotic syndrome (32.0%) and isolated proteinuria (17.0%). One hundred and ten patients (71.9%) had eGFR $<$60ml/min/1.72m2 at biopsy and a significantly higher proportion of older patients (85.5% vs 62.4%, $p<0.001$) had eGFR $<$30ml/min/1.72m2. Compared to the younger individuals $<$60 years old, older patients were more likely to be hypertensive (86.3% vs 58.4%, $p<0.001$) and diabetic (49.0% vs 28.1%, $p<0.001$).

Post biopsy, major bleeding was more frequent among older adults compared with younger adults (13.3% vs 5.7% respectively; p=0.04), although overall bleeding episodes between older and younger adults were not significantly different (15.9% vs 22.9% respectively; p=0.18).

Among older adults, minimal change disease (MCD) or focal segmental glomerulosclerosis (FSGS) was the most frequent diagnosis (23.5%), followed by membranous nephropathy (20.9%) and IgA nephropathy (9.8%), whereas MCD/FSGS (26.5%), lupus nephritis (24.5%) and IgA nephropathy (19.6%) were the top three diagnoses amongst younger adults. Co-existing glomerulonephritis (GN) with diabetic nephropathy and isolated diabetic nephropathy were seen in 12 (7.8%) and 20 (13.1%) elderly patients respectively. The majority (124 patients, 81.0%) of biopsies in older adults had histological diagnoses of glomerulonephritis that were potentially amendable to treatment although only 90 (58.8%) patients subsequently received immunosuppressants.

Among older adults with biopsy-proven glomerulonephritis, median follow up was similar between those treated and not treated with immunosuppressants (30.4 [27.3, 53.7] months versus 38.8 [30.7, 51.9] months, p=0.12). Among older adults with GN, ESRD was less frequent among those treated with immunosuppressants, compared to those who did not receive immunosuppressants, although the difference did not reach statistical significance (10.3% versus 18.9%, p=0.24). However, the combined endpoint of ESRD or mortality were similar (24.1% vs 21.6%, p=0.76).

Conclusion: Our findings support the utility of renal biopsy for diagnosis and to guide clinical care. Older adults undergoing kidney biopsy should be counselled and monitored for bleeding complications.

P0475 **CRESCENTIC GLOMERULONEPHRITIS FOLLOWING HCV TREATMENT WITH DAAS, THE NON-CLASSIC TALE**

Mohamed Elrggal[1], Mariam Emam[1], Wesam Ismail[2]

[1]Kidney and Urology Center, Nephrology, Alexandria, Egypt and [2]Beni-Suef University, Pathology, Egypt

Background and Aims: Observational studies suggest that acute kidney injury may occur in up to 15% of patients treated with sofosbuvir based regimens. Histological findings show features of acute interstitial nephritis (AIN) or acute tubular necrosis (ATN). Here, we report the first case of small vessel vasculitis following sofosbuvir treatment.

Method: A 65-year-old female with controlled T2DM was recently diagnosed with HCV. She attained sustained viral response (SVR) after a three-month course of (sofosbuvir + daclatasvir + ribavirin). Kidney functions were normal pre and post treatment. Three months later, she presented with puffiness, bilateral lower extremities edema (no rash) and vomiting. Labs showed acute kidney injury (AKI), nephrotic proteinuria and haematuria (table 1). Immunological investigations (C3, C4, ANA, ANCA and anti-GBM), paraproteinemia workup and cryoglobulins were all negative. Renal US was also normal. Kidney biopsy revealed focal necrotizing glomerulonephritis with 70% crescents (figure 3,4). No chronic changes were detected in the glomeruli, interstitium or tubules. The patient received pulse methylprednisolone 0.5 gm for 3 days followed by oral prednisolone 60 mg/day. Oral cyclophosphamide was initiated at 150 mg after biopsy result was obtained. Our patient showed clinical and laboratory improvement (figure 1,2), however, she developed bone marrow suppression that required cessation of cyclophosphamide. Valsartan initiated to control proteinuria with slight increase in serum creatinine to 1.4 mg/dl. The patient is still under close follow up every two weeks, with a plan to introduce rituximab if serum creatinine continued to increase.

Results: AKI following HCV treatment with DAA has been reported. Explanation includes AIN, ATN and cryoglobulinemic vasculitis (CV). AIN and ATN usually occur during the treatment course, which is not the case in our patient as she developed AKI three months following the end of the treatment, and the biopsy did not show signs of either ATN or AIN. New onset CV has been reported previously in 3 case reports following SVR after DAA treatment. Previous reports explained that HCV can induce B-cell clonal proliferation that may persist independent of viral eradication and produce IgM kappa which will result in cryoglobulinemic GN, again this is not true in our case. Our patient did not have a rash, her serum cryoglobulin was negative and complement levels (C3 and C4) were normal and biopsy did not show evidence of CV. As far as we know, this is the first case with suspected sofosbuvir associated small vessel vasculitis to be reported. Despite the patient had a negative serum ANCA levels, we suspect that this is a case of drug induced vasculitis. Drug induced vasculitis has been reported with hydralazine, propylthiouracil and cocaine, none of these drugs were used in our case. Also, there is no reported case of vasculitis associated with ribavirin or daclatasvir. Thus, we suspect Sofosbuvir is the cause of drug induced vasculitis in this patient.

Conclusion: Crescentic GN following HCV treatment using DAA is a serious complication that should be promptly diagnosed and managed. Physicians treating HCV infected patients should be aware of this possible complication and monitor for kidney function even after achieving SVR.

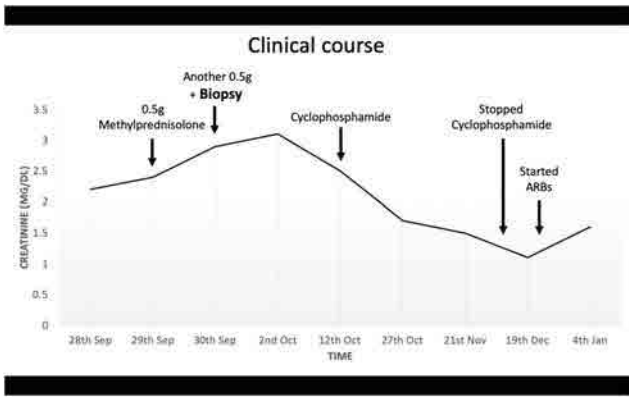


Figure 1: Treatment course against serum creatinine over time

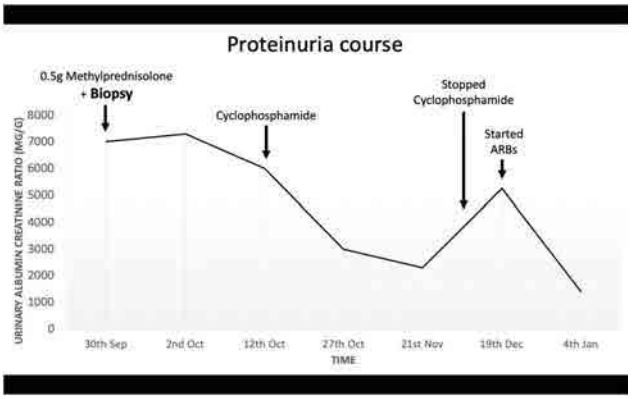


Figure 2: Proteinuria level against treatment and time

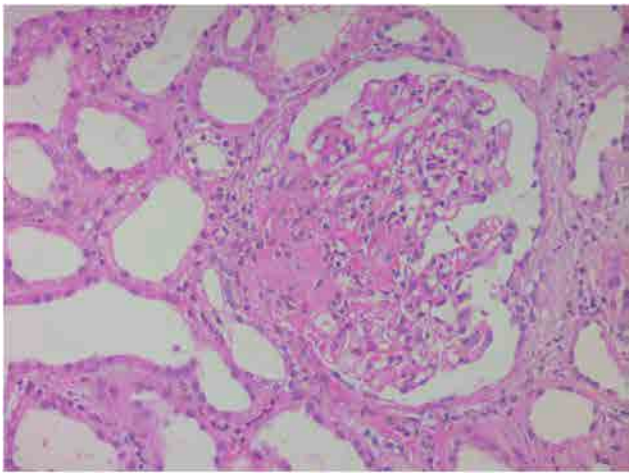


Figure 3: H&E stain of kidney biopsy

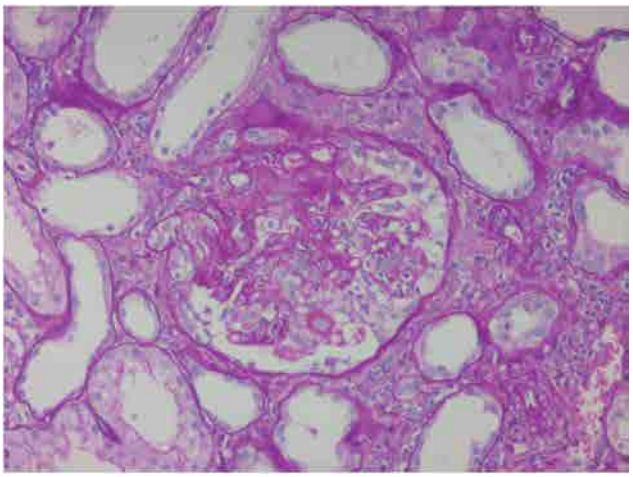


Figure 4: PAS stain of kidney biopsy

Table 1: Laboratory investigations of the patient

	4.2019	9.2019	10.2019	11.2019	12.2019
Urea (mg/dl)	25	86	112	62	53
Creatinine (mg/dl)	0.9	2.4	3.2	1.5	1.1
Uric acid (mg/dl)	4	6.5	7.1	5	5
Na (mEq/l)	140	122	133	127	133
K (mEq/l)	3.8	5.5	5	5.1	4.6
U-ACR (mg/g)		7000		2800	1403

P0476 **THE ABSENCE OF REMISSION PREDICTS MORTALITY IN RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS.**

Leydy Yohana Gil Giraldo[1], Patricia Muñoz Ramos[1], Antonio Carlos Fernández Perpen[1], Borja Quiroga[1]

[1]*Hospital de La Princesa, Nephrology, Madrid, Spain*

Background and Aims: Rapidly progressive glomerulonephritis (RPGN) encompasses a group of diseases with a common histology in which the absence of treatment progress to end-stage renal disease. Induction treatment includes the use of immunosuppressants, and in certain cases, plasmapheresis. The final objective of this study was to determine the long-term prognosis of the RPGN.

Method: A retrospective observational study was conducted, including patients diagnosed with RPGN between 2004 and 2019. Baseline epidemiological data and comorbidities were collected, as well as renal function and treatment at the time of diagnosis. During the follow up [median of 42 (5-101 months)], we analyzed the evolution of renal function, mortality and associated factors.

Results: Forty-three patients (65% women) were included, with a mean age of 70 $\pm$ 16 years. At the time of diagnosis, mean creatinine was 4.8 $\pm$ 2.6 mg/dl, proteinuria 1094 $\pm$ 856 mg/day and 37 patients (86%) presented hematuria Thirty-one patients (72%) presented positivity for antibodies against the neutrophil cytoplasm, 7 (16%) for antibodies against the glomerular basement membrane and 5 (12%) for both. Regarding the induction treatment, 41 patients received cyclophosphamide and corticoids and two patients received rituximab. Seventeen (31%) plasmapheresis were performed with a median of 7 (6-7 sessions).

At 6 months, 55% of the patients presented remission (15 patients complete remission and 8 patients partial remission). The median creatinine was 1.9 (1.2-3.1) mg/dl and the proteinuria was 380 (85 -542) mg/day ($p<0.0001$ compared to the initial data). At that time, 21% (9) of the patients needed dialysis. Associated factors with the absence of remission were diabetes mellitus ($p= 0.016$), creatinine at diagnosis ($p= 0.002$) and the need for hemodialysis at admission ($p<0.0001$). The only independent predictor of remission was initial creatinine (HR 0.5 [0.3-0.9], $p= 0.048$). During follow up, renal function improved with a median of creatinine at 18 months of 1.6 (1.2 – 2.9) mg/dl and 1.5 (0.8-2.4) mg/dl at the end. Twelve (28%) patients died during follow up. Associated factors with mortality were age ($p=0.02$), the need for hemodialysis ($p=0.015$) and the absence of remission at 6 months ($p=0.012$) (figure 1). An adjusted model using Cox regression demonstrated that the absence of remission was an independent predictor of mortality (HR 0.2 [0.5-0.8], $p= 0.032$).

Conclusion: Initial renal function and 6-month remission predicts mortality in the RPGN.

Figure 1: Kaplan Meier curves for the association between 6-month remission and long-term mortality.

P0477 CLINICOPATHOLOGICAL STUDY OF MIXED CRYOGLOBULINEMIC GLOMERULONEPHRITIS SECONDARY TO HEPATITIS B VIRUS INFECTION

Chao Li[1], Hang Li[1], Wei Su[2], Yu-bing Wen[1], Wei Ye[1], Wen-ling Ye[1], Xu-zhen Qin[2], Jian-fang Cai[1], Xuemei Li[1], Xuewang Li[1]

[1]Peking Union Medical College Hospital, Nephrology Department, Bejing, P.R. China and [2]Peking Union Medical College Hospital, Laboratory Department, Bejing, P.R. China

Background and Aims: To describe the clinical features, renal pathology findings and prognosis in patients with mixed cryoglobulinemic glomerulonephritis (Gn) caused by hepatitis B virus (HBV) infection.

Method: This was a retrospective study including seven Chinese patients with HBV infection associated mixed cryoglobulinemic Gn in a tertiary referral hospital from April, 2016 to March, 2019. The demographic, clinical, pathological characteristics, treatment and follow-up data were collected and analyzed.

Results: Age at renal biopsy was 47±12 years, including three females and four males. 24hUP was 5.6(3.0, 6.6)g/d and five cases presented with nephrotic syndrome. The median baseline eGFR(CKD-EPI) was 23.5(20.2, 46.3) ml/min per 1.73m^2. The extrarenal manifestations were: purpura (n=6), arthralgia (n=1), peripheral neuropathy (n=1), and cardiomyopathy (n=1). Six cases had type II cryoglobulinemia with IgMκ, the other one had type III. The median cryocrit was 4.0 (1.0, 15.0) %, rheumatoid factor was 368(117, 733) IU/ml, C3 was 0.48(0.41, 0.57) g/L, C4 was 0.013(0.003, 0.118) g/L. Renal pathologic findings on light microscopy: endocapillary proliferative Gn (n=3), membranoproliferative Gn (n=3), and mesangial proliferative glomerulonephritis(n=1). Hyaline thrombi were seen in four cases, while crescents were found in two cases. On immunofluorescence microscopy, the predominant types of immunoglobulin deposits were: IgM(n=5), IgA(n=1), and codominance of IgG and IgA(n=1). HBsAg and HBcAg deposits were found in only one case. Ultrastructural studies showed granular subendothelial and mesangial electron-dense deposits in all patients and organized microtubules was seen in only one case. All patients received antiviral medication (entecavir, n=6; lamivudine, n=1). They were given corticosteroid alone(n=2) or combined with cyclophosphamide(n=4) or mycophenolate mofetil(n=1). Two patients received plasmapheresis. The median follow-up time were 18 (6, 37) months. One patient died from pneumonia, and one progressed to end stage of renal disease (ESRD). At endpoint of follow-up, 24hUP was 2.1 (0.8-5.2) g/d, and eGFR (CKD-EPI) was 55.3 (20.7, 111.8) ml/min per 1.73m^2.

Conclusion: Mixed cryoglobulinemic Gn should be screened for HBV etiologies, especially in HBV-endemic country. Endocapillary proliferative Gn was the common pathologic type, as well as membranoproliferative Gn. Diagnosis and treatment in early stage benefit patients' renal outcome. Long-term prognosis should be investigated in further studies.

P0478 CLINICOPATHOLOGICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF IGM NEPHROPATHY

Amir Shabaka[1], Fabio Procaccini[2,3], Serena Gatius[2], Elena Valdes[2], Isabel Galan Carrillo[2], Clara Maria Cases Corona[1], Gema Maria Fernandez Juarez[1]

[1]Hospital Universitario Fundación Alcorcón, Nephrology, Alcorcón. Madrid, Spain, [2]Hospital Clinico San Carlos, Nephrology, Madrid, Spain and [3]Hospital del Sureste, Nephrology, Arganda del Rey, Madrid, Spain

Background and Aims: IgM nephropathy (IgMN) is a controversial clinicopathological entity that is characterized by the presence of dominant diffuse mesangial IgM deposits, with diverse clinical presentations and varying response to supportive or immunosuppressive treatment. The aim of our study was to determine the clinical features, histopathological characteristics and treatment outcomes in patients with IgMN.

Method: We conducted a multicenter retrospective observational study that included patients that had undergone a kidney biopsy between January 1990 and December 2018. We identified 40 patients with mesangial proliferative glomerulopathy with dominant IgM deposits. Patients with the presence of systemic diseases (systemic lupus erythematosus, rheumatoid arthritis, diabetes mellitus or paraproteinemia) were excluded, as well as those with incomplete histological or follow-up data. Demographic, clinical, analytical, and histological data were collected, and the different treatment regimens were compared for achieving clinical remission and prevention of kidney disease progression.

Results: 33 patients were identified with primary mesangial IgM nephropathy, with a median post-biopsy follow-up of 7.3 (2.8-11.1) years. Mean age of presentation was 34.9±19.0 years, 51.5% were females. The most frequent initial manifestation was nephrotic syndrome in 54.5% of cases, followed by proteinuria with microscopic hematuria in 21.2%, proteinuria in 19.1%, and isolated microhematuria in 3% of patients. On presentation, mean eGFR measured by CKD-EPI was 102.9±38.9 ml/min, median proteinuria was 3.3 g/24h (IQR 1.13-4.88), 69.7% had microscopic hematuria and 27.3% presented with hypertension. Light microscopy revealed mesangial hypercellularity and expansion in 81.8% and 78.8% respectively, 6.6% showed extracapillary proliferation, 33.3% showed segmental sclerosis, 39.4% had mild to moderate interstitial fibrosis, and 46.9% had vascular hyaline deposits. On immunofluorescence all patients showed diffuse mesangial IgM deposits, along with subdominant mesangial deposits of IgG (6.1%), IgA (6%), C3 (39.4%), C1q (27.3%) and Lambda (3%).

In nephrotic patients, 16.7% were steroid-resistant, whereas 40% of steroid-sensitive patients were steroid-dependent. 41.7% of steroid-sensitive and nondependent IgMN patients developed a median 3.5 relapses during follow-up. 12 nephrotic patients (3 steroid-resistant and 9 steroid-dependent) received immunosuppressive treatment; 5 patients were initially treated with oral cyclophosphamide, 5 with a calcineurin inhibitor (CNI) and 2 with chlorambucil. All steroid-dependent or resistant patients treated with cyclophosphamide or chlorambucil achieved partial or complete clinical remission. Out of the five patients treated with a CNI, 3 attained remission whereas the other two were switched to cyclophosphamide and chlorambucil respectively after which remission was obtained. No patients progressed to end-stage kidney disease.

Conclusion: IgMN is a rare mesangial proliferative glomerulopathy with a varying clinical and morphological spectrum. It commonly presents as nephrotic syndrome, and is frequently associated with microscopic hematuria. Clinical course is variable, with frequent relapses and a high prevalence of steroid dependence. Complete remission can be achieved with immunosuppressive therapy in cases of steroid-dependent or resistant IgMN, particularly with cytotoxic agents.

P0479 USTEKINUMAB INDUCED PAUCI IMMUNE ANCA NEGATIVE VASCULITIS IN PATIENT WITH CHRON'S DISEASE

Noshaba Naz[1], Ashwin Ajay[2]

[1]Wirral University teaching Hospital, Nephrology, Wirral, United Kingdom and [2]Wirral University teaching hospital, Nephrology, Wirral, United Kingdom

Background and Aims: Crohns disease is a chronic transmural inflammation which can affect any segment of the gastrointestinal tract in a discontinuous fashion. Treatment for crohns include steroids, Immunosuppresants (thiopurines and methotrexate) and biological agents such as TNF antagonist (adalimumab, infliximab and certrolizumab pegol) and anti-integrin antibodies (natalizumab and vedolizumab). However in cases of refractory disease the management can become difficult. In such case, use of Ustekinumab is indicated. Tumour necrosis factor-alpha are first line biological agents for managing adult patients with moderate to severe disease .

We present a rare case of Ustekinumab treatment and onset of renal disease secondary to crescentic glomerulonephritis in a 37-year-old female. We aim to discuss the presentation, diagnosis and management of the above condition. To the best of our knowledge, this type of presentation has not been described in existing literature.

Method: Patient's hospital case records and GP correspondence were used to analyze this case.

Results: This is a case of a 37-year-old female with a four year history of refractory crohns disease affecting colon and terminal ileum. She was treated with numerous treatment modalities such as budesonide, mesalazine, azathioprine, mercaptopurine, adalimumab and vedolizumab over the years. However, these treatments were not successful as she had multiple hospital admissions every year with flare up of crohns requiring intravenous steroids.

In January 2018, she was again admitted to hospital with a flare up of Crohns disease. Colonoscopy and imaging confirmed active disease with moderate severity. Further treatment strategies were discussed and Ustekinumab was decided as the best next treatment option. She had her first intravenous infusion in February 2018 and was planned for injections every 3 months. Her symptoms of Crohns disease improved with the Ustekinumab injections. After her second injection of Ustekinumab in May 2018, repeat blood tests showed acute kidney injury with creatinine of 127 umol/l from a baseline of 75 umol/l and a urea of 8.3 mmol/l from a baseline of 3 mmol/l. Urine dip in May was positive for protein and blood. She was referred to the renal team as an outpatient on the basis of these results for further management. Urea and creatinine had worsened to 10.4 mmol/l and 168 umol/l respectively. Urine protein creatinine ratio was 200. The initial impression was drug induced vasculitis versus Acute kidney injury (AKI) secondary to diarrhoea and poor intake.

Considering the possibility of glomerulonephritis, serology testing for immunoglobulins, complements, blood and urine electrophoresis, ANA, ANCA, anti-GBM and viral serology tests were arranged, which all came back negative. ultrasound-guided percutaneous kidney biopsy was performed.

Renal biopsy confirmed the diagnosis of pauci-immune glomerulonephritis with crescents (vasculitis).

A diagnosis of Ustekinumab induced ANCA negative crescentic glomerulonephritis was established. Ustekinumab was discontinued and she was treated with prednisolone 60mg for four weeks, followed by tapering regime for 6-12 weeks in the community.

Renal function improved with a creatinine of 120 umol/l, two months after stopping Ustekinumab. Repeated blood tests during these two months showed a steady and gradual decline in creatinine and eventually return back to normal level of 80 umol/l. Urinalysis showed proteinuria settling with no evidence of haematuria.

Conclusion/learning points

- This is the case of a renal limited pauci-immune glomerulonephritis caused by Ustekinumab treatment.
- Timely speciality advise can prevent long term organ damage
- It is essential to monitor kidney functions and urine dipsticks for proteinuria and haematuria in those receiving Ustekinumab or similar biological agents
- Safe profile of biological drugs are still not fully understood.

P0480

LENALIDOMIDE PLUS DEXAMETHASONE FOR PROLIFERATIVE GLOMERULONEPHRITIS WITH MONOCLONAL IG DEPOSITS

Houan Zhou[1], Manna Li[1], Xia Wang[1], Caihong Zeng[1], Xianghua Huang[1], Zhaohong Chen[1], Zhen Cheng[1]

[1]*National Clinical Research Center of Kidney Diseases, Jinling Hospital Research Institute of Nephrology, Nanjing University, School of Medicine, department of kidney, Nanjing, P.R. China*

Background and Aims: To evaluate the efficacy and safety of lenalidomide plus dexamethasone (LD) in patients with proliferative glomerulonephritis with monoclonal Ig deposits (PGNMID).

Method: Retrospectively analyzed the clinicopathological data of 6 PGNMID patients who treated with LD protocol from January 2010 to October 2019.

Results: All of the patients received LD treatment for ≥3 months after renal biopsy. 3 patients achieved renal remission. The renal remission rate was 50%. Light microscopy showed membranoproliferative glomerulonephritis and immunofluorescence showed single kappa type IgG3 was deposited in the mesangial region and the vascular loop. Before taking LD scheme, the median urinary protein were 7.76 (1.27,14.57) g/24h, the median serum creatinine 1.34 (0.8,3.27) mg/dL, the median albumin 34.5 (22.4,37.5) g/L. In 5 patients the concentration of serum free kappa and lambda light chain increased, but no patients with abnormal serum free light chain ratio. Complement C3 deteriorated in 2 patients, 2 cases of patients with monoclonal plasma cells, 0.7% and 0.5%, respectively. Immunofixation electrophoresis suggested that 1 patient had positive serum M protein for kappa type IgG3. At the last follow-up, median urine protein was 3.33 (0.33,11.23) g/24h, median serum creatinine was 1.23 (0.91,1.82) mg/dL, and median albumin was 35.9 (24.5,45.6) g/L. The concentration of 4 patients with elevated serum free light chain was lower than that before taking the drug. Two patients with decreased complement C3 increased to normal concentration at the last follow-up. However, the other two patients had a slight decrease in complement C3. The M spike did not turn negative during the follow-up in one patients. Adverse events included anemia, neutropenia, limb numbness, upper respiratory tract infection.

Conclusion: This study reported that lenalidomide plus dexamethasone may be effective in treating proliferative glomerulonephritis with monoclonal Ig deposits for the first time. More attention needs to be paid to the hematological adverse events during lenalidomide treatment.

Table SEQ * ARABIC 1 General information of 6 patients with PGNMID

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Gender	male	male	male	male	female	female
Age	40	62	51	61	48	38
Immunofluorescence	IgG3-κ	IgG3-κ	IgG3-κ	IgG3-κ	IgG3-κ	IgG3-κ
Scr (mg/dL)	1.73	1.23	1.46	3.27	1.22	0.8
ALB (g/L)	36.4	37.3	32.7	27.1	22.4	37.5
eGFR (mL/(min·1.73 m^2))	49	63	65	19	62	93
Urine protein (g/24h)	4.31	2.44	14.57	11.22	14.46	1.27
Serum C3 (g/L)	0.881	0.765	1.07	0.5	0.993	0.894
Serum C4 (g/L)	0.129	0.264	0.215	0.242	0.187	0.219
Serum free κ (mg/L)	14.1	25.4	20.1	66.2	23.8	21.8
Serum free λ (mg/L)	13.5	36.2	32.5	74	48.2	39.8
Serum free κ/λ ratio	1.04	0.7	0.62	0.89	0.49	0.55
M protein	-	-	-	-	-	Ig G-κ
Monoclonal plasma cells%	0.7	-	0.005	-	-	-

Table 2 Changes of baseline and last follow-up indexes in 6 patients with PGNMID

		Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Follow-up/ month		12	13	6	16	19	8
SCr (mg/dL)	baseline	1.73	1.23	1.46	3.27	1.22	0.8
	last follow-up	1.39	1.05	1.07	1.79	0.91	1.82
ALB (g/L)	baseline	36.4	37.3	32.7	27.1	22.4	37.5
	last follow-up	45.6	36.7	35.1	34.6	42.5	24.5
Urine protein (g/24h)	baseline	4.31	2.44	14.57	11.22	14.46	1.27
	last follow-up	0.42	0.33	5.44	1.22	8.05	11.23
Serum C3 (g/L)	baseline	0.881	0.765	1.070	0.500	0.993	0.894
	last follow-up	0.774	0.982	0.903	0.829	N	0.786
Serum C4 (g/L)	baseline	0.129	0.264	0.215	0.242	0.187	0.219
	last follow-up	0.216	0.290	0.225	0.194	N	0.320
Serum free κ (mg/L)	baseline	14.1	25.4	20.1	66.2	23.8	21.8
	last follow-up	12.2	16.6	21.7	28.0	10.7	35.3
Serum free λ (mg/L)	baseline	13.5	36.2	32.5	74.0	48.2	39.8
	last follow-up	16.0	20.4	22.0	43.1	25.0	46.9
Serum free κ/λratio	baseline	1.04	0.70	0.62	0.89	0.49	0.55
	last follow-up	0.94	0.81	0.99	0.65	0.43	0.75

Figure:

P0481 MORTALITY PREDICTORS IN ANCA-ASSOCIATED VASCULITIS AND ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE

Filipa Cardoso[1], Maria Do Mar Menezes[1], Miguel Bigotte Vieira[1], Mário Góis[1,2], Helena Viana[1,2], Fernando Nolasco[1]

[1]Hospital Curry Cabral, Centro Hospitalar Universitário de Lisboa Central, Nephrology, Lisbon, Portugal and [2]Hospital Curry Cabral, Centro Hospitalar Universitário de Lisboa Central, Laboratory of Renal Morphology, Lisbon, Portugal

Background and Aims:

The antineutrophil cytoplasmic antibody-associated vasculitis (AAV) and anti-glomerular basement membrane (GBM) disease are autoimmune diseases that cause necrotizing crescentic glomerulonephritis. These diseases portend an increased risk of end-stage kidney disease and death. The main objective of our study was to identify predictors of mortality in patients with these diseases.

Method:

Retrospective analysis of patients diagnosed with AAV and anti-GBM disease by renal biopsy performed between 2013 and 2019. The minimum duration of follow-up was 6 months. Demographic, laboratory and histological characteristics were studied. The primary endpoint was death due to any cause. Continuous variables were presented as means or medians, according to normality and categorical variables presented as frequencies. The comparison between subgroups of patients was performed using the Wilcoxon, Fisher exact test or t-test, chi-square test, according to normality. Univariate and multivariate logistic regression models were fitted to identify variables associated with death. STATA 14.2 statistical package was used and $p < 0.05$ was considered statistically significant.

Results:

We identified 40 patients, 37 (95%) were caucasian and 22 (55%) female. The mean age was 69 years, serum creatinine 3.4 (2.3 – 4.5) mg/dL, eGFR 14 (11-23) ml/min/1.73 m^2 and proteinuria 1.42 (0.75 – 3.38) g/day. Twenty-seven (68%) had a past medical history of hypertension and 3 (8%) type two diabetes. Thirty-three (83%) presented with constitutional symptoms and 12 (30%) had pulmonary manifestations, while the other manifestations were less frequent. The average time between symptoms presentation and therapy initiation was 119 days. Mean follow-up was 1094 days. Renal biopsy showed grade 0 interstitial fibrosis and tubular atrophy in 5 patients (13%), grade 1 in 13 (33%), grade 2 in 8 (20%) and grade 3 in 14 (35%). The majority had no vessel involvement (24, 60%) and grade 2 acute tubular necrosis (18, 45%). Inflammatory infiltrate was present in 25 patients (63%). At 6 and 12 months, 15 (38%) and 9 (23%) were dialysis dependent, respectively. All patients were treated with prednisolone, 14 (35%) with cyclophosphamide, 15 (38%) with rituximab and 14 (35%) underwent plasmapheresis. Eighteen (45%) patients were maintained on azathioprine. At the end of follow-up, 13 patients had died and 2 relapses occurred. Eleven (46%) patients presented at least one serious infectious episode. Older age (OR 1.10, 95% [1.01-1.20], p=0.035), higher diastolic blood pressure (OR 1.09, 95% [1.00-1.12], p=0.046), and lower C3 levels (OR 0.003, 95% [0.000-0.525], p=0.027) were associated with higher mortality on univariate analysis. On multivariate analysis, only higher diastolic blood pressure remained significant. Pathology findings and serum creatinine values were not associated with higher mortality

Conclusion:

Overall mortality in AAV and anti-GBM has decreased over the last two decades with the use of immunosuppressive therapies. However, mortality rates remain high and most deaths occur during the first year following diagnosis. Early detection of infections with prompt initiation of treatment may help to reduce mortality. Additionally, the identification of risk factors associated with a higher risk of mortality and that could allow individualization of therapy remains a challenge.

P0482 **INTERSTITIAL HSP70 EXPRESSION AT DIAGNOSIS ASSOCIATES WITH LONG TERM RENAL SURVIVAL IN AN ANCA VASCULITIS COHORT.**

Ioannis Petrakis[1], Ariadni Androvitsanea[2], Stavros Stratakis[3], Eugene Daphnis[3], Kostas Stylianou[3]

[1]Saarland University Hospital, Nephrology, Homburg, Germany, [2]University Hospital Erlangen, Nephrology, Erlangen, Germany and [3]University Hospital of Heraklion, Nephrology, Iraklio, Greece

Background and Aims: Heat shock proteins(HSP) present an evolving role in immune response. ANCA associated vasculitis(AAV) is often associated with kidney injury and progression to chronic kidney disease(CKD)

Method: Twenty nine patients with biopsy proven renal AAV were followed(1995-2015). Study end point was renal death. Renal tissue at diagnosis was stained with monoclonal antibodies against HSP60 and HSP70. Interstitial inflammatory cells and interstitial fibrosis graded were evaluated as mild(0-50%) or severe($\geq$50%). Healthy renal tissue served as control. Survival analysis(Kaplan-Meier), Fisher's exact test, or Test Chi-Square and bivariate analysis were performed. Statistical significance was set at $<$0,05.

Results: Mean age and mean eGFR at baseline was 57,8$\pm$19.2 years and 24,47 ml/min/1,73m^2 BSA respectively. Interstitial inflammatory infiltrates were present in most patients. Interstitial fibrosis was present in 10,3% of patients. Control biopsies showed a weak HSP expression. AAV-patients presented significantly higher HSP expression within crescents, proximal tubule, distal tubule and renal interstitium. Renal fibrosis associated with intense interstitial HSP70 expression(Pearsońs-R=0.521 p=0,004). Interstitial inflammatory infiltrates associated with increased distal tubular HSP60 expression(Pearsońs-R=0.672 p$<$0,001). Renal fibrosis associated with renal function loss(Mean time to renal replacement therapy 2.6 years, 95%CI 1.2-4.1 years, Log-Rank Chi-Square=4.33,p=0.038). Strong interstitial HSP70 expression associated with worsened renal survival in AAV-patients even in the absence of severe renal fibrosis(Mean time to renal replacement therapy initiation 0 years ; 95%CI 0, Log-Rank Chi-Square=11.45, p=0.001).

Conclusion: Interstitial HSP70 overexpression is associated with worse renal outcomes in renal AAV. To our knowledge this is the first study that shows an association of renal heat shock protein expression and renal outcomes in an AAV cohort.

P0483 PREGNANCY OUTCOMES IN PREGNANT WOMEN WITH DIFFERENT TYPES OF GLOMERULONEPHRITIS

Tatiana Kirsanova[1], Elizaveta Rumiantseva[2], Olga Ivanova[2], Maria Vinogradova[3], Tatiana Fedorova[4], Alina Balakireva[2]

[1]Federal State Budget Institution "Research Center for Obstetrics, Gynecology and Perinatology", Senior researcher, Moscow, Russia, [2]Lomonosov Moscow State University, Faculty of fundamental medicine, Moscow, Russia, [3]Federal State Budget Institution "Research Center for Obstetrics, Gynecology and Perinatology", Head of department of reproductive hematology and haemostasiology, Moscow, Russia and [4]Federal State Budget Institution "Research Center for Obstetrics, Gynecology and Perinatology", Head of department of transfusiology, Moscow, Russia

Background and Aims: Connection between active glomerulonephritis (GN) and adverse pregnancy outcomes is well known. The analysis of pregnancy outcomes for patients with different types of GN in remission has not been performed.

Aim: to investigate pregnancy outcomes in women with inactive lupus nephritis (LN), IgA nephropathy and unspecified types of GN.

Method: A retrospective single-center cohort study 11/2014 – 12/2019: 91 patients with GN in remission > 20 weeks of gestation. Proved IgA-nephropathy was observed in 14 patients, proved LN in 26 patients, 4 patients had proved antiphospholipid syndrome secondary to LN and 51 patients had unspecified types of GN (without morphological confirmation). Morphological class of LN was confirmed in 9 patients: 3rd in 5, 4th in 2, 5th in 2 patients. Renal function at conception, during pregnancy and after delivery, pregnancy outcomes, clinical and laboratory parameters were collected. PE was diagnosed by the 2008 WHO criteria. The sFlt-1/PlGF ratio was used as the main differential marker to exclude GN exacerbation in cases of increased proteinuria.

Results: Rate of preterm birth was significantly higher in patients with LN compared to patients with IgA nephropathy ($p = 0.002$) and patients with unspecified GN ($p < 0.0001$), and also in patients with APS plus LN compared to patients with unspecified GN ($p < 0.0001$) and IgA nephropathy ($p = 0.004$). PE was observed in 24 patients (25%), type of GN did not affect the incidence of PE. Week of delivery was significantly lower in women with LN compared to IgA-nephropathy ($p = 0.013$) and unspecified types of GN ($p = 0.001$) and almost significantly lower in patients with LN plus APS than patients with IgA-nephropathy ($p = 0.051$) and unspecified types of GN ($p = 0.06$). Birth weight was significantly higher in babies born to women with unspecified types of GN compared to women with LN ($p = 0.018$) and LN plus APS ($p = 0.047$).

Conclusion: Although the rate of PE is similar, the risks of preterm births are high in LN and LN plus APS patients. In this study, laboratory parameters and medical therapy did not significantly affect the pregnancy outcomes.

	IgA nephropathy (n = 14)	Lupus nephritis (n = 26)	LN with secondary APS (n = 4)	Unspecified types of GN (n = 51)
Age, *M ± SD*	31.6 ± 3.5	30.8 ± 4.6	30.2 ± 3.2	31.3 ± 4.3
Preterm birth, *n (%)*	1 (7%)*,#	11 (42%)*	3 (75%)#	4 (8%)*,#
Preeclampsia, *n (%)*	5 (36%)	5 (19%)	1 (25%)	11 (21.5%)
Week of delivery, *M ± SD*	38 ± 1.6*	35 ± 4*	34 ± 3	38 ± 1.6*
Birth weight, *M ± SD*	2559 ± 1143	2573 ± 805*	2342 ± 581*	3021 ± 777*

* – $p < 0.05$, # – $p < 0.05$

Figure:

P0484 CLINICAL FEATURES AND OUTCOME OF LUPUS NEPHRITIS IN MOROCCO: A SINGLE CENTER STUDY OF 207 CASES

Salma Naouaoui[1], Meriem Chettati[1], Wafaa Fadili[1], Inass Laouad[1]

[1]*Mohammed VI University Hospital, department of nephrology, dialysis and transplantation, Marrakesh, Morocco*

Background and Aims: renal involvement is a common and potentially severe complication of systemic lupus erythematosus (SLE). Few data for Lupus nephritis (LN) exist on North Africans, especially those from Morocco. The aim of our study was to report the long-term renal outcome of a cohort of Moroccan patients with LN.

Methods: the records of 207 patients (191 females, 16 males) with LN (American College of Rheumatology criteria) admitted to the departments of nephrology and internal medicine of Marrakesh University Hospital were reviewed and included in a retrospective analysis.

Results: the mean age at the time of renal biopsy was 31,7 ± 15,9 years. Time between diagnosis of SLE and the onset of renal disease was 29 ± 10 months. Renal involvement was observed concomitantly with the onset of SLE in 39 patients (18,8%). At presentation, 65 patients (31,4%) had hypertension. Hematuria was seen in 158 patients (76,3%), nephrotic syndrome in 82 patients (39,6%) and renal failure in 76 patients (36,7%). The most frequent extarenal manifestations were skin and joint manifestations in 89,3% and 83,6% respectively. The most common histological finding was type IV LN in 96 patients, followed by type III LN in 51 patients. 191patients (92,3%) received corticosteroids as initial therapy followed by immunosuppressive therapy in 127 patients (61,3%). During the follow-up period, partial or total remission was obtained in 56,5% of cases while 61 patients (29,4%) progressed to end stage renal disease (ESRD) and 29 patients (14%) died. Logistic regression detected that hypertension, high serum creatinine at admission and proliferative histological classes were the main risk factors for poor renal outcome.

Conclusion: Our results showed that LN was particularly severe in our population compared with other published data with predominance of proliferative forms.

P0485 ASSOCIATION BETWEEN ANTI-GBM TITERS AND KIDNEY INFLAMMATION MEASURED BY A NEW ACTIVITY SCORE

Evelyn Hermida-Lama[1], Diana Rodríguez[1], David Cucchiari[1], Miquel Blasco[1], Gaston Piñeiro[1], Esteban Poch[1], Miquel Lozano[1], Joan Cid[1], Estibaliz Ruiz-Ortiz[2], Adriana García-Herrera[3], Luis F. Quintana[1], Alā-cia Molina Andā°jar[1]

[1]Hospital Clínic de Barcelona, Nephrology and Renal Transplant Unit, Barcelona, Spain, [2]Hospital Clínic de Barcelona, Immunology, Barcelona, Spain and [3]Hospital Clínic de Barcelona, Pathology, Barcelona, Spain

Background and Aims: Anti-glomerular basement membrane (anti-GBM) disease is an aggressive and rare glomerulopathy characterized by rapidly progressive loss of kidney function, leading to end stage kidney disease (ESKD) in a significant amount of cases. The main objective of our study was to determine whether anti-GBM titer correlated with the rate of activity in renal biopsy and long-term kidney survival in patients with anti-GBM, hence identifying patients who would potentially benefit from more intensive treatments.

Method: A retrospective analysis was performed on the cases of anti-GBM from our center that had both a positive biopsy and serology, from 2007 to 2019. Epidemiological data, anti-GBM levels on admission, kidney function at admission, discharge and follow-up, treatment and kidney biopsy findings were collected. All biopsies were reevaluated by a single, blinded pathologist and nephrologist. Based on a recent study by van Daalen et al, a chronicity and activity histopathological score was developed. The score was divided in glomerular and interstitial sections. In the glomerular section, a sclerotic pattern (>50% of glomeruli) was given 0 points in activity and 3 in chronicity, a mixed pattern was given 1 point in activity and chronicity, and a crescentic pattern (>50% with cellular crescents) was given 3 points in activity and 0 in chronicity. In the interstitial section, the presence of fibrosis and atrophy was given between 0 and 3 points in chronicity and the presence of tubulitis or interstitial infiltrate were given points in activity (0 to 1 and 0 to 3 respectively). The presence of neutrophils in the infiltrate was given one extra point in activity. Spearman correlation was performed between anti-GBM levels and our biopsy score.

Results: Twelve cases were identified, with a median Anti-GBM titer at admission of 292 U/mL (IQR 40-1517). Ten patients were treated with cyclophosphamide, 1 with rituximab plus cyclophosphamide and 1 with only rituximab. All patients received treatment with metilprednisona and plasma exchange with a median number of sessions of 8 (range: 6-12). Only one patient was not in ESKD during follow-up (35 months), so correlation with long-term kidney survival could not be performed. On the other hand, high antibody titers correlated with more activity on biopsy (correlation coefficient 0.592, p= 0.042) and less chronicity (correlation coefficient -0.657, p= 0.02).

Conclusion: These results suggest that patients who present with higher titers have more acute inflammation and less chronicity in renal parenchima, and therefore could benefit from more intensive treatment that changes the natural history of this aggressive disease. It would be interesting to study this score in larger and multicentric cohorts in order to produce more definitive conclusions.

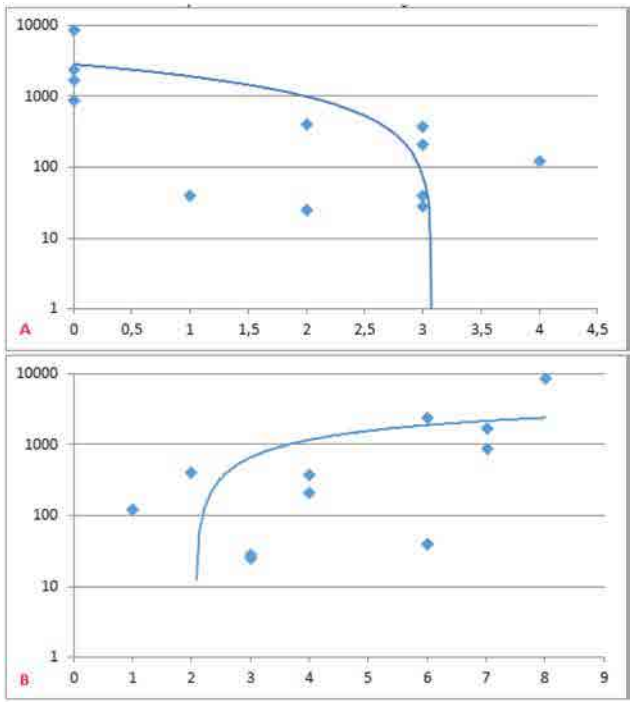


Figure. A: correlation between chronicity score and anti-GBM in logarithmic scale. B: Correlation between activity score and anti-GBM in logarithmic scale.

P0486

THROMBOTIC MICROANGIOPATHY IN A PATIENT WITH PERSISTENT CRYOGLOBULINEMIA AFTER HCV ERADICATION AND HETEROZYGOUS DELETION OF CFHR3-CFHR1 REGION: SHOULD WE TREAT WITH RITUXIMAB, ECULIZUMAB OR PLASMAPHERESIS?

Pamela Gallo[1], Pamela Gallo[1], Chiara Somma[1], Claudia Zullo[1], Marco Lombardi[1], Giuseppe Ferro[1], Pietro Claudio Dattolo[1]

[1]*Azienda USL Toscana Centro, Nephrology and Dialysis Unit Firenze II, Florence, Italy*

Background and Aims: Mixed cryoglobulinemia type II is a systemic vasculitis, caused by deposition of immune complexes in the endothelium of small vessels. Up to 90% are HCV infection related and usually resolve after eradication of the virus.

Method: We report the case of a patient with HCV related type II cryoglobulinemia, persistent despite the eradication of the virus with sofosbuvir and complicated by thrombotic microangiopathy.

Results: Since 2001 patient had cryoglobulinemic vasculitis treated with rituximab in 2002 and in 2011 for a relapse. In 2015 started antiviral therapy with sofosbuvir achieving sustained viral remission.

In December 2018 she admitted to hospital for fever, abdominal pain, diarrhea and oedema.

Blood exams showed acute kidney injury, (scar 3 mg/dl) proteinuria (2,6 g/24h) e microhematuria, haemolytic anaemia and thrombocytopenia, low C4, rheumatoid factor, cryocrit 4% (type II cryoglobulinemia), ANA, ENA e HCV RNA were negatives. On renal biopsy we found a thrombotic microangiopathy (fig.1,2). We rule out a lymphoma through PET total body e immunophenotype.

Conclusion: This report shows persistent cryoglobulinemia with vasculitis relapses, after HCV eradication with direct antiviral therapy (fig. 3), paying attention to complexity of immunological response, causing in this patient a TMA.

Intriguing in our report is the finding of TMA on renal biopsy, without other lesions, contrary to what expected. Cryoglobulinemic vasculitis are usually associated to membranoproliferative glomerulonephritis.

For this reason we search genetic mutation of complement genes, finding a heterozygous deletion on CHFR3-CHFR1 region. A pathogenic role of this deletion, is unknown, but it could mean a different target of therapy.



Fig 1 [optical microscopy]

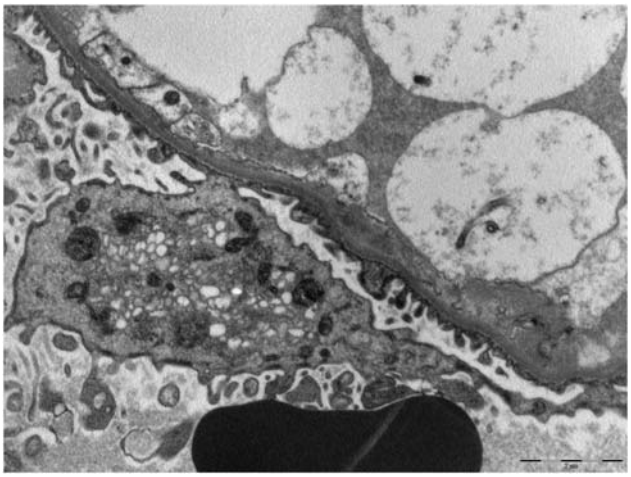


Fig 2 [electronic microscopy]

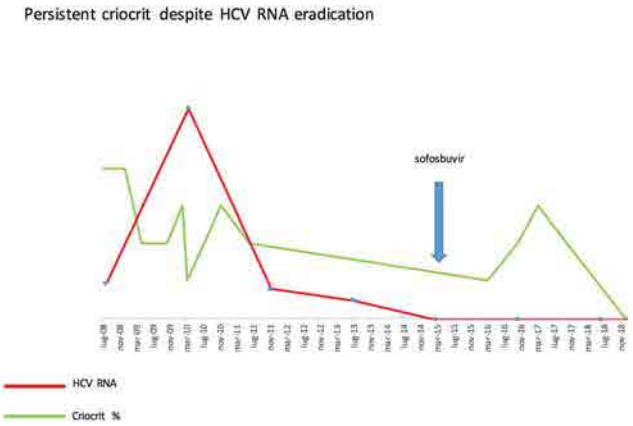


Fig 3

P0487 ROLE OF THERAPEUTIC PLASMAPHERESIS IN ANCA-ASSOCIATED VASCULITIS

AGLAIA CHALKIA[1], PANAGIOTA GIANNOU[1], Katerina Damianaki[1], ATHANASIA KAPOTA[1], KONSTANTINOS THOMAS[2], CHRISTINA TSALAPAKI[2], DIMITRIOS VASILOPOULOS[2], DIMITRIOS PETRAS[1]

[1]HIPPOKRATION GENERAL HOSPITAL OF ATHENS, NEPHROLOGY, ATHENS, Greece and [2]HIPPOKRATION GENERAL HOSPITAL OF ATHENS, JOINT RHEUMATOLOGY PROGRAM, NATIONAL AND KAPODISTRIAN UNIVERCITY OF ATHENS, CLINICAL IMMUNOLOGY - RHEUMATOLOGY UNIT 2ND DEPARTMENT OF MEDICINE ATHENS GREECE, ATHENS, Greece

Background and Aims: The role of plasmapheresis in the overall and renal survival of patients with ANCA-associated vasculitis (AAV) has not been fully elucidated. The aim of this study is to address whether plasmapheresis is associated with improvement in renal function and survival at 12 months in patients with severe manifestations of AAV and to record the indications, adverse events and treatment characteristics.

Method: Retrospective, descriptive study of 28 patients with AAV diagnosed over the last five years in a tertiary center. Patients were included if they had received therapeutic plasmapheresis adjunctive to conventional therapy (steroids and immunosuppressants) for the first episode of AAV or in relapse.

Results: 12 patients (75% male) were enrolled with average age at diagnosis 78.5±6.14 years. The patients were followed for a median period of 20 months. In 75% of the patients MPO-ANCA was positive, in 17% ANCA negative and in 8% double positive anti-GBM/ANCA. On admission, all patients had abnormal renal function with average serum creatinine 5mg/dl±2.12 and the majority of patients (9/12) were dialysis dependent. Indications for plasmapheresis were: alveolar hemorrhage in 33%, renal impairment in 25% and combination of the two above in 42%. 11 patients received plasmapheresis for the first episode of AAV and 1 patient for relapse. Plasmapheresis was performed using filtration and fresh frozen plasma as replacement fluid. The mean number of plasmapheresis treatment was 8 (range 1 to 19 days) and the average internal time between admission and first plasmapheresis treatment was 3 days. One patient had a severe allergic reaction resulting in early discontinuation and no episodes of severe infection or death were recorded during plasmapheresis. As far as treatment all patients received concomitant immunosuppressive therapy with cyclophosphamide (CYC) and corticosteroids while Rituximab (RTX) was added in 3 patients (3/12). Alveolar hemorrhage was resolved in all patients (100%). After one year, 75% of the patients had renal recovery (cre=5mg/dl±2.12 vs cre=2.6mg/dl±1.6, p=0.06) and 67% of the patients who required hemodialysis at the time of diagnosis, during the first year became independent of dialysis (75% vs 33%, p=0.5). Finally, survival at the end of the first year was 83% with cancer and ischaemic heart disease being the cause of death.

Conclusion: Plasmapheresis is quite often used in daily clinical practice with remarkable results in dialysis independence and survival, without serious complications. The actual role of plasmapheresis in ANCA-vasculitis therapeutic algorithm will be determined shortly with the expected results of a randomized multicenter study.

P0488 IG A NEPHROPATHY: ANALYSIS OF 501 BIOPSY

Marwa Omrane[1], Raja Aoudia[1], Mondher Ounissi[1], Soumaya Chargui[1], Mouna Jerbi[2], Hanene Gaied[2], Hafedh Hidri[1], Imen Gorsane[1], Taieb Ben Abdallah[1], Rim Goucha[2]

[1]Charles Nicole Hospital, Internal medicine A, Tunis, Tunisia and [2]Mongi Slim Hospital, Nephrology, La Marsa, Tunisia

Background and Aims: Mesangial deposits Ig A was described the first time in 1968 by Berger and Hinglais. It remains the most common primary glomerulonephritis worldwide. It is often idiopathic but can also be secondary. The aim of our study is to describe the epidemiologic characteristics, the incidence and the anatomopathological features of 501 IgA nephropathy (IgA N) patients.

Method: It is a retrospective mono-centric study including patients having IgA N in the renal biopsy done in our department among a period of 17 years.

Results: We analyzed data of 8427 patients who underwent renal biopsy. 81% had glomerular nephropathy with 7.3% (501) IgA N. A male-to-female ratio of 2.27. The average age was 28.7 years. IgA N was primary in 80.2% cases and secondary in 17.8% cases. The most frequent secondary IgA N was rheumatoid purpura (74.8%). There was a male predominance in Berger's disease as well as in rheumatoid purpura. Berger's disease was more common in adults, whereas rheumatoid purpura was more common in children. The main indication of renal biopsy was proteinuria with hematuria in 23.2% of cases and nephrotic syndrome in 23.8%. The association of non-nephrotic proteinuria, hematuria, arterial hypertension and renal injury was found in 9.3% whereas isolated macroscopic hematuria only in 6.4% of cases. According to HAAS classification, HAAS 3 was the most frequent. OXFORD classification used only from 2010, and M1, S1, E0, T0 and M1, S1, E0, T2 were the most frequent. Glomerular lesions were associated to tubulo interstitial and vascular lesions in 48.2% of cases.

Conclusion: IgA nephropathy is the most common glomerular disease and a frequent cause of end stage renal disease. Because of a clear increase of it's incidence in our country and the delay in the diagnosis, a systematic screening of urines is needed in our country as it's done in Singapore and Japan.

P0489 URINARY PROTEOMIC MARKERS OF MEMBRANOUS NEPHROPATHY

Barbara Moszczuk[1], Natalia Krata[2], Dominik Cysewski[3], Agnieszka Perkowska-Ptasinska[4], Leszek Pączek[2,3], Bartosz Foroncewicz[2,3], Radosław Zagożdżon[2,3,5], Krzysztof Mucha[2,3]

[1]Medical University of Warsaw, Immunology, Transplantology and Internal Medicine, Warsaw, Poland, [2]Medical University of Warsaw, Department of Immunology, Transplantology and Internal Medicine, Warsaw, Poland, [3]Polish Academy of Sciences, Institute of Biochemistry and Biophysics, Warsaw, Poland, [4]Medical University of Warsaw, Department of Transplantation, Nephrology and Internal Medicine, Warsaw, Poland and [5]Medical University of Warsaw, Department of Clinical Immunology, Warszawa, Poland

Background and Aims: Membranous nephropathy (MN) is considered one of the major conditions causing nephrotic-range proteinuria. Last years brought a huge progress in the field of non-invasive diagnostics, mainly due to the PLA2R antibody use in diagnostics and follow-up of primary MN. However, our understanding of MN is far from complete, especially that PLA2R-antibodies are found only in approximately 60-70% of all cases. Urinary proteomics is a promising tool that can help us to improve diagnostics, monitoring and understanding of MN. Our previous studies (Patent No. WO/2017/212463) suggested that specific urinary proteins can be used in the diagnostics of IgA nephropathy, lupus nephritis and ADPKD. The aim of this study was to evaluate with Mass Spectrometry (MS) patients diagnosed with MN in comparison to healthy controls.

Method: This study included patients with biopsy-proven MN (25) and healthy controls (7). Urine samples were obtained from a midstream of the second- or third-morning (SPOT) sample. The samples were processed up to 2 h after collection and stored at -80°C for further measurements with MS. The results were related to demographic data, standard laboratory tests and GFR estimated with use of Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Results: The signal intensity of urine protein A, B and C (patent pending and the name of proteins disclosed until the date of ERA-EDTA Congress) was found to be significantly higher ($p < 0.05$) in MN patients compared to healthy controls (Fig. 1). Mass spectrometry, according to the specific amino-acids fragments of each tested protein, confirmed the differences between tested and control group. Additionally, statistically significant differences exist between patients with different types of glomerulonephritides (comparative MS in progress).

Conclusion: The signal intensity of urine proteins A, B, C is elevated in MN and according to our study, vary depending on types of nephropathies. This observation might suggests their differential roles in the pathophysiology of MN and its' possible application as a non-invasive diagnostic and prognostic marker. Further studies are desired to establish the role of these urinary proteins.

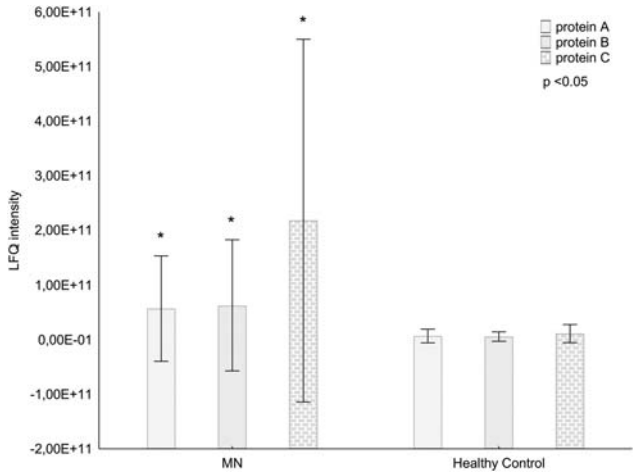


Figure: Signal intensity (Mean ± SD) of protein A, B, C in SPOT urine samples.

P0490

IS THE SEVERITY OF GLOMERULAR IGG STAINING IN PATIENT WITH IGA NEPHROPATHY USEFUL FOR PREDICTING POOR RENAL PROGNOSIS? THE DATA FROM TSN-GOLD WORKING GROUP

Kenan Turgutalp[1], Egemen Cebeci[2], Aydin Turkmen[3], Ülver Derici[4], Nurhan Seyahi[5], Necmi Eren[6], Fatih Dede[7], Mustafa Gullulu[8], Taner Basturk[9], Gulizar Manga Sahin[10], Mürvet Yılmaz[11], Savas Sipahi[12], Garip SAHIN[13], Memnune Sena Ulu[14], Erhan Tatar[15], Ali Gundogdu[16], Rumeyza Turan Kazancioglu[17], Can Sevinc[18], Ozkan Gungor[19], İdris Sahin[20], Sim Kutlay[21], Ilhan Kurultak[22], Zeki Aydin[23], Bulent Altun[24], Belda Dursun[25], Zulfikar Yilmaz[26], Ozcan Uzun[27], Gultekin Suleymanlar[28], Ferhan Candan[29], Siren Sezer[30], Derya Basak Tanburoglu[31], Zerrin Bicik Bahçebaşı[32], Dilek Guven Taymez[33], Deren Oygar[34], Esra Akcali[1], Zulal Istemihan[3], Omer Faruk Akcay[4], Mevlut Tamer Dincer[5], Metin Ergul[6], Ezgi Yenigun[7], Kultigin Turkmen[35], Savas Ozturk[2]

[1]Mersin University, Department of Nephrology, Mersin, Turkey, [2]Haseki Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [3]Istanbul University, Department of Nephrology, Istanbul, Turkey, [4]Gazi University Faculty of Medicine, Department of Nephrology, Ankara, Turkey, [5]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Nephrology, Istanbul, Turkey, [6]Kocaeli University, Department of Nephrology, Kocaeli, Turkey, [7]Health Sciences University, Ankara Numune Education and Research Hospital, Department of Nephrology, Ankara, Turkey, [8]Uludag University Faculty of Medicine, Department of Medicine, Bursa, Turkey, [9]Health Sciences University, Sıslı Hamidiye Etfal Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [10]Istanbul Abdulhamid Han Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [11]Health Sciences University, Bakirkoy Sadi Konuk Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [12]Sakarya University Medical Faculty Education and Research Hospital, Department of Nephrology, Istanbul, Turkey, [13]Eskisehir Osmangazi University, Department of Nephrology, Istanbul, Turkey, [14]Afyon Health Sciences University, Department of Nephrology, Afyon, Turkey, [15]Health Sciences University, Izmir Bozyaka Training and Research Hospital, Department of Nephrology, Izmir, Turkey, [16]Erciyes University, Department of Nephrology, Kayseri, Turkey, [17]Bezmialem Vakif University, Division of Nephrology, Istanbul, Turkey, [18]Atatürk University, Department of Nephrology, Erzurum, Turkey, [19]Kahramanmaras Sutcu Imam University, Department of Nephrology, Kahramanmaraş, Turkey, [20]Inonu University Faculty of Medicine, Department of Nephrology, Malatya, Turkey, [21]Ankara University, School of Medicine, Department of Nephrology, Ankara, Turkey, [22]Trakya University, Department of Nephrology, Edirne, Turkey, [23]Darica Farabi Training and Research Hospital, Department of Nephrology, Kocaeli, Turkey, [24]Hacettepe University, Department of Nephrology, Ankara, Turkey, [25]Pamukkale University, Department of Nephrology, Denizli, Turkey, [26]Dicle University, Department of Nephrology, Diyarbakır, Turkey, [27]Dokuz Eylül University, Department of Nephrology, İzmir, Turkey, [28]Akdeniz University, Department of Nephrology, Antalya, Turkey, [29]Cumhuriyet University, Department of Nephrology, Sivas, Turkey, [30]Atilim University Medicana International Hospital, Department of Nephrology, Ankara, Turkey, [31]Cukurova University, Department of Nephrology, Adana, Turkey, [32]Kartal Lutfi Kirdar Training and Research Hospital, Department of Nephrology, Istanbul, Turkey, [33]Kocaeli Government Hospital, Department of Nephrology, Kocaeli, Turkey, [34]Lefkosa BND Training and Research Hospital, Department of Nephrology, Lefkosa, Cyprus and [35]Necmettin Erbakan University, Meram School of Medicine, Department of Internal Medicine, Division of Nephrology, Konya, Turkey

Background and Aims: In IgA nephropathy (IgAN), which is characterized by mesangial IgA accumulation, there is the formation of circulating autoantibodies against galactose deficient IgA1s (Gd-IgA1). IgG / Gd-IgA1 immunocomplexes accumulate in the glomerular mesangium and play a role in the pathogenesis of IgAN. Recent studies have suggested a relationship between glomerular IgG deposition and the severity of glomerular inflammation. However, detection of the presence and severity of IgG in routine immunofluorescence microscopy (IFM) may fail. This study aims to investigate whether IgG positivity detected by IFM is associated with poor renal prognostic indicators and whether renal prognosis can be predicted according to IgG positivity.

Method: 4399 patients who were enrolled between May 2009-June 2019 in database of Turkish Society of Nephrology, Glomerular Diseases Working Group (TSN-GOLD) including 44 centers were evaluated. After exclusion criteria, 994 primary IgAN patients were included in the study. Glomerular IgG negative and positive patients were compared by means of Oxford classification scores, histopathological evaluations, proteinuria, creatinine, albumin, blood pressures. IgG positive patients were divided into subgroups according to the grade of the IFM positivity. The relationship between IgG positivity and poor prognosis criteria were evaluated.

Results: Demographic and biochemical findings of glomerular IgG positive and negative patients at the time of biopsy are shown in Table 1. No difference was found between the groups. There was no difference in the demographic and biochemical findings at the time of biopsy in IgG subgroup analyses (Table 2). There was no difference between the histopathological and Oxford MEST scores of the subgroups. Glomerular IgG positivity was not associated with diastolic blood pressure, systolic blood pressure, urea, uric acid, age, eGFR, albumin, proteinuria ($p > 0.05$ for all, r= -0.084, r= -0.102, r= -0.006, r=0.062, r= 0.014, r= -0.044, r= -0.061, r= -0.066, r= 0.150, respectively).

Conclusion: Glomerular IgG positivity detected by routine IFM in IgAN is not associated with poor renal prognostic indicators. It is difficult to predict renal prognosis by looking at the severity of IgG positivity at the baseline evaluation.

Table 1. Baseline demographic and biochemical findings

	IgG positive patients (n: 179)	IgG negative patients (n: 764)
Age (years)	38.5 ± 13.1	38.4 ± 12.8
Gender (male)	63.7%	62.7%
Body mass index (kg/m^2)	26.4 ± 5.1	26.7 ± 5.1
Systolic blood pressure (mmHg)	130 ± 22	130 ± 20
Diastolic blood pressure (mmHg)	82 ± 13	81 ± 12
Glucose (mg/dl)	97 ± 29	95 ± 23
BUN (mg/dl)	26 ± 22	24 ± 17
Creatinine (mg/dl)	1.51 ± 1.36	1.56 ± 1.25
eGFR (ml/min/1.73 m^2)	69.7 ± 37.9	66.5 ± 36.8
Proteinuria (g/day)	3.20 ± 0.48	3.24 ± 0.45
Albumin (g/dl)	3.9 ± 0.6	3.8 ± 0.7
Uric acid (mg/dl)	6.6 ± 1.9	6.6 ± 2.0
Total protein (g/dl)	7.6 ± 0.9	7.6 ± 0.9
Total cholesterol (mg/dl)	206 ± 49	215 ± 62
LDL (mg/dl)	129 ± 41	133 ± 50
HDL (mg/dl)	46 ± 17	46 ± 16
Triglycerides (mg/dl)*	163 ± 99	187 ± 123
Hemoglobin (g/dl)	13 ± 2	13 ± 2
Pyuria (leukocyte> 5)	17.7%	20.6%
C3 low	6.6%	8.4%
C4 low	0.9%	0.9%

*statistically significant

Table 2. Baseline demographic and biochemical analysis of the subgroups of IgG staining by IFM (differences between the parameters of the groups were not statistically significant)

	IgG (+) (n: 131)	IgG (++) (n: 36)	IgG (+++) (n: 12)
Age (years)	38.2 ± 12.8	40.3 ± 15.0	36.5 ± 11.2
Gender (male)	63.4%	63.9%	66.7%
Body mass index (kg/m^2)	26.4 ± 5.1	26.1 ± 4.6	27.5 ± 10.4
Systolic blood pressure (mmHg)	131 ± 23	128 ± 22	119 ± 15
Diastolic blood pressure (mmHg)	83 ± 12	80 ± 14	81 ± 13
Glucose (mg/dl)	99 ± 31	93 ± 22	90 ± 21
BUN (mg/dl)	26 ± 23	26 ± 20	24 ± 12
Creatinine (mg/dl)	1.56 ± 1.53	1.39 ± 0.69	1:32 ± 0.34
eGFR (ml/min/1.73 m^2)	70.4 ± 39.0	69.6 ± 38.7	61.6 ± 16.7
Proteinuria (g/day)	3.16 ± 0.50	3.27 ± 0.38	3.37 ± 0.48
Albumin (g/dl)	3.9 ± 0.5	3.9 ± 0.9	3.6 ± 0.7
Uric acid (mg/dl)	6.6 ± 2.0	7.6 ± 1.8	7.1 ± 1.5

P0491 **THE ROUTE TO INDIVIDUALIZED THERAPIES IN PRIMARY MEMBRANOUS NEPHROPATHY: BMI AND KIDNEY OUTCOMES.**

Rossella Siligato[1], Alfredo Laudani[1], Guido Gembillo[1], Vincenzo Calabrese[1], Alessandra Calderaro[1], Federica giada Vienna[1], Francesco Laurendi[1], Valeria Cernaro[1], Domenico Santoro[1]

[1]*Azienda Ospedaliera Universitaria Di Messina G. Martino - Facolta' Di Medicina E Chirurgia, D.A.I Medicina Clinica e sperimentale, U.O.C. Nefrologia e dialisi, Messina, Italy*

Background and Aims: A real progress in treating patients more than diseases, would rest on tailored medicine and go beyond the hypothesis that "one size fits all". Glomerular diseases are not an exception to this consideration, and deserve case-by-case evaluation for choosing both the most suitable therapeutic agent and its appropriate dose, because a standardized treatment may result in worse prognosis.

We analyzed the role of body mass index (BMI) in modifying renal outcomes of patients with nephrotic syndrome due to membranous nephropathy (MN) treated with immunosuppressive drugs.

Method: We performed a retrospective analysis of 29 MN patients related to our center (M 19, F 10), checking their anti PLA_2R status at kidney biopsy time and any change in proteinuria, serum creatinine (SCr) and body mass index (BMI) between diagnosis and at last follow-up visit, in search of a correlation with their response to immunosuppressive treatment. Data with non normal distribution are expressed as median and interquartile range [IQR].

Results: The median follow-up of our patients lasted 49 months [IQR 14-80]. At biopsy time, almost half of them was anti-PLA_2R positive (n=14 subjects) while the other resulted to be negative and were thus screened for secondary causes of MN (n=15). Irrespective either of anti-PLA_2R status or the administration of Ponticelli regimen or Rituximab, complete remission was achieved in 31% of patients, while 34.5% experienced a partial remission and 34.5% resulted non responder to at least a therapeutic protocol. Median proteinuria reduction was of 3.732g/24h [IQR 7.636-1.77 g/24h]. Median rise in SCr was 0.140 mg/dl [IQR -0.11 – 0.4 mg/dl]. Direct association between the proteinuria/BMI ratio at diagnosis and remission of proteinuria at last follow up was statistically significant (r=-0.7506; P<0.0001) (Fig.1).

Conclusion: Albeit remission is not directly correlated with basal BMI, our results appear to confirm that an appropriate drug posology, not only according to patients' renal or hepatic function but also to their body mass, may result in more effective individualized therapies in MN; nevertheless, this recorded association must be confirmed by large scale randomized clinical trials.

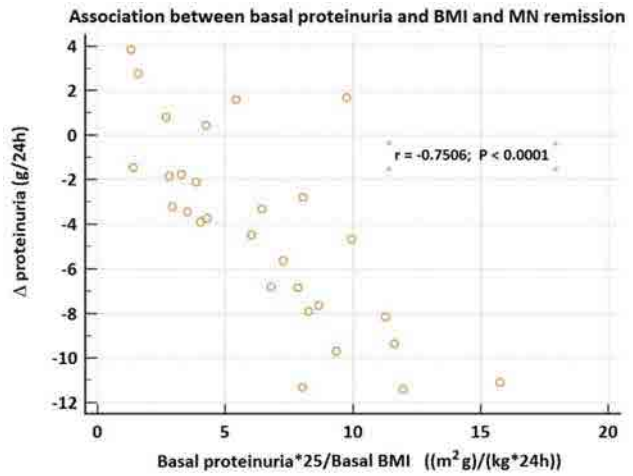


Figure:

P0492 ICAM-1 AND VEGF AS BIOMARKERS FOR PREDICTION LUPUS NEPHRITIS FLARE

Konstantin Chyzh[1,2,2], Tatyana Ryabceva[3], Nikolay Soroka[2], Pavel Viarshynin[4]

[1]Minsk, Minsk, Belarus, [2]Byelorussian State Medical University, 2nd Department of Internal Diseases, Minsk, Belarus, [3]Byelorussian State Medical University, Minsk, Belarus and [4]Minsk Scientific-Practical Center for Surgery, Transplantation and Hematology, State Institution, Nephrology and Hemodialysis, Minsk, Belarus

Background and Aims: Systemic lupus erythematosus (SLE) is autoimmune systemic disease of the connective tissue and characterized by the development of severe complications associated with damage to vital organs, in particular the kidneys. One of the important issues is an adequate assessment of the current activity and the objective prediction of the lupus nephritis (LN) flare. For this purpose molecular biomarkers are being searched. The work aim is the analyzing role of the intercellular adhesion molecule (ICAM-1) and vascular endothelial growth factor (VEGF) in the serum and urine of patients with SLE as a biomarker for lupus nephritis flare.

Method: The study group consisted of patients with SLE with LN (n = 23). The control group included patients with SLE without renal pathology (n = 13). The concentration of ICAM-1 and VEGF molecules was determined in blood serum and urine by enzyme-linked immunosorbent assay.

Results: The median concentration of ICAM-1in serum in patients with LN is 822.41 (580.50; 1300.95) ng/ml. That is two times higher than this indicator in the control group (378.97 (356.47; 439.52) ng/ml). The concentration of the VEGF molecule in serum in the group of LN is 91.99 (74.18; 132.58) ng/ml. That is three times higher than in the control group (31.13 (22.32; 132.58) ng/ml). An increase in the blood serum concentration of patients with SLE ICAM $\geq$577.7 ng/ml will indicate the presence of LN with a sensitivity of 82.61% and a specificity of 83.33%. ROC analysis showed the AUC coefficient is 0.927 (p = 0.0001). An increase in the blood serum in VEGF concentration of $\geq$66.43 ng/ml in patients with SLE will indicate the presence of LN with a sensitivity of 80.00% and a specificity of 83.33%. ROC analysis showed that the AUC coefficient is 0.916 (p = 0.006).

Conclusion: The results allow to conclude that it is possible to use the ICAM and VEGF concentration in serum and urine as early molecular markers of the LN and LN flare in patients with SLE.

P0493 EPIDEMIOLOGY OF IGA NEPHROPATHY IN THE MALTESE ISLANDS

Abigail Attard[1], Diana Vassallo[1], John Swayne[1], Jesmar Buttigieg[1], Edward Grech[1], Mario Pio Vella[1], Emanuel Farrugia[1]

[1]*Mater Dei Hospital, Nephrology, MSD2090, Malta*

Background and Aims: IgA nephropathy is the most common cause of glomerular disease worldwide. Natural history and clinical progression of this condition are highly heterogenous and can vary from asymptomatic haematoproteinuria, to a rapidly progressive glomerulonephritis that results in end-stage kidney disease (ESKD). The OXFORD MEST-C score is a set of consensus criteria that have been correlated with renal outcomes independent of baseline clinical features, proteinuria and blood pressure control. This is the first observational study carried out in the Maltese Islands that aims to evaluate the epidemiology and the histopathological distribution in Malta.

Method: All patients with biopsy-proven IgA nephropathy between January 2013 and July 2019 in our centre were recruited into this longitudinal retrospective observational study. Baseline data at time of biopsy included demographics, laboratory data and the MEST-C score. Study end-points included death, doubling of serum creatinine and ESKD. Data was censored on 31/12/2019.

Results: A total of 46 patients were recorded over this 6 year period, with a median follow-up of 2.7 years (Standard deviation 1.9). The median age of our cohort at time of biopsy was 46.1 years (Standard deviation 16.1). In total, 71.7% were males, 34.8% were hypertensive and 6.5% diabetic at baseline. At time of biopsy, 89.1% had an active sediment, 54.3% had established chronic kidney disease (CKD), 17.4% presented with acute kidney injury (AKI), 13% had a history of synpharyngitic haematuria, while 4.3% had a history of Henoch–Schönlein (HSP). In our cohort, 8 patients (17.4%) had progression of CKD. 4 of them had doubling of creatinine with 3 reaching ESKD. 1 patient died. Table 1 shows the distribution of histopathological findings in our cohort:

Conclusion: Despite the limited study sample, short follow-up time, and absence of treatment data, our results demonstrate that the distribution of histopathological variants in our cohort is similar to that reported elsewhere in the literature1.

Barbour SJ, Espino-Hernandez G, Reich HN, Coppo R, Roberts IS, Feehally J, et al. The MEST score provides earlier risk prediction in IgA nephropathy. Kidney Int. 2016 Jan;89(1):167–75.

Table 1: The histopathological distribution of IgA nephropathy in the Maltese Islands

	Cohort n=46	
	n	%
M	23	50
E	14	30.4
S	18	39.1
T	25	54.3
C	8	17.4

P0494 UNUSUAL CASE OF ACUTE KIDNEY INJURY (HISTOLOGICAL EVALUATION: COLLAPSING GLOMERULOPATHY) IN HEMOPHAGOCYTIC SYNDROME ASSOCIATED WITH NK/T LYMPHOMA

Elisabetta Ascione[1], Riccardo Magistroni[1], Marco Leonelli[1], Gianni Cappelli[1]

[1]*Modena, Nephrology Dialysis and Transplant Unit, University Hospital, Modena, Italy*

Background and Aims:

Hemophagocytic lymphohistiocytosis (HLH) is a severe hyperinflammatory syndrome induced by aberrantly activated macrophages and cytotoxic T cells. The primary (genetic) form, caused by mutations affecting lymphocyte cytotoxicity and immune regulation, is most common in children, whereas the secondary (acquired) form is most frequent in adults. Secondary HLH is commonly triggered by infections or malignancies but may also be induced by autoinflammatory/autoimmune disorders, in which case it is called macrophage activation syndrome.

The diagnosis of HLH in adults should be based on the HLH-2004 diagnostic criteria in conjunction with clinical judgment and the patient's history.

Renal involvement has previously been reported in 24 adult cases, mostly as acute renal failure. Collapsing glomerulopathy is extremely rare with only six previous cases reported in the literature.

Case presentation

We report the case of an African man, 31 years old, presented with fever, acute kidney injury: serum creatinine 10.3 mg/dl; urine protein 600 mg/dl, macrohematuria, ANA/ANCA were negative, low serum C3, organomegaly, anemia, thrombocytopenia, hypertriglyceridemia, hypofibrinogenemia, hyperferritinemia, direct and indirect antiglobulin (Coombs) tests were negative, low haptoglobin; elevated LDH; normal partial thromboplatin time. Peripheral blood smear examination reveal few schistocytes. ADAMTS13 activity was found to be 25%. HBV-DNA and HIV were negative. Anticardiolipin antibodies were negative. Lab exam suggested the relapse of an EBV infection and primary mycoplasma infection. Because of uremic symptoms and persisting oliguria we started replacement therapy by hemodialysis. Plasmapheresis was started because of suspected thrombotic microangiopathy. Suprisingly the kidney biopsy was consistent with collapsing glomerulopathy with evidence of tubular injury while the bone marrow biopsy diagnosed an EBV NK/T-Cell lymphoma.

During the course of his hospitalization, the patient suffered high fever. C-reactive protein, WBC and procalcitonin levels were elevated. Antimicrobial agents were initiated, starting with ceftriaxone then upgraded to piperacillin/tazobactam and then the shifted to teicoplanin and meropenem.

Blood, urine and stool cultures were negative.VRE positive, IgM Mycoplasma pneumoniae were positive; EBV PCR on bone marrow blood was positive. Malaria screening was negative. The antibiotic therapy was finally switched to doxycycline as unique agent.

Steroid therapy (dexamethasone daily 40 mg) and IVIG (daily 35g) were initiated then these drug were stopped. CHOP-like regimen (Etoposide 75 mg/m2, twice a week for two weeks then once a week until the seventh week) and Rituximab (375 mg/m2, once a week for 4 weeks) were initiated and continued for two weeks. Later on the patient died because of sepsis and multi-organ failure.

Conclusions

The multidisciplinary approach is very important. Physicians should be aware of HLH, because early recognition may prevent irreversible organ damage and subsequent death.[4,5] In adults, HLH-associated mortality remains high, especially in patients with underlying malignancies.

Collapsing glomerulopathy is the most commonly reported finding on renal biopsy. Renal prognosis appears to be poor with most patients remaining dialysis-dependent.

The increased awareness of HLH, together with a more rapid diagnostic workup and new therapeutic approaches, will improve the prognosis of HLH in adults.

P0495 PAUCI-IMMUNE GLOMERULONEPHRITIS - OUR EXPERIENCE IN A TERTIARY CARE CENTER

Umesh Lingaraj[1], Ricken Mehta[1], Shivaprasad SM[1], Leelavathi V[1], Kishan A[1], Sreedhara C[1], MYTHRI V[1]

[1]*Institute of Nephro Urology, Bengaluru, India*

Background and Aims:

- **Pauci-immune Glomerulonephritis, the most common etiology of primary RPGN, refers to a necrotizing glomerulonephritis with few or no immune deposits by immunofluorescence (IF) or electron microscopy (EM).**
- **In most patients, pauci-immune CGN is a component of a systemic small vessel vasculitis such as granulomatosis with polyangiitis (GPA), microscopic polyangiitis(MPA) or eosinophilic granulomatosis with polyangiitis(EGPA).**
- **Approximately 90% of patients with PICG have circulating ANCA antibodies, leading to the nomenclature ANCA-associated vasculitis (AAV).[1-3]**

Aims - To study the clinicopathological profile and short-term outcome of patients with Pauci-immune Glomerulonephritis at a tertiary care center

Method:

- A total of 30 Biopsy proven cases of Pauci-immune Glomerulonephritis were included during the study period from August 2017 to November 2019(28 months).
- Patients were treated based on the recent guidelines and were followed up (minimum follow up – 3months) to characterize their response to treatment.

Results: In our study group we found that majority of the patients had RPGN presentation (93.3%).

- 24.4% patients were ANCA negative. 50% had anti-MPO Abs.
- 50% had crescentic class, 23.3% had focal class of pauci-immune GN.
- 56.6% patients achieved remission(CR & PR) following treatment.
- 23.3% progressed to ESRD despite treatment.
- Patients with crescentic and focal class showed a higher probability to achieve remission.

Conclusion:

- Pauci-immune crescentic GN is the most common cause of primary RPGN in adults and elderly.
- A high percentage of these patients are ANCA negative.
- Despite the aggressive ISP therapy a large percentage of patients progress to ESRD.
- Focal and crescentic GN have a better prognosis and should be treated aggressively.
- We had a higher proportion of patients with antibodies against MPO-(pANCA) who have more glomerulosclerosis, relapsing course and poorer prognosis.

Treatment Outcome	Number	Percentage
Complete Remission	07/30 (3-F,4-C)	23.3%
Partial Remission	10/30 (2-F,8-C)	33.3%
CKD Stage 2 to 5 N/D	06/30 (2-F,3-C,1-M)	20%
CKD VD	07/30 (5-S,2-M)	23.3%
Death	06/30	20%

P0496 **THE IMPORTANCE OF COMPLEMENT LEVELS AND CLINICAL CHARACTERISTICS OF PRIMARY MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS IN TURKEY**

Erhan Tatar[1], Deren Oygar[2], Nurhan Seyahi[3], Necmi Eren[4], Yağmur Cantürk[5], Özkan Güngör[6], Ülver Derici[7], Murat Sipahioğlu[8], Abdülmecit Yıldız[9], Serhat Karadağ[10], Abdullah Sumnu[11], Ali Riza Odabas[12], Didem Turgut[13], Caner Cavdar[14], Garip SAHIN[15], Belda Dursun[16], Dilek Guven Taymez[4], Fatma Yılmaz Aydın[17], Memnune Sena Ulu[18], Taner Basturk[19], Serap Yadigar[20], Ilter Bozaci[1], Ahmet Behlül[2], Savaş Sipahi[21], Zerrin Bicik Bahçebaşı[20]

[1]Bozyaka Eğitim Ve Araştırma Hastanesi, nephrology, izmir, Turkey, [2]Burhan Nalbantoglu State Hospital, nephrology, Lefkoşa, , [3]Cerrahpaşa Tıp Fakültesi Hastanesi, nephrology, Turkey, [4]Kocaeli Üniversitesi Tıp Fakültesi, nephrology, koaceli, Turkey, [5]Çapa Tıp Fakültesi, Nephrology, İstanbul, Turkey, [6]Kahramanmaraş Sütçüimam University School of Medicine, nephrology, Kahramanmaraş, Turkey, [7]Gazi University Faculty of Medicine, nephrology, Ankara, Turkey, [8]Erciyes Üniversitesi Tıp Fakültesi Hastaneleri, nephrology, Kayseri, Turkey, [9]Uludag University Medical Faculty Hospital, nephrology, Bursa, Turkey, [10]Haseki Eğitim ve Araştırma Hastanesi, Nephrology, İstanbul, Turkey, [11]İstanbul Medipol University, Nephrology, İstanbul, Turkey, [12]Sağlık Bilimleri Üniversitesi Sultan Abdülhamid Han Eğitim ve Araştırma Hastanesi, nephrology, İstanbul, Turkey, [13]Başkent University Ankara Hospital, Nephrology, Ankara, Turkey, [14]Dokuz Eylul University Hospital, nephrology, İzmir, Turkey, [15]Eskişehir Osmangazi University Hospital, nephrology, Eskişehir, Turkey, [16]Pamukkale Üniversitesi Hastanesi, nephrology, Denizli, Turkey, [17]Dicle University Faculty of Medicine, Nephrology, Diyarbakır, Turkey, [18]Afyon Kocatepe Universitesi Tip Fakultesi, nephrology, afyon, Turkey, [19]Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi, Nephrology, İstanbul, Turkey, [20]Kartal Dr. Lütfi Kırdar Training and Research Hospital, Nephrology, İstanbul, Turkey and [21]Sakarya Eğitim Araştırma Hastanesi, Nephrology, Sakarya, Turkey

Background and Aims: Membranoproliferative glomerulonephritis (MPGN) may be caused by disturbances in the complement system. Hypocomplementemia is a characteristic of MPGN. Among these patients frequency of hypocomplementemia and their relation with clinical and histopathological findings are still not clearly known. The aim of this study is to evaluate the hypocomplementemia frequency among the primary MPGN patients in Turkey and its relation with histopathological subtypes, findings and demographic characteristics.

Method: The data was obtained from national multicentered (47 centers) records of primary glomerular diseases in Glomerulonephritis Study Group of the Turkish Society of Nephrology database from May 2009 to June 2019. Primary MPGN cases were evaluated and divided into 2 groups with and without hypocomplementemia.

Results: In total, 193 cases were included in the study. The indications for renal biopsy were isolated nephrotic syndrome (55.4%), nephritic syndrome (21.2%), nephrotic syndrome with a nephritic component (6.2%) and asymptomatic urinary findings (17.2%). 34.2% of the cases were reported as immune complex type, another 34.2% of the cases were reported as C3 glomerulopathy. 31.6% of patients were not specified. 82 (42.4%) of the cases presented hypocomplementemia. Hypocomplementemic patients were younger (34±14 vs 41±15, p=0.002) and most frequently female (56% vs 41%, p=0.03). At same time, serum albumin and hemoglobin levels were lower and anemic patient rates were higher (p<0.001). In this group, the nephrotic syndrome rates were higher (72% vs 54%, p=0,01). Hypocomplementemia rate in the C3 glomerulopathy was 52% (in DDD 40%, in C3GN 55%) whereas in immune complex type 41% and in non specified type 34%. In the pathological evaluation; among the hypocomplementemic group the endocapillary proliferation and glomerular exudative differentiation rates presented significant increase. However the chronicity index were lower in the kidney biopsy (Table 1).

Conclusion: This multicenter study provided important data about the epidemiology of MPGN with importance of hypocomplementemia in Turkey. Hypocomplementemia is associated with both subtypes of MPGN patern, anemia and nephrotic syndrome. At the same time, hypocomplementemia is a valuable parameter for active MPGN pattern in the histopathological evaluation. This may be important in determining the treatment.

Table 1. Laboratory Results and Demographic Evaluations of The Cases

	All Cases (n:193)	With Hypocomplementemia (n:82)	Without Hypocomplementemia (n:111)	P-value
Age (year)	38±15	34±14	41±15	0.002
Sex (F/M)	91/102	46/36	45/66	0.03
Nephrotic Syndrome frequency (n,%)	119 (61.6%)	59 (72%)	60 (54%)	0.01
Serum Creatinin (mg/dL)	1.43±1.02	1.37±1.18	1.47±0.89	0.50
Serum Albumin (g/dL)	3.1±0.9	2.9±0.8	3.2±0.9	0.02
Hemoglobine (g/L)	12.1±2.3	11.3±1.8	12.8±2.3	<0.001
Proteinuria (g/day)	5.3±4.8	5.4±4.1	5.1±5.3	0.65
C3 Glomerulopathy (n,%)	66(34.2)	34 (41.4%)	32(28.8%)	0.06
Kidney Biopsy Findings				
Glomerular endocapillary proliferation%, (+/-)	45	55	38	0.04
Glomerular exudative patern %, (+/-)	22	31	15	0.03
Interstisial Inflamation %, (+/-)	73	78	70	0.27
Vascular differentiation %, (+/-)	40	32	46	0.03
Interstitial fibrosis %, (+/-)	58	53	62	0.18
Tubular Atrophy %, (+/-)	56	53	59	0.38

P0497

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS IN A LMIC : EPIDEMIOLOGIC PROFILE, PROGNOSTIC FACTORS AND IMPACT OF ALPHA SMOOTH MUSCLE ACTIN

Agrebi Ikram[1], Kammoun Khawla[1], Dammak Najla[1], Yaich Soumaya[1], Boudawara Tahya[2], Fayçal Jarraya[1], Ben hmida Mohamed[1]

[1]Hedi Chaker university hospital, Nephrology department, Sfax, Tunisia and [2]Habib Bourguiba university hospital, anatomopathology, Sfax, Tunisia

Background and Aims: Mesangiocapillary glomerulonephritis (MCGN) is a rare kidney disease with a poor prognosis. Several factors have been described associated with poor renal prognosis. The contribution of alpha smooth muscle actin (α-SMA), which is involved in renal fibrogenesis, has been demonstrated in assessing the prognosis of several glomerular diseases, but few studies have concerned the MCGN.

The aim of our study is to determine the epidemiologic profile, to identify prognostic factors and to evaluate the contribution of α-SMA in predicting the prognosis the MCGN.

Method: Our study is retrospective over a period of 16 years (January 1996- December 2011) including all cases of primary MCGN aged more than 15 years, collected at the nephrology department of the university hospital Hedi Chaker Sfax. We reviewed available renal biopsies for the study of the expression of α-SMA by immunohistochemistry.

Results: We collected 118 cases of primary MCGN, with mean age of 45 ± 19 years. The incidence of MCGN has decreased from 10 cases / year between 1996 and 1999 to 5 cases / year between 2008 and 2011. 78.8 % of patients had renal failure at the moment of diagnosis. The study of the expression of α-SMA by immunohistochemistry was made in 16 cases. After a mean follow-up of 51.9 ± 44 months, progression to end stage renal failure (ESRF) was observed in 43.5% of cases. Poor prognostic factors were initial renal failure and sclerotic glomeruli (respectively p at 0,04 and 0,03), but interstitial fibrosis degree was not a prognosis predictor parameter while important interstitial expression of α-SMA was a marker of the evolution to ESRF ($p = 0.03$).

Conclusion: MCGN has significantly declined over recent years due to improve of socio-economic conditions. The presence of renal failure and sclerotic glomeruli at diagnosis were associated with a poor prognosis. The interstitial expression of α-SMA may be a useful marker to predict the progression of primary MCGN even before the installation of fibrosis.

P0498

CLINICAL PRESENTATION AND RENAL HISTOPATHOLOGICAL FINDINGS IN PATIENTS WITH MONOCLONAL GAMMOPATHY

Gaetano Alfano[1], Alice Delrio[1,2], Francesco Fontana[3], Annachiara Ferrari[1], Andrea Solazzo[1], Giacomo Mori[3], Gianni Cappelli[1]

[1], Surgical, Medical and Dental Department of Morphological Sciences, Section of Nephrology, University of Modena and Reggio Emilia, Modena, Italy;, Modena, Italy, [2]University of Modena and Reggio Emilia, Modena, Italy;, Modena, and [3]Nephrology Dialysis and Transplant Unit, University Hospital of Modena, Modena, Italy;, Modena,

Background and Aims: Monoclonal gammopathy is associated with renal lesions due to the toxic effect of M-protein. The aim of our study was to evaluate the prevalence and the clinical presentation of monoclonal gammopathy in patients who underwent kidney biopsy for renal impairment.

Method: We conducted a retrospective study at the Nephrology and Dialysis Unit of the University Hospital of Modena from 2005 to 2017. The diagnosis of renal disease was proved histologically.

Results: Monoclonal gammopathy was found in 179 out of 1334 patients (13.4%). Mean age was 66.1±13.4 years with a predominance of males (63.7%). There was no differences (P=0.16) between the age of patients with benign (64.9±14.3) and malignant lymphoproliferative diseases (67.6±12). The hematologic disorders involved in the production of M-protein were MGUS (51.9%), myeloma multiple (MM) (25.7%), amyloidosis (8.9%) smoldering MM (5 %), non-Hodgkin lymphoma (NHL) (6.7%) and HL (1.7%).

The prevalence of **MGUS** was estimated to be 6.97% (93/1334). Mean serum creatinine was 2.68±2.12 mg/dl (eGFR of 35.24±29.32 ml/min) and urine protein/creatinine ratio of 5.1±6.5. None of the study subjects progressed to MM or other lymphoproliferative diseases. The most common kidney disease was membranoproliferative (GN) (19.3%). MGRS has been identified in five patients (5.4%).

Mean age of **MM** was 66.84±13 years. Serum concentration M-protein was 1.47±0.98. Among patients with AKI (89.1%), 13 patients (28.2%) required urgent hemodialysis.

Histological evaluation showed cast nephropathy (71.7%), MM-associated AL amyloidosis (15.2%), MM-associated-light chain deposition disease (4.3%) and interstitial nephritis (8.7%).

Nine patients had a diagnosis of **smoldering MM**. Average age was 69.17±10.8 years old. At presentation, creatinine was 2.31±2.6 mg/dl (GFR of 41.35 ml/min). Evaluation of renal biopsies allowed us to identify different patterns of glomerular diseases, expression of an aspecific renal involvement of this hematological disease.

AL amyloidosis was secondary to MGUS (75%) and smoldering MM (33%). Mean age was 66.04±11.7 years old. At presentation mean urine protein/creatinine ratio was 8.33±3.2 concomitant to a serum albumin level of 2.74±0.84 gr/dl. Mean creatinine was 1.4 mg/dl corresponding to eGFR= 56.5 ml/min.

Average age of **NHL** patients was 72.6±9.6 years. Renal function was extremely variable at presentation; mean creatinine was 2.4±1.6 mg/dl (eGFR of 30.4±22.7 ml/min). Histological evaluation of biopsy specimen revealed amyloidosis (25%), cryoglobulinemic GN (25%), LCDD (16.6%), cast-nephropathy (8.3%), LCDD (8.3%) and other renal diseases (16.8%).

Three patients (1.12%) had a diagnosis of **HL** at mean age of 69.04±5.3 years. At presentation, renal function was normal in all patients with a creatinine of 0.93±0.07mg/dl (eGFR of 62.7.3±7.4 ml/min). Urine protein/creatinine ratio was 0.3±0.2. Kidney biopsy revealed cryoglobulinemic GN (75%) and hypertensive nephrosclerosis (25%).

ANOVA analysis did not found statistically significant differences in age (p=0.11) and serum concentration of M-protein (P=0.42) between groups. The differences in mean serum creatinine and mean urine protein/creatinine ratio were statistically significant between groups, (P<0.0001) and (P=0.003), respectively. A post hoc Tukey test showed that proteinuria was higher in AL amyloidosis compared to MM and HL, whereas renal function was worse in MM patients compared to the others.

Conclusion: MGUS was the most common monoclonal gammopathy. Surprisingly, it is frequently associated with membranoproliferative glomerulonephritis. MGRS is a rare histopathological entity (5.4%). MM manifests frequently with AKI whereas AL amyloidosis with nephrotic syndrome. Renal function was extremely variable in NHL patients; on the other hand, the limited number of HL patients with renal involvement in our cohort does not allow generalization of our findings.

P0499 SPONTANEOUS REMISSION IN PRIMARY MEMBRANOUS NEPHROPATY WITH POSITIVE ANTIPLA2R ANTIBODIES

SOFIA ORTEGO[1,2], Javier Villacorta[1,2], Milagros Fernandez Lucas[1,2], Angela Carrasco[1,3], NURIA RODRIGUEZ MENDIOLA[1,2], ESTHER CASILLAS[1,2], Vanessa Lopes[1,2], MARTA DIAZ[1,2], Claudia Rita[1,3], ISRAEL GAÑAN[1,3]

[1], Spain, [2]Ramon y Cajal Hospital, Nephrology and [3]Ramon y Cajal Hospital, Inmunology

Background and Aims: Patients with primary membranous nephropaty experience a spontaneous remission rate between 30-40%. AntiPLA2R antibodies are involved in the pathogenesis of the disease. Some studies demonstrated that levels of circulating anti-PLA2R in the beginning of the disease revealed a strong correlation with clinical disease activity, and it could help discriminate against those who will make spontaneous remission

Method: The principal objetive was to analize the spontaneous remission rate in patients with membranous nephropaty with positive antiPLA2R antiboidies and study clinical and serological variables associated. A retrospective analysis studied the associaition between analitis, clinical and serological variables of patients with with spontaneous remission and membranous nephropaty who were diagnosed in between 2015 and 2018 in Ramon y Cajal Hospital.

Results: We included 13 patients with primary positive antiPLA2R antibodies membranous nephropaty. Patients ha a mean age of 61,6 ± 20 and a 64.3% were males. All of them had nephrotic syndrome in the onset disease. Patients were aged 6,6 ± 3.8 gr/24horas, in serum albumine 2.3 ± 0.5 g/L and the serum Creatinine (Cr) was 1 ± 0.5 mg/dl. Medium AntiPLA2R tittle was ±. All the patients were treated at the diagnosis time with ARB/ACE inhibitors . 7 of the 13 (53.8%) patients experienced a spontaneous remission of the nephrotic syndrome. The mean time to spontaneous remission was 4.8 ± 2.4 months. Patients who presented spontaneous remission debuted with lower serum Cr at debut. No significative differences were found in between remisión rate in association with total proteinuria neither PLA2R titles in the beginning.

Conclusion: In our experience, approximately a 50% of patients with membranous nephropaty experienced an spontaneous remission. There was no significative association in between AntiPLA2R titles and spontaneous remission rate in our study. Patients with better renal function in the diagnosis were more frequently associated with spontaneous remission.

P0500

RESULTS OF A PHASE 1 TRIAL TO INVESTIGATE THE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF BION-1301 IN HEALTHY VOLUNTEERS

Jeannette Lo[1], Peter Van Zandvoort[1], Jos Van de Crommert[1], Aaron Endsley[2], Thomas Müller[1], Somayeh Honarmand[1], Angelique Mittan[1], Jonathan Barratt[3], Jackie Walling[1], David Essayan[1]

[1]Aduro Biotech, Inc, Berkeley, United States of America, [2]Certara, Princeton, United States of America and [3]University of Leicester, Leicester, United Kingdom

Background and Aims: IgA nephropathy (IgAN), the leading cause of primary glomerulonephritis, is an autoimmune disease with no approved treatments. Slow progression to end-stage-renal disease occurs in up to 50% of patients with IgAN over approximately 20-25 years, resulting in the need for dialysis or kidney transplant. A critical step in IgAN pathogenesis is the production of galactose-deficient IgA1 (Gd-IgA1) leading to the generation of anti-Gd-IgA autoantibodies and the formation of immune complexes that result in kidney inflammation and damage. Patients with IgAN have elevated levels of A proliferation-inducing ligand (APRIL), which may contribute to IgAN pathogenesis by regulating differentiation and proliferation of B cells. In a study of patients with IgAN, those with high plasma APRIL levels had higher levels of Gd-IgA1 and proteinuria and lower estimated glomerular filtration rates compared to those with lower plasma APRIL levels. BION-1301 is a first-in-class humanized antagonistic antibody targeting APRIL. BION-1301 reduced serum levels of IgA, IgM, and IgG with no drug-related toxicity in nonhuman primates and was well-tolerated with no dose-limiting toxicities in a Phase 1/2 first-in-human clinical study in patients with late-stage multiple myeloma. The Phase 1 trial described here will characterize the safety, pharmacokinetic (PK), and pharmacodynamic (PD) profiles of BION-1301 in healthy volunteers (HV) and patients with IgAN.

Methods: The protocol for this study (NCT03945318) is comprised of 3 parts, of which only Parts 1 and 2 are complete. Parts 1 and 2 assess BION-1301 in HV, and Part 3 will assess BION-1301 in patients with IgAN. Parts 1 and 2 are double-blind, randomized, placebo-controlled single and multiple ascending dose designs, respectively. Part 3 will assess a multiple dose regimen in IgAN patients. Part 1 enrolled 36 HV in 5 dose cohorts, randomized in a 3:1 ratio to receive a single dose of BION-1301 or placebo delivered by IV infusion. Part 2 enrolled 27 HV in 3 dose cohorts, randomized in a 2:1 ratio to receive 3 doses of BION-1301 or placebo delivered by IV infusion once every two weeks over a one month period. Dose escalation decisions were made by a Safety Review Team based on safety, tolerability, and PK-related stopping criteria.

Results: To-date, BION-1301 continues to be well tolerated. Its biological activity in the study is characterized by free APRIL, IgA, IgG, and IgM levels; unblinded safety, PK, and PD results for Parts 1 and 2 in Healthy Volunteers will be presented.

Conclusion: BION-1301, a humanized anti-APRIL antibody, may provide a novel avenue for the potential treatment of IgAN that offers potential advantages compared to currently used antihypertensive or immunosuppressive therapies.

P0501

THE EPIDEMIOLOGICAL FEATURES OF PIRMARY GLOMERULAR DISEASES IN TURKEY: THE MULTICENTER STUDY OF TURKISH SOCIETY OF NEPHROLOGY GLOMERULAR DISEASES (TSN-GOLD) WORKING GROUP

Aydin Turkmen[1], Abdullah Sumnu[2], Egemen Cebeci[3], Halil Yazici[4], Necmi Eren[5], Nurhan Seyahi[6], Kamil Dilek[7], Fatih Dede[8], Ülver Derici[9], Abdulkadir Unsal[10], Garip SAHIN[11], Murat Sipahioglu[12], Mahmut Gok[13], Erhan Tatar[14], Belda Dursun[15], Savaş Sipahi[16], Mürvet Yılmaz[17], Gultekin Suleymanlar[18], Memnune Sena Ulu[19], Ozkan Gungor[20], Sim Kutlay[21], Zerrin Bicik Bahçebaşı[22], İdris Sahin[23], Ilhan Kurultak[24], Kultigin Turkmen[25], Zulfikar Yilmaz[26], Rumeyza Turan Kazancioglu[27], Caner Cavdar[28], Ferhan Candan[29], Zeki Aydin[30], Deren Oygar[31], Cuma Bulent Gul[32], Mustafa Arici[33], Saime Paydas[34], Dilek Guven Taymez[35], Mehmet Kucuk[36], Sinan Trablus[37], Kenan Turgutalp[38], Leyla Koc[39], Siren Sezer[40], Murat Duranay[41], Simge Bardak[42], Luftullah Altintepe[43], Izzet Hakki Arikan[44], Alper Azak[45], Ali Riza Odabas[46], Gulizar Manga Sahin[13], Savas Ozturk[3]

[1]Istanbul University, Istanbul Faculty of Medicine, Nephrology, Istanbul, Turkey, [2]Medipol University Medical Faculty, Medipol Mega Hospital, Nephrology, İstanbul, Turkey, [3]Haseki Training and Research Hospital, Nephrology, Istanbul, Turkey, [4]Istanbul University, Istanbul Faculty of Medicine, Nephrology, Istanbul, , [5]Kocaeli University Medical Faculty, Nephrology, Kocaeli, Turkey, [6]Istanbul University, Cerrahpasa Faculty of Medicine, Nephrology, Istanbul, Turkey, [7]Uludag University, Medical Faculty, Nephrology, Bursa, Turkey, [8]Ankara Numune Training and Research Hospital, Nephrology, Ankara, Turkey, [9]Gazi University Medical Faculty, Nephrology, Ankara, Turkey, [10]Hamidiye Sisli Etfal Training and Research Hospital, Nephrology, Istanbul, Turkey, [11]Eskisehir Osmangazi University, Medical Faculty, Nephrology, Eskisehir, Turkey, [12]Erciyes University, Medical Faculty, Nephrology, Kayseri, Turkey, [13]Sultan Abdulhamit Han Research and Training Hospital, Nephrology, Istanbul, Turkey, [14]Bozyaka Training and Research Hospital, Nephrology, Izmır, Turkey, [15]Pamukkale University, Medical Faculty, Nephrology, Denizli, Turkey, [16]Sakarya University, Medical Faculty, Nephrology, Sakarya, Turkey, [17]Bakirkoy Sadi Konuk Training and Research Hospital, Nephrology, Istanbul, Turkey, [18]Akdeniz University, Medical Faculty, Nephrology, Antalya, Turkey, [19]Afyon University, Medical Faculty, Nephrology, Afyon, Turkey, [20]Sutcu İmam University, Medical Faculty, Nephrology, Kahramanmaras, Turkey, [21]Ankara University, Medical Faculty, İbni Sina Hospital, Nephrology, Ankara, Turkey, [22]Dr. Lutfi Kirdar Kartal Training and Research Hospital, Nephrology, Istanbul, Turkey, [23]Inonu University, Medical Faculty, Nephrology, Malatya, Turkey, [24]Trakya University, Medical Faculty, Nephrology, Istanbul, Turkey, [25]Necmettin Erbakan University, Meram Medicine Faculty, Nephrology, Konya, Turkey, [26]Dicle University, Medical Faculty, Nephrology, Diyarbakir, Turkey, [27]Bezmialem Vakif University, Medical Faculty, Nephrology, Istanbul, Turkey, [28]Dokuz Eylul University, Medical Faculty, Nephrology, Izmir, Turkey, [29]Cumhuriyet University, Medical Faculty, Nephrology, Sivas, Turkey, [30]Darica Farabi Training and Research Hospital, Nephrology, Kocaeli, Turkey, [31]Burhan Nalbantoglu State Hospital, Nephrology, Lefkosa, Cyprus, [32]Bursa Yuksek Ihtisas Training and Research Hospital, Nephrology, Bursa, Turkey, [33]Hacettepe University, Medical Faculty, Nephrology, Ankara, Turkey, [34]Cukurova University, Medical Faculty, Nephrology, Adana, Turkey, [35]Kocaeli State Hospital, Nephrology, Kocaeli, Turkey, [36]Okmeydanı Training and Research Hospital, Nephrology, Istanbul, Turkey, [37]Istanbul Training and Research Hospital, Nephrology, Istanbul, Turkey, [38]Mersin University, Medical Faculty, Nephrology, Mersin, Turkey, [39]Taksim Training and Research Hospital, Nephrology, Istanbul, Turkey, [40]Atilim University, Medicana International Hospital, Nephrology, Ankara, Turkey, [41]Ankara Training and Research Hospital, Nephrology, Ankara, Turkey, [42]Batman State Hospital, Nephrology, Batman, Turkey, [43]Selcuk University, Selcuklu Medicine Faculty, Nephrology, Konya, Turkey, [44]Marmara University, Medical Faculty, Nephrology, Istanbul, Turkey, [45]Balikesir Training and Research Hospital, Nephrology, Balikesir, Turkey and [46]Medeniyet University Medical School, Goztepe Training and Research Hospital, Nephrology, Istanbul, Turkey

Background and Aims: The largest data on the epidemiology of primary glomerular diseases (PGD) are obtained from the databases of countries or centers. Here, we presented the extended results of the Primary Glomerular Diseases Study of the Turkish Society of Nephrology Glomerular Diseases (TSN-GOLD)Working Group.

Method: The data of patients who underwent renal biopsy and diagnosed as primary glomerular disease were recorded in the database prepared for the study. Between May 2009 and May 2019, a total of 4399 patients from 47 centers were evaluated. Basal data of 3875 patients were analyzed after exclusion of those lacking light microscopy and immunofluorescence findings.

Results: The mean age was 41.5 ± 14.9 years. Of the patients, 1690 were female (43.6%) and 2180 (56.3%) were male. Nephrotic syndrome was the most common biopsy indication (51.7%). This was followed by asymptomatic urinary abnormalities (18.3%) and nephritic syndrome (17.8%). The most common PGH was IgA nephropathy (25.7%), followed by membranous nephropathy (25.6%) and FSGS (21.9%). The mean total number of glomeruli per biopsy was 17 ± 10. Mean baseline systolic blood pressure was 130 ± 20 mmHg and diastolic blood pressure was 81 ± 12 mmHg. Median proteinuria was 3300 (IQR: 1467-6307) mg / day, mean serum creatinine, estimated GFR and albumin values were 1.4 ± 1.5 mg / dl, 80.7 ± 39.1 ml / min and 3.2 ± 0.9 g / dl, respectively.

Conclusion: In Turkey, the incidence of IgA nephropathy patients have become more common than membranous nephropathy among PGD patients diagnosed with renal biopsy.

Table 1. Basal characteristics of patients

	Mean±SD
Systolic blood pressure (mmHg)	130±20
Diastolic blood pressure (mmHg)	81±12
Body mass index (kg/m^2)	27.3±9.7
Glucose (mg/dl)	97±31
BUN (mg/dl)	23±19
Creatinine (mg/dl)	1.4±1.5
eGFR (CKD-EPI)	80.0±39.1
Number of glomeruli per biopsy	17±10
Uric acid (mg/dl)	6.2±1.8
Trigliserid (mg/dl)	208±133
LDL-Cholesterol (mg/dl)	163±85
ALT (IU/l)	22±59
Calcium (mg/dl)	8,8±0.8
Hemoglobin (g/dl)	12.9±2.1
Proteinuria (mg/per day)*	3300 (IQR: 1467-6307)
Serum albumin (g/dl)	3.2±0.9

*median value (%25-%75)

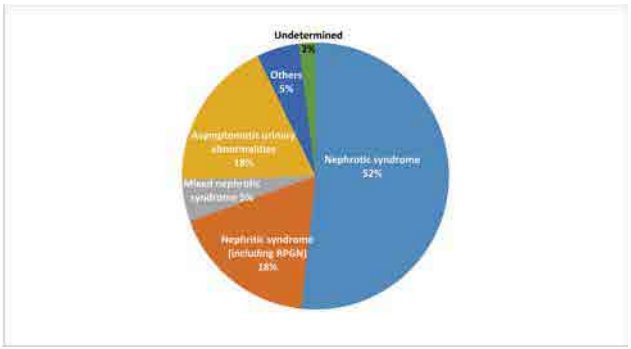


Figure 1. Indications for renal biopsy.

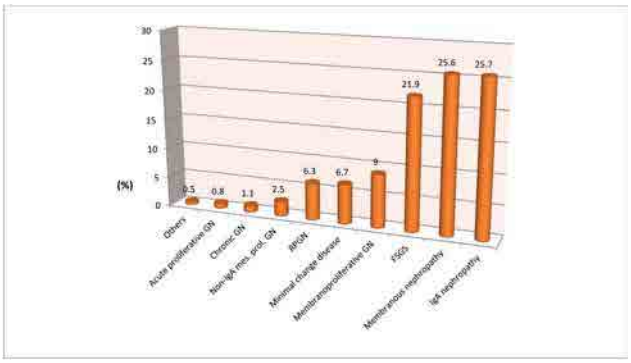


Figure 2. Pattern of primary glomeruler disease in Turkey.

P0502

BIOBANKING FOR GLOMERULAR DISEASES: A STUDY DESIGN AND PROTOCOL FOR KOREA RENAL BIOBANK NETWORK SYSTEM TOWARD NEXT-GENERATION ANALYSIS (KORNERSTONE)

Eunjeong Kang[1], Yaerim Kim[2], Yong Chul Kim[1], Soojin Lee[1], Seungyeup Han[2], Minsun Choe[3], Jin Ho Hwang[4], Sunhwa Lee[5], Ji In Park[5], Jung Tak Park[6], Beom Jin Lim[7], Jung Pyo Lee[8], Jung Nam An[8], Dong-Ryeol Ryu[9], Jung-Hyun Kim[10], Hee Gyung Kang[11], Hyun Soon Lee[12], Kyung Chul Moon[13], Kwon Wook Joo[1], Kook-Hwan Oh[1], Seung Seok Han[1], Hajeong Lee[1], Dong Ki Kim[1]

[1]Seoul National University Hospital, Internal Medicine, Seoul, Korea, Rep. of South, [2]Keimyung University School of Medicine, Internal Medicine, Daegu, Korea, Rep. of South, [3]Keimyung University School of Medicine, Pathology, Korea, Rep. of South, [4]Chung-Ang University Hospital, Internal Medicine, Seoul, Korea, Rep. of South, [5]Kangwon National University Hospital, Internal Medicine, Chuncheon, Korea, Rep. of South, [6]Institute of Kidney Disease Research, Yonsei University, Internal Medicine, Seoul, Korea, Rep. of South, [7]Institute of Kidney Disease Research, Yonsei University, Pathology, Seoul, Korea, Rep. of South, [8]Seoul National University Boramae Medical Center, Internal Medicine, Seoul, Korea, Rep. of South, [9]College of Medicine, Ewha Womans University, Internal Medicine, Seoul, Korea, Rep. of South, [10]Major of Food and Nutrition, Pai Chai University, Home Economics Education, Daejeon, Korea, Rep. of South, [11]Seoul National University Children's Hospital, Pediatrics, Seoul, Korea, Rep. of South, [12]Hankook Renal Pathology Lab, Pathology, Seoul, Korea, Rep. of South and [13]Seoul National University Hospital, Pathology, Seoul, Korea, Rep. of South

Background and Aims: Glomerular diseases, a set of debilitating and complex disease entities, are related to mortality and morbidity. To gain insight into pathophysiology and novel treatment targets of glomerular disease, various types of biospecimens linked to deep clinical phenotyping including clinical information, digital pathology, and well-defined outcomes are required. We provide the rationale and design of the KOrea Renal biobank NEtwoRk System TOward Next-generation analysis (KORNERSTONE).

Method: The KORNERSTONE, which has been initiated by Korea Centres for Disease Control and Prevention, is designed as a multi-centre, prospective cohort study and biobank for glomerular diseases. Clinical data, questionnaires will be collected at the time of kidney biopsy and subsequently every one year after kidney biopsy. All of the clinical data will be extracted from the electrical health record and automatically uploaded to the web-based database. High-quality digital pathologies are obtained and connected in the database. Various types of biospecimens are collected at baseline and during follow-up: serum, urine, buffy coat, stool, glomerular complementary DNA (cDNA), tubulointerstitial cDNA. All data and biospecimens are processed and stored in a standardised manner. The primary outcomes are mortality and end-stage renal disease. The secondary outcomes will be deterioration renal function, remission of proteinuria, cardiovascular events and quality of life.

Disussion: Ethical approval has been obtained from the institutional review board of each participating centre and ethics oversight committee. The KORNERSTONE is designed to deliver pioneer insights into glomerular diseases. The study design allows comprehensive, integrated and high-quality data collection on baseline laboratory findings, clinical outcomes including administrative data and digital pathologic images. This may provide various biospecimens and information to many researchers, establish the rationale for future more individualised treatment strategies for glomerular diseases.

Conclusion: In conclusion, we describe the objectives and clinical protocol for the KORNERSTONE. As the first large-scale glomerulonephropathy cohort study with the integration of clinical data, biospecimens and digital pathologic images in Korea, the KORNERSTONE will help to clarify the natural course, complication profiles, and novel treatment targets of the Asian population with glomerular disease.

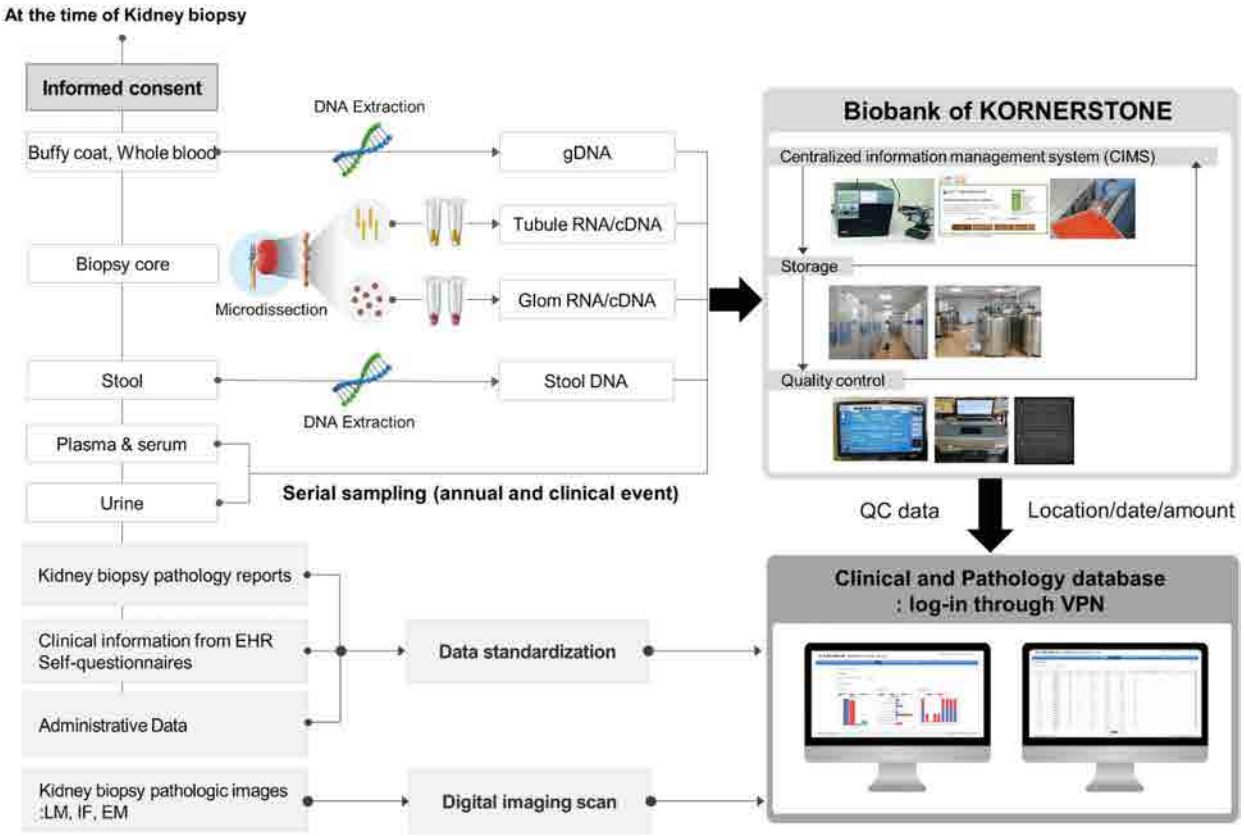


Figure:

P0503

PROGNOSTIC VALUE OF HISTOPATHOLOGICAL CLASSIFICATION OF ANCA-ASSOCIATED GLOMERULONEPHRITIS: A SINGLE-CENTER RETROSPECTIVE STUDY

Xanthi Benia[1], Vasiliki Papanikolaou[1], Stavros Pantelakos[2], Christina Vourlakou[2], Theofanis Apostolou[1], Christallenia Christodoulidou[1]

[1]Evaggelismos General Hospital, Department of Nephrology, Athens, Greece and [2]Evaggelismos General Hospital, Department of Pathology, Athens, Greece

Background and Aims: Kidney biopsy is the gold standard for establishing the diagnosis of ANCA-associated glomerulonephritis (GN). Previous studies have validated the prognostic significance of histopathological classification for the development of end stage renal disease (ESRD). We sought to evaluate the prognostic value of the EUVAS histopathological classification in terms of renal and overall survival (OS) in a single center retrospective cohort study.

Method: Forty-six consecutive patients (mean age 69, range; 29-84 years) with biopsy-proven ANCA-associated GN diagnosed at our hospital between January 2003 and January 2019 were included in the study. All biopsies had $\geq$10 glomeruli and were reviewed by two independent pathologists blinded to clinical data. Renal morphology was classified as sclerotic (if $\geq$50% globally sclerotic glomeruli), focal (if $\geq$50% normal glomeruli), crescentic (if $\geq$50% crescents with cellular component) and mixed. Probabilities of renal and overall survival were estimated using Kaplan-Meier method. Cumulative incidence function for ESRD was estimated using death as competing risk.

Results: Three biopsies were classified as focal (6%), twenty-nine as crescentic (63%), ten as mixed (22%) and four as sclerotic (9%). With a median follow-up of 39 months the 3-year probability of renal survival was 100% for the focal class, 66,37% for the crescentic class, 64% for the mixed class and 50% for the sclerotic class ($p>0.05$). Other parameters associated with increased probability of ESRD were interstitial fibrosis (IF) and eGFR at time of diagnosis. IF of $\geq$40% at diagnosis was associated with high incidence of ESRD, while IF of 20-40% and $<$20% had significantly lower incidence of ESRD (100% vs 34.2% vs 17.6%, $p=0.014$). Half (50%) of the patients with eGFR$<$15ml/min at diagnosis developed ESRD at 36 months compared to only 8% of the patients with eGFR$\geq$15ml/min ($p=0.024$) at diagnosis. Median overall survival for the entire cohort reached 128 months (95% CI; 35-221). Twelve patients died at median time of 19,5 months (range; 3-129) after diagnosis. Three patients died before developing ESRD and nine patients developed ESRD prior to death. Leading cause of death was sepsis (8/12). Other causes included sudden death (n=2), malignancy (n=1) and intestinal obstruction (n=1). In terms of histopathological classification, OS at 3 years was 100% (95% CI; N/A) for the focal class, 73.5% (95% CI; 57-94.8) for the crescentic class, 100% (95% CI; N/A) for the mixed class and 37,5% (95% CI; 83,9-100) for the sclerotic class ($p>0.05$).

Conclusion: Our results suggest that the focal class has the best and the sclerotic the worst outcome, while both crescentic and mixed subtype are of intermediate risk. Although our results did not reach statistical significance, due to primarily the small number of patients included, the incidence of ESRD and the probability of renal survival in each histopathological subtype in our cohort are comparable to those reported by larger studies. Thus, the EUVAS histological classification of ANCA-associated glomerulonephritis appears to be a useful predictor of renal outcome at the time of diagnosis. As previously reported, no significant prognostic difference was observed between the crescentic and mixed subtype. Thus, this classification system should be optimized by inclusion of other histological characteristics, such as the specific percentage of normal glomeruli, tubular atrophy and interstitial fibrosis. These characteristics may prove useful in highlighting significant differences between mixed and crescentic classes.

P0504

FACTORS ASSOCIATED WITH THE LONG-TERM RENAL OUTCOME OF IDIOPATHIC FOCAL SEGMENTAL GLOMERULOSCLEROSIS WITH NEPHROTIC SYNDROME

HIROAKI TANAKA[1], Takayuki Fujii[1], JUNYA KOSHIZAKA[1], NOBUAKI YAMAUCHI[1], MAYU MORIMOTO[1], NORIKO TERASAKI[1], SATOSHI SUZUKI[1]

[1]*Seirei Sakura citizen hospital, kidney center, Sakura city, Japan*

Background and Aims: In the treatment of idiopathic focal segmental glomerulosclerosis (FSGS) with nephrotic syndrome, the remission of proteinuria is considered to be an important goal. The partial remission of proteinuria improves renal survival, whereas it may progressively reduce the renal function. A study searched for a novel partial remission more accurately reflecting the long-term renal outcome. The goal of proteinuria reduction for improving the renal prognosis remains to be clarified.

We examined factors associated with the long-term renal outcome of idiopathic FSGS.

Method: Of 148 patients with FSGS diagnosed based on kidney biopsy between 1981 and 2018, a retrospective cohort study was conducted involving 33 who had undergone immunosuppressive therapy for nephrotic syndrome, and had been followed-up for $\geq$1 year, excluding those with secondary FSGS. We examined the renal prognosis, regarding a 50% decrease in the estimated glomerular filtration rate (eGFR) as an outcome. We calculated the rate of decrease in the urinary protein level 4 and 8 months after the start of treatment, and estimated the rate of decrease associated with renal hypofunction using ROC analysis. Based on the results of ROC analysis, Cox's proportional hazard analysis was performed using factors contributing to renal hypofunction as covariates.

Results: Concerning the background of the 33 patients, the mean follow-up period was 11.4 years, and there were 24 males. The mean age was 49.8 years, and the mean blood pressure was 100.5 mmHg. The mean urinary protein level, albumin (Alb) level, eGFR, and total cholesterol (TCho) level were 7.4 g/day, 2.1 g/dL, 44.3 mL/min/1.73 m^2, and 369 mg/dL, respectively. Corticosteroid therapy was selected in 21 patients, whereas it was combined with steroid pulse therapy in 12. The daily dose of prednisolone was 37.3 mg.

On ROC analysis, the rate of decrease in the urinary protein level after 4 months was 83.1% (AUC: 0.74, sensitivity: 0.80, specificity: 0.74), and that after 8 months was 85.7% (AUC: 0.78, sensitivity: 0.90, specificity: 0.65).

Cox's proportional hazard analysis, in which the data were adjusted with the sex, blood pressure, urinary protein level at the start of treatment, Alb level, eGFR, and treatment methods, showed that the rate of decrease in the urinary protein level after 4 months was significantly correlated with renal hypofunction: after 4 months: hazard ratio, 0.19 (95%CI: 0.04-0.77); p=0.0202; after 8 months: hazard ratio, 0.34 (95%CI: 0.05-1.37); p=0.1359.

Conclusion: In the treatment of idiopathic FSGS with nephrotic syndrome, the rate of decrease in the urinary protein level 4 months after the start of treatment was correlated with the long-term renal outcome.

P0505 COST ANALYSIS OF SCREENING FOR IGA NEPHROPATHY USING NOVEL BIOMARKERS

Mami Ishida[1], Keiichi Matsuzaki[2], Hiroshi Ikai[3], Hitoshi Suzuki[4], Yusuke Suzuki[4]

[1]Kyoto University, Graduate school of medicine, Kyoto, Japan, [2]Kyoto University, Health Service, Kyoto, Japan, [3]Kyoto Prefectural University of Medicine, Kyoto, Japan and [4]Juntendo University, Department of Nephrology, Faculty of Medicine, Tokyo, Japan

Background and Aims: IgA nephropathy (IgAN) is the most common primary chronic glomerulonephritis and a major cause of end-stage kidney disease worldwide. Recently, novel biomarkers including aberrantly glycosylated IgA1 and the glycan-specific antibodies can be measured and will predict the IgAN. However, little is known about the cost-effectiveness of this screening method from the societal perspective. This is the cost analysis of additional novel biomarkers to the conventional IgAN screening strategy.

Method: Cost analysis was carried out to compare the two diagnostic strategies with or without biomarkers. We developed an analytical decision model to estimate the lifetime medical expense of each strategy. The decision tree was started at forty years old with first time hematuria, and simulated the clinical strategy after the screening using the novel biomarkers (Group N: N), and conventional strategy (Group C: C). The result of the analysis is presented as the lifetime medical expenses from societal perspective. Discount was not considered.

Results: Lifetime medical expenses per person during forty years were calculated as 31.6 million JPY (≈287,270 USD) for using the novel biomarkers, 33.9 million JPY (≈307,903 USD) for conventional strategy. They were lower by 2.3 million JPY (≈20,633 USD) in Group N. Moreover, by using the novel biomarkers, the expected value of IgAN led to increase by 5.67 percent points (N: 48.44%, C: 42.77%), and the expected value of the dialysis led to decrease by 0.85 percent points (N: 19.91%, C: 19.06%). One-way sensitive analysis showed that the prevalence of IgAN was the most influential variable. In the sensitivity analysis, the rate of tonsillectomy with steroid pulse therapy and achieved clinical remission was higher, the expected lifetime expenses were reduced by 3.3 million JPY (≈30,355 USD) and the expected value of the dialysis led to decrease by 1.76 percent points (N: 11.80%, C: 13.56%).

Conclusion: Screening for IgAN using novel biomarkers is expected to reduce the lifetime medical expenses.

P0506

PATTERNS AND OUTCOMES OF GLOMERULAR DISEASES IN ADULTS PRESENTING TO MANSOURA UNIVERSITY HOSPITAL: A SINGLE-CENTER PROSPECTIVE STUDY

Hoda M. M. Abd-Elaziz[1], Mohammed Kamal Nassar[1], Dina Abdallah Ibrahim[2], Nagy Sayed-Ahmed[1]

[1]Faculty of Medicine, Mansoura University, Mansoura Nephrology and Dialysis Unit (MNDU), Egypt and [2]Faculty of Medicine, Mansoura University, Pathology, Egypt

Background and Aims: Glomerular diseases (GDs) impose a substantial burden on patients and health care systems, and they are considered a major cause of end-stage renal disease (ESRD) worldwide. Morbidity and mortality have shown to be substantially higher in patients with GDs than in the general population. In Egypt, there is yet no available national registry for GDs, and GDs outcome is not adequately studied. Therefore, it is of considerable interest to study patterns and outcomes of GDs in our locality.

Method: Patients with features suggesting GDs presenting to Mansoura nephrology and dialysis unit (MNDU) were recruited in this study between 1 July 2017 and 30 June 2018, and those with biopsy-proven GDs were prospectively followed up for a minimum of 6 months or until either death or reaching ESRD. ESRD was defined as initiation of long-term dialysis or eGFR persistently <15 ml/min per 1.73 m^2 during follow up visits. Enrolled patients were subjected to through history taking and clinical examination. Biopsies were independently examined by two pathologists blinded to the clinical data. The study outcomes were to identify the GDs subtype frequencies, and to identify the frequency of those achieving either renal recovery, progression to ESRD or death from all-cause mortality. Logistic regression analysis was carried out to identify the potential predictors for renal recovery.

Results: Sixty-six patients (21 males and 45 females) with biopsy-proven GDs were included and completed the required period of follow up. The median age of the studied patients was 32 years (IQR 23 - 46.45). Fifty percent of the cases had hypertension and only one patient had was diabetic. The main indications for renal biopsy were unexplained kidney function decline (62%) followed by subnephrotic (23%) and nephrotic presentation (15%). Diffuse proliferative GN followed by MPGN and sclerosing GN were the most frequently encountered histopathological patterns. Primary and secondary GDs constituted 30.3% and 69.7% respectively. Lupus nephritis (LN) was the most common cause of secondary GDs and class IV LN was the most frequently encountered class accounting for 16 cases (51.6%) of patients with lupus. By the end of 6-month follow up, renal recovery was achieved in 30 patients (45.5%), 21 patients (31.8%) progressed to ESRD and 7 patients (10.6%) had died. Urban residency and total renal chronicity score were the most significant predictors of renal recovery.

Conclusion: Diffuse proliferative GN is the most common histopathological pattern, and secondary GDs, particularly those related to lupus, are more frequently encountered than primary GDs in our center. Unfortunately, quick complete recovery is not the rule and is possibly predictable by less chronic changes in biopsy.

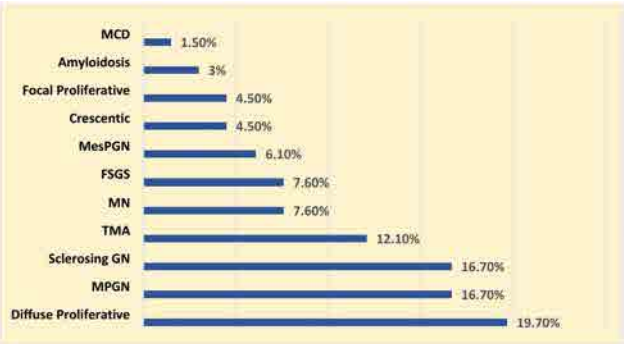


Figure 1. Frequency of different histopathological patterns.

P0507 ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE. ABOUT 32 CASES

Mohamed Iotfi Amiri[1], Raja Trabelsi[1], Mondher Ounissi[1], Soumaya Chargui[1], Mouna Jerbi[2], Hanene Gaied[2], Hafedh Hedri[1], Imen Gorsane[1], Taieb Ben abdallah[1], Rim Goucha[2]

[1]charles Nicolle hospital, Nephrology, tunis, Tunisia and [2]Mongi slim Hospital, Nephrology, tunis, Tunisia

Background and Aims: Anti-Glomerular basement membrane disease « anti-GBM » is a rare autoimmune disease. It most often results in a rapidly progressive glomerulonephritis syndrome associated with intra-alveolar hemorrhage. The diagnostic confirmation is histological, by the demonstration of linear deposits of immunoglobulins (IgG) along the glomerular basement membrane. The aim of our study was to describe its epidemiological, clinical, biological, immunological, histological, and evolutionary characteristics and to identify the different prognostic factors for predicting patient survival and renal survival.

Method: It was a retrospective, descriptive and analytical study including patients over 16 years old with anti-GBM disease proved by kidney biopsy and followed up over a period of 32 years (January 1985 to July 2017), in Internal Medicine Department of Charles Nicolle Hospital of Tunis.

Results: We collected 32 patients with a sex ratio H/F = 1.13. The mean age at diagnosis was 42 years old with extremes of 18 to 81 years old. The most frequent extra-renal manifestations were pulmonary (53%), neurological (12.5%) and ocular (6%) manifestations. Hematuria associated with proteinuria was constantly found.

The latter was nephritic in 31% of patients. All patients had renal insufficiency on admission, oligo-anuric in 60% of cases. The use of extra-renal treatment at admission was necessary in 75% of patients. On the immunological level, the search for anti-MBG antibodies, performed in 20 patients, was positive in 65% of cases. All our patients had undergone a renal biopsy puncture with direct immunofluorescence study.

Diffuse extra-capillary glomerulonephritis was observed in 93% of patients.

Corticotherapy was initiated in 27 cases, associated with plasma exchange in 21 cases and cyclophosphamide in 17 cases. Nine of our patients died in the first year. Renal outcome was marked by partial remission in 2 cases and end-stage renal failure in 19 cases. In univariate analysis, an age greater than 60 years and the occurrence of respiratory distress were predictors of death.

Oligo-anuria and need dialysis on admission were predictive factors for progression to end-stage renal failure.

Conclusion: Anti-GBM disease is a serious illness. Current therapeutic modalities have significantly improved patient survival. These must be intensive and rapid in order to hope for a favorable renal evolution whose prognosis remains reserved.

P0508 NEPHROTIC SYNDROME DUE TO HEAVY AND LIGHT CHAIN (AHL) AMYLOIDOSIS

Csilla Markóth[1], László Bidiga[2], Piroska Pettendi[3], Éva Rékasi[4], László Ujhelyi[1], Jozsef Balla[1], János Mátyus[1]

[1]University of Debrecen, Institute of Internal Medicine, Nephrology Department, Debrecen, Hungary, [2]University of Debrecen, Institute of Pathology, Debrecen, Hungary, [3]Jász-Nagykun-Szolnok County Hospital, Internal Medicine Department, Szolnok, Hungary and [4]Jász-Nagykun Szolnok County Hospital, Nephrology Department, Szolnok, Hungary

Background and Aims: Kidney diseases with heavy chain deposition are rare, including AHL amyloidosis also. The mutation/deletion of the constant domain (C_H1/C_H2) of the heavy chain causing high tissue affinity seems most likely in its pathogenesis. The very low serum level is responsible for the difficult diagnosis, which is often based on kidney biopsy or laser microdissection / mass spectrometry.

Method: Case study of a 76-year-old male patient, examined in January, 2019.

Results: Besides treatment for Ménière syndrome and benign prostatic hyperplasia there was no other important event in patient's history. Significant proteinuria and microscopic haematuria were observed from May 2016, but eGFR was 70 ml/min/1,73 m2 at that time. By April, 2018 nephrotic range proteinuria (10 g/day) with full nephrotic syndrome developed. Screening tests for cancer were negative. Despite symptomatic treatment, half year later eGFR decreased to 27 ml/min/1,73 m2, therefore he was referred to nephrology. Serum protein electrophoresis verified IgG lambda (8,1 g/l) and free lambda (0,5 g/l) monoclonal light chains, and in addition the possibility of IgG heavy chain accumulation. Urine electrophoresis showed also IgG lambda (1720,1 mg/l), and free lambda light chain (552,1 mg/l) monoclonality. Serum free lambda and kappa light chain ratio was 0,06, complement serology was normal. Kidney biopsy was done, which showed IgG heavy and light chain restriction, Congo red stain positivity and apple green birefringence under the polarized microscope in the expanded mesangium, in the interstitium and along the tubular basement membrane and the blood vessels. The electron microscope detected fibrillary deposits (10 nm) in the same structures, therefore diagnosis of AHL amyloidosis was established. He had no extrarenal symptoms. Bone marrow aspiration flow cytometry verified 1,11% plasma cell accumulation, 93% of them had pathological immunphenotype. Bone marrow morphology assay showed 30-40% plasma cell infiltration, and chromosome assay detected monoallelic deletion of IgH and MAF and gains of 1q region, suggesting myeloma multiplex in the background of AHL amyloidosis. VCD (bortezomib-cyclophosphamide-dexamethason) treatment was started, so far he has received 8 cycles. He is asymptomatic, proteinuria decreased, kidney function stabilized, eGFR 23 ml/min/1,73 m2.

Conclusion: only about 20 cases of AHL amyloidosis have been reported in the literature so far. In the context of longstanding kidney failure with nephrotic syndrome, we should consider renal disease associated with plasma cell dyscrasia also. If case of an AHL amyloidosis caused by myeloma multiplex, effective anti-plasma cell therapy can improve the hematological and the renal outcome.

P0509 CLINICAL ANALYSIS FOR PROGNOSTIC FACTORS BASED ON RESULTS OF VERY SHORT-TERM TREATMENT IN MEMBRANOUS NRPHROPATHY

Takatsugu Iwashita[1], Kaori Takayanagi[1], Maiko Yamasaki[1], Mai Aoyagi[1], Taisuke Shimizu[1], Hajime Hasegawa[1]

[1]*Saitama Med Center, Saitama Med Univ, Department of Nephrol and Hypertens, Blood Purification Center, Kawagoe, Japan*

Background and Aims:

Membranous nephropathy (MN) is known to affect frequently in elderly patients.

Since the duration of MN treatment is likely to be prolonged, it is desirable that the treatment duration would be shortened by the concomitant use of immunosuppressant and prednisolone (PSL). Therefore, we evaluated prognostic factors using the results of treatment in a very short period of time in patients with membrane nephropathy at our hospital.

Method:

Biopsy-proven 66 cases with MN, hospitalized between April 2009 and December 2017, were enrolled in this study.

All cases were divided between two groups, high responder and low responder, based on the 50% proteinuria-reduction ratio at a month after the beginning of therapy including sole administration of PSL and concomitant use of immunosuppressants such as Cyclosporin or Mizoribine.

High responder and low responder were comparatively studied.

All biopsy specimens were stained by anti-phospholipase A2 receptor (PLA2R) and thrombospondin type 1 domain containing 7A (THSD7A) antibodies by standard protocol.

Results:

Estimated glomerular filtration rate (eGFR) was 70.5 vs 60.4 ml/min ($p = 0.087$), showing no difference.

Baseline urine protein-to-Cr ratio (PCR) and degree of hematuria in high responder were significantly higher than those in low responder; baseline PCR: (6.95 vs 3.86, $p = 0.003$), degree of hematuria: (1 vs 0, $p = 0.036$)

There was no difference in intensity of immunofluorescent staining of IgG, A, M, C3 between high responder and low responder. We also studied the difference in immunofluorescent intensity of PLA2R, THSD7A and IgG subclass. Intensity of IgG3 and ratio of PLA2R/IgG4 intensity in low responder were significantly higher than those in high responder; IgG3 intensity: (0 vs 0.5, $p = 0.049$), PLA2R/IgG4 ratio: (0.58 vs 1.00, $p = 0.029$)

Conclusion:

Obtained results showed that higher baseline PCR and degree of hematuria might be related to the rapid therapeutical response.

On the other hand, higher staining intensity of IgG3 and PLA2R/IgG4 intensity ratio might reduce the response of treatment.

P0510 INFLAMMATORY BOWEL DISEASE IN KIDNEY TRANSPLANTATION:CASE REPORT

Abir Gana[1,2]

[1]SAHLOUL HOSPITAL, nephrology, sousse, Tunisia and [2]SAHLOUL HOSPITAL, nephrology departemznt, Sousse, Tunisia

Introduction: Kidney transplantation has become the treatment of choice for chronic end-stage renal disease because it improves not only the quality of life of patients but also their survival rate. However, several complications can be observed in transplant patients such as immune rejection, infections and recurrence of initial nephropathy etc.

Case summary:A 21-year-old man diagnosed with chronic end-stage renal failure 5 years ago with a renal biopsy showing an aspect of proliferative glomerulonephritis.

The study of the alternate complementary path show a C3 low level, C4 and CH50 normal level, H factor and I factor was normal too. The patient presented purpuric skin lesions with a biopsy of granular deposits of C3. We started extra renal purification by peritoneal dialysis and the patient had, one year later, a kidney transplant from his mother. Ten month later, we have notice a progressive renal function decline with an aspect of proliferative membranous glomerulonephritis with deposits predominant of c3 in graft biopsy. The diagnosis of the recurrence of the initial nephropathy was made but the treatment was delayed by the onset of cutaneous leishmaniosis. Few months later the patient was presented with diarrhea lasting more than a month, which led us to do a colonoscopy, which objectified an aspect of chronic inflammatory bowel disease evoking earlier a Crohn's disease.

Therefore, we stopped tacrolimus and put the patient on full dose corticosteroid therapy and azathioprine without having a remission, and appearance of skin lesions at the elbow and pelvis evoking pyoderma gangrenosum in skin biopsy. In addition, the patient has presented an ischemic retinal damage probably related to a deregulation of the alternate complement pathway.

Discussion: The complement system is not only a host defense system against microbes, but also a surveillance system that contributes to maintain tissue homeostasis and tissue repair. However, uncontrolled complement activation can induce tissue damage, and inappropriate activation is involved in the pathogenesis of various conditions like autoimmune diseases, sepsis and transplant and extensive inflammation and tissue damage. The impairment of alternative path can explain the extra-renal manifestation of this patient especially the appearance of inflammatory bowel disease witch can be explained by impaired local immune defense in the gut.

Conclusion: Immune system abnormalities can occur after kidney transplantation this leads to the appearance of several inflammatory abnormalities such as chronic inflammatory bowel disease which may in our case be due to an abnormality of the alternate pathway of the complement.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii821–iii878, 2020

AKI. EXPERIMENTAL

P0518

VNN1 MEDIATES RENAL MALADAPTIVE REPAIR AFTER AKI BY INDUCING PREMATURE SENESCENCE OF RENAL TUBUAR CELLS

Yani He[1], Kehong Chen[1], Jia Chen[1]

[1]*Nephrology, Daping Hospital, Army Medical University, Chongqing, P.R. China*

Background and Aims: Renal maladaptive repair after acute kidney injury (AKI) can easily progress to chronic kidney disease. Sustained renal interstitial damage caused by accelerated senescence of renal tubular cells leads to renal fibrosis. Vanin-1 (VNN1) is an extracellular enzyme with panthenylmethylamine activity that indirectly reduces the synthesis of glutathione, causing oxidative stress. The purpose of this study was to investigate the expression and of VNN1 in renal tissue and to study its role in senescence of renal tubular cells after ischemia reperfusion (I/R).

Method: hirty male wild BALB/c mice were randomly divided into control group, sham group and I/R group. In the I/R group, the bilateral renal pedicle was ligatured for 35 min followed by reperfusion. The expression of VNN1 and aging markers (P16, P21, SA-b-gal) were detected. Furthermore, wild type mice and VNN1 knockout mice were used to compare the degree of renal tissue and functional damage and the senescence of renal tubular cells after I/R injury.

Results: Compared with sham group, Scr, BUN and renal injury score increased significantly in I/R group at the early stage (3d) of renal injury. Renal fibrosis was observed in the later stage (28-42d). The expression of VNN1 in renal tubular cells of I/R group increased after I/R injury. VNN1 was coexpressed with P16, suggesting that VNN1 might be related to cellular stress senescence. The SCr, BUN of VNN1 KO mice was significantly lower than that of wild type mice at 7-28 d after renal reperfusion. The renal interstitial injury score of VNN1 KO mice was significantly lower than that of wild type mice, and the renal interstitial fibrosis level was significantly higher than that of wild type mice at 42d after reperfusion. The results suggest that VNN1 KO promotes renal repair of AKI. The ratio of P16 positive tubule cells in VNN1 KO mice was significantly higher than that in wild-type mice at 7d after renal reperfusion, suggesting that VNN1 could promote the senescence of renal tubule cells during AKI repair.

Conclusion: VNN1 mediates renal maladaptive repair after AKI by inducing premature senescence of renal tubular cells.

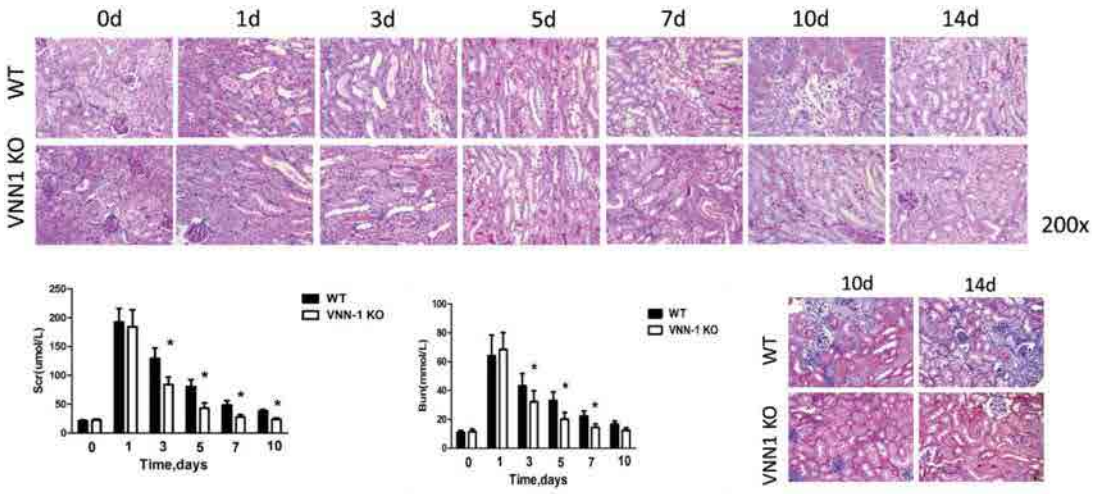


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P0519 **HEXARELIN PROTECTS ISCHEMIA REPERFUSION INDUCED ACUTE KIDNEY INJURY BY TARGETING 14-3-3Σ**

Chen Guan[1], Yan Xu[1]

[1]*The Affiliated Hospital of Qingdao University, Department of Nephrology, Qingdao, P.R. China*

Background and Aims: Acute kidney injury (AKI), manifested as a sudden decline in renal function on the order of days or a week, is one of the most common complications and is strongly associated with renal prognosis, medical expenses and length of stay of hospitalized patients. However, incidence of AKI can be reduced by early intervention. Hexarelin is a synthetic analogue of ghrelin with a potent GH releasing activity, which is also found to exhibited a significant protectant activity against postischemic ventricular dysfunction in isolated perfused hearts subjected to low flow ischemia and reperfusion. This study aims to explore the effects of hexarelin on ischemia reperfusion induced acute kidney injury (I/R-AKI) and the underlying mechanism of it.

Method: Thirty healthy male SPF SD aged at 8 weeks weighing 250-300g rats were divided into 5 groups including normal group, sham operation group, acute kidney injury (AKI) group, acute kidney injury group after hexarelin (HEX + AKI), and acute kidney injury group after saline (Saline + AKI). Bilateral kidney artery clamping was applied for 50 min to induce AKI. The drug-administered group and the saline-controlled group rats were treated with intraperitoneal injections 7 days before modelling and the Hex + AKI group and the saline + AKI group were given Hexarelin (dose 100 μg/kg. d) and equal volume of saline, respectively. To explore the underlying mechanism of HEX on I/R-AKI, gene expression profiling of AKI samples were searched from Pubmed, GEO dataset. Differential expression genes were used to predict canonical signal transduction pathways and signalling networks. Molecular docking was used to predict the combination of hub proteins and HEX.

Results: 1) Renal function in HEX-pretreated rats was significantly improved compared with control group: HE results showed that renal tubules were less dilated and rebuilt after pretreatment, and the infiltration area was significantly reduced; serum creatinine ($P = 0.0005 < 0.05$), urea nitrogen ($P < 0.0001$) concentration were significantly reduced; RT-qPCR showed that relative expression of Kim-1 ($P < 0.0001$), caspase3 ($P = 0.007$), Bax ($P < 0.0001$), Bad ($P = 0.0168 < 0.05$) in HEX+AKI group were significantly decreased while the relative expression of Bcl-2 ($P < 0.05$) was significantly increased compared with saline treated rats;

2) Microarray data analysis showed that 63 differential expression genes including SFN, Cyr61, Kim-1 were hub genes in the development of I/R-AKI;

3) Three-dimensional structure of the hub proteins HEX were obtained from the SWISS-MODEL database and the PubChem compound database, and Autodock software was used to calculate the molecular docking between proteins and HEX. Results showed that HEX and the protein that encoded by the gene SFN (SFN, 14-3-3σ) binding stably with a binding energy of -8.51;

Conclusion: Hexarelin protects ischemia reperfusion induced acute kidney injury by targeting 14-3-3σ.

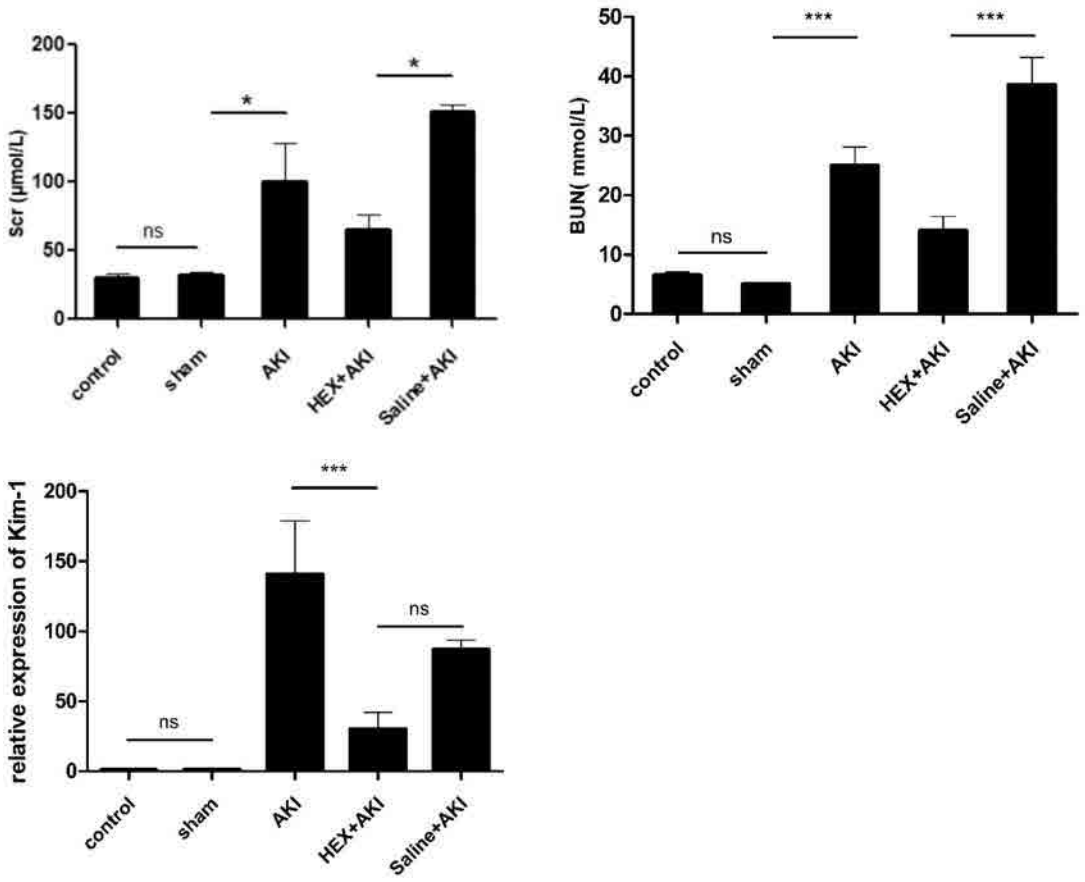


Fig.1 Hex pretreatment can significantly improve kidney function

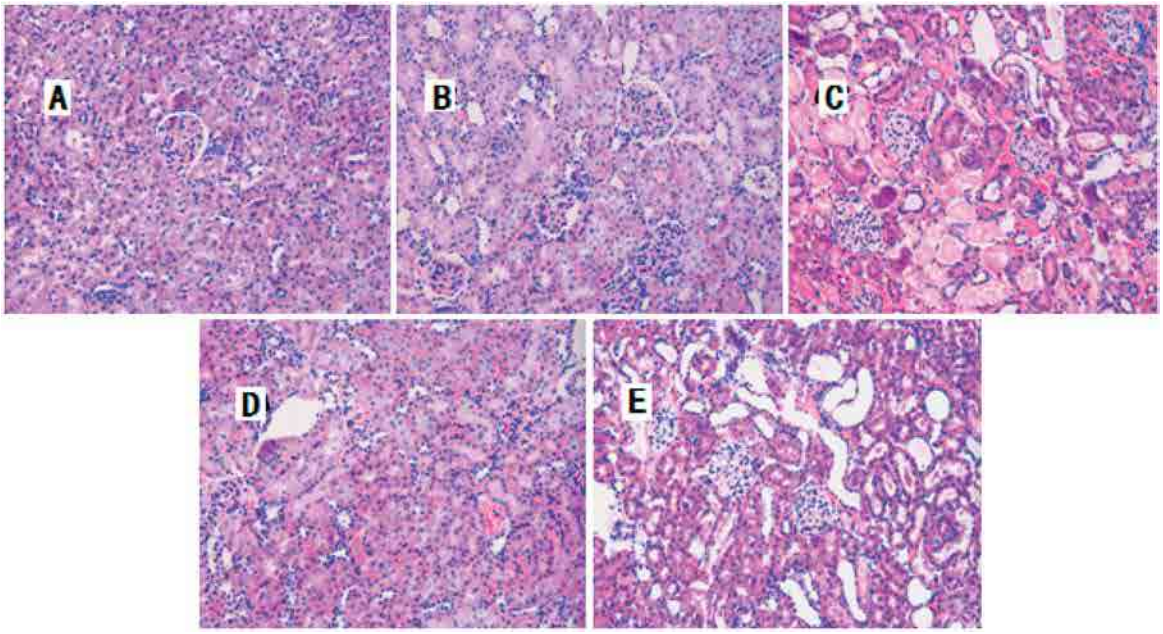


Fig.2 HEX can bind to 14-3-3σ protein

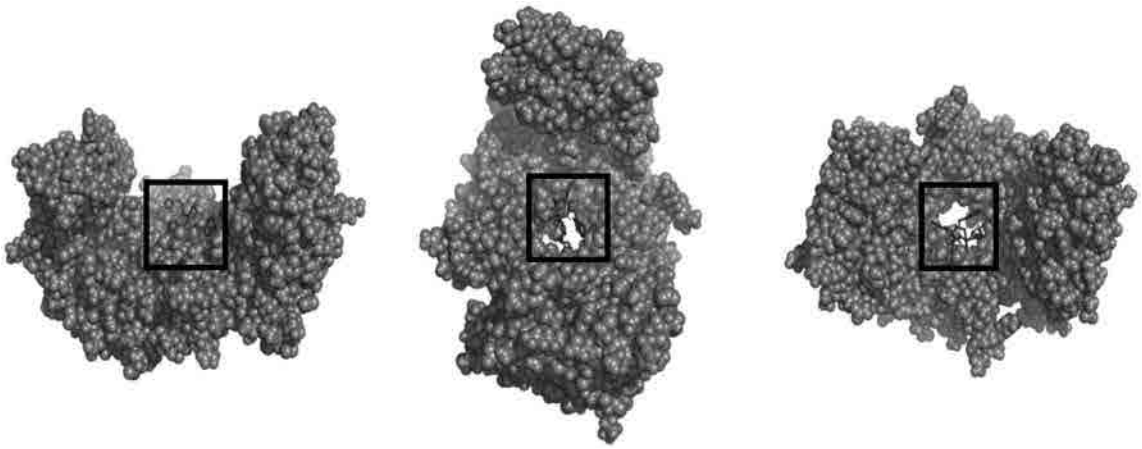


Fig.3 HEX pretreatment can reduce the relative expression of SFN and mitigate apoptosis

P0520 **EFFECT OF HUMAN UMBILICAL CORD MESENCHYMAL STEM CELLS ON SECONDARY ACUTE KIDNEY INJURY IN RATS WITH LIVER CIRRHOSIS**

Yan Mi[1]

[1]*Nephrology, The First Affiliated Hospital of Baotou Medical College, Baotou, P.R. China*

Background and Aims: Acute kidney injury(AKI) is one of the most common complications of decompensated cirrhosis, and it primarily presents as a sharp decrease in glomerular filtration rate, rapid increase in serum creatinine(SCr) and urea nitrogen. And the search for specific and safe treatment has been a research hot spot in recent years. In this article, the effect of human umbilical cord mesenchymal stem cells on carbon tetrachloride (CCl4)-induced liver fibrosis (HF) in rats with acute kidney injury and the possible mechanism are investigated.

Method: Human umbilical cord blood mesenchymal stem cells were sub-cultured by adherent method, and the cells were identified by morphological observation, cell phenotypic analysis and multi-directional differentiation potential analysis methods. WASTA rats were randomly divided into control group, cirrhosis model group and treatment group, with 10 rats in each group. Model group and treatment group were injected with CCl4-olive oil (1:1) solution 3 mL·kg $^{-1}$, and the control group was given the same amount of olive oil for intervention, twice a week for 8 weeks. Rats in treatment group were administrated wth Human umbilical cord mesenchymal stem cells (2×10^9 /L) via the tail vein at the 5th week after injection of CCl4-olive oil solution, but the other rats were injected with 0.9% normal saline, once a week for 6 weeks. After the intervention, Serum, kidneys and 24 hours urine of rats in each group were collected, which were applied for a detection of serum creatinine and urea nitrogen, malondialdehyde (MDA), NO content and superoxide dismutase (SOD), as well as renal pathological examination.

Results: 1.In vitro, umbilical cord blood mesenchymal stem cells was passaged to the third generation, and the morphology was uniform and spiraled. Phenotypic analysis showed that the positive rates of stem cell markers CD29, CD44 and CD105 were all greater than 95%, the positive rate of HLA-DR (graft-versus-host disease-associated factor) less than 10%, and the positive rate of CD34 and CD45 lower than 20% (Figure 1).

2. Compared with the cirrhotic model group, MDA content of serum and kidney in model group significantly decreased under the effect of mesenchymal stem cell ($p < 0.01$) (Table 1).

3. The normal group had normal liver tissue structure, ordered liver cells, no hepatic edema, and no lesions. In the model group, large-area lesions, including edema of liver cells, rupture of cell membranes, and infiltration of inflammatory cells, had appeared. Compared with the model group, Hepatocellular necrosis, edema, and inflammatory cell infiltration were significantly improved after transplanting Human umbilical cord mesenchymal stem cells (Figure 2).

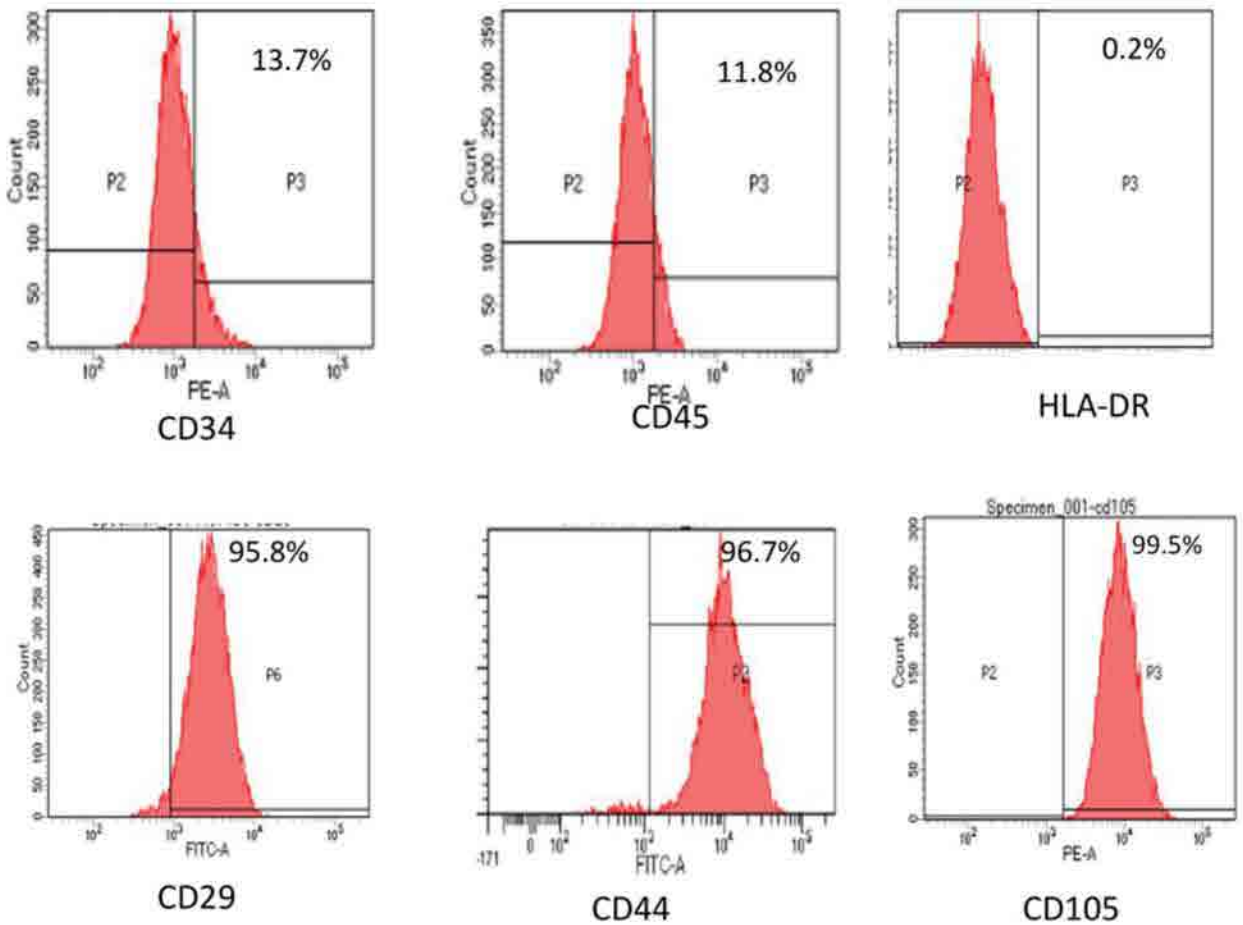


Figure 1. HUMSCs identification by appearance and immune-phenotype.

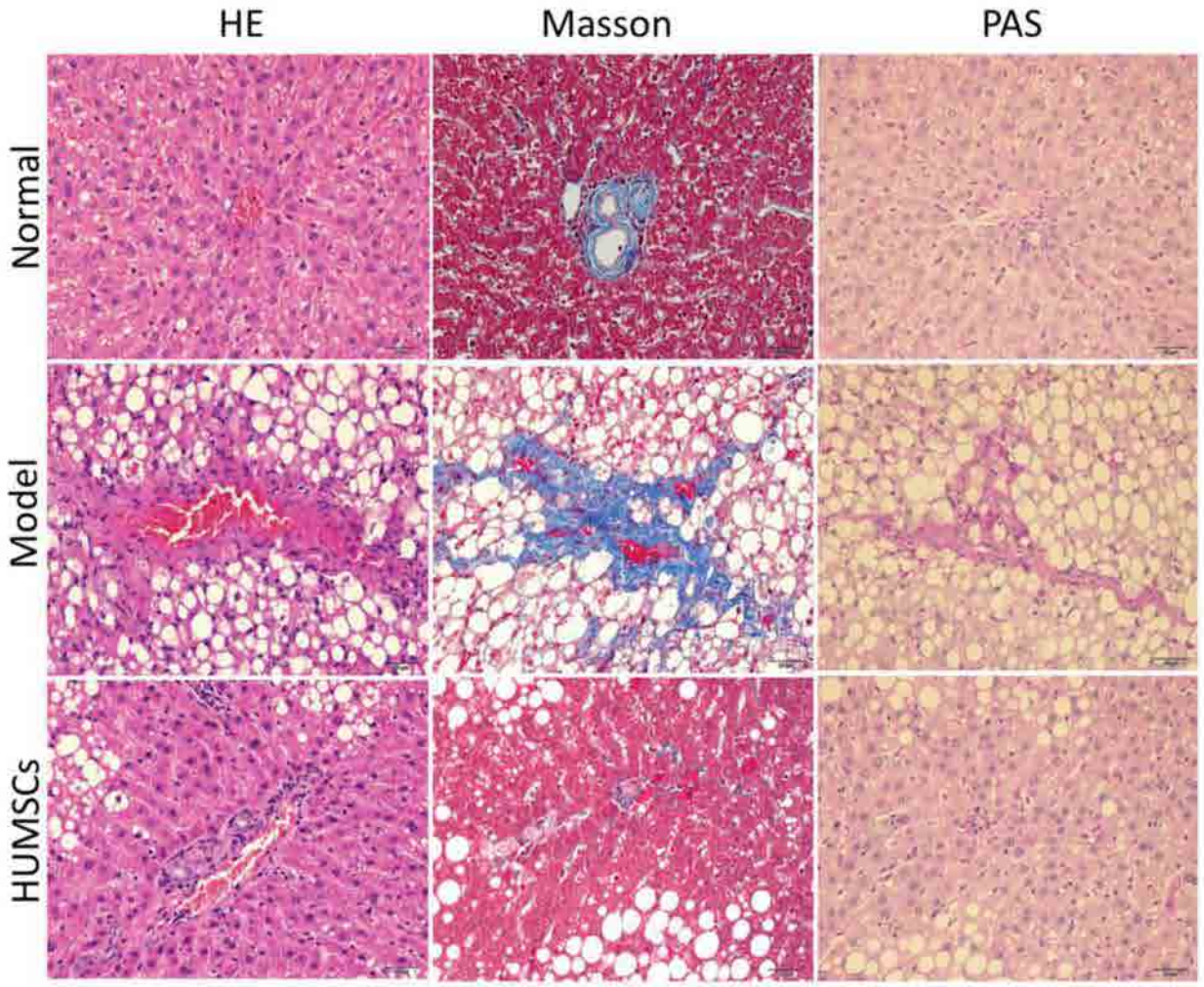


Figure 2 Liver pathology using periodic acid-Schiff (PAS) and Masson staining.

4.In the model group, the rat renal tubules disappeared and the lumen was disordered. After injection of Human umbilical cord mesenchymal stem cells, renal tubular and renal interstitial damage is improved and the thickening of glomerular basement membrane is reduced (Figure 3).

Table 1 Effect of human umbilical cord mesenchymal stem cells on SOD activity and MDA and content in rat serum and kidney (x ± s)

group	Serum		Kidney	
	MDA (nmol/ml)	SOD (U/ml)	MDA (nmol/ml)	SOD (U/ml)
Normal	5.77±1.20	145.72±18.97	13.89±5.23	105.20±48.25
Model	9.07±2.20	165.42±21.42	23.17±5.74	123.52±22.09
HUMSCs	7.02±1.91*	155.21±19.66	15.77±6.02*	115.33±12.79

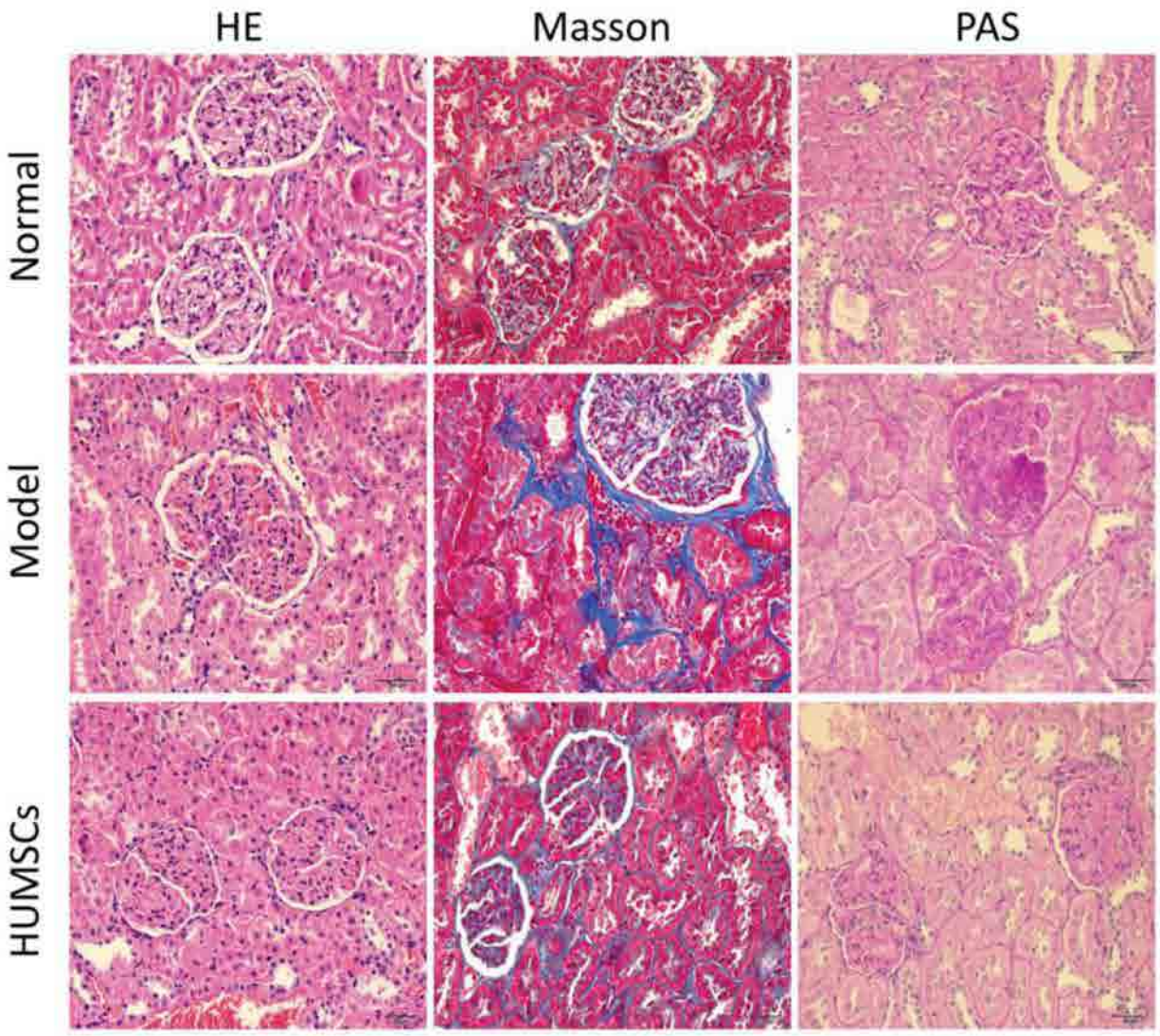


Figure 3 Kidney pathology using periodic acid-Schiff (PAS) and Masson staining.

Conclusion: In CCl4-induced liver cirrhosis model rats, human umbilical cord mesenchymal stem cells can protect the kidney by reducing free radicals and cellular lipid peroxidation in vivo.

P0521

TICAGRELOR PROTECTS KIDNEY FROM SEPSIS INDUCED ACUTE KIDNEY INJURY THROUGH ADENOSINE DEPENDENT WAY

Yuhan Cao[1], Qiancheng Xu[2], Yuwei Wang[1], Cong Fu[3]

[1]Yi Ji Shan hospital, nephrology, Wuhu, P.R. China, [2]Yi Ji Shan hospital, Intensive care unit, Wuhu, P.R. China and [3]Yi Ji Shan hospital, Cardiology, Wuhu, P.R. China

Background and Aims: Sepsis induced acute kidney injury (AKI) is common in intensive care unit in multiple organ failure patients. Ticagrelor is an anti-platelet drug that widely applied in coronary artery disease. In addition, ticagrelor can increase the level of adenosine. Recent study had indicated that ticagrelor can protect renal function in sepsis induced AKI. However, the detailed mechanism was still unknown. Accordingly, we designed this trial to investigate if the ticagrelor alleviated sepsis induced AKI and demonstrated the potential mechanism that how ticagrelor works.

Method: C57BL6J mouse received oral ticagrelor (20mg/kg and 50mg/kg) for 7 days and caecum ligation and puncture (CLP) were performed. Adenosine-receptor antagonist was administered (10mg/kg, intraperitoneal injection) to block the adenosine pathway 2h before CLP. After 24h, serum creatinine was measured. PAS staining was used and TUNEL staining was applied to determine the pathological changes and cell apoptosis. Plasma concentrations of TNF-α and IL-1β were detected. Kidney tissue level of TNF-α and IL-1β were determined via qRT-PCR. Western blot was used to determine the expression of signal molecular in kidney.

Results: In ticagrelor group, PAS staining (fig. 1) showed that less swelling of renal tubules and TUNEL staining (fig. 2) showed the less cell apoptosis compared to CLP. Serum creatinine was significantly lower in ticagrelor group. Plasma TNF-α and IL-1β and kidney expression of TNF-α and IL-1β were significantly lower in ticagrelor group. Adenosine-receptor antagonist significantly blocked the effect of ticagrelor (fig. 3 ang 4). Western blot showed that ticagrelor activate the phosphorylation of AKT and mTOR in kidney. Adenosine-receptor antagonist inhibited the activation of AKT and mTOR (fig. 5).

Conclusion: The protective effect of ticagrelor was dependent on adenosine-receptor activation with downstream upregulation of phosphorylation of AKT and mTOR in sepsis induced AKI.

Figure 1

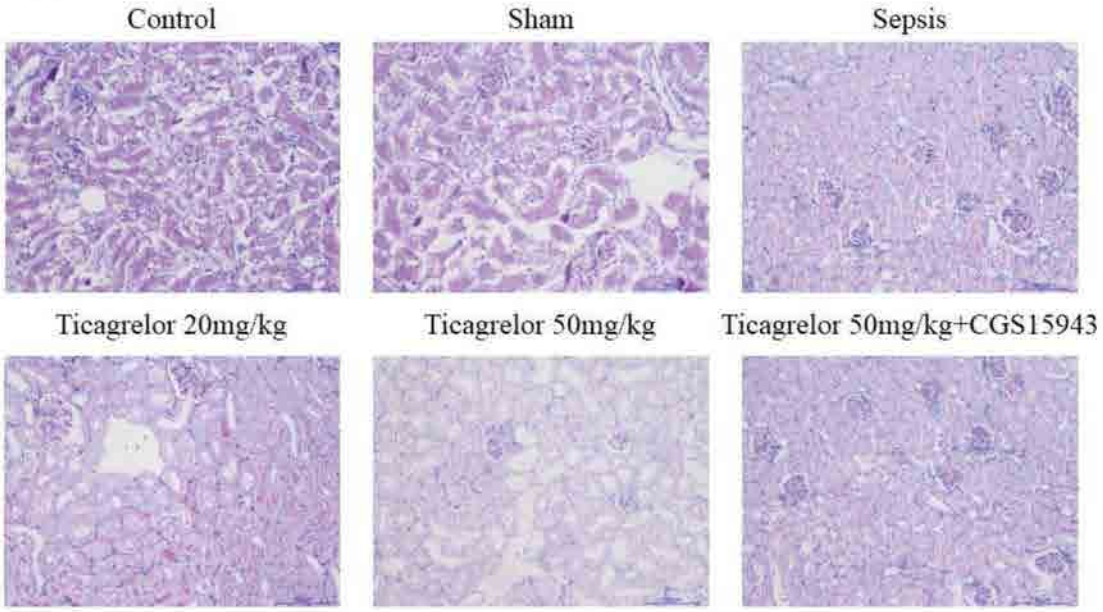


Figure 2

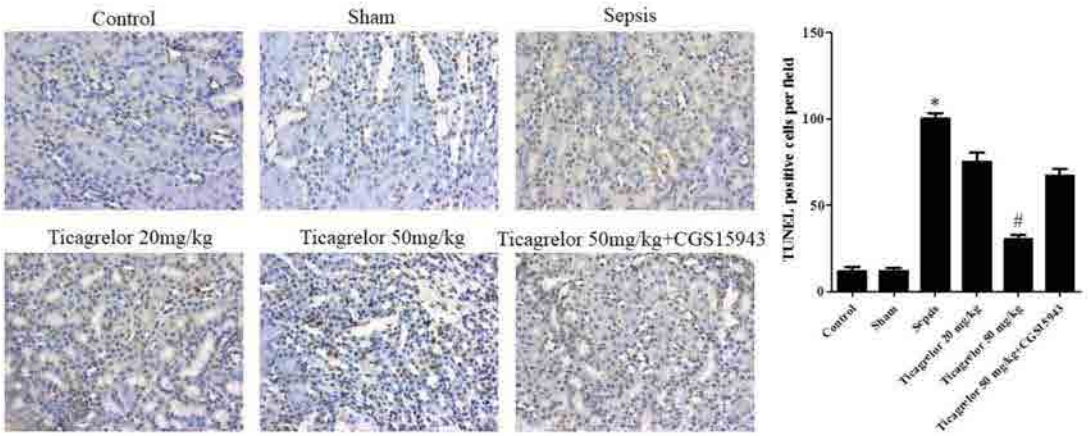


Figure 2

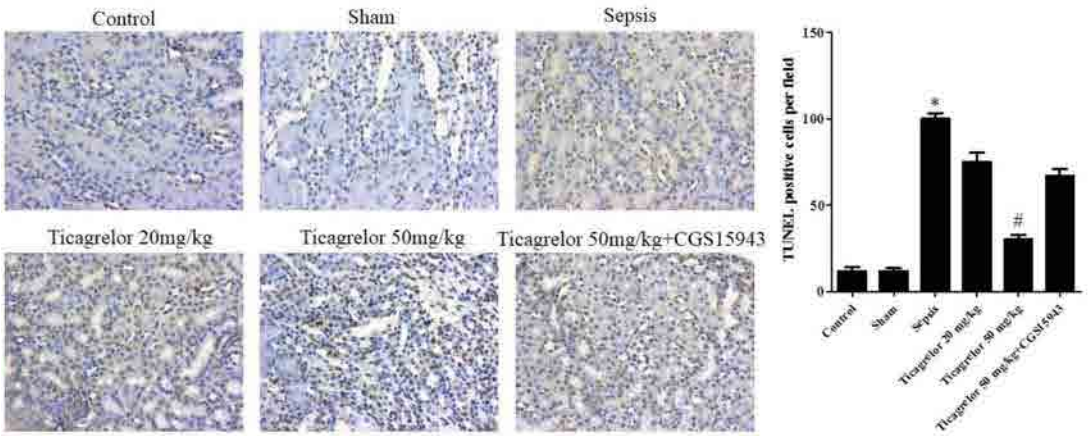


Figure:

P0522

INHIBITING 15-PGDH PREVENTS ISCHEMIC RENAL INJURY BY A PGE2/EP4 SIGNALING PATHWAY MEDIATING VASODILATION, INCREASED RENAL BLOOD FLOW, AND INCREASED ADENOSINE/A2A RECEPTOR.

Byeong Woo Klm[1], Sun hee Kim[2], Ki beom Bae[2]

[1]Haeundae Bumin Hospital, Nephrology, Busan, Korea, Rep. of South and [2]Paik Hospital, General surgery, Busan, Korea, Rep. of South

Background and Aims: We demonstrate the marked activity of SW033291, an inhibitor of 15-hydoxyprostaglandin dehydrogenase (15-PGDH), in preventing acute kidney injury (AKI) in a murine model of ischemia reperfusion injury (IRI). AKI due to ischemic injury represents a significant clinical problem. Prostaglandin E2 (PGE2) is vasodilator in the kidney, but is rapidly degraded in vivo due to catabolism by 15-PGDH. We investigated the potential of SW033291, a potent and specific 15-PGDH inhibitor, as prophylactic treatment for ischemic AKI.

Method: 10-week aged male C57/BL6 mice were randomly allocated to five groups (n=8 to 15 in each group): the sham-control group, sham-SW033291 group, IRI-vehicle group, IRI-indomethacin group and the IRI-SW033291 group. IRI were induced by clamping bilateral renal artery for 30 min followed by 24 hours of reperfusion. Vehicle, indomethacin, or SW033291 were intraperitoneally administered three times at 1 hour before, immediately after, and 12 hours after IRI. Renal function, histological changes, and renal blood flow were compared and the relevant parameters of oxidative stress and inflammation were detected.

Results: Prophylactic administration of SW033291 significantly increased renal tissue PGE2 levels and increased post-AKI renal blood flow and renal arteriole area. In parallel, prophylactic SW033291 decreased post-AKI histologic injury score and tubular apoptosis and markedly reduced biomarkers of renal injury that included BUN, creatinine, NGAL and KIM-1. Prophylactic SW033291 also reduced post-AKI induction of proinflammatory cytokines, high mobility group box 1 (HMGB1), and malondialdehyde (MDA). Protective effects of SW033291 were mediated by PGE2 signaling as they could be blocked by pharmacologic inhibition of PGE2 synthesis or of the EP4 type PGE2 receptor. Consistent with activation of PGE2 signaling, SW033291 induced renal levels of both EP4 and of cyclic adenosine monophosphate (cAMP), along with other vasodilatory effectors including AMP, adenosine, and the adenosine A_{2A} receptor (A_{2A}). Protective effects of SW0333291 could largely be achieved with a single prophylactic dose of the drug.

Conclusion: Inhibiting 15-PGDH may thus represent a novel strategy for prophylaxis of ischemic AKI in multiple clinical settings, including renal transplantation and cardiovascular surgery.

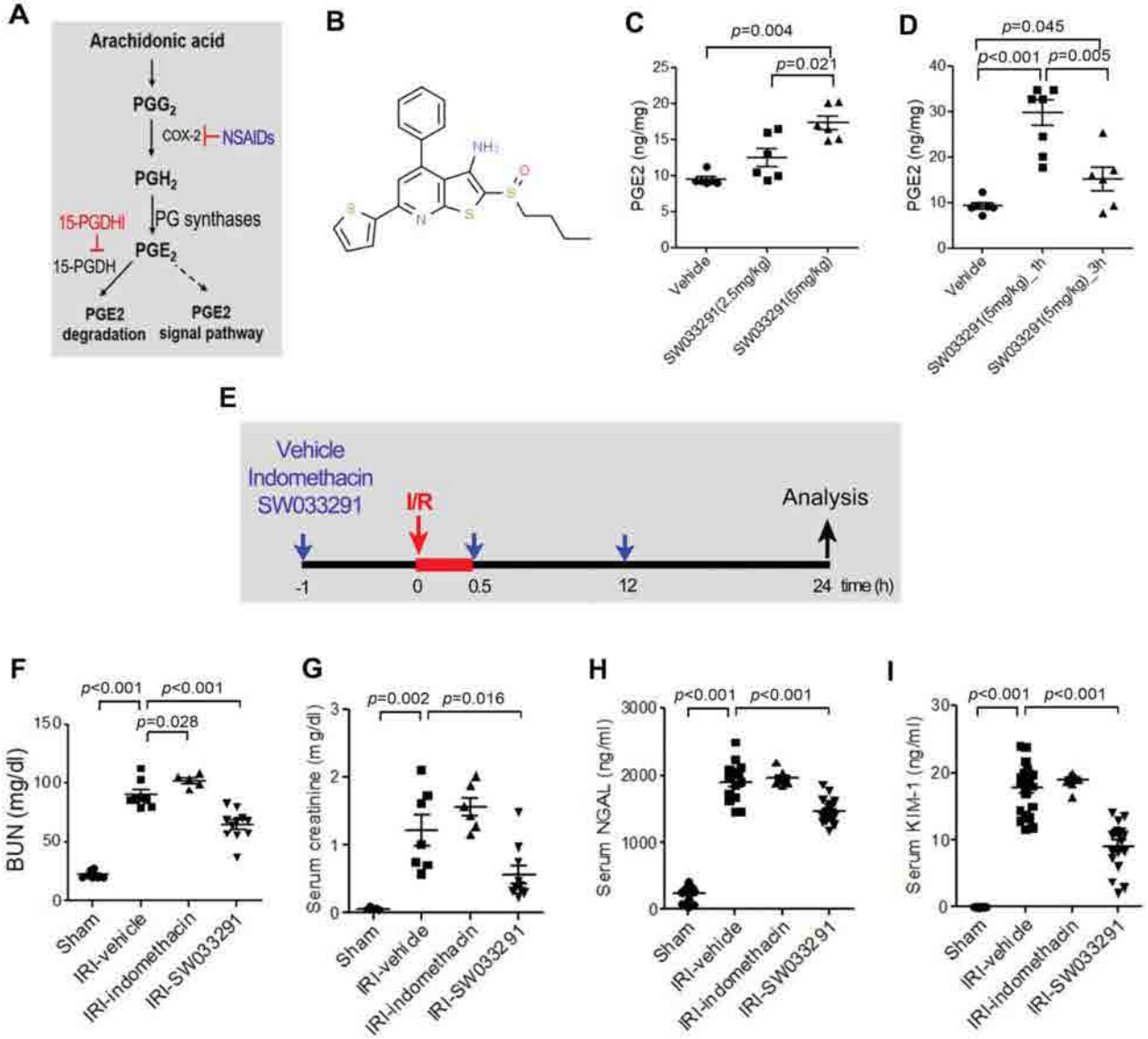


Fig. 1. 15-PGDH inhibition on renal IRI decreases the levels of renal injury biomarkers.

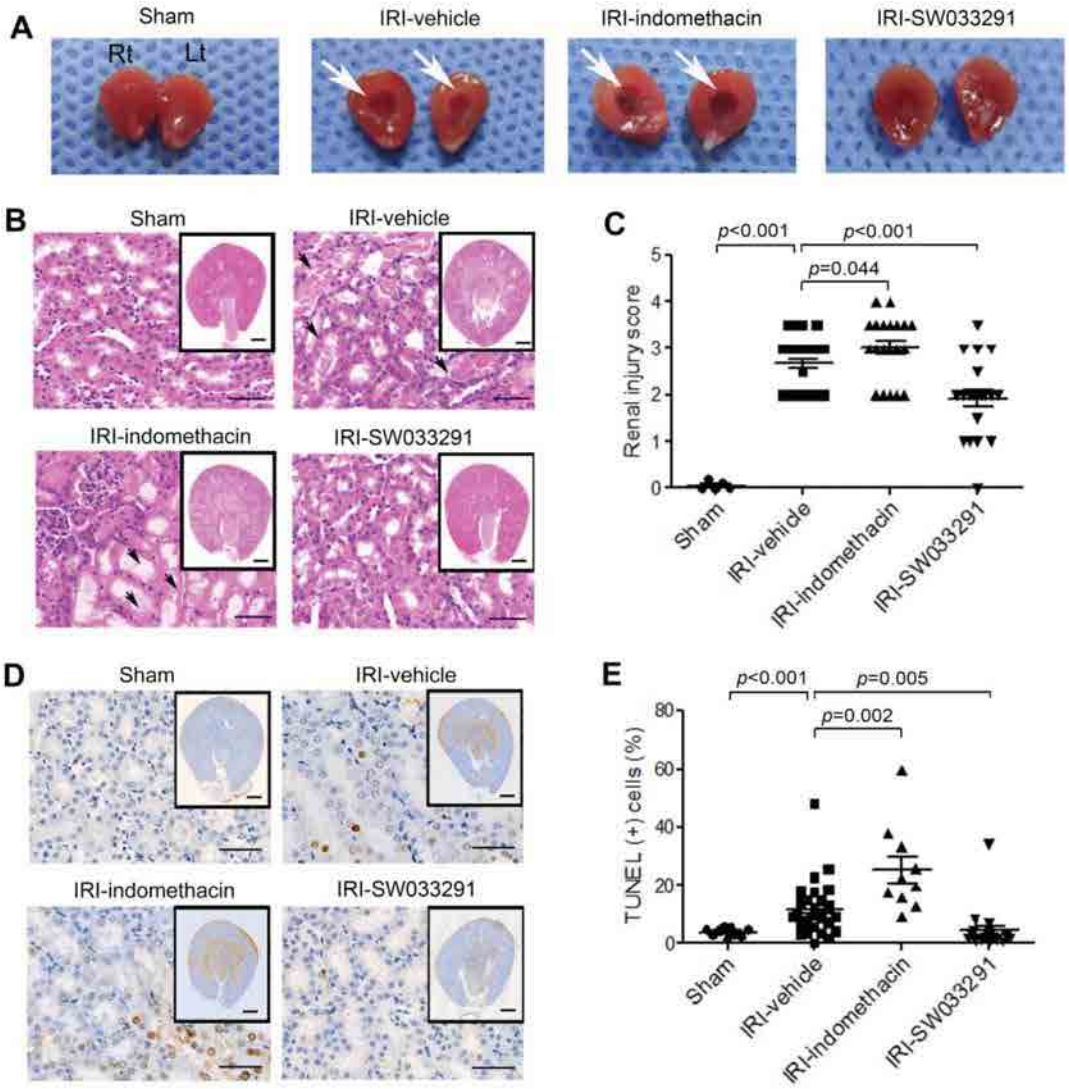


Fig. 2. 15-PGDH inhibition ameliorates renal tubular cell death in mice with ischemic AKI.

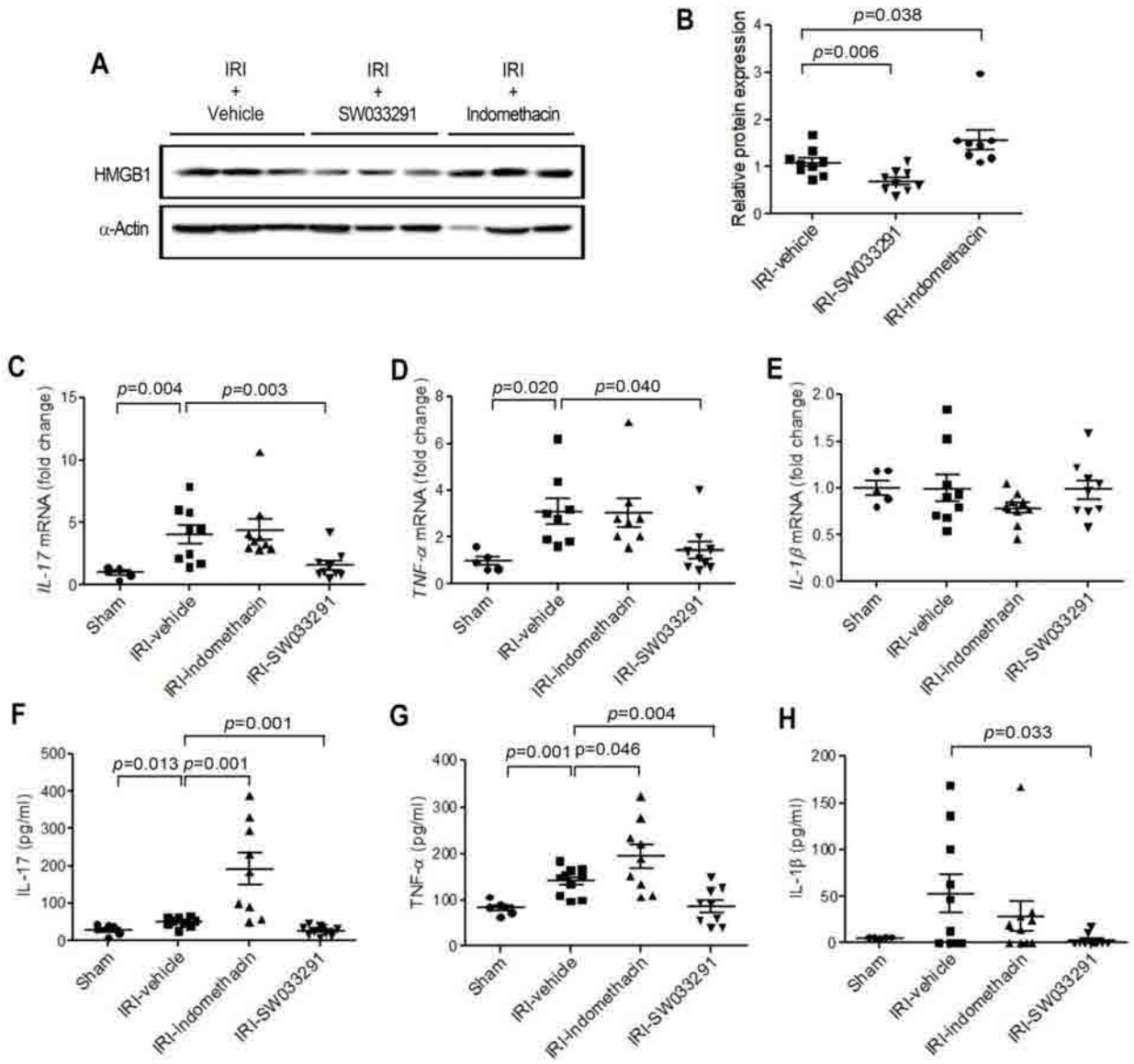


Fig. 3. 15-PGDH inhibitor pretreatment ameliorates the inflammatory response in mice with ischemic AKI.

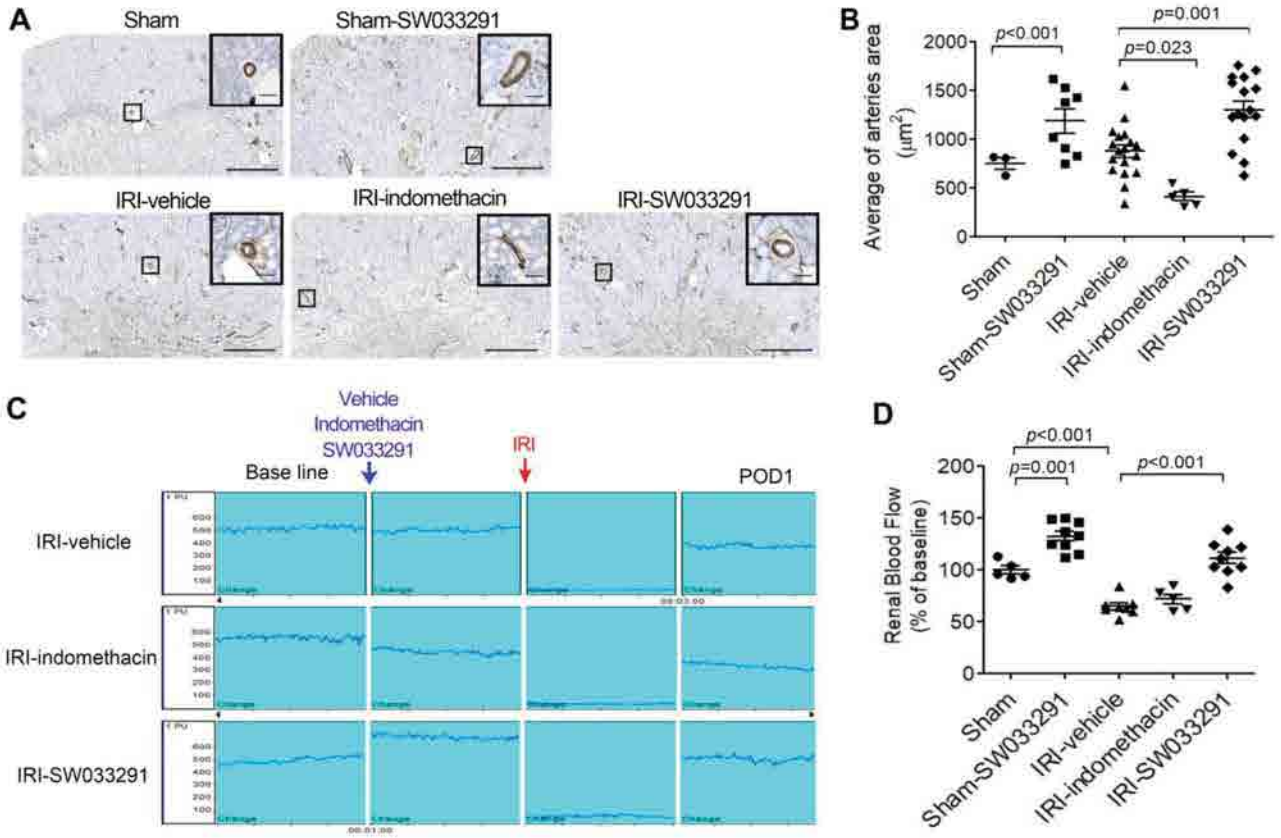


Fig. 4. 15-PGDH inhibition induces renal vasodilation in the outer medulla of mice with ischemic AKI.

P0523

PROTECTIVE ROLE OF REGULATORY B CELLS ON THE RENAL TISSUE REPAIRMEN AFTER ISCHEMIA REPERCUSSION INJURY

Yokota Yunosuke[1], Goh Kodama[1], Sakuya Itou[1], Yosuke Nakayama[1], Nobukazu Komatsu[2], Atsushi Mizoguchi[2], Kei Fukami[1]

[1]Kurume University School of Medicine, Division of Nephrology, Department of Medicine, Kurume, Fukuoka, Japan and [2]Kurume University School of Medicine, Department of immunology, Kurume, Fukuoka, Japan

Background and Aims: Acute kidney injury (AKI), even if followed by renal recovery, is a risk factor for the future development of chronic kidney disease (CKD) and end-stage renal disease. It has been postulated that interleukin-10 (IL-10)-producing Regulatory B cells (Breg) play an important role for the tissue repairment in several tissues and organs. Basically, protective role of Breg has been reported in inflammatory bowel disease. In the kidney, it has been shown that IL-10 suppresses renal function decline and improves renal prognosis in IRI model, a typical model of AKI. However, the identity of Breg in the kidney and their origin have not been clarified. Further, how the Breg works during the transition from AKI to CKD is not known. Therefore, first we investigated whether Breg existed in renal tissue on the progression from AKI to CKD in IRI model mice. Further, we performed splenectomy, and examined the renal injury, Breg, and plasma IL-10 levels in this model.

Method: To examine the existence of Breg in the kidney of IRI model, we used 8-10 weeks-old GFP / IL-10 mice based on C57BL / 6J mice. They are reporter mice for IL-10 producing cells, and can visualize IL-10 producing cells under a fluorescence microscope without fluorescent immunostaining. We prepared following three groups, sham, IRI (unilateral), and IRI + SN (splenectomy) groups. Mice were anesthetized with chloral hydrate (4 g/kg,, intraperitoneal). After making a midline incision, exposed a blood vessel of the left renal pedicles and clamped it for 30 min by clips. one day, 7 days, and 14 days after the surgery, mice were sacrificed, and renal function and plasma IL-10 levels as well as tissue damages by PAS and Masson's Trichrome staining were assessed. Tissue IL-10-producing cells were detected by flow cytometry.

Results: There was no difference of plasma IL-10 levels and renal tubulointerstitial injury in IRI group and IRI+SN group on day 1 after IRI. However, on day 7 and day 14, plasma IL-10 levels became gradually higher in IRI group, and SN decreased the increase in IL-10 levels. Tubulointerstitial injury was induced by IRI and SN further worsened tubular damages. Serum Cr and BUN levels were not different in three groups due to normal right kidney. On day 1, number of IL-10-producing B cells increased in the spleen and renal medulla in IRI group confirmed by flow cytometry, which was completely diminished by SN, suggesting that origin of the infiltrated Breg might be spleen, thereby being involved in the protective role in IRI injury in the kidney.

Conclusion: We report for the first time that Breg might be recruited from spleen by AKI, which may be one of the mechanisms to prevent the progression to CKD.

P0524 **PERICYTE IS ESSENTIAL FOR RENAL TUBULAR CELL REGENERATION AFTER ACUTE KIDNEY INJURY**

Yu-Hsiang Chou[1], YU-HAN SHAO[2], SHUEI-LIONG LIN[3]

[1]National Taiwan University Hospital, Jin-Shan Branch, Department of Internal Medicine, Taipei City, Taiwan, R.O.C., [2]College of Medicine, National Taiwan University, Graduate Institute of Physiology, Taipei City, Taiwan, R.O.C. and [3]National Taiwan University Hospital, Department of Internal Medicine, Taipei City, Taiwan, R.O.C.

Background and Aims: Pericyte-myofibroblast transition is activated after acute kidney injury (AKI) and is the major mechanism of ensuing chronic kidney disease (CKD). Nevertheless, the role of pericyte in renal regeneration after AKI has not been deeply investigated. Many studies have shown that pericyte can secret growth factors such as fibroblast growth factor 1 and 7 (FGF-1, FGF-7) and is essential for structure support and vascular integrity in normal kidney. We supposed that the ablation or inhibition of pericytes during AKI would retard renal repair.

Method: Our study demonstrated that activated pericytes/myofibroblast was beneficial for renal regeneration after AKI. We here performed pericyte ablation and pericyte inhibition after ischemia-reperfusion renal injury by using transgenic mice such as Gli1-Cre^{ERT2};iDTR mice and blockade of platelet-derived growth factor receptor β (PDGFRβ), respectively.

Results: Renal injury was more severe and renal recovery was worse in groups of pericyte ablation or inhibition compared to control groups. Ki67 positive tubular cells which indicated renal regeneration were much more in control groups than that in groups of pericyte ablation or inhibition. We also found higher macrophage number as well as higher inflammatory factor including tumor necrosis factor-α and interleukin-1β which indicated more severe inflammation in groups of pericyte ablation or inhibition.

Conclusion: These studies suggest that pericytes play a beneficial role during renal recovery after AKI. These findings delineate the adequate timing when we target on pericyte/myofibroblast to ameliorate renal fibrosis and avoid to impede renal regeneration at the same time. Further research is still needed to clarify the change of specific gene and signalling pathway after pericyte ablation or inhibition. These are promising findings that provide opportunities to develop new targets to promote AKI recovery and to ameliorate renal fibrosis.

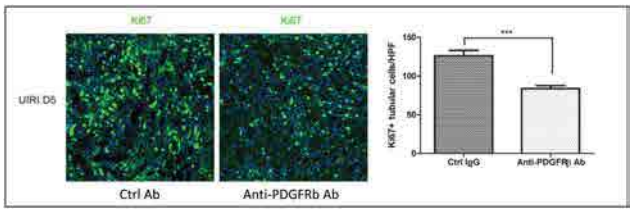


Figure:

P0525 ROLE OF NADPH OXIDASE 4 IN ACUTE KIDNEY INJURY ASSOCIATED TO MASSIVE INTRAVASCULAR HEMOLYSIS

Cristina García Caballero[1], Melania Guerrero Hue[2], Alejandra Palomino Antolín[3,4], Matilde Cabanillas[2], Cristina Vazquez Carballo[5], Carmen Herencia[6], Lucas Opazo-Ríos[6], Javier Egea[4,7], Pablo Cannata-Ortiz[8], Manuel Praga[9], Alberto Ortiz[6], Jesus Egido[6,10], Juan Antonio Moreno[2,11,12]

[1] Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Department of Cell Biology, Physiology, and Immunology, Córdoba, Spain, [2]Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Department of Cell Biology, Physiology, and Immunology, Córdoba, Spain, [3]Instituto de Investigación Sanitaria (IIS), Madrid, Spain, [4]Instituto Teófilo Hernando, Departament of Pharmacology and Therapeutics, Medicine Faculty, Autónoma University, Madrid, Spain, [5] Fundación Instituto de Investigaciones Sanitarias, Fundación Jiménez Díaz, Autónoma University, Renal, Vascular, and Diabetes Research Laboratory, Madrid, Spain, [6]Fundación Instituto de Investigaciones Sanitarias-Fundación Jiménez Díaz, Autonoma University, Renal, Vascular and Diabetes Research Lab, Madrid, Spain, [7]Instituto de Investigación Sanitaria (IIS), Hospital Universitario de la Princesa, Madrid, Spain, [8]Fundación Instituto de Investigaciones Sanitarias-Fundación Jiménez Díaz, Autónoma University, Pathology Department, Madrid, Spain, [9]12 de Octubre Hospital, Department of Nephrology, Madrid, Spain, [10]Centre of Biomedical Research in network of Diabetes and Metabolic disease associated (CIBERDEM), Madrid, Spain, [11]Hospital Universitario Reina Sofia, Córdoba, Spain and [12]Centre of Biomedical Research in network of Cardiovascular disease (CIBERCV)

Background and Aims: Massive intravascular hemolysis is a common condition of several pathologies. It is associated with acute kidney injury (AKI) and progressive impairment of renal function. In this context, free hemoglobin (Hb) can exert harmful effects by accumulating in the kidney, where induces oxidative stress and it becomes cytotoxic. NADPH oxidase 4 (Nox4) is the principal source of reactive oxygen species (ROS) in the kidney. Nox4 is mostly expressed in proximal tubular cells with lower levels in glomerulus. The role of Nox4 in renal damage is not clear, with studies reporting beneficial or deleterious actions depending of the environmental conditions. For that reason we aimed to investigate the role of Nox4 in massive intravascular hemolysis-associated AKI.

Method: To study the role of Nox4 in AKI caused by massive intravascular hemolysis, we performed an experimental model of intravascular hemolysis by intraperitoneal injection of phenylhydrazine (200 mg/kg) in wild type (Nox4+/+) and Nox4 knockout mice (Nox4-/-). Mice were sacrificed 24 and 72 hours after intravascular hemolysis induction. We collected serum, urine and tissues sample. We analyzed renal function, oxidative stress, cell death and inflammation in these samples. In other experiments, wild type mice were treated with GKT137831 (10mg/kg/day), a potent Nox4 and Nox1 inhibitor, and mice were sacrificed 72h after induction of hemolysis. We also performed *in vitro* experiments in murine tubular epithelial cells (MCT) and murine podocytes cells to investigate the regulation of Nox4 in Hb-stimulated cells treated or not with GKT137831.

Results: Induction of intravascular hemolysis in Nox4+/+ mice increased creatinine and BUN levels and enhanced the expression of tubular injury markers, such as NGAL. These pathological effects were reduced in Nox4 knockout mice. Then, we analyzed oxidative stress in our experimental model thought determination of HO-1, ferritin, GSH and lipid peroxidation levels. All of these oxidative markers were reduced in Nox4-/- mice with intravascular hemolysis as compared with Nox4+/+ mice. We also observed that inflammatory markers such as IL-6, cell death and podocytes injury markers were reduced in Nox4-/- mice than in wild type mice, specially 72 hours after phenylhydrazine injection. In line with these results, GKT137831 administration ameliorated intravascular hemolysis-associated renal function impairment. Moreover, oxidative stress, tubular injury markers and podocyte injury were reduced in hemolytic mice treated with GKT137831. GKT137831 also reduced Hb- and heme-mediated oxidative stress in MCT and podocytes.

Conclusion: Our results show the important role of Nox4 in renal injury associated to massive intravascular hemolysis. Moreover, the inhibition of Nox4 may be a potential therapeutic target to prevent renal damage associated to Hb accumulation. These findings provide new insights into novel aspects of Hb-toxicity and may have important pathogenic and therapeutic implications for intravascular hemolysis related diseases

P0526

MIR-181D-5P TARGETS KLF6 TO IMPROVE ISCHEMIC/ REPERFUSION AKI THROUGH EFFECTS ON RENAL FUNCTION,APOPTOSIS AND INFLAMMATION

Yan Xu[1,2], Yue Zhang[1]

[1], The Affiliated Hospital of Qingdao University, QingDao, P.R. China and [2]The Affiliated Hospital of Qingdao University, nephrology, P.R. China

Background and Aims: Inflammation and renal tubular cell death is the most crucial pathophysiological changes in acute kidney ischemic/reperfusion injury(IRI). The miR-181d family plays diverse roles in cell proliferation, apoptosis and inflammation, but its renal target and potential role in IRI are unknown.

Method: We built hypoxia/reoxygenation (H/R) renal cell model (HK-2 cells) and renal ischemia/reperfusion (I/R) injury mice model. We used observe the expression location of miR-181d-5p and KLF6 by in situ hybridization and immunohistochemistry, the blood creatinine and urea nitrogen levels through fully automatic biochemical detector, the severity of kidney injury by HE staining, the apoptosis and necrosis of renal tubular epithelial cells by TUNEL and Annexin V-FITC/PI flow cytometry, the concentrations of pro-inflammatory factors in the cell supernatant by ELISA and the mRNA and protein levels of related factors and predicted and verified the relationship between miR-181d-5p and KLF6 via bioinformatics systems and luciferase reporter genes.

Results: We showed that the expression of miR-181d-5p decreased in HK-2 cells of H/R and renal mouse model of I/R injury. Mechanistically, KLF6 was predicted as a new potential target gene of miR-181d-5p through bioinformatics and the Luciferase reporter verification. After renal ischemia/ reperfusion, overexpression of microRNA-181d significantly attenuated the level of KLF6 and inhibited inflammatory mediators such as IL-6, TNF-α, reducing apoptosis and further improving renal function. Critical NF-κB signaling pathways mediated this inflammatory response.

Conclusion: In conclusion, upregulation of microRNA-181d inhibits KLF6 expression, which have protective anti-apoptosis and anti-inflammatory effects against I/R kidney in vivo, and H/R HK-2 cells in vitro, thereby providing novel insights into the molecular mechanisms associated with ischemia/reperfusion injury and a potential novel therapeutic target.

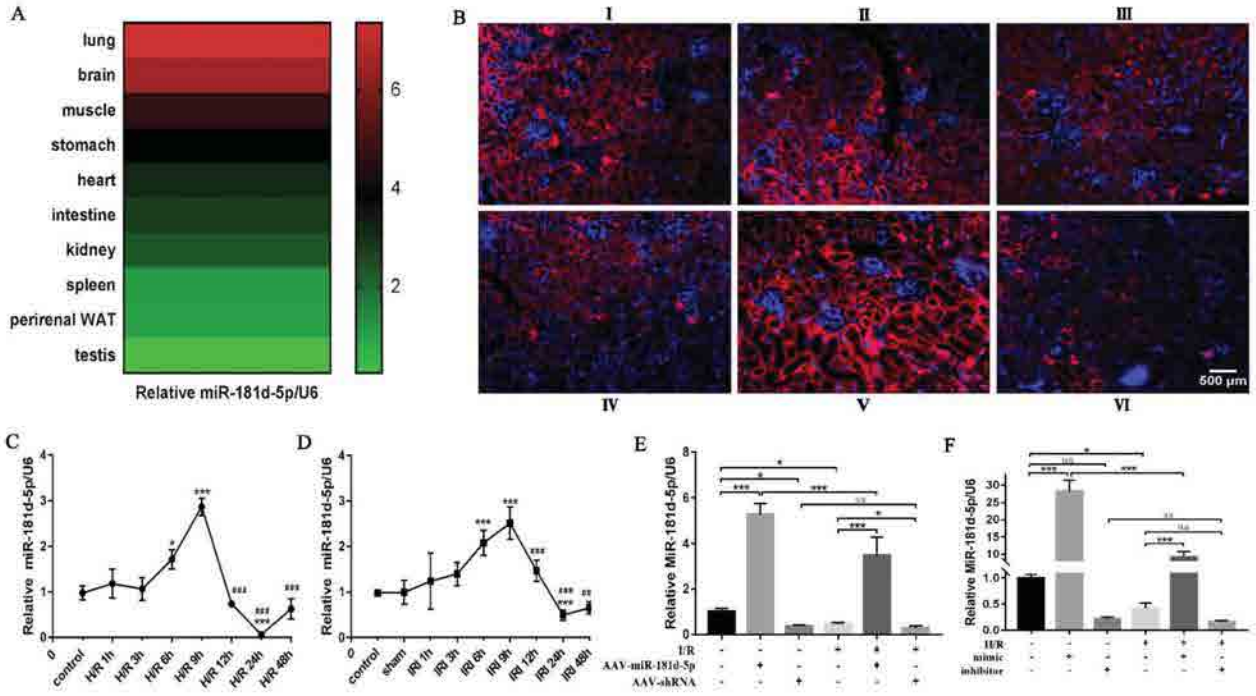


Figure 1

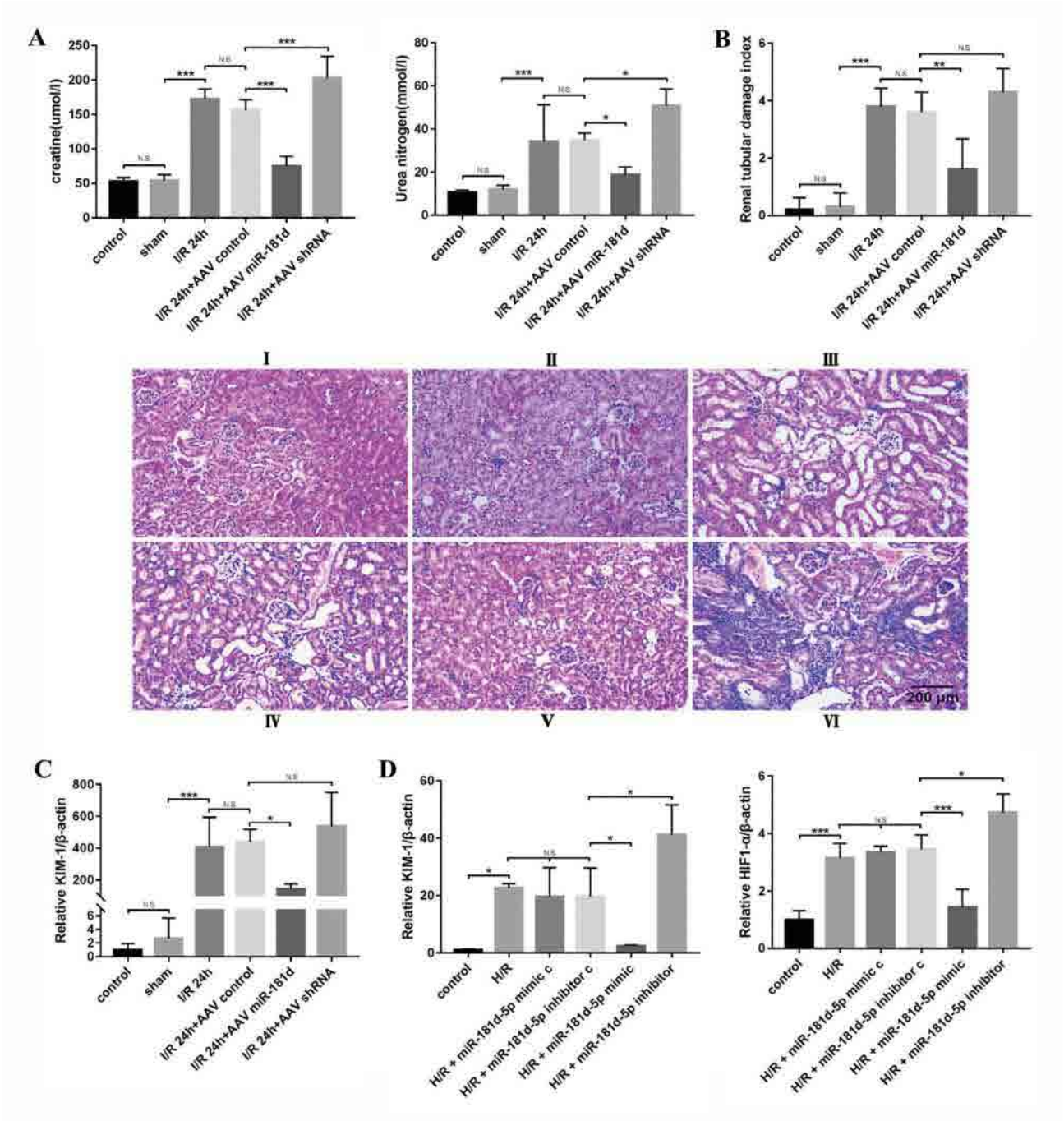

A
creatine(umol/l)
250
200
150
100
50
0
N.S
***
***
N.S
***
***
control
sham
I/R 24h
I/R 24h+AAV control
I/R 24h+AAV miR-181d
I/R 24h+AAV shRNA
Urea nitrogen(mmol/l)
80
60
40
20
0
N.S
***
N.S
*
*
control
sham
I/R 24h
I/R 24h+AAV control
I/R 24h+AAV miR-181d
I/R 24h+AAV shRNA
B
Renal tubular damage index
6
4
2
0
N.S
***
N.S
**
N.S
control
sham
I/R 24h
I/R 24h+AAV control
I/R 24h+AAV miR-181d
I/R 24h+AAV shRNA
I
II
III
IV
V
VI
200 μm
C
Relative KIM-1/β-actin
800
600
400
200
6
4
2
0
N.S
***
N.S
*
N.S
control
sham
I/R 24h
I/R 24h+AAV control
I/R 24h+AAV miR-181d
I/R 24h+AAV shRNA
D
Relative KIM-1/β-actin
60
40
20
0
*
N.S
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control
H/R
H/R + miR-181d-5p mimic c
H/R + miR-181d-5p inhibitor c
H/R + miR-181d-5p mimic
H/R + miR-181d-5p inhibitor
Relative HIF1-α/β-actin
6
4
2
0
***
N.S
***
*
control
H/R
H/R + miR-181d-5p mimic c
H/R + miR-181d-5p inhibitor c
H/R + miR-181d-5p mimic
H/R + miR-181d-5p inhibitor

Figure 2:

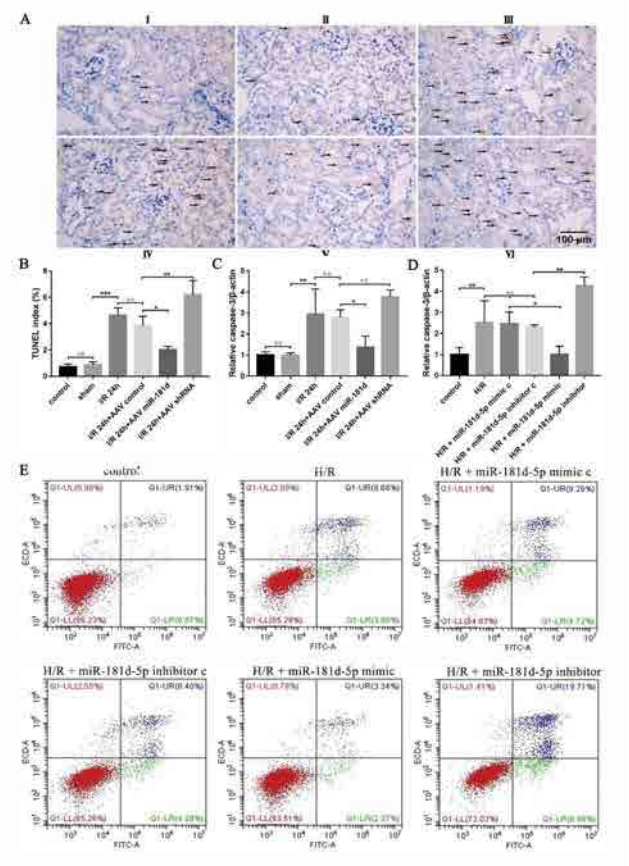

A
I
II
III
100 μm
B
IV
TUNEL index (%)
control
sham
I/R 24h
I/R 24h+AAV control
I/R 24h+AAV miR-181d
I/R 24h+AAV siRNA
C
V
Relative caspase-3/β-actin
D
VI
Relative caspase-3/β-actin
control
H/R
H/R + miR-181d-5p mimic c
H/R + miR-181d-5p inhibitor c
H/R + miR-181d-5p mimic
H/R + miR-181d-5p inhibitor
E
control
H/R
H/R + miR-181d-5p mimic c
H/R + miR-181d-5p inhibitor c
H/R + miR-181d-5p mimic
H/R + miR-181d-5p inhibitor
ECD-A
FITC-A

Figure 3:

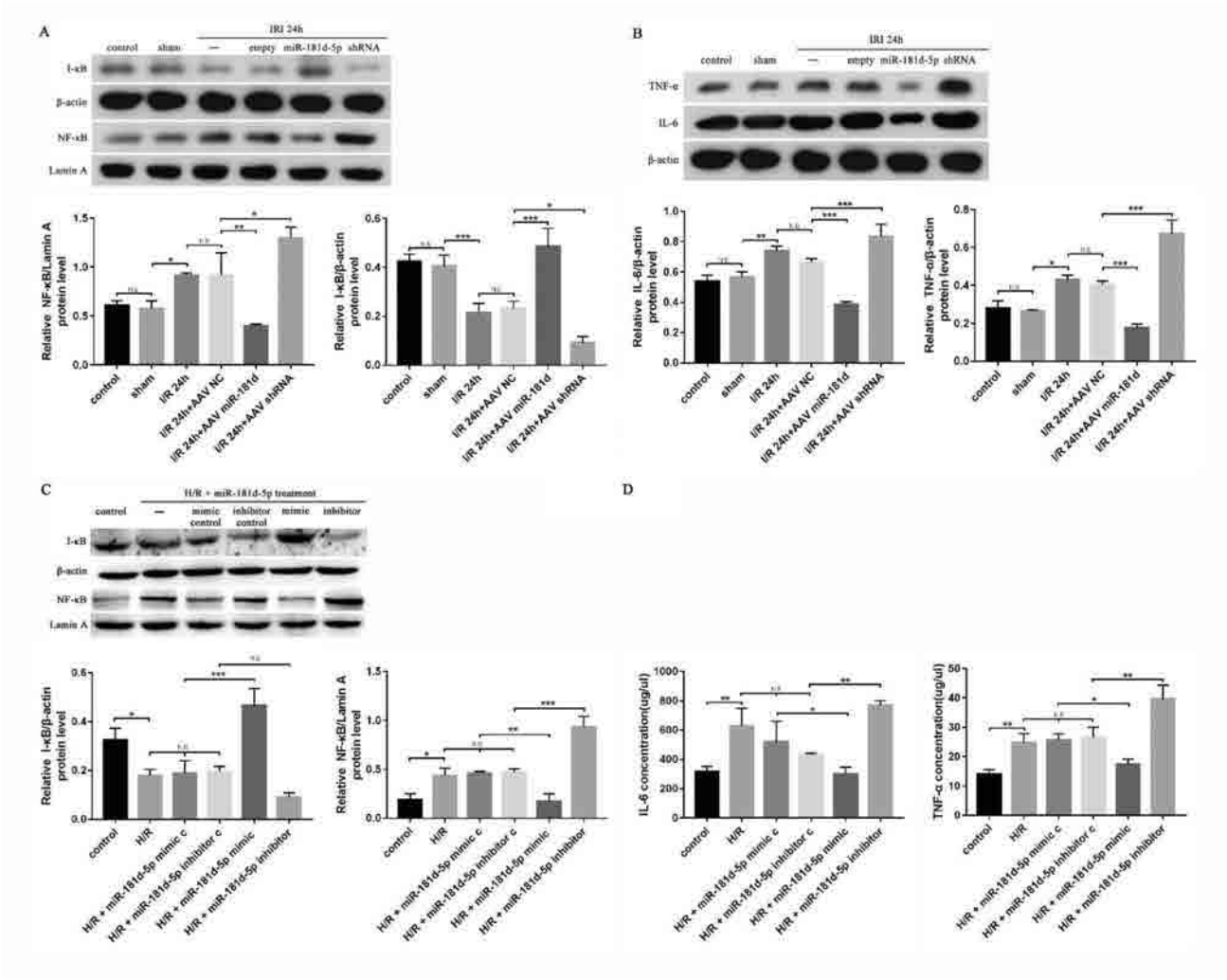


Figure 4:

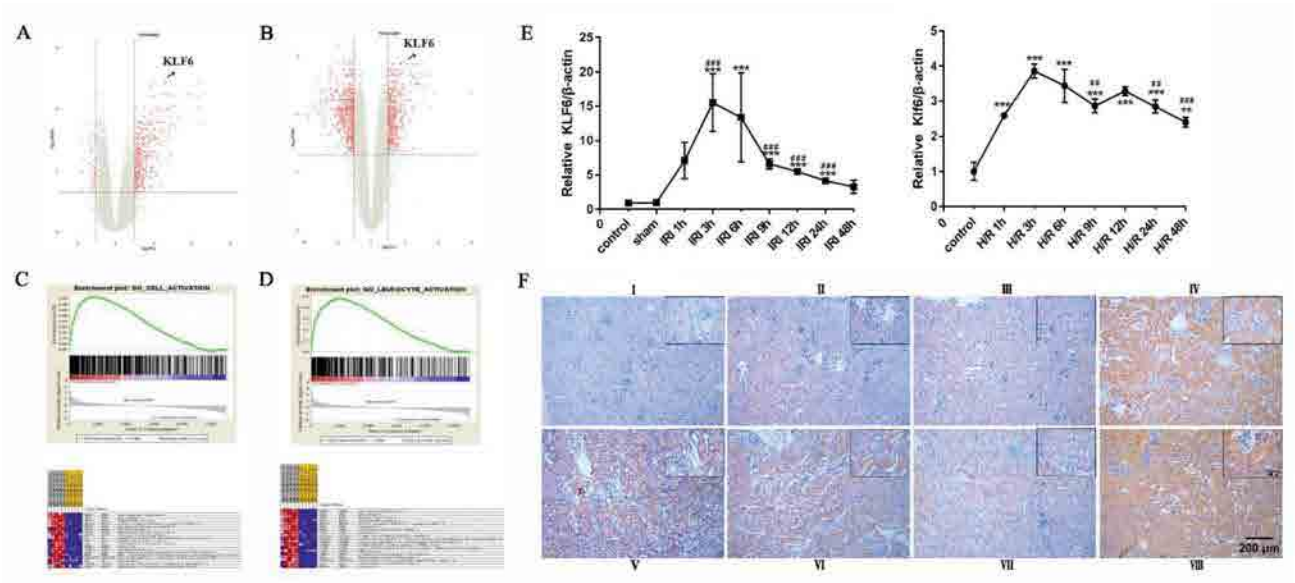


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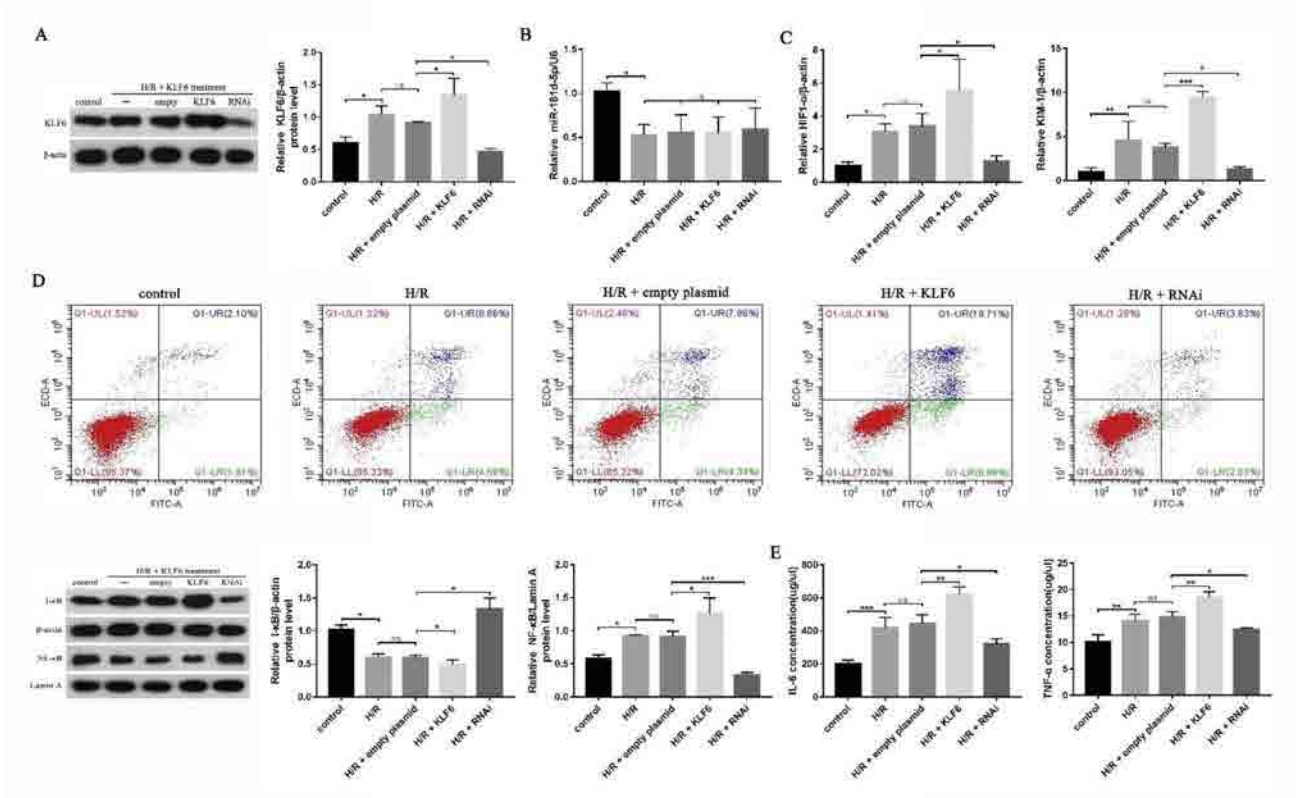


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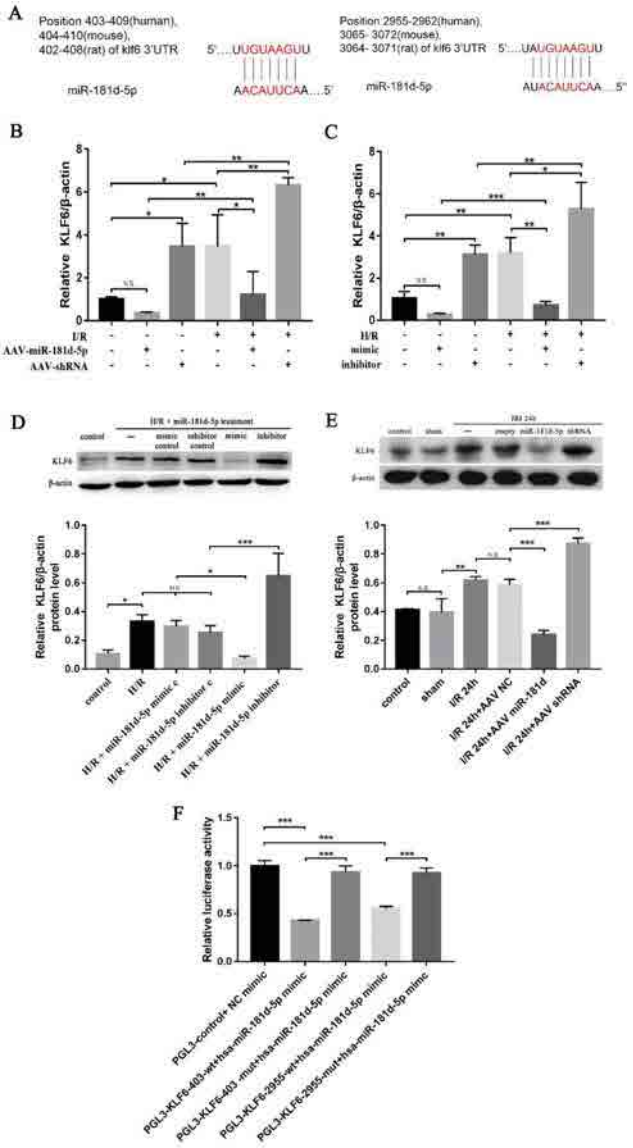


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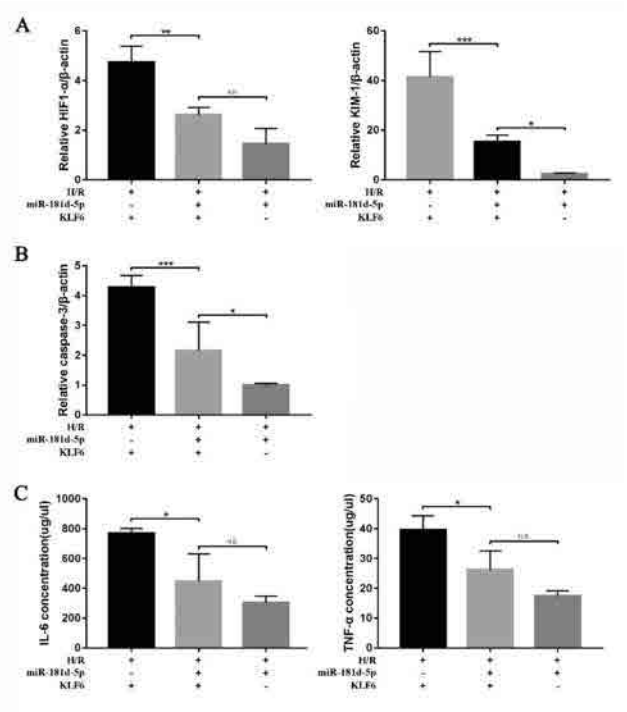


Figure 8:

P0527

HYPERGLYCEMIA-ASSOCIATED ACUTE KIDNEY INJURY INCREASES THE SUSCEPTIBILITY TOWARDS NEUROLOGICAL DYSFUNCTION: ROLE OF ANGIOTENSIN II TYPE 2 RECEPTOR AND ANGIOTENSIN-CONVERTING ENZYME 2.

Nisha Sharma[1], Anil Bhanudas Gaikwad[2]

[1]BITS Pilani, Pharmacy, Pilani, India and [2]BITS Pilani, Pilani, India

Background and Aims: In clinical settings, diabetics remain on higher risk of ischemic renal injury (IRI) than nondiabetic patients. In addition, IRI predisposes distant organs to dysfunction such as neurological impairments via activation of the pressor arm of renin-angiotensin system (RAS). In contrast, the role of depressor arm of RAS on IRI-associated neurological sequalae remains elusive. Hence, this study explored the role of angiotensin II type 2 receptor (AT2R) and angiotensin-converting enzyme 2 (ACE2) in IRI-associated neurological dysfunctions under nondiabetic (ND) and diabetes mellitus (DM) condition.

Method: Type 1 diabetes was induced by injecting streptozotocin (55 mg/kg *i.p.*). ND and DM rats with bilateral IRI were treated with AT2R agonist-Compound 21 (C21) (0.3 mg/kg/day, *i.p.*) or ACE2 activator-Diminazene Aceturate (Dize), (5 mg/kg/day, *p.o.*) *per se* or in combination therapy. Behavioural, biochemical, and histopathological analysis were done to assess IRI-induced neurological impairment. Moreover, immunohistochemistry, ELISA and qRT-PCR experiments were conducted for molecular mechanism analysis.

Result: In ND and DM rats, IRI caused hippocampal complications as evidenced by increased MDA and nitrite levels, augmented inflammatory cytokines (granulocyte colony stimulating factor, glial fibrillary acidic protein), altered protein and mRNA expressions of Ang II, Ang-(1-7), AT1R, AT2R and MasR. In contrast, concomitant therapy of C21 and Dize effectively normalised aforementioned hippocampal alterations. The protective effect of combination therapy was exerted due to augmented protein and mRNA levels of depressor arm components.

Conclusion: The current study demonstrated the protective role of AT2R agonist and ACE2 activator in IRI-associated neurological dysfunction through preventing oxidative stress, inflammation and upregulating brain depressor arm of RAS under ND and DM conditions.

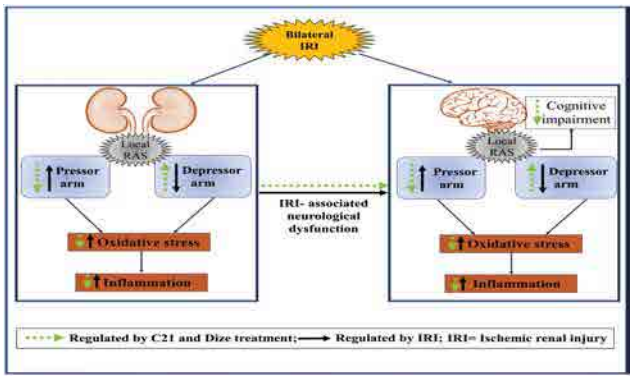


Figure:

P0527A

ROLE OF PROMOTING INFLAMMATION OF KLF6 IN ACUTE KIDNEY INURY

Dan Li[1], Chenyu Li[2], Yan Xu[3]

[1]Qingdao Central Hospital, Department of Nephrology, Qingdao, P.R. China, [2] Medical Clinic and Polyclinic IV, University Hospital, Munich, Division of Nephrology, Munich, Germany and [3]Affiliated Hospital of Qingdao University, Department of Nephrology, Qingdao, P.R. China

Background and Aims: Acute kidney injury (AKI), commonly appeared in cardiac arrest, surgery and kidney transplantation which involved in ischemia-reperfusion (IR) injury of kidney. However, the mechanisms underlying inflammatory response in IR AKI is still unclear.

Method: Public dataset showed kruppel-like factor 6 (KLF6) was significantly highly expressed ($P<0.05$) in AKI, implies KLF6 might be associated with AKI. To evaluate the mechanism of KLF6 on IR AKI, 30 rats were randomly divided into sham and IR group, and were sacrificed at 0 h, 3 h, 6 h, 12 h or 24 h after IR.

Results: The results showed KLF6 expression was peaking at 6 h after IR, and the expression of pro-inflammatory cytokines MCP-1 and TNF-α were increased both in serum and kidney tissues after IR, while anti-inflammatory cytokine IL-10 was decreased after IR. Furthermore, in vitro results showed KLF6 knock-down reduced the pro-inflammatory cytokines expression and increased the anti-inflammatory cytokines expression.

Conclusion: These results suggest that (1) KLF6 might be a novel biomarker for early diagnosis of AKI and (2) targeting KLF6 expression may offer novel strategies to protect kidneys from IR AKI

Figure: KLF6, AKI, Control Inflammation

P0528 RENOPROTECTIVE EFFECT OF IL-34 INHIBITION ON CISPLATIN-INDUCED NEPHROTOXICITY IN MICE

Yukihiro Wada[1], Masayuki Iyoda[1], Kei Matsumoto[2], Taihei Suzuki[1], Ken Iseri[1], Shohei Tachibana[1], Nobuhiro Kanazawa[1], Motonori Sugiyama[1], Hirokazu Honda[1]

[1]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Tokyo, Japan and [2]Showa University Koto Toyosu Hospital, Division of Nephrology, Department of Medicine, Tokyo, Japan

Background and Aims: Interleukin (IL)-34, a macrophage (Mø) mediator, is expressed by tubular epithelial cells (TECs). However, the influence of IL-34 on TECs injury has not been fully elucidated. We investigated the physiological properties of IL-34 on TECs damage caused by cisplatin-nephrotoxicity (CP-N).

Method: 7-week-old male C57BL/6 (B6) mice (n=16) were fasted for 8 hours and then induced CP-N by intraperitoneal injection (IP) of CP (25 mg/kg) on day 0. Groups of animals were given either anti-mouse IL-34 antibody (CP+anti-IL-34 Ab, 400 ng/kg, n=8) or vehicle (CP+V, equal volume of saline, n=8) daily by IP from day -1 to day 2. Three age-matched male B6 mice were used as normal control (NC). All mice were sacrificed on day 3. In addition, mouse renal proximal TECs (MRTEpiC) were cultured to analyze the inhibitory effects of IL-34 on CP-induced TEC apoptosis. Cells were stimulated with CP (2 μg/mL), then treated with or without anti-IL-34 Ab (1000 pg/mL).

Results: Compared to the NC, CP+V mice exhibited marked acute kidney injury (AKI) and upregulated expression of IL-34 and its two receptors, cFMS and PTP-ζ. Compared to the vehicle treatment, anti-IL-34 Ab treatment significantly suppressed the intrarenal expression levels of IL-34 and its two receptors in CP-N mice; it also significantly suppressed serum IL-34 levels (72.1 ± 5.6 vs. 40.4 ± 7.5 pg/mL, p=0.013). Additionally, treatment with anti-IL-34 Ab significantly improved serum Cr levels (1.3 ± 0.2 vs. 0.7 ± 0.1 mg/mL, p=0.033), ameliorated tubulointerstitial injury (numbers of casts/HPF: 11.9 ± 2.6 vs. 6.5 ± 1.8, p=0.048), and suppressed the number of F4/80+ Mø (17.5 ± 2.7 vs. 11.1 ± 1.1/HPF, p=0.041) and TUNEL+ apoptotic cells (29.2 ± 4.9 vs. 16.7 ± 2.7/HPF, p=0.036) in CP-N mice. The renal cortical transcript levels of Kim-1, MIP-1/CCL3, TNF-α, and Bax were significantly lower in the CP+anti-IL-34 Ab mice than in the CP+V mice. Furthermore, the CP+anti-IL-34 Ab mice showed significantly less renal infiltration of CD11b+F4/80+TNF-α+ cells. In vitro, stimulation with CP induced the expression of IL-34 and its two receptors in MRTEpiC. Treatment with anti-IL-34 Ab significantly suppressed CP-induced caspase-3 and Bax expression with degradation of ERK1/2 phosphorylation in the damaged MRTEpiC.

Conclusion: IL-34 secreted from damaged TECs was involved in the progression of CP-N. Inhibition of IL-34 with neutralizing antibody directly prevented CP-induced TEC apoptosis by inhibiting the phosphorylation of ERK1/2. Blocking of IL-34 might suppressed proliferation of cytotoxic Mø, which indirectly led to the attenuation of CP-N. Thus, IL-34 represents a potential as therapeutic target for AKI with TECs injury.

P0529

THE DIFFERENCE IN DIETARY RESTRICTION-INDUCED NEPHROPROTECTIVE MECHANISMS IN YOUNG AND OLD ANIMALS

Nadezda Andrianova[1,2], Ljubava Zorova[2], Irina Pevzner[2], Vasily Popkov[2], Denis Silachev[2], Dmitry Zorov[2], Egor Plotnikov[2]

[1]Lomonosov Moscow State University, Faculty of Bioengineering and Bioinformatics, Moscow, Russia and [2]Lomonosov Moscow State University, A.N. Belozersky Institute of Physico-Chemical Biology, Moscow, Russia

Background and Aims: Acute kidney injury (AKI) is a widespread disease affecting mostly old people. Dietary restriction (DR), based on the reduction of food intake, is believed to be one of the most efficient approaches ameliorating damage in different pathological conditions including age-associated diseases. The aim of the study was to investigate the protective mechanisms of DR in the model of AKI in young and old rats.

Method: All experiments were made on young (3-4 months) and old (22-24 months) male rats. DR was performed by limiting the amount of food for 35% of the ad libitum (AL) daily intake. Since earlier, we showed ineffectiveness of 4-weeks DR in old rats, in this study we applied 35% DR lasting 8 weeks for old rats and 4 weeks for young rats. During DR, we registered the weight loss and measured the level of adiponectin, as this hormone is closely associated with adipose tissue metabolism.

Renal ischemia/reperfusion (I/R) was used as a model of ischemic AKI. I/R was performed by clamping the left renal pedicle for 40 minutes followed by reperfusion with simultaneous contralateral nephrectomy. The severity of AKI was evaluated by measuring blood urea nitrogen (BUN), serum creatinine (SCr) and the levels of protein biomarkers of AKI (NGAL and L-FABP) in urine. Proliferation in kidney epithelium in response to I/R was analyzed by PCNA protein level in kidney tissue.

We evaluated the function of mitochondria by measuring TMRE/MitoTracker Green ratio in vital kidney slices; in kidney homogenates, we also analyzed levels of Bcl-X_L and Bcl-X_S proteins. The production of reactive oxygen species (ROS) was evaluated by staining vital kidney slices with DCF. The content of lipid peroxidation products was measured using Image-iT Lipid Peroxidation Kit, and the level of carbonylated proteins was determined by OxyBlot Protein Oxidation Detection Kit.

The activation of autophagic-lysosomal system was estimated by western blotting to LC3 II/LC3 I ratio and LAMP1 level, as well as by staining vital kidney slices with LysoTracker Green probe.

Results: The body weight of rats during DR dropped as far as 20% by the end of 4 weeks in young rats and 30% by the end of 8 weeks in old rats. Nevertheless, adiponectin concentration elevated during DR only in the serum of young rats.

DR strongly influenced mitochondria function, in particular, elevated mitochondrial membrane potential both in kidney cells of young and old rats. DR also resulted in increasing the Bcl-X_L level. We revealed the decrease of ROS and lipid peroxidation products in vital kidney slices, but only in kidneys of young rats. However, DR reduced the content of carbonyl groups more than 2 times in animals of both ages.

We showed that activation of autophagy in response to DR and I/R occurred only in the kidneys of young rats, indicating deterioration of autophagy signaling in old animals. We also found that 48 h after I/R PCNA level increased 19 times in young kidney, although old rats showed only 4-fold elevation of kidney cells proliferation.

Estimation of kidney injury markers (NGAL, L-FABP) in urine revealed that 2-month DR led to some protection in old rats. Nonetheless, despite all positive alterations in kidney tissue of old rats, DR was not able to ameliorate impairment of kidney function after I/R, whereas all young rats showed significant improvement of SCr and BUN levels.

Conclusion: Short-term DR has a significant nephroprotective effect against renal I/R in young rats. Old animals require longer periods of food restriction, after which some protective alterations are observed. We propose, protection of kidney in old and young rats is implemented through slightly different mechanisms and some of them are missing in old animals.

P0530 A NOVEL LNCRNA(LRAN9884) PROMOTES AKI VIA MAINTAINING MINCLE-DEPENDENT M1 MACROPHAGE PHENOTYPE

Yingying Zhang[1], Chen Yu[2]

[1] Shanghai Tongji Hospital, Tongji University School of Medicine, Department of Nephrology, Shanghai, P.R. China and [2]Shanghai Tongji Hospital, Tongji University School of Medicine, Department of Nephrology, Shanghai, P.R. China

Background and Aims: Macrophages are key inflammatory cells and play a critical role in renal inflammation in acute kidney injury (AKI). M1 inflammatory macrophage and M2 anti-inflammatory macrophage act reverse role. Phenotype of macrophages is highly flexible and can be changed over time. However, the underlying mechanism of M1 and M2 macrophage phenotype switching during AKI is still largely unclear. In our previous study, we identified a novel lncRNA (LRNA9884) might contribute to inflammation according to modifying macrophages. The present study was designed to uncover the pathogenic role and the underlying mechanism of LRNA9884 in cisplatin-induced AKI.

Method: Expression level and pattern of LRNA9884 were examined in cisplatin-induced AKI mice. The regulatory mechanisms of LRNA9884 was investigated in cultured bone marrow–derived macrophages (BMDMs) *in vitro* by silencing or overexpressing of LRNA9884. Flow Cytometer, fluorescence in situ hybridization (FISH) and other multiple molecular biological techniques were applied to figure out the role of LRNA9884 under acute kidney injury.

Results: LRNA9884 was significantly upregulated in the kidney of cisplatin-induced mice and was associated with the progression of the renal inflammation by using RT-PCR and ISH assay. FISH assay with immunofluorescence co-staining detected that LRNA9884 was largely expressed in the nucleus of macrophage in cisplatin-induced mice kidney compared with the sham group at day 1 after AKI injury. LRNA9884 was remarkedly induced by TNF-α (10ng/ml) in BMDMs as time- and dose- dependent. Western blot and RT-PCR showed that silencing of LRNA9884 effectively inhibited upregulated of macrophage-inducible C-type lectin (Mincle) and iNOS induced by TNF-α. More importantly, we identified that LRNA9884 maintained M1 macrophages phenotype by triggering mincle production at transcriptional level as evidenced by ChIP assay.

Conclusion: LRNA9884 is a mincle-dependent lncRNA that highly-expressed in macrophages under AKI development. Targeting of LRNA9884 effectively blocked the inflammatory response via promoting the transition M1 macrophage to M2 macrophage phenotype. This study will shed new lights on the understanding of pathological role of novel LRNA9884 in AKI.

P0531

CONTINUOUS HEMODIAFILTRATION WITH PMMA HEMOFILTER MODULATED COMPLEMENT ACTIVATION AND RENAL DYSFUNCTION IN A SWINE MODEL OF SEPSIS-INDUCED ACUTE KIDNEY INJURY.

Alessandra Stasi[1], ROSSANA FRANZIN[1,2], Fabio Sallustio[3], Chiara Divella[1], Claudia Curci[4], Antonio Crovace[5], Claudio Ronco[6], Francesco Staffieri[5], Vincenzo Cantaluppi[2], Massimo De Cal[6], Mauro Neri[6], Anna Lorenzin[6], Pertosa Giovanni[5], Giovanni Stallone[7], Loreto Gesualdo[1], Giuseppe Castellano[7]

[1]University of BARI, Department of Emergency and Organ Transplantation, Nephrology Unit, Bari, , [2]University of Piemonte Orientale, Department of Translational Medicine, Italy, [3]University of BARI, Interdisciplinary Department of Medicine, Italy, [4]University of BARI, Department of basic medical sciences, neurosciences and sense organs, Italy, [5]University of BARI, Department of Emergency and Organ Transplantation, Veterinary Unit, Italy, [6] International Renal Research Institute of Vicenza, Department of Nephrology Dialysis & Transplantation, Italy and [7]University of Foggia, Department Medical Science, Italy

Background and Aims: Sepsis-induced acute kidney injury (AKI) is a growing health care problem, refractory to conventional treatments. This disease is characterized by an overwhelmed immune response against a primary insult that become responsible for renal dysfunction and poor outcome. Therapeutic strategies based on blood purification have been developed for the treatment of this disease. The use of polymethyl methacrylate (PMMA) membrane hemofilter in continuous hemodiafiltration (CHDF) modality showed better hemodynamic stability and efficient renal support in chronic dialysis maintenance. Here we investigated the efficacy of Hemofeel PMMA membrane (TORAY, Japan) in interfering with Complement activation and renal damage in a swine model of sepsis-induced AKI.

Method: After 3 hours from LPS infusion, 7 hours of PMMA-CVVH treatment or 7 hours of polysulfone (PSF)-CVVH were performed. Animals were sacrificed after 24h from LPS infusion. Histologic and renal function parameters were analyzed in all pigs. Pentraxin-3 (PTX3) and C5b-9 deposits were assessed on renal biopsies. Systemic Complement activation was evaluated by Wieslab kit. Gene expression profile was obtained from isolated PBMCs by Agilent SurePrint G3 Porcine Gene Expression Microarrays. Genespring and R software were used for the analysis. Results were validated by Real-time PCR.

Results: Analysis of renal biopsies from septic pigs presented increased interstitial leucocyte infiltrate, extensive collagen deposition and diffuse glomerular thrombi compared to healthy pigs ($p<0.05$). Confocal analysis showed extensive PTX-3 and C5-b9 deposits at tubulo-interstitial level associated with significant activation of systemic complement classical and alternative pathways ($p<0.05$). Interestingly, PMMA-CVVH treatment significantly reduced local and systemic complement activation, leucocyte infiltrate and tubule-interstitial fibrosis ($p<0.05$). On the contrary, no significant improvement was observed by PSF-CVVH treatment. Then, we compared the whole-genome gene expression profiles of swine PBMC. We identified 711 differentially expressed genes comparing PBMC before LPS infusion (LPS T0) and after 24 hours from LPS infusion (LPS T24) and 913 genes comparing gene expression profiles of LPS T24 group with that of septic pigs treated with PMMA-CVVH (PMMA T24 group) (fold change >2 ; false discovery rate <0.05). The most modulated genes were Granzime B, Complement Factor B, Complement Component 4 Binding Protein Alpha, IL-12, SERPINB-1 and TIMP-2 that were closely related to sepsis-induced immunological process. Finally, quantitative PCR confirmed the microarray data indicating that Granzime B and Complement Factor B upregulation in PBMC was significantly hampered by PMMA treatment.

Conclusion: Our data suggest that LPS induced AKI is characterized by activation of Classical and alternative Complement pathways resulting in significant renal tissue damage. By interfering with complement activation and inflammatory response, PMMA membrane might prevent dysfunctional activation of resident renal cells with prevention of sepsis-induced AKI.

P0532 **CD8+CD103+ INDUCED REGULATORY T CELLS BUT NOT NATURE REGULATORY T CELLS AMELIORATE IR-INDUCED KIDNEY INJURY.**

Tongtong Xu[1], Zhenjian Xu[1], Liling Chen[1], Anping Xu[1]

[1]*Sun Yat-sen Memorial Hospital, nephrology, Guangzhou, P.R. China*

Background and Aims: Acute kidney injury (AKI) is one of the most common complications in clinical practice, but current approaches offer no cures for AKI. Inflammatory response is the key mechanism of ischemia reperfusion (IR)-induce AKI, known as hypoxia/reoxygenation injury. T lmphocytes are crucial mediators of IR-induced AKI. It is reported that regulatory T cell (Treg) has potential ability to ameliorate IR-induced AKI. Tregs consist of nature Treg (nTreg) and induced Treg (iTreg), which are well established to blunt immune responses. We confirmed that CD8+CD103+iTreg remain steadily and barely transfer into Th17, which produce proinflammatory response, under inflammatory response. It is studied that nTreg tends to transfer into Th17 under inflammatory condition, which clarifies the instability of nTreg. Thus, the instability of nTreg under inflammatory response hints us that nTreg are not suitable for recovery from IR-induced AKI. Accordingly, we studied the role of CD8+CD103+iTreg in repair after IR-induced kidney.

Method: In vitro study, we test the expression of CD103, Foxp3 and IL-17a in CD8+CD103+iTreg under 1% O_2 concentration. In vivo study, SPF C57BL/6J male mice (8-10 weeks old, body weight 20-25g) were divided into four groups, sham-operated control group, AKI group, iTreg treatment group and nTreg treatment group, with 6 mice in each group. On the day of surgery, we anesthetize the mice (pen-tobarbital sodium, 50 mg/kg body weight). Mice in the AKI group were reperfused after 25 minutes of bilateral renal artery ischemia. We injected CD8+CD103+iTreg (2×10^6/mouse) or nTreg (2×10^6/mouse) intraperitoneally after 24 hours of modeling to the treatment group and euthanized the mice on the third day of anesthesia.

Results: We discovered that the expression of CD103 is stable in CD8+iTreg in vitro under 1% O_2 concentration (Figure 1, 2). In addition, their inhibiting abilities of T cells proliferation in vitro remain steadily (Figure not shown). However, CD8+CD103+iTreg seldom transfer into Th17, but remain Foxp3 under hypoxic condition (Figure 2). Adoptively transferring CD8+CD103+iTregs, a new subpopulation of CD8+iTreg we have identified, to AKI mice, we found that these cells can ameliorate the development of AKI by mitigating the level of serum creatine, alleviating acute tubular necrosis (ATN) and decreasing the mortality of AKI.

Conclusion: Therefore, we confirmed that CD8+CD103+iTreg is stable under inflammatory(hypoxic) environment. Thus, CD8+CD103+iTreg targeting may be a novel therapeutic approach to enhance recovery from IR-induced AKI.

Fig 1

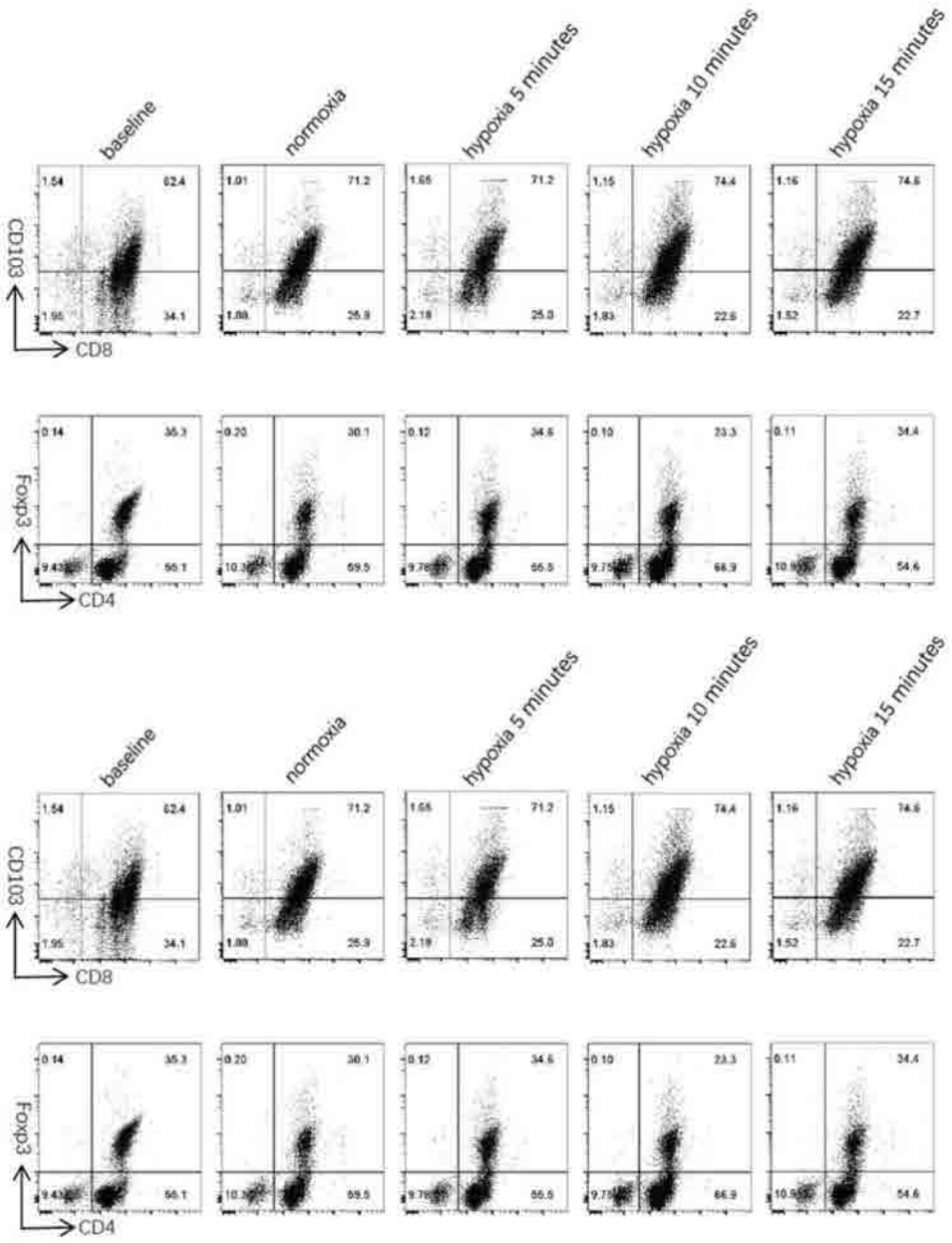


Fig 1

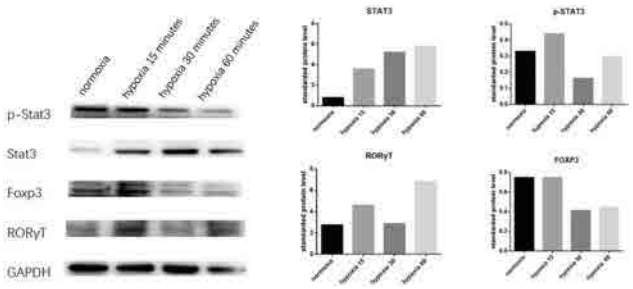

normoxia
hypoxia 15 minutes
hypoxia 30 minutes
hypoxia 60 minutes
p-Stat3
Stat3
Foxp3
RORγT
GAPDH
STAT3
p-STAT3
RORγT
FOXP3

Fig 2

P0533

SCUTELLARIN PROTECTS ISCHEMIA/REPERFUSION INDUCED ACUTE KIDNEY INJURY FROM OXIDATIVE STRESS BY TARGETING NRF2.

Dai Jie[1]

[1]Nephrology Institute, Department of Nephrology, Qingdao, P.R. China

Background and Aims: Ischemia/reperfusion (I/R) may cause acute kidney injury(AKI) by mediating the oxidative stress and related inflammation then inducing apoptosis. The present study is to explore the preventive effect and mechanism of Scutellarin(Scu),on AKI induced by I/R.

Method: ①The renal ischemia-reperfusion model GSE98622 data set was selected from NCBI GEO DateSets, and the genes with significantly increased expression in acute kidney injury were selected. Further, dozens of hub-genes were identified as candidate proteins by protein-protein interaction network(PPI network). The molecular docking between the protein and the Scu was performed using the Autodock software. As the results of the molecular docking,the binding energy between the protein Nrf2 and Scu molecule is -9.84, suggesting that there is a high probability of interaction between the two molecules.

②Experiment in vivo. Wistar rats were randomly divided into 5 groups: normal group, sham group, AKI group (bilateral renal pedicle clip 45 min), Scu + AKI group (Intraperitoneal injection of 50 mg/kg.d Scu daily for 7 days before surgery,the same surgery with AKI group),Saline + AKI group (the same concentration of DMSO-normal saline solution daily for 7 days before surgery, the same surgery with AKI group), 6 rats in each group.The rats were sacrificed together 24h after surgery.

③Experiment in vitro.Human kidney tubular epithelial cells (HK-2) were firstly divided into 7 groups:hypoxia for 3 hours (h), 6h, 9h, 12h, 24h, 36h and 48h reoxygenation for 1h. RT-PCR detect Hihf1α, Nrf2, HO1,SOD-1,caspase3, Bcl2/BAX, NF-κB and TNFα levels to determine the best hypoxia time. To screen the safe concentration of the drug,after pretreatment with 200μmol/l, 150μmol/l,120μmol/l, 100μmol/l,80μmol/l,60μmol/l, 40μmol/l,20μmol/l, 10μmol/l,5μmol/l Scu for 12 h, use CCK8 to measure the absorbance. Then the optimal protective concentration in hypoxia was searched in maximum safe concentration to determine the final drug concentration.Finally,after the cells were randomly divided into normal group, hypoxia group, hypoxia + DMSO group, hypoxia + Scu group, RT-PCR ,Western Blot and ROS probe was used to detect related indicators.

Results: ①Bioinformatics analysis suggests that Nrf2 protein is one of the key factors in acute kidney injury induced by ischemia-reperfusion, which may be a target for the prevention and treatment of diseases.

②The results of experiments in vivo showed that compared with the normal group and the sham group, the serum creatinine level increased after AKI, and the HE staining showed that the renal tubular injury score increased . The creatinine and renal tubular injury score of Scu group were significantly relieved. Scu also reduces the level of MDA increased by AKI.KIM-1 increased, Nrf2 and HO-1 increased,SOD-1 decreased,Caspase3 increased, Bcl2/BAX decreased, NF-κB and TNFα increased after AKI, all $P<0.05$, suggesting obvious renal injury.However, the Scu+AKI group significantly up-regulated the Nrf2/HO-1 to combat oxidative stress damage.Moreover,Scu further down-regulated the inflammatory and apoptotic level.

③The pre-test choosed ischemia for 24h and re-oxygenation for 1 hour as the experiment time. And Compared with the normal group,the PCR results showed that in the hypoxia group and the hypoxia+DMSO group, the expression of hif1α increased, Nrf2 and HO-1 increased, caspase3 increased, Bcl2/BAX decreased, and NF-κB and TNFα increased, both $P<0.05$. The H+Scu group significantly reduced the oxidative stress through the results of ROS probe and increasing Nrf2/HO-1 and SOD-1 level.Scu also ameliorates the indicators of inflammation and apoptosis ($P<0.05$). The WB results are consistent with the PCR.

Conclusion: Scu has obvious protective effect on acute kidney injury induced by ischemia-reperfusion. The mechanism is probably alleviating oxidative stress by targeting Nrf2/HO-1 pathway.

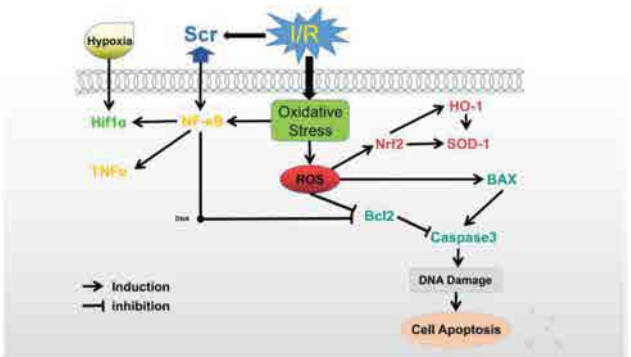


Figure:

P0534 THE EFFECT OF HIGH FAT DIET INTAKE AND FOOD SUPPLY RESTRICTION ON CISPLATIN NEPHROTOXICITY IN MICE

Ji Su Kim[1], Min Jung Kong[1], Kwon Moo Park[1]

[1]*School of Medicine, Kyungpook National University, Anatomy, Daegu, Korea, Rep. of South*

Background and Aims: Nephrotoxicity is a major side effect of cis-diamminedichloroplatinum (II) (cisplatin), which is widely used for cancer therapy. The nephrotoxicity is associated with the excessive formation of reactive oxygen species (ROS) and oxidation of cell components. Here, we investigate whether cisplatin nephrotoxicity can be controlled by the regulation of food supply which is associated with cellular production of ROS.

Method: Male mice were administered with either cisplatin or saline. Before cisplatin administration, mice were high-fat diet (HFD) feeding for 7 days, no-food supply for 2 days, 2 days no-food supply and refeeding with normal diet (ND), and normal diet. Renal function was analyzed by plasma creatinine (PCr) and blood urea nitrogen (BUN) concentration. Kidney cell damage was evaluated by periodic acid shiff staining and transmission electron microscope analysis.

Results: Cisplatin injection induced the disruption of kidney tubular cells and also increased BUN and PCr concentration. These increases were greatest in the HFD feeding mice, whereas .these increases were lowest in the food restricted mice. Levels of DNA oxidation and lipid peroxidation increased in the kidney after cisplatin injection and these increase were also greatest in the kidney of HFD feeding mice and lowest food restricted mice. Mitochondrial damage was observed in the proximal tubule cells after cisplatin injection and this mitochondria damage was more severe in the HFD feeding mice than ND feeding mice. Cisplatin increased the expression of fission 1 in the kidney, whereas reduced the expression of opa-1 expression. These cisplatin induced changes were greater in the HFD feeding mice than the ND feeding mice.

Conclusion: High fat diet feeding worsens cisplatin-induced nephrotoxicity along with increased oxidative stress and mitochondrial damage, whereas food restriction reduces this cisplatin nephrotoxicity. These data indicate that cisplatin nephrotoxicity is controlled by food supply, suggesting that energy metabolism is associated with cisplatin nephrotoxicity.

P0535 ATG5 OVEREXPRESSION IN PACS SIGNIFICANTLY IMPROVES CELL-MEDIATED AKI PROTECTION

Daniel Patschan[1], Katrin Schwarze[2], Oliver Ritter[1], Susann Patschan[1], Gerhard Anton Müller[2]

[1]MHB Theodor Fontane, Neuruppin, Germany and [2]Universitätsmedizin Göttingen, Göttingen, Germany

Background and Aims: Acute Kidney Injury (AKI) significantly worsens the prognosis of hospitalized patients. Cell-based strategies have been established as reliable option for improving AKI outcomes in experimental AKI. Own studies performed in recent years utilized Pro-angiogenic Cells (PACs). Autophagy (AP) is commonly regarded as process of en-dogenous self-defense. The AP cascade, which may be stimulated by either substrate deprivation or certain exogenous / endogenous stressors, involves the activation of numerous proteins, the so-called Autophagy-related proteins (Atg proteins). Among these, Atg5 has been suggested to play a key role in augmenting AP. The current study evaluated whether selective Atg5 activation in syngeneic murine PACs may result in improved cell-mediated AKI protection.

Method: Cultured murine PACs were selectively transfected for Atg5. Successful transfection was verified by detecting red fluorescing cells. AKI was induced in male C57/Bl6N mice (8-12 weeks) by bilateral renal ischemia (IRI - 40 minutes). Transfected cells were i.v. injected post-ischemia. Mice were analyzed 48 hours and 6 weeks later.

Results: IRI induced significant kidney excretory dysfunction as reflected by higher serum cystatin C levels (48 hours and 6 weeks). Cell administration (either native or after transfection) did not improve AKI outcomes at 48 hours. At 6 weeks, injection of native cells resulted in lower serum cystatin C, this effect was even more pronounced if transcfected cells were applied.

Conclusion: Together, our data show that selective Atg5 overexpression in murine PACs sub-stantially augments cell-mediated AKI protection in the long-term. Thus, a new strategy for improving AKI protective effects of PACs has been identified.

P0536 **HYPOTHERMIA DURING RENAL ISCHEMIA-REPERFUSION IN MICE: A PROTECTIVE EFFECT ON RENAL AND MITOCHONDRIAL FUNCTIONS**

Maxime Schleef[1,2], Delphine Baetz[1], Bruno Pillot[1], Christelle Leon[1], Noelle Gallo-Bona[1], Michel Ovize[1,3], Laurent Juillard[1,2], Fitsum Guebre-Egziabher[1,2], Sandrine Lemoine[1,4]

[1]B13 Opera / Inserm U1060 Carmen, Université Lyon 1, Bron, France, [2]Edouard Herriot Hospital, Hospices Civils de Lyon, Nephrology Department, Lyon, France, [3]Louis Pradel Hospital, Hospices Civils de Lyon, Cardiovascular Functional Explorations Department, Bron, France and [4]Edouard Herriot Hospital, Hospices Civils de Lyon, Renal Functional Explorations Department, Lyon, France

Background and Aims: Renal ischemia reperfusion (RIR) can induce mitochondrial stress triggering cell death and eventually leading to acute kidney injury (AKI). It has been suggested that mild hypothermia could be protective in RIR without clear underlying mechanisms. We aimed to show that mild hypothermia (34°C) during RIR protects renal mitochondrial function and prevents AKI.

Method: Male C57BL6 mice were assigned to 4 groups: normothermic ischemic (RIR-37°C) group (n=14) and hypothermic ischemic (RIR-34°C) group (n=14) with body temperature maintained at respectively 37°C or 34°C during 20 minutes of renal ischemia by bilateral renal clamping under general anesthesia; normothermic sham (Sham-37°C) group (n=10) and hypothermic sham (Sham-34°C) group (n=10) with only anesthesia and laparotomy at 37°C or 34°C respectively. Renal function (serum urea concentration) and isolated renal mitochondria function (capacity of mitochondria to retain calcium *i.e.* calcic retention capacity (CRC), and oxidative phosphorylation capacity of electron transport chain complexes (complex I, II and IV)) were assessed 2 hours and 24 hours after reperfusion. All animal procedures were approved by local Ethics Committee. Data are presented as median with IQR.

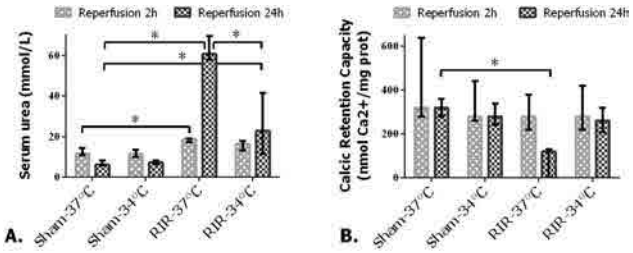
Results: All the parameters monitored were not modified by the temperature in the sham groups, and there was no mortality in those 2 groups. Mortality was 33% in the RIR-37°C group and 11% in the RIR-34°C group 24 hours after reperfusion (p=0.58).

Renal ischemia was responsible for a significant increase of serum urea level 2 hours after reperfusion at 37°C [18.7 (17.3–19.0) mmol/L] compared to sham groups (p=0.02), whereas no significant increase was observed in the RIR-34°C group. After 24 hours of reperfusion serum urea level was improved in the RIR-34°C group [22.7 (11.5–42.0) mmol/L] compared to RIR-37°C [60.8 (58.0–69.7) mmol/L, p=0.001].

CRC was not modified by RIR after 2 hours of reperfusion in both groups. CRC was preserved 24 hours after reperfusion in the RIR-34°C group [260 (210–320) nmol Ca2+/mg protein] with no difference compared to Sham-37°C [320 (280–360) nmol Ca2+/mg protein p=0.18] whereas CRC was significantly decreased in the RIR-37°C group compared to Sham-37°C [120 (0–130) vs 320 (280–360) nmol Ca2+/mg protein p=0.004).

Complexes I, II and IV were lowered after 2 hours of reperfusion in the RIR-37°C group ($p<0.05$), and complexes II and IV activities remained altered 24 hours after reperfusion, compared to Sham-37°C (p=0.009 and p=0.02 respectively). In the RIR-34°C group, complexes I, II and IV activities were preserved 2 hours after reperfusion but complex I activity decreased 24 hours after reperfusion. We found significant difference between complexes II and IV activities between IRI-34°C and RIR-37°C.

Conclusion: Mild hypothermia (34°C) during RIR significantly protected renal mitochondrial respiration and mitochondrial stress, associated with a preserved renal function after 2 hours of reperfusion and an improved renal function 24 hours after reperfusion compared to normothermic mice (37°C).



A. Serum urea concentration and **B. Renal mitochondrial calcic retention capacity** at 2 hours and 24 hours of reperfusion, after a 20-minute bilateral renal ischemia conducted in mice with core body temperature maintained at 37°C (RIR-37°C) or at 34°C (RIR-34°C), or after a sham laparotomy at 37°C (Sham-37°C) or 34°C (Sham-34°C).
Data are shown as median with IQT
* $p < 0.05$ (Mann-Whitney test)

Figure:

P0537 **LINARIN PROTECTS KIDNEY AGAINST ISCHEMIA/ REPERFUSION INJURY VIA INHIBITION OF ETS2**

Chengyu Yang[1], Yan Xu[2]

[1]The Affiliated Hospital of Qingdao University, Department of Nephrology, Qingdao, P.R. China and [2]The Affiliated Hospital of Qingdao University, Department of Nephrology, Qingdao, P.R. China

Background and Aims: Ischemia/reperfusion injury (IRI), a participant in acute kidney injury (AKI), can occur as a series of pathological processes such as inflammation. Linarin (LIN) has been widely used for different diseases. To confirm the anti-inflammatory value and relevant mechanism of LIN during IRI, in vivo and vitro model were established.

Method: LIN or isovolumetric DMSO was given, and histologic analysis, quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR), serum creatinine (SCr) testing and blood urea nitrogen (BUN) were used to evaluate kidney injury. Microarray analysis, protein-protein interaction (PPI) analysis and molecular docking were used to identify target protein of LIN.

Results: At first, we find that LIN could inhabit the kidney injury in vivo IRI model and decrease the expression of IL-12 p40 in vitro IRI model. To explore the mechanism of LIN, we collected raw data from public microarray database and identified E26 oncogene homolog 2 (ETS2) as a target protein of LIN according to microarray analysis, PPI and molecular docking. The contact area is highly conserved and located on a protein-protein interaction domain of ETS2 which indicated that LIN may alter the interaction with synergistical protein in the regulation of IL-12 p40 expression.

Conclusion: Our study demonstrated the anti-inflammatory effect of LIN during IRI-triggered AKI, broadening the medicinal value of LIN and the therapeutic options for IRI-triggered AKI.

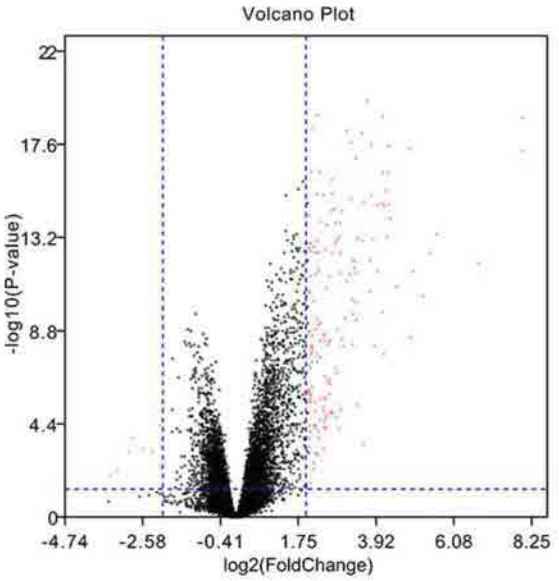


Figure 5 Molecular docking between LIN and ETS2.

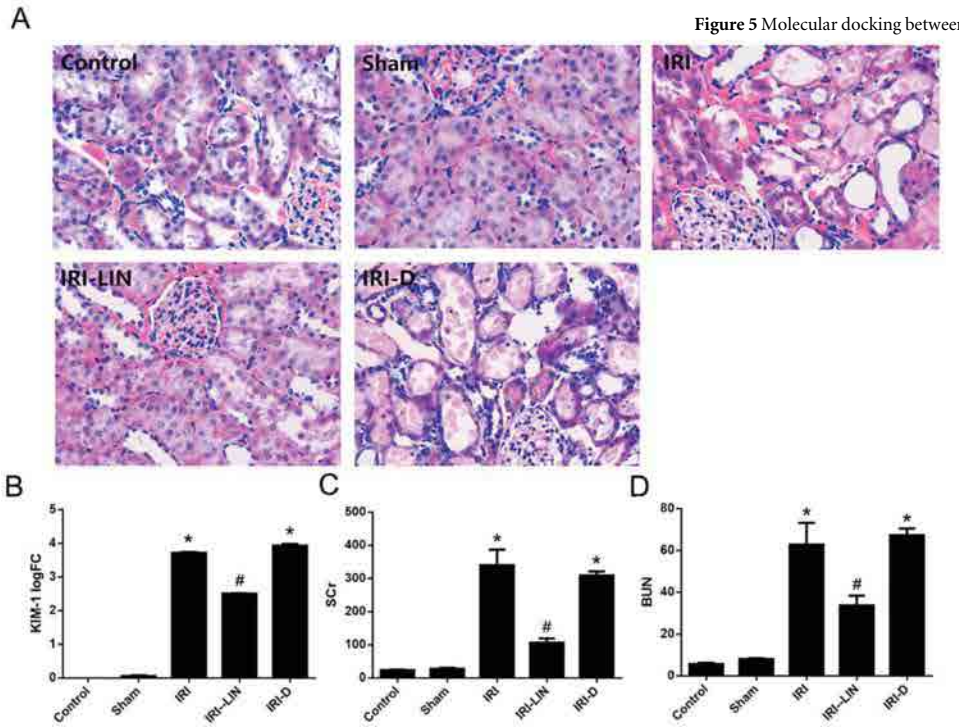


Figure 3 Volcanic plot of microarray data

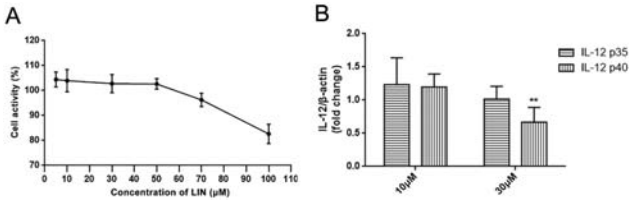


Figure 4 PPI networks and hub gene selection.

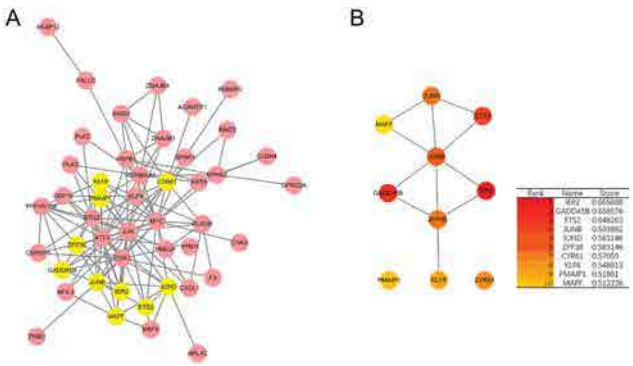


Figure 6 LIN contact domain of ETS2.

P0538 HYPERIN PREVENTS ISCHEMIC/REPERFUSION AKI VIA STK40

Yan Xu[1], Yue Zhang[1]

[1]*The Affiliated Hospital of Qingdao University, nephrology, P.R. China*

Background and Aims: Ischemia-reperfusion injury (IRI) is the outcome of an inflammatory process and tubular cell death that is triggered by undergoing a transient reduction or cessation of blood flow and following by reperfusion. Unresolved IRI can contribute to chronic kidney disease even death. Our aims is to investigate the protective effect of hyperin on ischemia-reperfusion renal injury (IRI) and its possible mechanism.

Method: ① The transcriptome chip data of multiple IRI models were selected from the NCBI GEO DateSets database and a number of key proteins that could participate in IRI were screened out (the fold increase was greater than 2 fold and was statistically significant). Network and transcript binding motif analysis was performed to determine the best binding protein. ② C57BL / 6J mice were selected and randomly divided into normal group, sham operation group, IRI group (bilateral renal pedicle clamping for 45min), hyperin + IRI group (50mg / kg.d per day, 7 days before surgery), DMSO + IRI group (7 days before the operation, the same amount of DMSO was administered to the stomach every day, and the operation was the same as AKI), with 6 rats in each group. Renal tissue and blood were collected 24 hours after operation for testing. ③ In vitro experiments, human proximal tubule epithelial cells (HK-2) were selected and divided into hypoxia 3, 6, 9, 12, 24, 36, and 48h for reoxygenation of 1, 3, and 6h respectively. Relevant indicators for RT-PCR detection were determined Optimal hypoxia time. The drug safe concentration was selected according to 0, 5, 10, 25, 50, 100, 200, 400 μg / ml hyperin pre-treatment for 12 hours, and the CCK8 reagent was added for 2 hours to measure the absorbance at 450 nm. The cells were randomly divided into normal group, hypoxia group, hypoxia + DMSO group, hypoxia + hyperin group, and related indexes were detected by RT-PCR and Western Blot. ④ Obtain the tertiary structure of the protein and the three-dimensional structure of the hyperin molecule from the RCSB Protein Data Bank website and the PubChem compound database, and use molecular docking technology to determine the proteins that can bind to hyperin using autodock software and analyze their binding ability.

Results: Bioinformatics analysis suggested that STK40 protein is one of the key factors of IRI and may be a target for preventing and treating diseases. In vivo experiments showed that compared with the normal group and the sham operation group, the levels of serum creatinine, blood urea nitrogen, and kim-1 in rats were significantly increased after AKI, and HE staining of pathological sections showed an increase in renal tubular injury scores. Significantly decreased ($P<0.05$); RT-PCR results showed that kim-1, caspase-3, NF-κB, IL-6, TNF-α increased significantly after AKI, STK40, Bcl2 / BAX decreased, and the above after hyperin The indicators changed in opposite directions ($P<0.05$). In vitro experiments: The best time for hypoxia is 24h hypoxia + 1h reoxygenation; compared with the control group, the drug concentration is <100 μg / mL and the cell proliferation activity rate is> 90%, so the hyperin concentration was selected as 50 μg / mL ($P < 0.05$); RT-PCR results showed that Hif1-α, caspase-3, NF-κB, IL-6, TNF-α significantly increased, and STK40, Bcl2 / BAX decreased compared with the normal group. After administration of hyperin, the above indexes changed in opposite directions ($P<0.05$).

Conclusion: In this study, using molecular docking technology and constructing IRI mice model, it was confirmed that hyperin can reduce IRI and exert a protective effect on IRI by inhibiting STK40 expression.

P0539

NICOTIFLORIN ATTENUATES RENAL ISCHEMIA/ REPERFUSION INJURY THROUGH REDUCING CELL APOPTOSIS

Lin Wang[1], Yan Xu[1]

[1]*The Affiliated Hospital of Qingdao University, Department of Nephrology, Qingdao, P.R. China*

Background and Aims: Renal ischemia/reperfusion (I/R) is the main cause for acute kidney injury, Nicotiflorin can ameliorate ischemia/reperfusion injury in other organs, just like in cerebral ischemic damage. Therefore, this article intends to explore whether Nicotiflorin has protective effects on renal tubular epithelial cell after ischemia-reperfusion. On the one hand, We use C57 mice to establish the Nicotiflorin group, DMSO group, AKI group, sham group and control group to investigate whether Nicotiflorin can ameliorate ischemia-reperfusion injury of kidney. In other hand, we use CCK8 to explore the optimal concentration of Nicotiflorin in renal tubular epithelial cells and find optimal hypoxia oxygenation time, in order to analysis the influence of Nicotiflorin. The results indicate that Nicotiflorin can alleviate ischemia-reperfusion injury by reducing apoptosis of renal tubular epithelial cells.

Method: In this study, we investigated the protective mechanism of Nicotiflorin on ischemic acute kidney injury by analyzing gene chip in patients with acute kidney injury and proving in vitro and in vivo experiments. The main methods are as follows: (1) Multiple nucleus ischemia-reperfusion model transcriptase data were selected from the NCBI GEO Datasets database and analyzed to screen out related proteins that may be involved in ischemia-reperfusion kidney injury; (2) The tertiary structure of Nicotiflorin and related proteins was obtained from the SWISS-MODEL database and the PubChem compound database. The molecular docking between protein and Nicotiflorin was performed using Autodock software, and the binding energy between Nicotiflorin and the selected protein was analyzed to determine Nicotiflorin binds to each other; (3) We set different groups, such as control group, sham group, AKI group, Nicotiflorin group and DMSO group in animals. The blood function was used to detect renal injury related function indicators 24 hours after modeling. Renal tissue samples were collected for real-time fluorescent RT-PCR, Western blotting and histopathological analysis; (4)Renal tubular epithelial cells were treated with different concentrations of Nicotiflorin, CCK8 was screened for the most appropriate concentration, and the hypoxic and reoxygenated cells were intervened at the concentration to explore the interaction between Nicotiflorin and the docking protein, and to observe the protective mechanism of Nicotiflorin on the kidney

Results:

1. 390 differential genes were obtained by microarray analysis of AKI gene chip; (2) Molecular docking results showed that Nicotiflorin binds to ATF3 protein most stably among dozens of proteins that may be involved in renal ischemia-reperfusion. It has a lower binding energy and a minimum binding energy of -9.2. (3) The kidney ischemia-reperfusion model in mice showed that the renal function of Nicotiflorin was significantly improved compared with the control group, mainly due to decreased serum creatinine, decreased expression of renal injury molecule-1 (KIM-1), and renal tubular injury score. While the apoptosis indicators were significantly reduced, which indicated that Nicotiflorin had protective effects on ischemic reperfusion injury; (4) ATF3 expression was significantly increased in renal ischemia-reperfusion injury compared with the control group, interference the protective effect of ATF3 on the kidney was significantly weakened by Nicotiflorin, indicating that Nicotiflorin exerts a protective effect on the kidney through ATF3.

Conclusion: Nicotiflorin binds to ATF3 and promotes the expression of Cyr61 through protein interactions to improve renal ischemia-reperfusion injury.

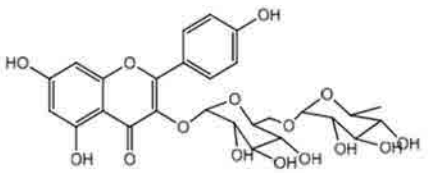


Figure1 Chemical structure of Nicotiflorin

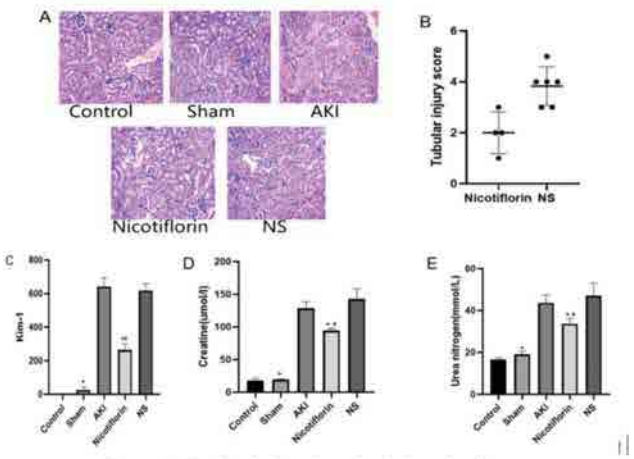


Figure 2. Histological and serological evaluation

Figure:

P0540

EFFECT OF MEMBRANE MATERIALS ON VANCOMYCIN, TEICOPLANIN AND LINEZOLID REMOVAL DURING CONTINUOUS RENAL REPLACEMENT THERAPIES: AN IN VITRO STUDY

Llaria Godi[1,2], Anna Lorenzin[1], Massimo De Cal[1,3], Claudio Ronco[1,2,3]

[1]International Renal Research Institute of Vicenza, San Bortolo Hospital, Vicenza, Italy, [2]University of Padova, Medicine, Padova, Italy and [3]San Bortolo Hospital, Nephrology, Dialysis and Transplantation, Vicenza, Italy

Background and Aims: In a continuous renal replacement therapy (CRRT) scenario, removal of anti-methicillin resistant Staphylococcus Aureus agents can be quantitatively important, thereby contributing to clinically relevant decreases in their plasma concentration during treatment. Extracorporeal elimination of antimicrobial agents is influenced by the dose and modality prescribed, as well as the sieving coefficient (SC) and adsorptive properties of the membrane used.The aim of this study was to document the specific SC and adsorptive capacity of three different membrane materials related to vancomycin, teicoplanin and linezolid.

Method: This in vitro study used a model of continuous veno-venous hemofiltration. 500 ml of whole blood from healthy donor spiked with one antibiotic under investigation was pumped (blood flow of 50 ml/min and ultrafiltrate flow of 10 ml/min) in a closed-circuit using polysulfone (PS), polymethylmethacrylate (PMMA) and polyacrylonitrile (PAN) membranes. Samples were collected from in-flow, out-flow and ultrafiltrate lines in a 360 min period. Antibiotic concentrations were measured to calculate SCs. Mass balance analysis was assessed to evaluate the adsorptive capacity of PS, PMMA and PAN membrane related to each antibiotic.

Results: The SCs were substantially affected by the hemodialyzers material in the case of Vancomycin, where PMMA membrane had higher SC (SC=0.89±0.01) compared to PAN (SC=0.79±0.02) and PS (SC=0.62±0.03) membranes. The effect of material was minor for Teicoplanin (Sc=0.12±0.05 for PS, Sc=0.17±0.05 for PMMA, Sc=0.19±0.00 for PAN) and no noticeable difference within hemodialyzers was found for Linezolid (Sc=0.92±0.03 for PS, Sc=0.95±0.01 for PMMA, Sc=0.95±0.00 for PAN). In terms of adsorptive capacity, PS and PMMA membranes showed higher interaction with Vancomycin and Teicoplanin compared with PAN membrane, while a small amount of Linezolid was adsorbed by all the three filters. The cumulative adsorbed amount of PS and PMMA of Teicoplanin were also clinically relevant (99.15 mg/m2 and 51.33 mg/m2 respectively) compared to PAN membrane (9.14 mg/m2).

Conclusion: PS, PMMA and PAN membranes behave differently in terms of sieving and adsorptive properties related to vancomycin, teicoplanin and linezolid. These differences may have a clinical influence on vancomycin and teicoplanin removal during CRRT, while linezolid variability during CRRT hasn't to be ascribed for membrane material.

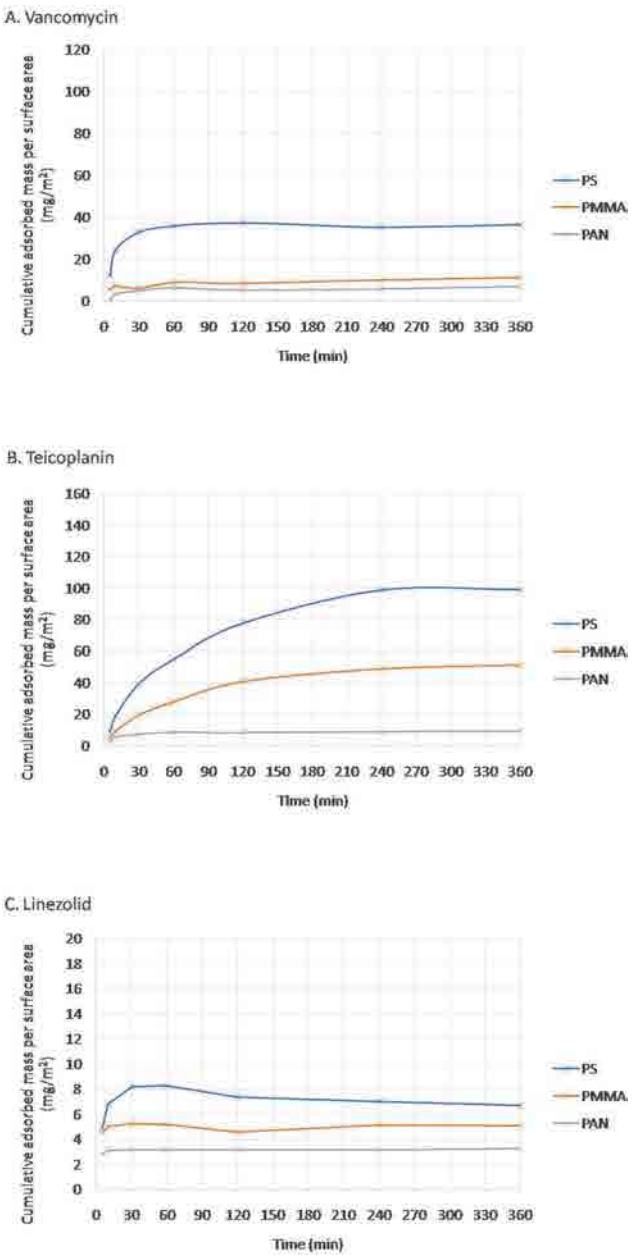


Figure:

P0541 KLOTHO IS INVOLVED IN EARLY AND LONG-TERM PROTECTION AGAINST RHABDOMYOLYSIS ASSOCIATED AKI

Melania Guerrero Hue[1], Cristina García Caballero[1], Alfonso Rubio Navarro[2], Juan Manuel Amaro Villalobos[2], Raul Rodrigues Diez[2], Carmen Herencia[2], Cristina Vazquez Carballo[2], Lucas Opazo-Ríos[2], Gema Ruiz-Hurtado[3], Juan. R Muñoz-Castañeda[4], Mariano Rodriguez[4], Pablo Cannata-Ortiz[5], Manuel Praga[3], Alberto Ortiz[2], Jesus Egido[2,6], Juan Antonio Moreno[1,7]

[1]Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Department of Cell Biology, Physiology and Immunology, Córdoba, Spain, [2]Fundación Instituto de Investigaciones Sanitarias-Fundación Jiménez Díaz, Renal, Vascular and Diabetes Research Lab, [3]12 de Octubre Hospital, Department of Nephrology, Madrid, Spain, [4]Instituto Maimónides de Investigación Biomédica de Córdoba/Hospital Universitario Reina Sofia/Universidad de Córdoba, Servicio de Nefrología (Red in Ren), GC13, Metabolismo del calcio, Calcificación Vascular, Córdoba, Spain, [5]Fundación Instituto de Investigaciones Sanitarias-Fundación Jiménez Díaz, Pathology Department, Madrid, , [6]Centre of Biomedical Research in network of Diabetes and Metabolic disease associated (CIBERDEM) and [7]Centre of Biomedical Research in network of Cardiovascular disease (CIBERCV)

Background and Aims: Rhabdomyolysis is characterized by the breakdown of the skeletal muscle and the subsequent myoglobin (Mb) release into the bloodstream. A common complication of this syndrome is acute renal injury (AKI). Once filtered by the kidney, Mb causes oxidative stress, inflammation and tubular cell death. There is no specific treatment for rhabdomyolysis-AKI, so it is crucial a better understanding of this syndrome to identify new therapeutic targets. Klotho is an anti-aging protein mostly expressed by the kidney. In addition to its functions in the regulation of mineral metabolism, Klotho protects from AKI-harmful effects. However, no previous studies analyzed the role of Klotho in rhabdomyolysis.

Method: We performed a pre-clinical model of rhabdomyolysis in C57BL/6J mice (male, 12 weeks old, n=30) by intramuscular injection of 10 ml/kg of 50% glycerol ($\geq$99.5% m/v). Mice were sacrificed 3 and 6 hours or 1, 3, 7 and 30 days after glycerol administration. To evaluate to beneficial effect of Klotho in rhabdomyolysis, C57BL/6J mice were injected intraperitoneally with 0.1 mg/kg recombinant mouse Klotho (1819-KL, R&D Systems), or vehicle (PBS) 30 minutes before and 1, 3 and 5 days after glycerol injection. Blood, urine and renal samples were collected to analyze renal function, Klotho/FGF23 levels, oxidative stress, inflammation, fibrosis and cell death, all of them pathological processes affecting Klotho expression. In addition, we carried out studies in murine tubular cells (MCTs) to study the molecular mechanisms involved in Klotho regulation.

Results: Our results indicate that rhabdomyolysis induces an early decrease in Klotho renal mRNA and protein expression as well as Klotho serum levels. Klotho levels decreased in line with augmentation of creatinine concentration, kidney inflammation (CCL2 and IL-6 mRNA expression) and tubular injury marker NGAL. Moreover, patients with rhabdomyolysis-AKI also showed lower plasma Klotho levels and increased FGF23 plasma concentration than age-matched healthy individuals. Renal klotho protein expression remained reduced one month after rhabdomyolysis-induction, in line with long term renal fibrosis and pro-inflammatory macrophage accumulation ($F4/80^+$ cells). Exogenous recombinant Klotho administration ameliorated renal function and reduced rhabdomyolysis-mediated tubular cell death oxidative stress (4-HNE staining) and tubular injury 24h after glycerol injection. In the same line, Klotho administration during AKI development reduced long term renal fibrosis and macrophage infiltration one month later. Antioxidant therapies with N-acetylcysteine (NAC) and sulforaphane, a potent Nuclear factor erythroid-2-related factor 2 (Nrf2) inducer, reduced Mb-mediated Klotho decrease in cultured tubular cells. Inhibition of TNF-α and IL-6 with infliximab and tocilizumab, respectively, also reverted Mb-mediated Klotho decrease. Inhibition of the inflammatory NFkB and p38 pathways also prevented Mb-mediated Klotho reduction.

Conclusion: Our findings are the first to demonstrate decreased renal and soluble Klotho levels not only in the early phases of rhabdomyolysis-induced AKI, but also when renal function was recovered, indicating that long-term consequences of AKI, such as inflammation and fibrosis, are also involved in Klotho downregulation. In addition, our results also indicate that Klotho administration may be a potential strategy to decrease rhabdomyolysis- long term negative effects.

P0542

EVALUATION OF BLOOD CELL ADHESION AND SOLUTE REMOVAL PERFORMANCE BY AN EX VIVO EXPERIMENT OF A POLYSULFONE HEMOFILTER USING AN NV POLYMER MEMBRANE FOR CONTINUOUS RENAL REPLACEMENT THERAPY

Yoshitaka Kurihara[1], Shunichi Ueki[1], Kozue Kobayashi[1], Kokubo Kenichi[1], Hirosuke Kobayashi[1], Masaru Kubota[1]

[1]*Kitasato University Graduate School of Medical Sciences, Sagamihara, Japan*

Background and Aims: Since hemofilters used for continuous renal replacement therapy (CRRT) come in prolonged contact with blood during treatment, clotting and cell adhesion induced by contact of blood with the membrane often occur, increasing the risk to the patient and burden on the staff. Suppressed platelet adhesion and better biocompatibility have been reported with the use of a dialysis membrane whose surface has been modified with an NV polymer in patients on maintenance hemodialysis. Therefore, it may be advantageous to use the NV membrane as a hemofilter for CRRT. In the present study, we evaluated the solute removal performance change and blood cell adhesion on the NV membrane after it comes in contact with blood, to clarify the characteristics of the NV membrane for long-time use.

Methods: A new polysulfone membrane containing the NV polymer (SNV) and a conventional polysulfone membrane (SHG) were used for the *ex vivo* blood filtration experiment. To compare the solute removal performance change and blood cell adhesion after blood comes in contact with the membranes, porcine blood collected from a single animal was divided into two portions, and a 24-hour of continuous hemofiltration (CHF) experiment was performed. The circulation conditions were as follows; blood flow rate, 100 mL/min; filtrate flow rate, 20 mL/min; heparin dose adjusted as appropriate to maintain the activated clotting time from 300 to 400 sec during the experiment. We evaluated the time-courses of the transmembrane pressure (TMP) and pressure drop at the hemofilter and the change in the sieving coefficients of dextran of different molecular weights (molecular weight cutoff curve) before and after the experiment, and blood cell adhesion. The amount of blood cell adhesion was evaluated based on the hemoglobin content and lactate dehydrogenase (LDH) activity in the eluate from the residual blood clots on the hemofilter 24 hours after the CHF experiment.

Results: The changes in the TMP and the pressure drop were significantly lower with the use of SNV as compared to SHG ($n = 9$, $p < 0.01$). From the molecular weight cutoff curves before and after the experiment, the molecular weights when the sieving coefficient was 0.1 to 0.4, which reflect the pore size of the pores through which relatively small molecules can pass, decreased to a lower extent after blood contact with SNV as compared to SHG ($n = 3$, SC = 0.1-0.3, $p < 0.05$; SC = 0.4, $p < 0.01$).The hemoglobin content and LDH activity in the blood clots adhering to the membrane after the experiment were significantly lower in SNV as compared to SHG ($n = 9$; Hb, $p < 0.01$; LDH, $p < 0.05$), indicating that blood cell adhesion on SNV was less pronounced than that on SHG.

Conclusion: SNV suppressed the increase in the TMP and also the pressure drop, allowed a high rate of solute removal performance to be maintained, and suppresses blood cell adhesion to a greater extent as compared to the conventional polysulfone membrane.

P0543 **NQO1ATTENUATES RENAL INJURY BY RENAL ISCHEMIA REPERFUSION OF MICE.**

Kang Wook Lee[1], Jin Young Jeong[2], DAE EUN CHOI[1], Ki Ryang Na[1], Haeri Kim[1], Young Rok Ham[1], Wonjung Choi[1], Yoon-Kyung Chang[3], JAE WAN JEON[1]

[1]Chungnam National University, Nephrology, Daejeon, Korea, Rep. of South, [2]Chungnam National University, Department of Medical Science, Daejeon, Korea, Rep. of South and [3]The Catholic University of Korea, Daejeon Saint Mary Hospital, Nephrology, Daejeon, Korea, Rep. of South

Background and Aims: Ischemia-reperfusion (I-R)-induced reactive oxygen species (ROS) are thought to be a major factor in the development of acute renal injury by promoting the initial tubular damage. NAD(P)H:quinone oxidoreductase 1 (NQO1) is a well-known antioxidant protein that regulates ROS generation. We investigate whether NQO1 modulates the renal I-R injury.

Method: C57BL/6N NQO1-deficient mice (NQO1/) were generated. Mice were sacrificed at 4, 12, 24, and 48 h after the surgical procedure. I-R was performed using vascular clamp for 30min. We analyzed renal function, oxidative stress, and tubular apoptosis after I-R injury.

Results: NQO1/ mice showed increased blood urea nitrogen and creatinine levels, tubular damage, oxidative stress, and apoptosis. In the kidneys of NQO1/ mice, the cellular NADPH/NADPþ ratio was significantly higher and NOX activity was markedly higher than in those of NQO1þ/þ mice. The activation of NQO1 by β-lapachone (βL) significantly improved renal dysfunction and reduced tubular cell damage, oxidative stress, and apoptosis by renal I-R. Moreover, the βL treatment significantly lowered the cellular NADPH/NADPþ ratio and dramatically reduced NOX activity in the kidneys after IRI. From these results, it was concluded that NQO1 has a protective role against renal injury induced by I-R and that this effect appears to be mediated by decreased NOX activity via cellular NADPH/NADPþ modulation.

Conclusion: NQO1 activation might be beneficial for ameliorating renal injury induced by I-R.

P0544 **INHIBITION OF 15-HYDROXYPROSTAGLANDIN DEHYDROGENASE (15-PGDH) PROTECTS MICE AGAINST CONTRAST-INDUCED ACUTE KIDNEY INJURY.**

Byeong Woo Klm[1], Sun hee Kim[2], Ki beom Bae[2]

[1]Haeundae Bumin Hospital, Nephrology, Busan, Korea, Rep. of South and [2]Paik Hospital, General surgery, Busan, Korea, Rep. of South

Background and Aims: Although the mechanism of contrast-induced acute kidney injury (CI-AKI) is not fully known, the imbalance of vasoconstrictive and vasodilative mediators plays a major role. Prostaglandin E2 (PGE2) is one of the vasodilators involved in this process. Inhibition of 15-hydroxyprostaglandin dehydrogenase (15-PGDH) causes elevation of PGE2 level in tissue by delaying the rapid degradation of PGE2 by the enzyme. We tested the hypothesis that the 15-PGE2 inhibitor would protect against CI-AKI in a mouse model and attempted to elucidate the mechanism involved.

Method: 10-week aged male C57/BL6 Mice were injected with 10gI/kg of iodixanol by tail vein. Renal blood flow measurement, right nephrectomy, and blood sampling were taken at 48 hours after iodixanol injection. The 15-PGDH inhibitor was injected before and after iodixanol administration. Plasma creatinine, NGAL, KIM-1 were measured as biomarkers for renal function. Histological evaluation was analyzed by the necrosis scoring system and TUNEL assay. Arteriolar area of outer medulla was analyzed by α-smooth muscle actin stain. Renal blood flow was measured by the non-invasive laser doppler.

Results: Plasma creatinine (1.94±0.75 vs 1.11±0.44 mg/dL, p=0.005), NGAL (299.7±115.87 vs 140.4±76.56 ng/mL, p=0.004), and KIM-1 (2.09±2.34 vs 0.43±0.89 ng/mL, p=0.024) levels were significantly lower when the 15-PGDH inhibitor was injected before and after iodixanol administration than the vehicle group. But no significant renal protective effect was shown when the 15-PGDH inhibitor was injected before or after iodixanol administration. The 15-PGDH inhibitor administration before and after iodixanol injection showed a significantly wider renal arteriolar area (683.63±248.46 vs 1132.97±357.46 μm^2, p=0.039) and larger renal blood flow (360.0±49.72 vs 635.1±27.20, p=0.011) than vehicle administration.

Conclusion: The 15-PGDH inhibitor has a renal protective effect against CI-AKI in mice by increasing renal blood flow when injected intravenously before and after iodine contrast media administration.

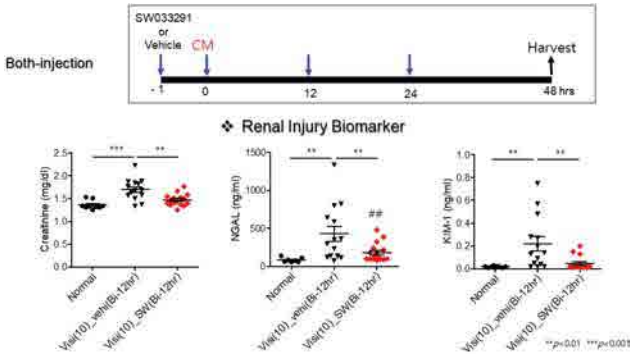


Figure 1. Renal injury biomarkers after injection of the 15-PGDH inhibitor in CI-AKI model and control

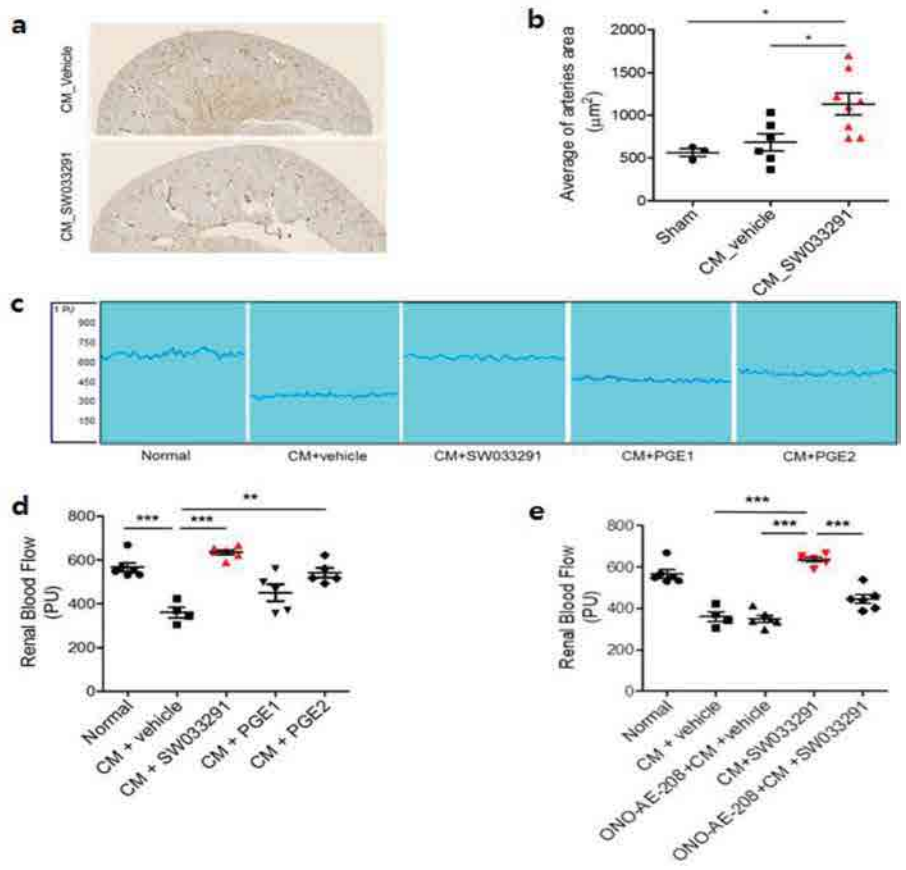


Figure 2. Renal arteriolar area and renal blood flow after injection of the 15-PGDH inhibitor in CI-AKI model and control

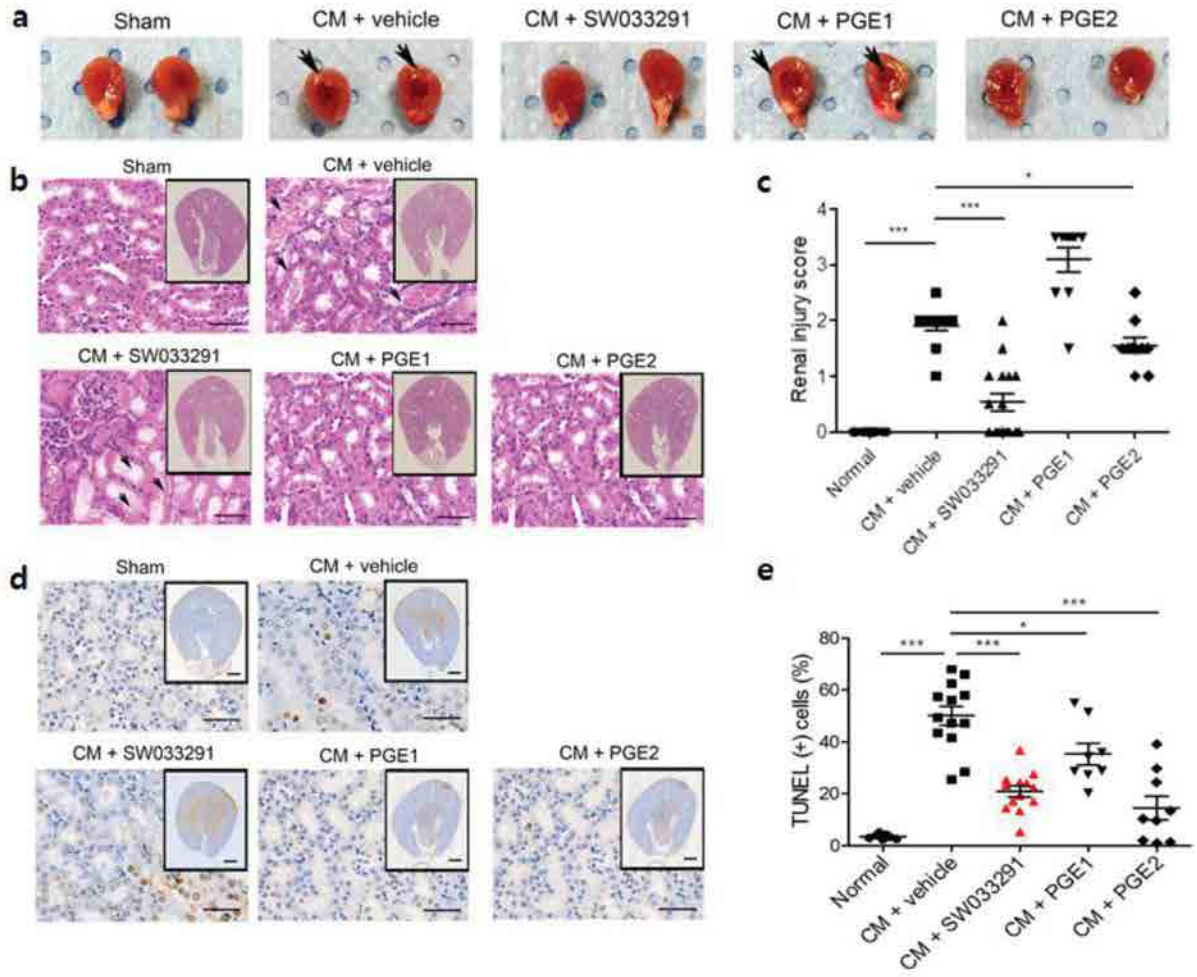


Figure 3. Histologic renal injury score and TUNEL assay in study groups.

P0545 **DPP-4 INHIBITOR ATTENUATED RENAL VASOCONSTRICTION FOLLOWING ISCHEMIA-REPERFUSION INJURY IN CIRRHOTIC RATS**

CHIAO-LIN CHUANG[1,2], Hui-Chun Huang[2,3]

[1]Taipei Veterans General Hospital, Medicine, Taipei, Taiwan, R.O.C. and [2]National Yang-Ming University, Medicine, Taipei, Taiwan, R.O.C.

Background and Aims: Cirrhotic patients may develop gastroesophageal varices to cope with portal hypertension. Annual risk of variceal bleeding among small and large varices is 5% and 15%, respectively. Bleeding from varices is a medical emergency and is associated with a high morbidity and mortality. In those who survive the initial bleeding event, the risks of further bleeding and other serious complications remain high, such as hypotension and ischemia-reperfusion injury. Ischemia-reperfusion injury is a leading cause of acute kidney injury. In patients with advanced liver cirrhosis, variceal bleeding associated hypotension and ischemia-reperfusion injury may activated endogenous vasoconstrictors, leading to severe renal vasoconstriction and subsequent renal failure (so called hepatorenal syndrome). There was not effective treatment yet.

Dipeptidyl peptidase-4 (DPP-4) inhibitors, a new class of oral hypoglycemic agents, have shown potential pleiotropic effects, such as anti-inflammatory and anti-oxidant properties. Previous studies reported that inhibition of DPP-4 could attenuate the development of ischemia-reperfusion injury in kidney. Cumulated evidences indicates that DPP-4 inhibitors could attenuate the endothelin-1 induced contraction and increase endothelial-dependent vasodilation related to activation of endothelial nitric oxide synthase and increased production of nitric oxide. In addition, DPP-4 inhibitors may suppress inflammation and fibrosis in the kidneys independently of glycemic control. The aim of this study is to delineate the effect of DPP-4 inhibitors in renal vascular reactivity of cirrhotic rats following ischemia-reperfusion injury.

Method: Male Sprague-Dawley rats weighing 240-270 g were used for experiments. Secondary biliary cirrhosis were created by common bile duct ligation (CBDL). Rats receiving sham surgery (SHAM) were used as the control group. Linagliptin (3 mg/kg/day) or distilled water (DW) was administered via oral gavage since the 1st day throughout the 28th day after surgery. On the 29th day, all rats were randomized to control group or ischemia-reperfusion injury. Bilateral renal pedicles of rats in the ischemia-reperfusion injury group were clamped for 45 minutes with microvascular clamps. Thereafter, the clamps were removed and reperfusion was allowed by visual control. After 60 minutes of reperfusion period, kidneys were perfused in situ via right renal artery for continuous monitoring of renal perfusion pressure using a non-recirculating system.

Results: There was no significant difference in mean arterial pressure, heart rate, and portal pressure between DW and DPP-4 inhibitor treated groups in both SHAM and CBDL rats. Ischemia-reperfusion injury enhanced renal vascular reactivity to endothelin-1 in both SHAM ($p = 0.027$) and CBDL ($p = 0.016$) rats, implying renal vasoconstriction. Compared with corresponding DW-treated rats, DPP-4 inhibitor treatment abrogated renal hyper-reactivity following ischemia-reperfusion injury in BDL rats ($p = 0.038$), but not in SHAM rats ($p = 0.17$).

Conclusion: We concluded that DPP-4 inhibitors may attenuate the development of renal vasoconstriction following ischemia-reperfusion injury in cirrhotic rats. The potentially mechanisms remained to be elucidated.

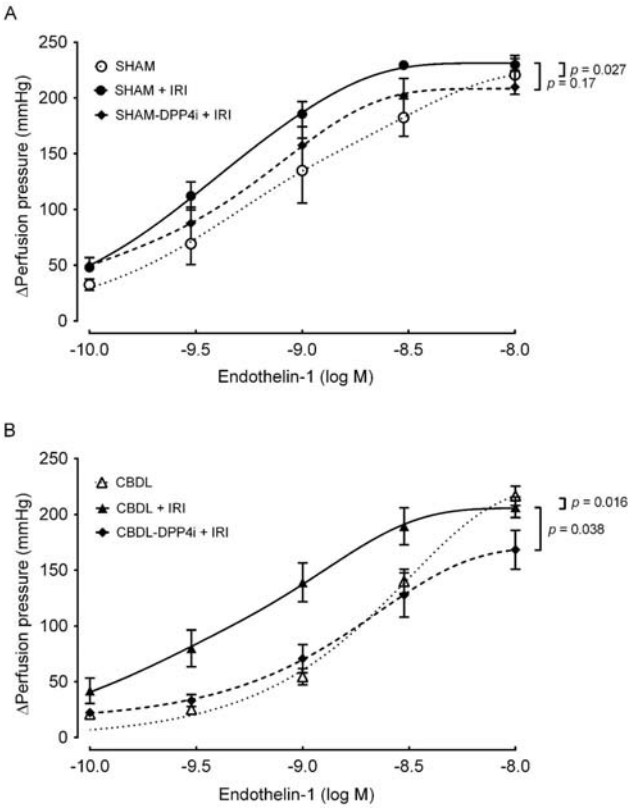


Figure:

P0546

EARLY, BUT NOT LATE, CONTRALATERAL NEPHRECTOMY OVERCOMES PROGRESSION TO CKD AFTER UNILATERAL ISCHEMIC INJURY

Lies Moonen[1], Cristina Cuesta-Apausa[2], Francisco J. Lopez-Hernandez[2], Carlos Martinez Salgado[2], Patrick D'Haese[1], Benjamin Vervaet[1]

[1]University of Antwerp, Laboratory of Pathophysiology, Antwerpen, Belgium and [2]Instituto de Investigación Biomédica de Salamanca, Physiology and Pharmacology, Salamanca, Spain

Background and Aims: It is increasingly clear that acute kidney injury (AKI) can result in the development of chronic kidney disease (CKD) in humans. Murine renal unilateral ischemia-reperfusion injury (UIRI) models this AKI-to-CKD progression in the injured kidney in the presence of its healthy counterpart (Le Clef et al, Plos One 2016). In mice, we and others demonstrated that contralateral nephrectomy (Nx), when performed shortly after UIRI (i.e. 3 days), is able to significantly attenuate the progression to CKD. Although non-translatable, Nx can be considered an experimental therapeutic intervention that incites inherent physiological recovery mechanisms in the kidney. Here, we investigate in rats to what extent contralateral Nx is able to attenuate or revert CKD progression when performed well beyond the acute injury phase, i.e. with increased Nx delay time after UIRI.

Method: AKI was induced in male Wister rats by left UIRI for 60 min at 35°C core body temperature after which contralateral Nx was performed 3, 10 or 20 days later, or no Nx was performed. Control animals underwent sham-UIRI and sham-Nx 3 days later. Renal function was assessed by serum creatinine and transcutaneous GFR measurement 24h and 72h after Nx and weekly thereafter. Rats were euthanized 11 weeks after Nx. Kidneys were weighed and histology was evaluated by PAS stain for overall morphology and Sirius Red stain for interstitial fibrosis.

Results: When no Nx was performed, renal function of the injured kidney decreased 44% compared to control animals at week 11. Nx at day 3 induced full functional recovery from week 5 after Nx on, whereas Nx at day 10 and 20 both lead to a persistent 20% loss of renal function at week 9 after Nx ($p<0.05$). Nx at day 3 was able to attenuate renal atrophy and fibrotic tubulointerstitial expansion. Nx at day 10 and 20 were less efficient and led to 1.6 ($p>0.05$) and 2.6 ($p<0.05$) fold increase of tubulointerstitial area compared to controls. Nx at day 3 and 10 induced a significant increase in renal mass-to-body weight ratio compared to control from 2.9 ± 0.1 mg/g (control) to 4.6 ± 0.4 mg/g (day 3) and 4.8 ± 0.3 mg/g (day 10) respectively. When Nx was performed at day 20 or no Nx was performed, renal mass-to-body weight ratio did not differ significantly from control animals, however, parallel with renal function, histopathology was considerably worse.

Conclusion: Early contralateral Nx after UIRI rescues renal function and morphology, whereas delayed Nx does not allow full recovery of the injured kidney. There was no additional functional loss when Nx was performed on day 20 versus day 10, though, histopathology aggravated. These results imply that a damaged kidney loses its intrinsic (compensatory) recovery potential over time and that an early intervention is crucial for averting CKD outcome after AKI.

P0547

THE DELETION OF AKT1 ATTENUATES RENAL FIBROSIS AND TUBULAR EPITHELIAL-MESENCHYMAL TRANSITION DURING ACUTE KIDNEY INJURY TO CHRONIC KIDNEY DISEASE PROGRESSION

Byung Min Ye[1], Il Young Kim[1], Min Jeong Kim[1], Soo Bong Lee[1], Dong Won Lee[1], Sang Heon Song[2], Eun Young Seong[2]

[1]Pusan National University Yangsan Hospital, Yangsan, Korea, Rep. of South and [2]Pusan National University Hospital, Korea, Rep. of South

Background and Aims: Acute kidney injury (AKI) is an underestimated, yet important risk factor for the development of chronic kidney disease (CKD), which is characterized by the tubulointerstitial fibrosis and tubular epithelial-mesenchymal transition (EMT). Akt has been reported to be involved in renal fibrosis and EMT. Thus, we investigated the role of Akt1, one of the three Akt isoforms, in the murine model of AKI to CKD progression.

Method: We subjected the wild type and *Akt1*$^{-/-}$ mice to unilateral ischemia-reperfusion injury (UIRI). UIRI was induced by clamping the left renal artery for 30 min followed by reperfusion. After 6 weeks of UIRI, the renal fibrosis and EMT were assessed by histology, immunohistochemistry, and western blot.

Results: After 6 weeks after UIRI, we found that Akt1, not Akt2 or Akt3, was activated in UIRI-kidney. The tubulointerstitial fibrosis was significantly alleviated in *Akt1*$^{-/-}$ mice compared with the wild type (WT) mice. Besides, the deletion of Akt1 decreased the expression of the vimentin and α-SMA and increased the expression of E-cadherin, indicating the suppression of tubular EMT. However, there was no difference in the activity of TGF-β1/Smad signalling, which is the potent inducer of renal fibrosis and EMT, between WT mice and *Akt1*$^{-/-}$ mice. The deletion of Akt1 also increased the GSK-3β activity and decreased the expression of β-catenin, Snail, and twist1.

Conclusion: Our findings demonstrate that the deletion of Akt1 attenuates the renal fibrosis and tubular EMT independently of TGF-β1/Smad signalling during the AKI to CKD progression. Akt1 may be the therapeutic target against the AKI to CKD progression.

P0548

PAC-MEDIATED AKI PROTECTION IS CRITICALLY MEDIATED BUT DOES NOT EXCLUSIVELY DEPEND ON CELL-DERIVED MICROVESICLES

Daniel Patschan[1], Katrin Schwarze[2], Oliver Ritter[1], Susann Patschan[1], Gerhard Anton Müller[2]

[1]MHB Theodor Fontane, Neuruppin, Germany and [2]Universitätsmedizin Göttingen, Göttingen, Germany

Background and Aims: Acute Kidney Injury (AKI) significantly worsens the prognosis of hospitalized patients. In recent years, cell-based strategies have been established as reliable option for improving AKI outcomes in experimental AKI. Own studies focused on so-called Proangiogenic Cells (PACs). Mechanisms that contribute to PAC-mediated AKI protection include production / secretion of extracellular vesicles (EV). In addition, the cells most likely act by paracrinic processes (secretome). The current study evaluated whether AKI may be preventable by the administration of either PAC-derived EV and / or the secretome alone.

Method: AKI was induced in male C57/Bl6N mice (8-12 weeks) by bilateral renal ischemia (IRI - 40 minutes). Syngeneic murine PACs were stimulated with either melatonine, Angiopoietin-1 or -2, or with Bone Morphogenetic Protein-5 (BMP-5) for one hour, respectively. The four mediators were chosen since previous own studies showed improved PAC-mediated AKI protection after cell preconditioning with these substances. PAC-derived EV and the vesicle-depleted supernatant were subsequently collected and i.v. injected post-ischemia. Mice were analyzed 48 hours later.

Results: IRI induced significant kidney excretory dysfunction as reflected by higher serum cystatin C levels. The only measure that improved AKI was the injection of EV, collected from native PACs. The following conditions worsened post-ischemic renal function even further: EV+Ang-1, EV+BMP-5, EV+melatonin, and EV+secretome+Ang-1.

Conclusion: Together, our data show that PAC-mediated AKI protection substantially depends on the availability of cell-derived EV. The secretome, either collected from native or preconditioned cells does not prevent mice from ischemia-induced dysfunction. However, since previous data showed improved AKI-protection by PACs after cell preconditioning with certain mediators (Ang-1 and -2, melatonine, BMP-5), other than exclusively vesicle-dependent mechanisms must be involved in PAC-mediated AKI protection. We suggest, that the mere presence of intact cells in the post-ischemic tissue is necessary for improving functional and structural outcome parameters under certain conditions.

P0549 ESSENTIAL ROLES OF TESTOSTERONE IN MALE KIDNEY MATURATION AND REPAIR AFTER INJURY

Yuki Sato[1], Eiichiro Uchino[1], Yuichiro Kitai[1], Akiko Oguchi[1], Motoko Yanagita[1]

[1]*Graduate School of Medicine Kyoto University, Department of Nephrology, Kyoto, Japan*

Background and Aims: The newborn kidneys are structurally and functionally immature. They mature after birth to adapt to extra-uterine life, yet the comprehensive changes of the kidney have not been defined. We investigated the structural and functional changes in the kidney after weaning and examined the effect of testosterone in this maturation process in male mice.

Method: We performed phenotypic analysis of male mouse kidneys as well as those subjected to castration utilizing a combination of histological analysis, bulk transcriptome analysis, charged metabolite analysis by CE-TOFMS and brush border membrane vesicles LC-MS/MS analysis.

Results: Bulk transcriptome analysis of postnatal 3 and 8 week male kidneys showed the gene sets enriched in 8w included those associated with metabolic process and transporters in proximal tubule, and structural analysis revealed proximal tubule elongation and hypertrophy in 8 weeks. Most differentially expressed genes (DEGs) identified above were induced between postnatal day 28 and 40, a period of testosterone surge, and were closely correlated with DEGs between adult male and female kidneys. These structural and gene expression changes during maturation were mostly cancelled by castration before testosterone surge. Proximal tubules expressed androgen receptor, and some of these DEGs were upregulated or downregulated by the administration of testosterone in cultured proximal tubules. Consistent results with DEGs were also confirmed at protein levels and related metabolites in vivo. For instance, induction of cystine transporter SLC7A13 expression as well as the increase in cysteine and cysteine-glutathione disulphide-Divalent in the kidney were confirmed during this period. Fatty acid β-oxidation enzymes were also increased during this period. Some of the down-regulated genes across puberty were reactivated after injury and returned to the basal levels with repair.

Conclusion: Proximal tubules are the main site of maturation after weaning, and acquire the abilities to absorb and metabolize a variety of filtered substances and to increase energy metabolism, which were mainly driven by testosterone.

P0550

ISCHEMIC PRECONDITIONING ATTENUATES RENAL ISCHEMIA-REPERFUSION INJURY THROUGH ACTIVATING THE NRF2/HO-1 PATHWAY ENHANCED AUTOPHAGY

Jeong Kye Hwang[1], HyunSu Choi[2], Mi-hyeong Kim[3]

[1]Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Transplant surgery & vascular surgery, Seoul, Korea, Rep. of South, [2]The Catholic University of Korea Daejeon St. Mary's Hospital, clinical research center, Daejeon, Korea, Rep. of South and [3]Eunpyeong St. Mary hospital, Seoul, Korea, Rep. of South

Background and Aims: Ischemic preconditioning (IPC), which is a brief and nonlethal episode of ischemia, confers protection against subsequent ischemia-reperfusion (I/R) through the up-regulation of endogenous protective mechanisms. Recent studies have reported that the activation of autophagy is associated with IPC. However, the underlying mechanisms still need to be determined. In this study, we investigated the role of IPC in renal I/R injury and demonstrated that IPC could ameliorate renal I/R injury by activating the Nrf2/HO-1 pathway and induction of autophagy.

Method: In order to gain insights into IPC–induced alterations at the cellular level, an in vitro model for IPC was designed using the human proximal tubule epithelial cell line HK-2. In vitro I/R was induced by layering mineral oil (for 60 min) over a thinfilm of media covering the cells followed by 120 min of reperfusion in normal media. IPC was performed by a 10-min period of incubation of cells under mineral oil followed by a 30-min recovery period prior to the 120 min reperfusion. To further determine the role of autophagy in IPC-induced renoprotection, the cells were treated with bafilomycin A1 (200 nM), prior to I/R injury. In a renal I/R injury model, mice were subjected to 30 min of renal ischemia followed by 24 h of reperfusion. IPC was produced by 5 min of ischemia followed by 10 min of reperfusion prior to sustained ischemia.

Results: We found that IPC significantly attenuated I/R-induced kidney injury and suppressed oxidative stress and inflammatory responses. IPC also increased LC3-II and decreased SQSTM/p62 and cleaved caspase-3 during renal I/R injury, as well as increased the number of intracellular double-membrane vesicles in injured renal cells. IPC-induced renal protection was efficiently attenuated by pretreatment with Bafilomycin A1 (0.3 mg/kg, IP). Pretreatment with IPC also dynamically affected the expression of Nrf2/HO-1 signaling components. The beneficial effects of IPC were abolished by Brusatol (2 mg/kg, IP), potent inhibitors of Nrf2. Moreover, the Nrf2 agonist t-BHQ (50 mg/kg, IP) showed similar activity as IPC.

Conclusion: In summary, the present study shows that Nrf2 plays a critical role in regulating the HO-1 production induced by I/R. Also, upregulation of Nrf2 expression might represent one of the major mechanisms whereby IPC confers protection against I/R-induced kidney injury. The beneficial effects of IPC could be attributed to its anti-oxidative stress and anti-inflammatory properties

P0551

THE EFFECTS OF HYPERBARIC OXYGEN PRECONDITIONING AND APOCYNIN TREATMENT IN POSTISCHEMIC ACUTE KIDNEY INJURY INDUCED IN SPONTANEOUSLY HYPERTENSIVE RATS

Sanjin Kovacevic[1], Milan Ivanov[2], Zoran Miloradovic[2], Predrag Brkic[3], Una-Jovana Vajic[2], Maja Zivotic[4], Rada Jeremic[3], Nevena Mihailovic-Stanojevic[2], Djurdjica Jovovic[2], Danijela Karanovic[2], Jelena Nesovic - Ostojic[1]

[1]Faculty of Medicine, University of Belgrade, Department of Pathophysiology, Belgrade, Serbia, [2]Institute for Medical Research, University of Belgrade, Department of Cardiovascular Physiology, Belgrade, Serbia, [3]Medical Faculty, University of Belgrade, Department of Medical Physiology, Belgrade, Serbia and [4]Medical Faculty, University of Belgrade, Department of Pathology, Belgrade, Serbia

Background and Aims: Acute kidney injury (AKI) is associated with significant in-hospital morbidity and mortality, particularly in those admitted to the Intensive care units, where mortality rates may exceed 50%. Besides increased mortality rates, there are chronic consequences that carry high risk of developing or exacerbating chronic kidney disease and accelerated development of the end-stage renal disease. Renal ischemia/reperfusion injury is a common cause of AKI and hypertension might contribute to the increased incidence of AKI. The purpose of this study was to investigate the effects of combined hyperbaric oxygen (HBO) preconditioning and apocynin treatment on kidney hemodynamics, function and structure in spontaneously hypertensive rats (SHR) after renal ischemia reperfusion injury.

Method: Male SHR were randomly selected in three experimental groups: sham-operated group (SHAM, n=9), AKI control group (AKI, n=11) and AKI group with HBO preconditioning and apocynin treatment (AKI+APO+HBO, n=13). HBO preconditioning was performed by exposing to pure oxygen (2.026 bar) twice a day for two consecutive days for 60 minutes and day before AKI induction. All surgical procedures were performed in anaesthetized rats and AKI was induced by removal of the right kidney and atraumatic clamp occlusion of the left renal artery for 45 minutes. NADPH oxidase inhibitor, apocynin (40 mg/kg b.m., intravenously) was applied as a bolus injection 5 minutes before clamp removal. All hemodynamic parameters were measured 24 hours after reperfusion. After hemodynamic measurements, blood samples were collected and used for further analysis. Animals were sacrificed by pentobarbital overdose injection. Kidney tissue was removed and then prepared for histological examination.

Results: AKI significantly increased renal vascular resistance (RVR, $p<0.001$) and reduced renal blood flow (RBF, $p<0.001$), which were significantly improved in group with HBO preconditioning with apocynin treatment (RVR, $p<0.05$; RBF, $p<0,01$). AKI induction significantly increased plasma creatinine ($p<0.001$), urea ($p<0.001$), phosphate ($p<0.001$) levels. Remarkable improvement, with decrease in creatinine ($p<0.001$), urea ($p<0.01$) and phosphate ($p<0.001$) levels was observed in treated group. While AKI induction significantly increased plasma KIM – 1 levels ($p<0.001$), HBO preconditioning with apocynin treatment decreased its levels ($p<0.05$). Considering renal morphology, in SHAM operated rats, normal morphology of glomeruli, tubulointerstitium, and blood vessels were observed including rare kidney specimens with a few PAS positive casts in the lumen of the tubules. In animals with AKI significant morphological alterations were present: tubular cells necrosis, dilatation of certain segments of the proximal and distal tubules, mostly with loss of brush-border. The most notable changes were present in the cortico-medullary zone, where the broad areas of tubular necrosis and a large number of PAS positive casts in the collecting ducts were observed. In treated animals degrees of morphological changes were significantly lower compared to AKI control. There were reduced tubular dilatation, tubular necrosis in the cortico-medullary zone and PAS positive cast formation.

Conclusion: HBO preconditioning and apocynin treatment improve renal hemodynamics, function and in SHR which suffer AKI. These results suggest that it is reasonable to assume that HBO preconditioning and NADPH oxidase inhibition potentially may have beneficial effects, but further comprehensive experimental and clinical studies are needed to confirm these promising results.

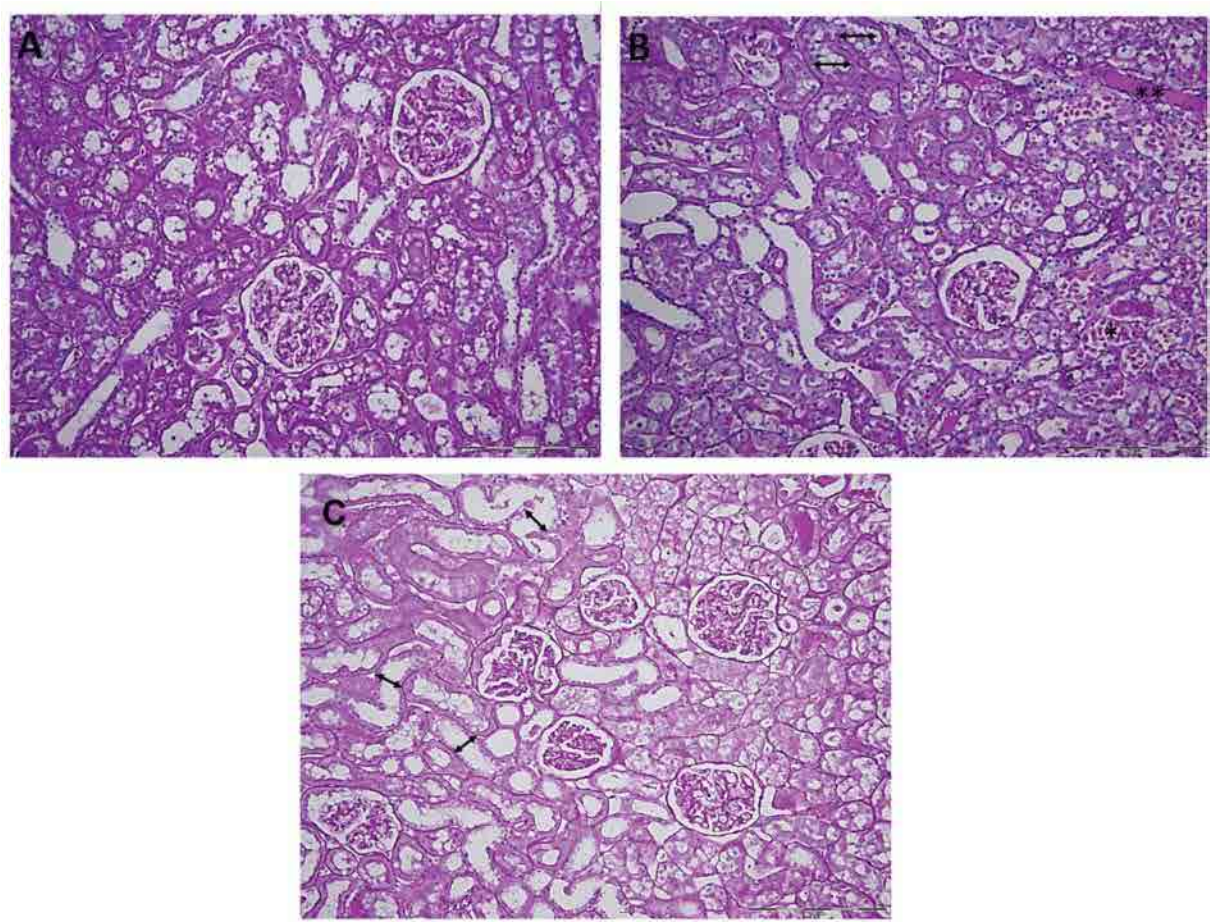


Figure 1. Histopathology of the representative kidney samples collected in different experimental groups: SHAM (A), AKI (B), AKI+APO+HBO (C). proximal tubular dilatation (↔), necrosis of tubular epithelial cells (*) and PAS-positive casts (**)

P0552

EXPRESSION OF CNDP1 PROTEIN IS REGULATED BY AGE-DEPENDENT AND AKI-RELATED ASTRAGALUS MEMBRANACEOUS EFFECTS IN MICE

Kagemasa Kajiwara[1], Makoto Arai[2], Yoshinobu Nakada[2], Go Nagashima[3], Takeaki Kinoue[4]

[1]Tokai University, School of Medicine, Molecular Life Sciences, Isehara, Kanagawai, Japan, [2]Tokai University, School of Medicine, Kampo Medicine, Isehara, Kanagawa, Japan, [3]Tokai University, School of Science, Chemistry, Hiratsuka, Kanagawa, Japan and [4]Tokai University, School of Medicine, Community Health, Isehara-shi, Japan

Background and Aims: *Astragalus membranaceus* (AM) is widely used for herbal medicine in Asia (see http://nccih.nih.gov/health/astragalus). Until now, numerous findings about the AM effects have been provided in various tissues and organs; however, the therapeutic effects of AM against chronic kidney disease (CKD) remain unclear. Recent findings suggest that acute kidney injury (AKI), which has been previously believed to heal completely, is a promoting factor for CKD pathogenesis or progression. Our recent findings have been observed that susceptibility to AKI as well as AM effects against AKI was significant in old mice, suggesting that AM effects exert an age-dependent manner in kidney. Therefore, we further examined the therapeutic effect of AM against age-dependent AKI pathogenicity.

Method: Female C57BL/6 mice were collected blood in advance (0.2 ml as normal), separated to two groups, and administered with AM powder-mixed sterilized 0.5% methylcellulose 400 (w/v) (AM-administered group) or with sterilized 0.5% methylcellulose 400 (control group), respectively by two hours before surgery. Left renal artery was exposed and occluded by non-traumatic small clips for 20 minutes. Twenty hours after the renal reperfusion, we collected blood (0.2 ml as reaction) and acquired kidney from each mouse. These serum samples were measured to detect serum creatinine and urea nitrogen. The dissected kidneys were used for Western blot analysis to determine the expression of AM-target protein candidates, which were selected as both age-dependent and renal disease-related factors from research data base (NCBI, Bethesda MD USA).

Results: Sorting with the data base, we isolated a metabolic product, carnosine (beta-alanyl-L-histidine), which is abundant in young human blood samples and exerted a scavenger effects against the anti-oxidative stress. Carnosine is degraded by carnosinase encoded by CNDP1 gene, and its metabolism revealed renoprotective characterization including scavenger of reactive oxygens in various tissues. Furthermore, recent epidemiologic studies showed association between pathogenesis of diabetic nephropathy and CNDP1 gene polymorphism. Therefore, here we examined the levels of CNDP1 protein by Western blot analysis. CNDP1 protein was upregulated in ischemia-reperfusion kidneys significantly from old mice (52 weeks old), compared to those from young mice (6-8 weeks old) which showed little increased levels. The levels of CNDP1 protein were down-regulated by AM administration prior to ischemia-reperfusion in both old and young kidneys. These findings suggest that pharmacological effects of AM normalized carnosine metabolism by regulating expression of CNDP1, which plays a critical role in AKI pathogenesis of aged kidney.

Conclusion: AM administration can reduce day-to-day generated AKI by carnosine upregulation at least in part. The AM effects involved in carnosine metabolism would play a critical role in prolonging activity of aged kidney.

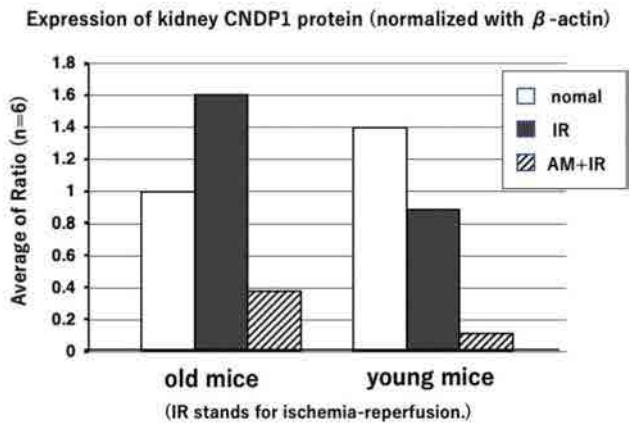


Figure:

P0553 PROTECTIVE EFFECT OF (-)-ALPHA-BISABOLOL OVER RENAL CYTOTOXICITY INDUCED BY AMPHOTERICIN B

Emanuel Paula Magalhães[1], Brenna Pinheiro Silva[1], Ramon Paula Pessoa Bezerra de Menezes[1], Tiago Lima Sampaio[1], Danya Bandeira Lima[1], Geraldo Bezerra da Silva Junior[1,2], Elizabeth De Francesco Daher[1], Alice Maria Costa Martins[1]

[1]Federal University of Ceará, School of Medicine and Pharmacy, Fortaleza, Brazil and [2]Universidade de Fortaleza, Public Health and Medical Sciences Graduate Programs, Fortaleza, Brazil

Background and Aims: Drug-induced acute kidney injury (AKI) is a health problem that increases morbidity and mortality rates as well as costs to health systems. Amphotericin B (AnB) is a widely used antifungal, which its therapy is closely associated with nephrotoxicity. The mechanisms of nephrotoxicity are not yet fully understood and there is a need to search for substances that prevent and / or reverse the associated renal damage. (-) - α-Bisabolol (BIS) has been demonstrated nephroprotective effect due to its antioxidant action. Thus, the aim of this study was to evaluated the effect of BIS as a protective substance on renal cell injury induced by amphotericin B.

Method: LLC-MK2 tubular renal cells were treated with different concentrations of BIS and AnB and its viability was measured by MTT assay to define the working concentrations of BIS and AnB. Then, cells were pretreated or post treated with BIS (31.25 - 125 μM) and AnB (13.97 μM) for 24 hours to evaluate the protective effect of BIS. Control (CT) was treated with sterile PBS. The experimental groups were further submitted to flow cytometry assays for membrane integrity evaluation using 7-AAD and measurement of cytoplasmic ROS production using DCFH-DA. The experiments were performed in triplicate (n = 3), and the data analyzed by One-Way ANOVA with Bonferroni post-test.

Results: BIS concentrations from 31.25 to 125 μM were selected, as well as the IC50 for AnB (13.97 ± 1.45 μM) for the furthers assays. Pretreatment with BIS increased cell viability by about 10% (31.25 – 63.31 ± 2.04%; 62.5 – 64.75 ± 2.10%; 125 – 63.92 ± 2.72%) compared to the AnB-only group (49.79 ± 1.25%), which had its cell viability reduced by about 50% (CT – 100.70 ± 0.83%). BIS was also able to increase the whole cell population at concentrations of 62.5 (83.10 ± 1.10%) and 125 μM (84.67 ± 0.98%) when compared to the AnB group (76.54 ± 1.18%). In DCF labeling, it was observed that AnB increased the production of ROS in 20% (IFR = 1.21 ± 0.02) when compared to the control (IFR = 1.00 ± 0.01), and BIS (31.25 μM) was able to reduce in 41% (IFR = 0.79 ± 0.01) when compared to the AnB group.

Conclusion: The (-)-α-bisabolol was able to prevent the renal cytotoxicity induced by amphotericin.

P0554 IN VITRO ASSESSMENT OF HA330 CARTRIDGE ADSORPTION CAPACITY REALTED TO VANCOMYCIN

Anna Lorenzin[1], Llaria Godi[1,2], Massimo De Cal[1,3], Claudio Ronco[1,2,3]

[1]International Renal Research Institute of Vicenza, San Bortolo Hospital, Vicenza, Italy, [2]University of Padova, Medicine, Padova, Italy and [3]San Bortolo Hospital, Nephrology, Dialysis and Transplantation, Vicenza, Italy

Background and Aims: The rationale for blood purification as adjunctive therapy during sepsis involved the capacity in removing endogenous and exogenous toxins, but currently no recommendations exists [1]. A critical point may be the potential interaction with antimicrobial therapy, which remains the mainstay of sepsis treatment. HA330 cartridge (Jafron, Zhuhai City, China), widely used in China and actually available in Europe, is used in hemoperfusion for blood purification in septic patients.The aim of this in vitro study was to investigate the adsorptive capacity of HA330 related to vancomycin (VAN).

Reference: 1. Rhodes A et al. Crit Care Med 45:486-552. 2017

Method: This is an experimental study, simulating an hemoperfusion treatment with HA330. We circulated (250 ml/min) in a closed loop 500 ml of normal saline solution enriched with VAN, stirred and maintained at 37°C. We spiked 100 mg of VAN every 15 minutes to increase the antibiotic load until reaching 1500 mg, the last injection was 500 mg to get a total amount of 2 g. Samples were collected from the inlet line at each VAN adjunct, after system stabilization. Measured VAN concentrations were used to get the adsorption isotherm: for each VAN load, the adsorbed amount of VAN was obtained by multiplying VAN reduction ratio and the quantity of VAN injected.

Results: Figure 1 shows VAN adsorption isotherm obtained with HA330 cartridge. We observed that, at each injection, after 15 minutes VAN was almost entirely adsorbed by the cartridge, with an average reduction ratio of 0.96. Interestingly, this was confirmed even adding 500 mg at once. Even increasing the VAN load to 500 mg at once, the reduction ratio was maintained.

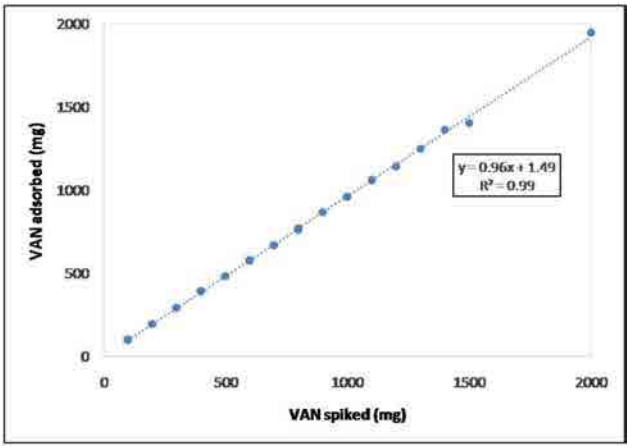


Figure 1. Vancomicyn adsorption isotherm obtained with HA330 blood purification device. The isotherm is described by the following equation : $y = 0.96x + 1.49$ (R^2=0.99).

Conclusion: In our study, simulating hemoperfusion using HA330, a rapid and clinically relevant removal of VAN has been shown. A significant amount of VAN (2g) was adsorbed without reaching membrane saturation nor reducing its adsorptive capacity.

In a clinical setting, we recommend a therapeutic drug monitoring to optimize VAN levels during blood purification with HA330 and a VAN loading dose may be considered. Further in vivo studies are warranted to confirm these findings.

P0555 **HYPOTHERMIA ATTENUATES CHRONIC RENAL INJURY AFTER ISCHEMIA-REPERFUSION IN KIDNEY.**

Ki Ryang Na[1,2], DAE EUN CHOI[2], Kang Wook Lee[2], Dabi Kim[3], Eunji Kim[3], Jin Young Jeong[3], Young Rok Ham[2], Haeri Kim[1], Wonjung Choi[1], Yoon-Kyung Chang[4]

[1]Chungnam National University Hospital, Nephrology, Daejeon, Korea, Rep. of South, [2]Chungnam National University, Nephrology, Daejeon, Korea, Rep. of South, [3]Chungnam National University, Department of Medical Science, Daejeon, Korea, Rep. of South and [4]The Catholic University of Korea Daejeon St. Mary's Hospital, Nephrology, Daejeon, Korea, Rep. of South

Background and Aims: Hypothermia attenuates the renal injury induced by ischemia-reperfusion(IR). However, the detailed molecular pathway remains unknown. Although there has been reported that hypothermia protects acute renal damage, there is little known that hypothermia reduce renal fibrosis in IR kidney injury. We evaluated hypothermic protection against renal fibrosis in renal IR injury.

Method: C57Bl/6 mice were divided into the following groups: sham-operated (cold, 32C) vs normal temperature (37C); IR mice (32C vs 37C). Kidneys were harvested 10 and 27 minutes after induction of renal ischemia and 24, 72, 168 hours after iIR injury. Functional and molecular markers of kidney injury were evaluated.

Results: The blood urea nitrogen and serum creatinine levels and the histologic renal injury scores were significantly lower in 32C IR than 37C IR kidneys (all P values < .05).In kidney harvested 10 and 27 min, the extent of renal AMPK,ERK, and HIF1 phosphorylation was significantly increased in the kidneys of 32C compared to 37C IR mice. In kidney harvested 27 min, 24hr, 72hr, and 168hr, the expression levels of SOX9, TGF beta, alpha SMA, collagen IV, and fibrinogen decreased in 32C IR compared to 37C IR mice. In addition, in kidney harvested 72hr, and 168hr, the stained area of TGF beta, alpha SMA, and masson trichrome, were significantly decreased in 32C IR compared to 37C IR mice.

Conclusion: Hypothermia attenuates the renal fibrosis induced by Ischemia reperfusion.

P0556 **MULTI-ORGAN DAMAGE FOLLOWING PERINATAL ASPHYXIA IN RAT MODEL**

Tamas Lakat[1,2], Adam Hosszu[1,2], Agnes Molnar[1,2], Akos Roland Toth[1], Adar Saeed[1], Kornel Demeter[3], Hanga Kelemen[2,4], Eva Mikics[4], Attila Szabo[2,5], Adam Denes[6], Andrea Fekete[1,2]

[1]MTA-SE, "Lendület" Diabetes Research Group, Budapest, Hungary, [2]Semmelweis University, 1st Department of Pediatrics, Budapest, Hungary, [3]MTA Institute of Experimental Medicine, Behavioral Studies Unit, Budapest, Hungary, [4]MTA Institute of Experimental Medicine, Translational Behavioural Neuroscience, Budapest, Hungary, [5]MTA-SE, Pediatrics and Nephrology Research Group, Budapest, Hungary and [6]MTA Institute of Experimental Medicine, Neuroimmunology, Budapest, Hungary

Background and Aims: Perinatal asphyxia (PA) leads to the death of more than half a million mature newborns yearly. PA is associated with several serious complications, including hypoxic encephalopathy, renal- hepatic- and cardiovascular injury, as well as respiratory distress. Basic research and clinical trials mainly focus on mitigating central nervous system damage by selective head or whole body cooling, which is currently the only routinely used treatment in clinical practice. However, the extent of PA-associated multi-organ damage is not clarified yet and effective therapies are lacking. The aim of the present study was to determine the acute renal, hepatic and cardiac impairment following PA and to identify pathways involved in the pathomechanism. In addition, we aimed to investigate long-term effects of PA on permanent organ damage and susceptibility to ischemia/-reperfusion injury in adulthood.

Method: Postnatal 7 day-old male Wistar rat pups (n=5-10/group) were randomly grouped as follows: **(i) Baseline**; or separated from the dam and placed in a treatment chamber for 15 minutes **(ii) Control**: normal air; **(iii) PA:** 4% O_2; 20% CO_2 in N_2 gas mixture. Serum and tissue samples were collected after 4 (T4) and 24 (T24) hours respectively. In a second experiment 35 min bilateral renal ischemic insult was performed on control and PA rats aged 6 months (n=6-7/group). Serum and tissue samples were collected 24 (T24 IR) hours after reperfusion (**Figure 1**).

Serum levels of electrolytes, kidney and liver functional parameters, and myocardial ischemic protein Troponin I were determined. Highly selective tubular injury markers (Kim1, Ngal) were measured. Expressions of hypoxic (Hif1a, Hif2a) inflammatory (Il1α, Il1β, Il6, Tnfα, Mcp1, Tlr2), apoptotic (Bax, Bcl-2) and angiogenic genes (Vegf, Epo) and heat shock proteins (Hsp27, Hsp72) were investigated. Periodic-Acid Schiff staining and CD45 immunostaining on kidney tissue sections, and Hematoxylin & Eosin staining on liver tissue sections were performed.

Results: Blood urea nitrogen (BUN) and serum GPT were elevated at T4 following PA. Kim1, Ngal and heat shock protein expressions were increased, inflammatory and angiogenic pathways were activated in the kidney after PA. CD45 staining showed increased leukocyte infiltration. In the liver hypoxic and apoptotic pathways were activated at T24 in controls and after asphyxia, but not in the Baseline group. Vacuolisation, cytoplasmic degradation, and the onset of necrosis were observed in the liver following PA. Serum Troponin I was elevated indicating myocardial damage, moreover inflammatory cytokines and heat shock proteins increased in the heart. In adult PA rats BUN levels were elevated, suggesting a long-term detrimental effect of PA on renal function. In addition, adult PA rats were more susceptible to renal ischemic insult, confirmed by higher serum creatinine and GPT levels, as well as increased expression of tubular injury, hypoxic and inflammatory markers compared to Control rats subjected to ischemia.

Conclusion: Acute renal, hepatic and myocardial impairment was observed after PA. These results may justify the need for clinical follow-up and novel treatment strategies for possible multi-organ damage. The molecular pathways described here are potential targets for therapeutic intervention. In addition, birth asphyxia may increase sensitivity to renal injury even in adulthood, which may be worth considering in clinical situations with potential renal impairment such as major surgeries.

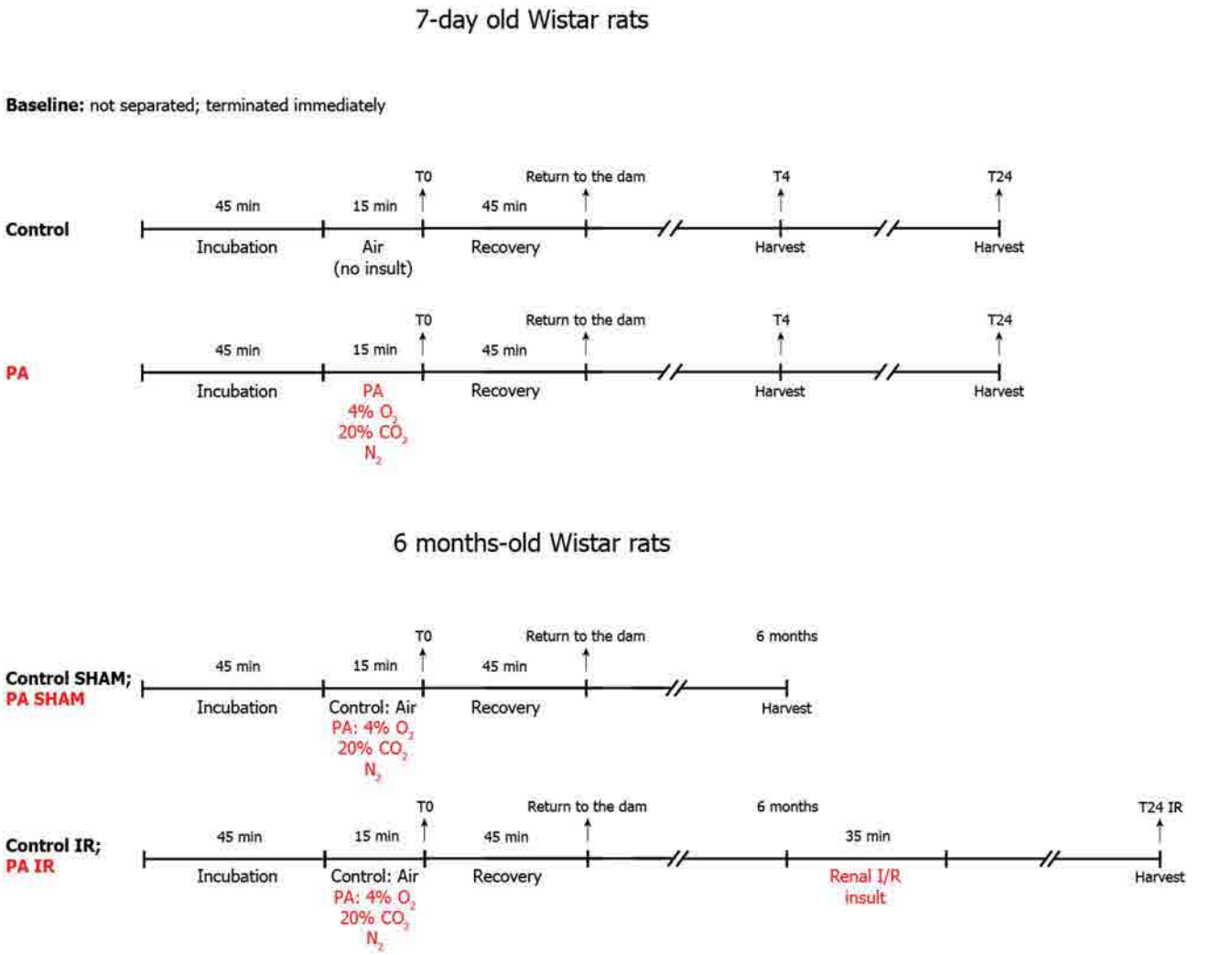


Figure 1: **Experimental models.** PA, Perinatal Asphyxia; I/R, ischemia-reperfusion.

P0557

HYPERBARIC OXYGEN PRECONDITIONING INCREASES HEME OXYGENASE 1 EXPRESSION IN KIDNEY TISSUE AND IMPROVES KIDNEY FUNCTION IN SPONTANEOUSLY HYPERTENSIVE RATS WITH ISCHEMIC ACUTE KIDNEY INJURY

Milan Ivanov[1], Zoran Miloradovic[1], Nevena Mihailovic-Stanojevic[1], Djurdjica Jovovic[1], Danijela Karanovic[1], Una-Jovana Vajic[1], Rada Jeremić[2], Marina Djelic[2], Predrag Brkic[2]

[1]Institute for medical research, University of Belgrade, Cardiovascular physiology, Belgrade, Serbia and [2]Faculty of Medicine, University of Belgrade, Institute of Medical Physiology, Belgrade, Serbia

Background and Aims: Renal ischemia–reperfusion (RIR) injury is one of the factors in the development of acute kidney injury (AKI). AKI is multifactorially caused, but the mechanism of pathogenesis and development of this disease is still incompletely defined. AKI is characterized by the sudden appearance, rapid progression of disease and very uncertain and often fatal outcome. Heme oxygenase-1 (HO-1) is a cytoprotective enzyme that catalyzes the breakdown of heme to biliverdin, carbon monoxide, and iron. HO-1 is now recognized as a protection factor in acute kidney injury. The aim of this study was to determine the effect of preconditioning with hyperbaric oxygen (HBO) on HO-1 expression in kidney tissue and kidney function in spontaneously hypertensive rats (SHR) during kidney ischemia–reperfusion injury.

Method: An experiment was performed in anesthetized, adult six-month-old male SHR. The right kidney was removed and the renal ischemia was performed by clamping the left renal artery for 40 minutes. SHR were randomly selected in three experimental groups: sham operated group (SHAM; n=7); AKI control group (AKI; n=9); and AKI group with HBO (AKI+HBO; n=9). Treated group were placed into experimental HBO chambers and exposed to pure oxygen, twice a day (in a 12 hour period, 8AM and 8 PM) for two consecutive days in the following manner: 10 minutes slow compression, 2.026 bar for 60 minutes, 10 minutes slow decompression. Mean arterial pressure (MAP) and HO-1 expression in kidney tissue were measured 24h after reperfusion. Clearance of creatinine (CCr), urea (CUr) and phosphate (CPh) were calculated 24h after reperfusion.

Results: After AKI induction reduction of blood pressure was recorded in both groups with AKI. Preconditioning with HBO significantly improved kidney function in rats with AKI compared to control group. HO-1 expression in kidney tissue was significantly higher in the treated group ($p<0,01$) compared to SHAM and AKI control group.

Conclusion: Our results suggest that HBO treatment improves kidney function in the AKI+HBO vs. AKI control group. This implies that increased level of HO-1 due to preconditioning with hyperbaric oxygen may have beneficial effects on kidney function, and potentially protective effect in an ischemic model of AKI with hypertension.

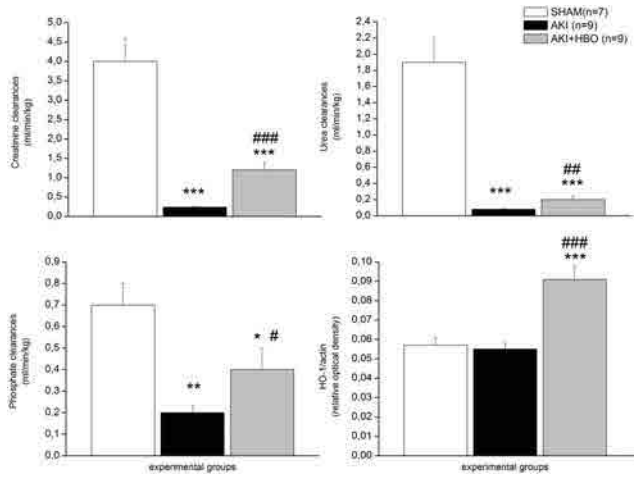


Figure:

P0558 DICLOFENAC ENHANCES RENAL INFLAMMATION IN EXPERIMENTAL SUBCLINICAL ACUTE KIDNEY INJURY (AKI)

Johanna Störmer[1], Faikah Gueler[1], Song Rong[1], Mi-Sun Jang[1], Nelli Shushakova[1], Sonja Schmidt[2], Hermann Haller[1], Robert Greite[1]

[1]Hannover Medical School, Nephrology, Hannover, Germany and [2]Phenos GmbH, Hannover, Germany

Background and Aims: Diclofenac is frequently used for pain control. In a previous study, we showed that already a single oral dose of diclofenac could reduce renal perfusion in healthy individuals. To investigate the influence of oral diclofenac administration on renal inflammation in the setting of pre-existing renal damage, we used a mouse model of subclinical acute kidney injury (AKI) induced by renal ischemia-reperfusion injury (IRI) followed by diclofenac administration.

Method: Male CD1 mice (7-8 weeks old) underwent unilateral renal pedicle clamping for 15min to induce subclinical AKI. After reperfusion mice received a single oral dose of 100 or 200mg/kg diclofenac via oral gavage. Vehicle treated mice with unilateral IRI served as control. At day 1, mice were placed into metabolic cages to collect urine. Histology was performed on day 1 and 14 for renal morphology. Inflammation and fibrosis were investigated by immunohistochemistry and qPCR.

Results: Diclofenac treated mice showed reduced urine production. Morphologically, signs of AKI were more pronounced in diclofenac treated kidneys which also showed more Cox-2 positive tubuli in the cortex. On mRNA expression level the pro-inflammatory markers IL-6 and CXCL2, the chemoattractant for neutrophils, were elevated in the diclofenac group. Early upregulation of the pro-fibrotic markers CTGF and PAI-1 was detected already on d1 after IRI in the diclofenac group and tubular atrophy was pronounced after two weeks.

Conclusion: Already, a single oral dose of diclofenac causes aggravation of renal inflammation and progressive renal fibrosis in the setting of pre-existing subclinical acute kidney injury.

AKI. CLINICAL. EPIDEMIOLOGY AND OUTCOME

P0560

POST-DISCHARGE FOLLOW UP AFTER AKI. AN EXTERNAL VALIDATION AND DECISION CURVE ANALYSIS OF TWO RISK MODELS.

Simon Sawhney[1], Zhi Tan[2], Corri Black[1], Brenda Hemmelgarn[3], Angharad Marks[4], David Mclernon[1], Matthew James[2]

[1]University of Aberdeen, [2]University of Calgary, [3]University of Alberta and [4]University of Swansea

Background and Aims: There is limited evidence to inform which people should receive follow up after AKI and for what reasons. Here we report the external validation (geographical and temporal) and potential clinical utility of two complementary models for predicting different post-discharge outcomes after AKI. We used decision curve analysis, a technique that enables visualisation of the trade-off (net benefit) between identifying true positives and avoiding false positives across a range of potential risk thresholds for a risk model. Based on decision curve analysis we compared model guided approaches to follow up after AKI with alternative strategies of standardised follow up – e.g. follow up of all people with AKI, severe AKI, or a discharge eGFR<30.

Method: The Alberta AKI risk model predicts the risk of stage G4 CKD at one year after AKI among those with a baseline GFR>=45 and at least 90 days survival (2004-2014, n=9973). A trial is now underway using this tool at a 10% threshold to identify high risk people who may benefit from specialist nephrology follow up. The Aberdeen AKI risk model provides complementary predictions of early mortality or unplanned readmissions within 90 days of discharge (2003, n=16453), aimed at supporting non-specialists in discharge planning, with a threshold of 20-40% considered clinically appropriate in the study. For the Alberta model we externally validated using Grampian residents with hospital AKI in 2011-2013 (n=9382). For the Aberdeen model we externally validated using all people admitted to hospital in Grampian in 2012 (n=26575). Analysis code was shared between the sites to maximise reproducibility.

Results: Both models discriminated well in the external validation cohorts (AUC 0.855 for CKD G4, and AUC 0.774 for death and readmissions model), but as both models overpredicted risks, recalibration was performed. For both models, decision curve analysis showed that prioritisation of patients based on the presence or severity of AKI would be inferior to a model guided approach. For predicting CKD G4 progression at one year, a strategy guided by discharge eGFR<30 was similar to a model guided approach at the prespecified 10% threshold (figure 1). In contrast for early unplanned admissions and mortality, model guided approaches were superior at the prespecified 20-40% threshold (figure 2).

Conclusion: In conclusion, prioritising AKI follow up is complex and standardised recommendations for all people may be an inefficient and inadequate way of guiding clinical follow-up. Guidelines for AKI follow up should consider suggesting an individualised approach both with respect to purpose and prioritisation.

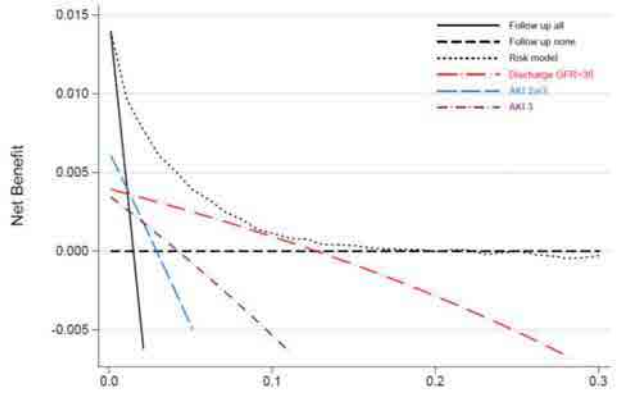


Figure 1 Threshold probability for CKD G4 progression at one year

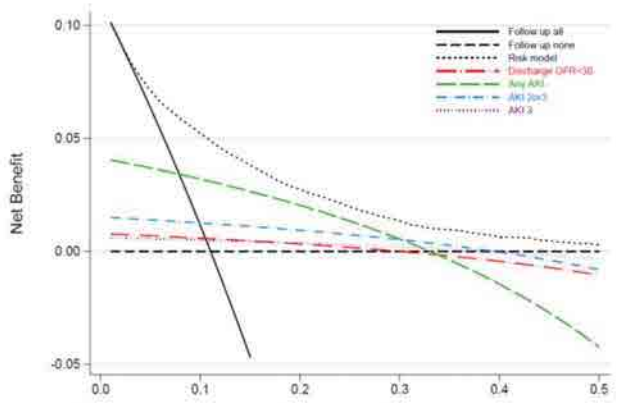


Figure 2 Threshold probability for unplanned readmission or death within 90 days

Figure:

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P0561 **ACUTE KIDNEY INJURY AS A RISK FACTOR FOR KIDNEY STONES: A PROPENSITY MATCHED ANALYSIS**

Cheikh Hassan Hicham Ibrahim[1,2], Maureen Lonergan[1], Judy Mullan[3], Brendan McAlister[3], Kelly Lambert[2,3], Thomas Suesse[4]

[1]Wollongong Hospital, Illawarra Shoalhaven Local Health District, Australia, [2]University of Wollongong, Wollongong, Australia, [3]CHRISP, University of Wollongong, Australia and [4]National Institute for Applied Statistics Research Australia, School of Mathematics and Applied Statistics, University of Wollongong, Australia

Background and Aims: Kidney stones affects 6-9% of the population, with an almost 30% risk of reoccurrence. Factors associated with kidney stone formation include male gender, ethnicity, family history and stone type. The underlying pathology of stone formation is complex and includes increased urine saturation, decreased urine stone inhibitors in addition to metabolic factors.

Acute kidney injury (AKI) refers to the abrupt decrease in kidney function, resulting in retention of urea and other waste products and the dysregulation of fluid and electrolyte balance. AKI affects 10-15% of the hospitalised population and is associated with long-term outcomes, such as chronic kidney disease, end-stage kidney disease (ESKD), cardiovascular disease, fractures and earlier mortality.

There is evidence that AKI may result in long-term renal damage and fibrosis. A potential effect is impairment in urine concentration which would limit kidney stone formation. However there has been no previous investigation about this potential association. We aim to investigate if there is an association between AKI and kidney stone formation.

Method: Retrospective clinical data available for all adult ($\geq$18 years of age) hospital admissions to a local health district in Australia between January 2008 and December 2017 was used in the analysis. We excluded 1) non-residents, 2) stone diagnosis pre-AKI, 3) death within 1 month of an AKI episode, 4) dialysis dependent ESKD prior to an AKI episode and 5) incomplete patient information. AKI episode was diagnosed from ICD-10 coding and kidney stone from ICD-10 and SNOMED coding. Our outcome was a kidney stone episode. We examined the entire cohort in addition to propensity score matching (PSM) using 1:1 optimal matching, caliper 0.1 and without replacement based on covariates known to be associated with renal calculi and AKI. Balance before and after PSM was assessed between the groups to evaluate quality using standardised means. Baseline characteristics were compared with chi-square and Mann Whitney U. Multivariate analysis was compared using Logistic regression.

Results: For the cohort of 180,927 patients, after exclusions, 12,338 (6.8%) patients were diagnosed with an AKI and 4,495 (2.5%) patients with a kidney stone. Patients with an AKI (12,338), compared to patients with no AKI (168,523), were more likely to be older (75.0 vs 50.0 years, $p<0.001$) with more comorbidities such as hypertension (31.8% vs 12.7%, $p<0.001$), diabetes (21.5% vs 9.4%, $p<0.001$), coronary artery disease (14.6% vs 7.0%, $p<0.001$) and peripheral vascular disease (5.4% vs 1.8%, $p<0.001$).

The risk of kidney stone formation for the entire cohort in patients with a history of AKI was lower when compared to the no AKI patients (1.1% vs 2.6%, Hazard ratio 0.42, 95% confidence interval 0.36- 0.52, $p<0.001$). After PSM 12,336 patients with AKI were matched with 12,336 patients with no AKI with good balance of covariates. Patients with a history of AKI had a lower risk of kidney stone formation when compared to no AKI patients (Hazard ratio 0.57, 95% Confidence Interval 0.36- 0.51, $p<0.001$)

Conclusion: Our findings suggest that patients with AKI appear to be at a significantly lower risk of developing subsequent kidney stone formation when compared to patients with no previous AKI episodes. Further analysis on a greater scale are required to confirm these findings and their implications.

Table 1: Comparison of patient characteristics between patients with acute kidney injury and patients with no acute kidney injury.

	Unmatched Data		Matched Data	
	No AKI n=168,523	AKI n=12,338	No AKI n=12,336	AKI n=12,336
Gender (Male)	43.8% (73,877)	55.3% (6,819)	44.5% (55495)	44.7% (5,519)
Age first admission (years)	50.0 [31.0, 68.0]	75.0 [66.0, 82.0]	76.0 [66.0, 83.0]	75.0 [66.0, 82.0]
Hypertension	12.7% (21,435)	31.8% (3920)	29.9% (3,693)	31.7% (3,915)
Diabetes	9.4% (15,784)	21.5% (2649)	18.7% (2,305)	21.4% (2,645)
Coronary Artery Disease	7.0% (11,820)	14.6% (1796)	13.4% (1,657)	14.6% (1,796)
Congestive heart Failure	3.8% (6446)	14.6% (1806)	12.2% (1,511)	14.6% (1,801)
Arrythmia	8.4% (14,210)	19.0% (2342)	18.0% (2226)	19.0% (2341)
Peripheral Vascular Disease	1.8% (2,963)	5.4% (12,342)	4.5% (554)	5.4% (661)
Dementia	3.3% (5521)	4.6% (566)	4.5% (554)	4.6% (566)
Neurological Disease	4.7% (7876)	5.6% (693)	5.9% (731)	5.6% (693)
Liver Disease	2.4% (4,023)	3.1% (385)	2.7% (335)	3.1% (384)
Peptic Ulcer Disease	0.7% (1,134)	1.2% (153)	1.3% (161)	1.2% (153)
Cancer	8.2% (13,905)	8.5% (1,054)	8.3% (1,029)	8.5% (1053)
Anaemia Deficiency	2.1% (3,476)	5.0% (619)	4.0% (490)	5.0% (615)
Obesity	0.9% (1,527)	2.6% (327)	1.9% (230)	2.6% (322)
Weight Loss	6.1% (10,297)	8.9% (1,097)	8.9% (1,100)	8.9% (1,096)
Alcohol Abuse	9,033 (5.4%)	4.6% (565)	4.1% (507)	4.6 (565)

Figure:

P0562

DIFFERENT POTENTIAL INTERPRETATIONS OF CRITERIA FOR AKI WHEN USING AUTOMATED DECISION SUPPORT: IMPACT ON ASSOCIATED MORTALITY

Wim Van Biesen[1], Johan Steen[1], Johan Decruyenaere[2], Dominique Benoit[2], Eric Adriaan J. Hoste[2], Jill Vanmassenhove[1]

[1]Ghent University Hospital, Renal Division, Gent, Belgium and [2]Ghent University Hospital, Intensive Care Unit, Gent, Belgium

Background and Aims: The reported associated mortality risks of Acute Kidney Injury (AKI) in the intensive care unit (ICU) are variable. Although the Kidney Disease Improving Global Outcome (K-DIGO) improved harmonisation of the definition, there is remaining variability in the actual implementation of this AKI definition, with variable use of the urinary output (UO) criterion, and different interpretations of the baseline serum creatinine (Screa). This hampers progress of our understanding of the clinical concept AKI and leads to confusion and unclarity when interpreting models to predict AKI associated outcomes. With the advent of big data and artificial intelligence based decision algorithms, this problem will only become more of interest, as the user will not know what exactly the construct AKI in the application used means. Therefore, we intended to explore the impact of different interpretations of the Screa and the UO criterium as presented in the K-DIGO definition on the associated ICU mortality risk of AKI stage 2 in the ICU.

Method: We included all patients of an electronic health data system applied in a tertiary ICU between 2013 and 2017. Sequential Organ Failure Assessment (SOFA) score was calculated, and gender, age, weight and mortality at ICU and in hospital were extracted. All serum creatinine (sCrea) values during ICU stay and hospitalisation were extracted, as were UO data, with their time stamps. In addition, all Screa data up to 1 year before ICU admission were retrieved from a dataset external to ICU. AKI was defined according to KDIGO stage 2, using different possible interpretations of the Screa and/or the UO criterion. For the evolution of Screa as compared to a baseline value, we either used a value directly available to ICU staff (def 1), a presumed eGFR of 75ml/min (def 2), the first available value after admission to ICU (def 3), the lowest value during the current hospitalisation before ICU admission (def 4), the lowest value before the hospitalisation episode as found in an external dataset (def 5). For the UO criterion, we used either (in line with K-DIGO stage 2) a UO below 6ml/kg during a 12 hour block (def 6) or a UO below 0.5ml/kg/hour during each of 12 consecutive one hour intervals (def 7). Definition 8 and 9 identified patients who complied with at least one out of the Screa criteria 1-5 (def 8) or out of the UO criteria (def 9). Definition 10 identified patients who complied both with at least one Screa and one UO criterium.

Results: Our dataset comprised 16433 admissions (34.7% female, age 60.7±16.4 years). Overall, 8.1% of patients died in Intensive Care Unit (ICU). The SOFA score at admission was 6.9±4.1. The mortality risk associated with AKI according to the stage 2 definition of K-DIGO varied according to the interpretation of the diagnostic criteria (table). Most important, associated mortality risk was comparable whether a UO (RR 2.31, 95% CI 1.90-2.81) or a Screa (RR 2.00, 95% CI 1.57-2.55) criterium was used, and was highest in patients who complied with both at least one UO and one Screa criterium (RR 7.28, 95% CI 6.12-8.65).

Conclusion: Unclarity on the actual interpretation of the Screa and UO criteria used in the K-DIGO definition of AKI leads to substantial differences in AKI associated mortality risk. Omitting the UO criterium leads to substantial underestimation of associated risk.

Definition (see text)	Exp Beta adjusted for age, gender, and SOFA score	95% CI	Unadjusted mortality positive patients	Unadjusted mortality negative patients
1	4.58	3.87-5.43	27.6%	5.0%
2	3.33	2.91-3.80	20.3%	5.0%
3	2.87	2.35-3.49	28.5%	6.8%
4	6.14	5.22-7.88	26.9%	4.2%
5	4.96	4.24-5.80	22.7%	4.0%
6	3.63	3.16-4.17	15.6%	4.0%
7	5.09	4.46-5.81	24.7%	5.0%
8	3.53	3.09-4.03	18.3%	4.4%
9	3.64	3.17-4.18	15.8%	4.0%
10: none of 1-9	1		3.3%	
10: only UO	2.31	1.90-2.81	7.3%	
10: only Screa	2.00	1.57-2.55	7.1%	
10: both UO and Screa	7.28	6.12-8.65	26%	

Figure: mortality according to different interpretations of the Screa and UO criteria of K-DIGO AKI stage 2

P0563 **THE SHORT AND LONG-TERM EFFECTS OF HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY ON RENAL FUNCTION IN PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER**

Federica Di Maio[1], Anna Fagotti[2], Carlo Ronsini[3], Nicola Panocchia[1], Giuseppe Grandaliano[1,4], Giovanni Scambia[4,5], Pietro Manuel Ferraro[1,4]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Nefrologia, Roma, Italy, [2]Fondazione Policlinico Universitario A Gemelli IRCCS, Dipartimento Scienze della Salute della Donna e del Bambino, Roma, Italy, [3]Università G. d'Annunzio, Gynecologic and Obstetrics Unit, Chieti, Italy, [4]Università Cattolica del Sacro Cuore, Roma, Italy and [5]Fondazione Policlinico Gemelli IRCCS, Roma, Italy

Background and Aims:

Cytoreductive surgery (CRS) with platinum based Hyperthermic Intraperitoneal Chemotherapy (HIPEC) represents a valid therapeutic approach in the treatment of ovarian cancer patients with peritoneal spread (vanDriel NEJM). Nevertheless, cisplatin nephrotoxicity represents one limitation to the diffusion of HIPEC in clinical practice. To date, few studies evaluated the nephrotoxicity of hyperthermic intraperitoneal cisplatin and the risk of acute kidney injury (AKI) in patients treated with HIPEC. The aim of our study is to evaluate short- and long-term changes in serum creatinine (SCr) levels in a cohort of patients with a first relapse of platinum-sensitive ovarian cancer, receiving CRS plus or minus HIPEC.

Method:

We compared a cohort of patients with a first relapse of platinum-sensitive ovarian cancer, receiving CRS plus/minus HIPEC in a period from January 2013 to October 2018. The HIPEC technique required the perfusion of the abdominal cavity with a 4 L/m2 of a heated saline solution containing cisplatin 75 mg/m2. We assessed the estimated glomerular filtration rate (eGFR), using the CKD-EPI formula, and SCr from the preoperative value, at 24, 48, 72 hours, 7 days and the last SCr value available on the electronic record, at least 3 months after the procedure. We analyzed the effect of HIPEC treatment on SCr values over time and we used logistic regression models to investigate the effect of HIPEC treatment on clinical outcomes. No patient in the HIPEC group had kidney protective treatment with thiosulphate.

Results:

Our analyses included complete data of 110 patients treated in our Institution from January 2013 to October 2018. The two groups had significant differences in baseline SCr (p-value = 0.002), with lower average values in the CRS+HIPEC group (mean 0.68, standard deviation [SD] 0.14 mg/dL) compared to the CRS group (mean 0.76, SD 0.13 mg/dL). The baseline eGFR was significantly higher in the CRS+HIPEC group (mean 95, SD 16 mL/min/1.73 m2) than in the CRS group (mean 88, SD 14 mL/min/1.73 m2) (p-value = 0.014) and three patients in each group had chronic kidney disease (CKD) before surgery. SCr values in the HIPEC group were significantly higher at post-operative day #7 (1.22 ± 1.10 mg/dL vs 0.69 ± 0.16 mg/dL; p-value <0.001) and the differences remained during follow-up at least three months after randomization (0.96 ± 0.55 vs 0.69 ± 0.19 mg/dL; p-value <0.001). Seventeen patients (31%) developed Acute Kidney Injury (AKI), according to the KDIGO Guidelines, in the first week after CRS+HIPEC versus seven patients (13%) after CRS alone. No patients who developed AKI post-HIPEC needed renal replacement treatment, although 5 (9%) had AKI stage III and 7 (13%) stage II. The CRS+HIPEC group had a significantly higher risk of developing AKI [OR: 3.48 (2.30-5.27)] compared with the CRS group (p-value <0.001). There were no statistically significant differences between the two groups with regard to risk of complications other than AKI.

Conclusion:

To our knowledge, our study represents the first investigation on short- and long-term changes in SCr and on the risk of AKI in patients with a first relapse of platinum-sensitive ovarian cancer, treated with CRS and HIPEC. There is a strong correlation between the intraperitoneal cisplatin at elevated temperatures and the rise of SCr over the time. However, this event was no reversible and influenced following treatments in only eight women.

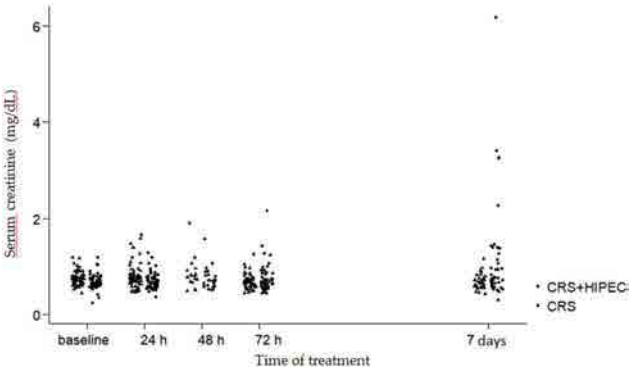


Figure 1. Scatter plot of serum creatinine values as function of the time of treatment

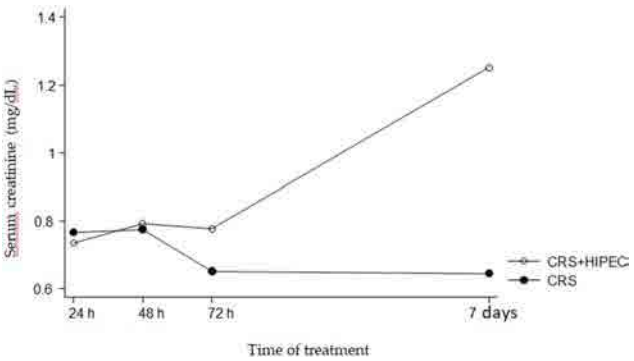


Figure 2. Linear prediction of serum creatinine as function of the time of treatment

P0564 **INCIDENCE AND PROGNOSIS OF ACUTE KIDNEY INJURY VERSUS ACUTE KIDNEY DISEASE AMONG 71,041 INPATIENTS**

Chenyu Li[1,2], Long Zhao[1], Lingyu Xu[1], Chen Guan[1], Zhibo Zhao[2], Na Li[2,3], Xiaosu Zhang[4], Jing Wang[5], Jun Zhao[6], Junyan Huang[7], Zhihua Zheng[3], Hans-Joachim Anders[2], Yan Xu[1]

[1]The Affiliated Hospital of Qingdao University, Nephrology, Qingdao, P.R. China, [2]Ludwig-Maximilians-Universität München, Division of Nephrology, Medizinische Klinik und Poliklinik IV, Klinikum der Universität, München, Germany, [3]The Seventh Affiliated Hospital, Sun Yat-sen University, Division of Nephrology, P.R. China, [4]Yidu Central Hospital of Weifang, Department of Kidney Internal Medicine, [5]Haiyang People's Hospital, Renal Department of Internal Medicine, [6]Shandong Weifang People's Hospital, Department of Nephrology and [7]Qingdao Central Hospital, Department of Nephrology

Background and Aims: The current diagnostic criteria for acute kidney injury (AKI) predict the need for dialysis and early mortality, but are less useful to predict long-term outcomes. Acute kidney disease (AKD) defines patients with AKI or subacute loss of kidney function lasting for more than 7 days, which should predict better subsequent chronic kidney disease (CKD). The aim of this study was to investigate the risk factors and prognosis of AKD and to compare different types of acute/subacute renal impairment among Chinese inpatients.

Method: From a cohort of 450,000 patients consecutive admitted from June 1, 2012, to March 31, 2018 to five district hospitals, complete data were available from 71,041 inpatients. AKI and AKD were diagnosed based on the Acute Disease Quality Initiative Criteria 2017.

Based on this diagnostic criterion of AKI and AKD, patients were classified as having (1) AKI Recover, if Scr back to baseline value within 7 days (renal impairment duration of less than 7 days or rapid recovery within 7 days), and (2) AKD with AKI, if a condition in which stage 1 or greater AKI was present $\geq$ 7 days after an AKI initiating event (continuous AKI progressing to AKD), (3) AKD without AKI, if Scr levels increased slowly but lasted more than 7 days (subacute AKD without meeting the AKI criterion).

Results: Of 71,041 inpatients, 16,098 (22.66%) patients developed AKI or AKD. 5,895 (8.30%) AKI patients recovered within 7 days (AKI Recover), 5,623 (7.91%) were followed by AKD and 4,580 (6.44%) patients developed AKD without AKI. Thus, AKI and AKD are frequent complications in Chinese inpatients (Fig 1).

Compared to AKI recover or AKD without AKI, patients with AKI followed by AKD had higher hospital mortality (16.59% vs. 3.82% vs. 2.12%, P<0.05) and more *de novo* CKD (8.95% vs. 7.29% vs. 5.48%, P<0.05). Mortality was proportional to stages of AKI and AKD (P for trend <0.05), while AKI followed by AKD was associated with a higher risk of long-term mortality (hazard ratio (HR) 4.51, 4.32-4.71, P<0.05) as compared to AKD without AKI (HR 2.25, 2.13-2.39, P<0.05) and AKI Recover (HR 1.18, 1.09-1.26, P<0.05).

The AKI criterion yielded a higher risk for overall survival and a lower risk for *de novo* CKD than the AKD criterion, indicating that both criteria imply persistent kidney damage but that a rapid decline in excretory kidney function implies higher mortality risks while a persistent decline may rather result in *de novo* CKD (Fig 2). Meanwhile, these associations between different kidney injury criteria and outcomes had good generalizability and were constant across different genders, surgeries, and comorbidities (Fig 2).

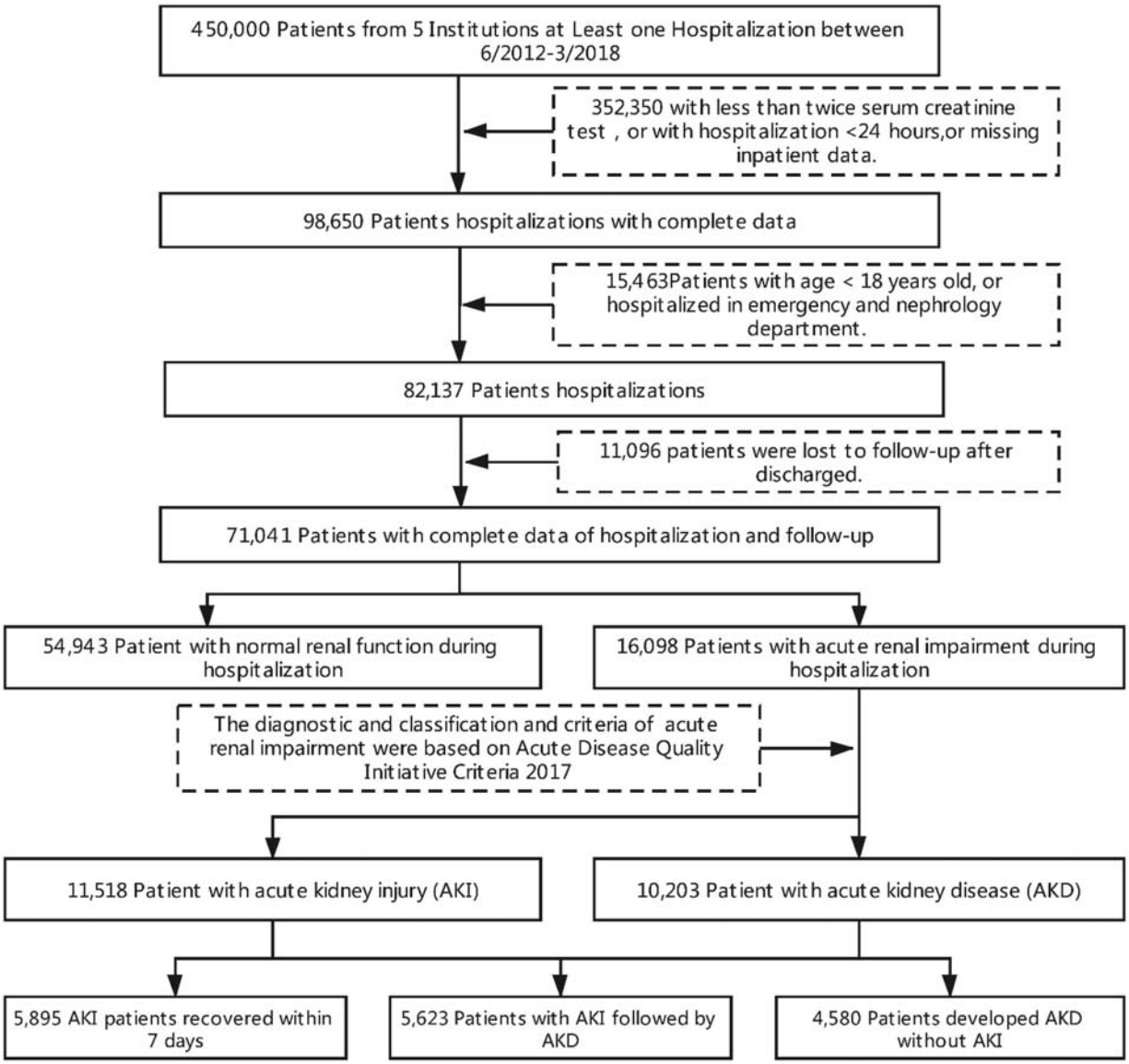


Figure 1. Flow diagram of patient selection

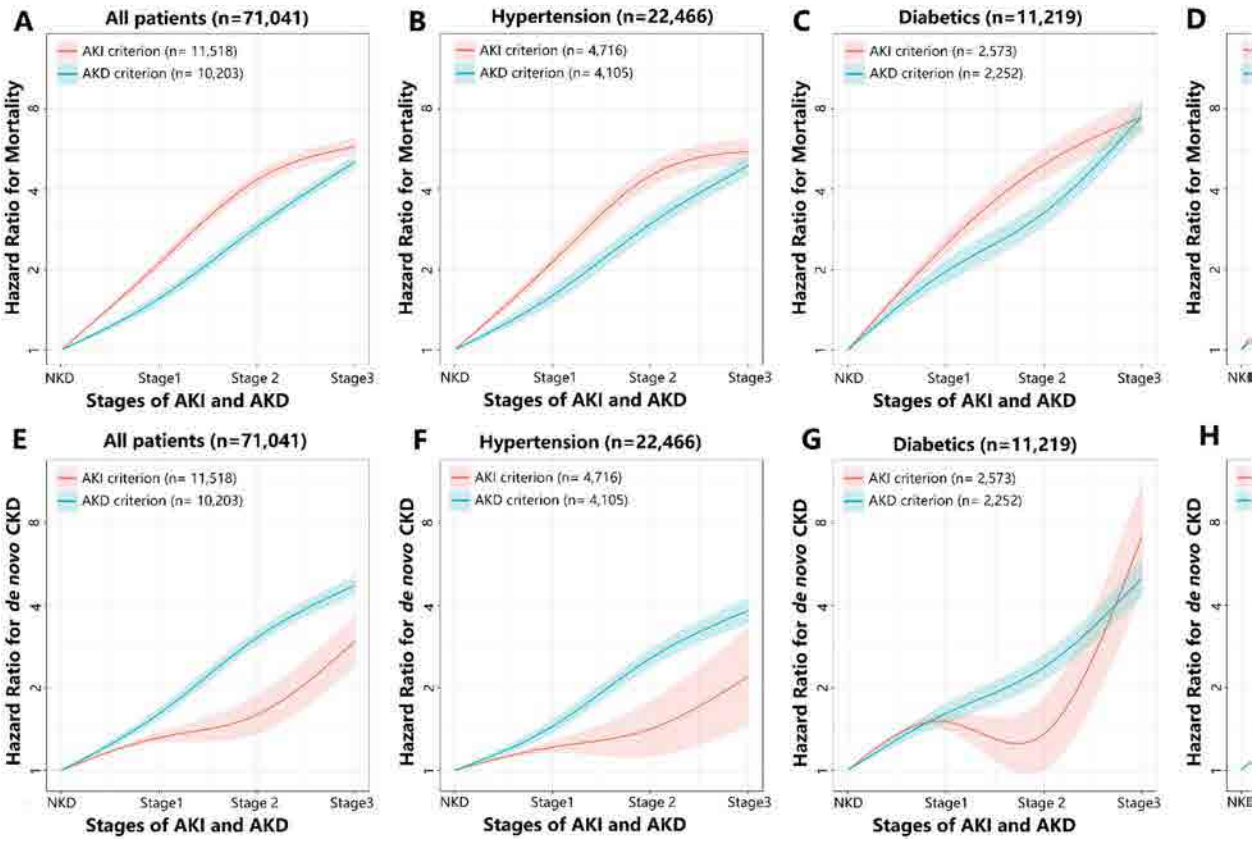


Figure 2. Distributions and hazard ratios of AKI and AKD for survival (A-D) and *de novo* CKD (E-H) by using restricted cubic splines in different clinical setting.

The AKD criterion was robustly associated with overall survival (area under the receiver operating characteristic curve (AUROC) 0.71) and *de novo* CKD (AUROC 0.71), while AKI criterion showed a relatively lower ability to fitting risk of overall survival (AUROC 0.65, P<0.05) and CKD (AUROC 0.63, P<0.05). Moreover, combining AKI and AKD was strongly associated with long-term mortality (AUROC 0.725) and *de novo* CKD (AUROC 0.72) compared to each single criterion of AKI or AKD (Fig 3).

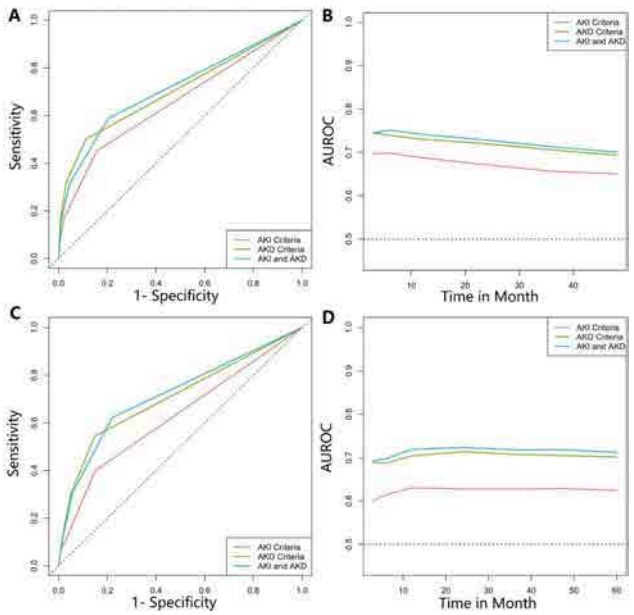


Figure 3. Abilities of AKI and AKD criterion to predict clinical outcome. (A) ROC and (B) time-dependent ROC analyses for survival. (C) ROC and (D) time-dependent ROC analyses for de novo CKD.

Conclusion: (1) Adding AKD as a definition for renal failure lasting >7 days up to 90 days is of clinical importance in addition to the existing definitions for AKI and CKD. (2) These findings suggest research activities and clinical practice should also focus on AKD, which is far more accurate to predict subsequent *de novo* CKD.

P0565 **EVALUATION OF THE WNT SIGNALING PATHWAY AS A PROGNOSTIC MARKER IN PATIENTS WITH UROSEPSIS**

Dong-Jin Oh[1], Jungho Shin[2]

[1]Myongji Hospital, Hanyang University College of Medicine, Internal Medicine, Goyang, Korea, Rep. of South and [2]Chung-Ang University Hospital, Chung-Ang University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Sepsis is a serious condition characterized by a dysregulated inflammatory response to infection, leading to life threatening organ dysfunction. Acute kidney injury (AKI) is one of sepsis-induced organ dysfunction and results in extremely high morbidity and mortality. Emerging evidence demonstrated the relationship between the Wnt signaling pathway and inflammation. In vitro and in vivo studies reported that inhibition of canonical Wnt/β-catenin signaling attenuates the sepsis-induced organ injury and systemic inflammation. On the other hand, Wnt5a, a typical glycoprotein of the non-canonical pathway, may have proinflammatory functions. Studies showed that Wnt5a levels are elevated in patients with sepsis. Despite potentials, there is a paucity of studies evaluating these pathways and correlating it with clinical data, particularly in patients with sepsis. Therefore, this prospective observational study investigated the association between the Wnt pathway and clinical outcomes in patients with urosepsis.

Method: Adult patients (>18 years of age) with urinary tract infection admitted to the intensive care unit of the Myongji Hospital were screened for sepsis according to the 2012 Surviving Sepsis Campaign Guidelines. Thereafter, 38 subjects who were diagnosed with urosepsis were included in the study. Twenty healthy volunteers (10 males and 10 females, aged 55–64 years) were recruited into the control group. In patient serum creatinine levels at day 0, day 5, and at discharge day were obtained for accessing renal recovery. Wnt3a and Wnt5a levels were measured at admission. Levels of Wnt3a and Wnt5a proteins were evaluated using the enzyme-linked immunosorbent assay (ABclonal Biotechnology, Woburn, MA, USA). The primary composite outcome was the incidence of Major Adverse Kidney Events (MAKE), which was defined as new renal replacement therapy, stage 3 AKI by the guideline of the Kidney Disease Improving Global Outcomes, or death. Thereafter, the levels of Wnt3a and Wnt5a were evaluated to predict the primary composite outcome.

Results: 1) Both Wnt3a and Wnt5a levels were significantly increased in the urosepsis group ($P = 0.001$ and $P < 0.001$ respectively) compared to normal individuals. 2) Out of 38 included patients with urosepsis, MAKE occurred in 13 (34.2%) subjects. The patients were divided into two groups, with MAKE (13 patients, 34.2%) and without MAKE (25 patients, 65.8%). No significant difference in the levels of Wnt3a was observed between the two groups ($P = 0.927$); however, the levels of Wnt5a were higher in the patients with MAKE than in those without MAKE ($P = 0.015$). 3) Results showed that Wnt5a levels could be a predictor for the occurrence of MAKE, while Wnt3a levels are not ($P = 0.927$). The area under the curve of Wnt5a was 0.74 (95% confidence interval 0.57– 0.92; $P = 0.016$). 4) The levels of serum creatinine at discharge were higher in the Wnt5a high group than in the Wnt5a low group ($P = 0.030$) although the levels on day 0 and day 5 were similar ($P = 0.201$ and 0.233 respectively).

Conclusion: This study confirmed the elevated levels of Wnt3a and Wnt5a in patients with urosepsis. It furthermore identified that the elevated levels of Wnt5a could predict a higher incidence of MAKE and non recovery of renal function in the patients; however, Wnt3a levels are not associated with MAKE and renal recovery. Accordingly, we suggest that Wnt5a levels can be used as a prognostic marker in patients with sepsis. Further studies with a larger number of subjects are required to confirm the utility of Wnt5a as a biomarker in various diseases including sepsis. This study also suggests the potentials of the Wnt signaling pathway as novel therapeutic targets in sepsis.

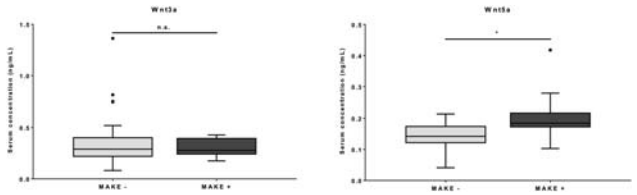


Fig. 1. The levels of Wnt3a and Wnt5a according to the occurrence of Major kidney adverse events (MAKE) (* $p < 0.05$; n.s, non-significnat)

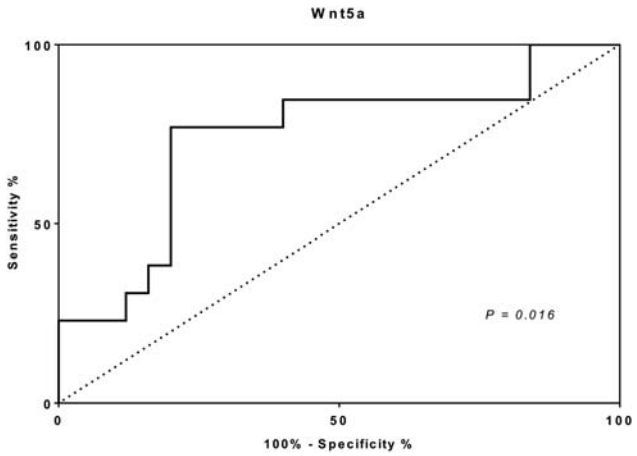


Fig. 2. Receiver operating curves for major kidney adverse events (MAKE)

P0566 INCIDENCE AND IMPACT OF ACUTE KIDNEY INJURY (AKI) IN ANDALUSIA

Wenceslao Aguilera Morales[1], Alfonso Lara Ruiz[1], Irene Díaz Díez[1], Mercedes Salgueira Lazo[1]

[1]*Hospital Universitario Virgen Macarena, Nefrología, Sevilla, Spain*

Background and Aims: Acute Kidney Injury (AKI) is an insufficiently reported clinical entity with significant impact on overall mortality, hospital stay and associated costs, increasing the risk of progression to Chronic Kidney Disease. It is especially relevant in hospitalized patients, where the incidence has doubled in the last decade, reaching 22-25%. Aims: Know the reported incidence of AKI in the Andalusian Autonomous Community, and its impact on mortality, average stay and associated costs.

Method: Cross-sectional descriptive study that analyzes data from all Andalusian hospitals, extracted from CMBDA corresponding to 2017. Hospitalization episodes, reference units, episodes with AKI at discharge, exitus and average stays were collected. An associated cost estimate analysis was also carried out using as reference the costs/day hospitalization in each SAS Assistance Unit according to BOJA Number 218 (14nov2016). The groups were compared according to the presence of the diagnosis of AKI.

Results: There were 525,757 hospital admissions in Andalusia; 25,727 reported the diagnosis of AKI at discharge, assuming an incidence of 4.89%. Patients with AKI total 316,938 stays, with an average stay of 15.5 + 13.8 days, compared to 6.5 + 6 days in which they have no associated diagnosis ($p < 0.01$). The estimated costs associated with the diagnosis of AKI were 168,922,706 euros, with a cost / episode of 24,693 euros vs 3796 in the rest ($p < 0.01$) (AKI/noAKI cost ratio: 6.5), and a cost / day / patient of 823 + 437 euros for AKI compared to 571 euros in the rest. The overall mortality associated with AKI was 26.8% (median 16.6%) vs. 4.76% (median 0.7%) in the rest ($p < 0.01$). AKI/noAKI mortality ratio: 16.

These data may be underestimated since the completion of the CMBDA is not complete in all hospitals and also the diagnosis of AKI may have been present and not reported upon discharge. Estimated costs did not include dialysis sessions.

Conclusion: The incidence of hospital AKI in our Autonomous Community is lower than that reported in the literature, probably due to inadequate reporting to CMBD. In spite of the limitations, our data show the impact of the diagnosis of AKI in hospitalized patients, multiplying by 2.5 the average stay, by 6.5 the associated costs and by 16 mortality, assuming a big problem Public Health that makes it imperative to develop measures to reduce the impact it entails.

P0567 ACUTE KIDNEY INJURY IN OBSTRUCTIVE UROPATHY; EPIDEMIOLOGY, RENAL OUTCOME AND MORTALITY

Bong Gyun Sun[1], Hyeon-jin Min[1], Young-Bin Son[1], Eunho Choi[1], Jihyun Yang[1], Se Won Oh[1], Myung-gyu Kim[1], Sang-Kyung Jo[1], Won-Yong Cho[1]

[1]*Korea University Anam Hospital, Seoul, Korea, Rep. of South*

Background and Aims: Urinary tract obstruction (UTO) is a common clinical problem leading to acute or chronic renal impairment. Unlike pediatric population in which congenital anomalies of urinary tract account for a majority of UTO and contribute to end stage renal disease (ESRD), etiologies, clinical manifestation and outcome in adult UTO remain uncertain due to lack of large epidemiological data.

Method: We performed a multi-center, retrospective study analyzing 1,711 patients who underwent percutaneous nephrostomy (PCN) from 2001 to 2015.

Results: The most common cause of UTO was malignancies (55.6%) followed by urolithiasis (28.5%) and others. Metastatic colorectal cancer were the most common type of malignancies. Patients with UTO caused by malignancies were significantly older, had more advanced stage acute kidney injury (AKI) and higher mortality rate, while those with urolithiasis had higher prevalence of hypertension, diabetes, cardio-cerebro-vascular diseases. Eighty two percentage of patients developed AKI and 15.2% of patients needed a temporary dialysis. Older age, malignancy associated UTO and high uric acid level were independently associated with AKI. Among patients with AKI, 38.2% patients showed a renal functional recovery defined as eGFR $\geq$60ml/min/1.73m2 on day 7 after PCN. Multivariate analysis showed that older age and lower hemoglobin level were independent factors predicting a nonrecovery of renal function. During the median follow up period of $\sim\sim$months, overall mortality rate was 33.9% with the highest rate was found in malignancy associated UTO (51.9%), followed by other causes (15.9%) and urolithiasis (8.8%). Malignancy associated UTO (OR 4.754, 95% CI 3.151-7.174, $p<0.001$), lower albumin level (OR 0.731, 95% CI 0.568-0.942, $p<0.001$) and stage 3 AKI (OR 2.529, 95% CI 1.332-4.803, $p=0.005$) were found to be independently associated with mortality. However, the impact of AKI on overall mortality was more prominent in non-malignancy associated UTO with stepwise increase of mortality as KDIGO stage increased.

Conclusion: In conclusion, malignancy is the most common cause of upper UTO in adults and AKI is frequently associated. Short term renal recovery after PCN was observed only in 38.2% patients and older age, lower hemoglobin level were associated with nonrecovery of renal function. Malignancy associated UTO showed the highest mortality rate compared to urolithiasis or other causes and stage 3 AKI as well as lower hemoglobin and lower albumin level were found to be independent predictors of mortality in UTO.

P0568

INCIDENCE AND RISK FACTORS OF ACUTE KIDNEY INJURY AND TUMOR LYSIS SYNDROME IN PATIENTS WITH MULTIPLE MYELOMA TREATED WITH BORTEZOMIB

SEUNGMIN SONG[1], Hyo jin Boo[1], Hye Ryoun Jang[1], Wooseong Huh[1], Dae Joong Kim[1], Yoon-Goo Kim[1], Jung Eun Lee[1]

[1]*Samsung Medical Center, Nephrology, Seoul, Korea, Rep. of South*

Background and Aims: Nephrotoxicity of bortezomib, a proteasome inhibitor, has not yet been described frequently, while tumor lysis syndrome (TLS) associated with multiple myeloma (MM) has been increased after introduction of the drug. This study compared the incidence and risk factors of acute kidney injury (AKI) and TLS in patients with MM after bortezomib-based chemotherapy to investigate the drug-related nephrotoxicity.

Method: From 2006 to 2017, 276 patients who underwent first cycle of bortezomib-based chemotherapy for MM were identified in single tertiary hospital. Laboratory TLS was defined according to the Cairo-Bishop definition. Development of AKI was assessed by AKI Network (AKIN) criteria within 7 days after first chemotherapy.

Results: The age was 65 [56-72] years old, and 47% (n=131) of participants were female and baseline estimated glomerular filtration rate (eGFR) was 61.3 [34.1-89.1] mL/min/1.73m^2. The incidences of AKI and laboratory TLS were 17% (n=47) and 13% (n=36), respectively. Ten (3.6%) subjects corresponded to the both AKI and TLS criteria. Multivariate analyses showed that lower eGFR category (30∼59, odds ratio [OR]=3.063 [1.278-7.339]; 15∼29, OR=3.417 [1.088-10.726]; <15, OR=10.080 [2.677-37.951] vs ≥ 60), lower serum albumin level (OR=0.491 [0.278-0.868], P=0.0144) and renal amyloidosis (OR=11.174 [3.974-31.420], P<0.0001) were predictors of development of AKI. MM stages and β2-microglobulin were not associated with AKI occurrence.

Regarding laboratory TLS, MM stage and β2-microglobulin were higher in those with TLS. In multivariate analyses, β2-microglobulin levels (OR=1.194 [1.066-1.337], P=0.0021) and any chromosomes abnormalities at high risk (OR=0.115 [0.026-0.503], P=0.0041) were associated with higher risk of TLS.

Conclusion: Development of AKI was often observed without being accompanied by TLS in patients with MM after treatment of bortezomib. In addition, risk factors of AKI and TLS were widely different. These findings implicated the potential nephrotoxicity of bortezomib besides TLS in patients with decreased kidney function. The efforts to prevent bortezomib associated AKI are needed in patients at high risk.

Table. Risk factors of AKI and laboratory TLS after bortezomib treatment: multivariate regression analyses

	AKI			Laboratory TLS		
	OR	95% CI	P value	OR	95% CI	P value
Sex (female)	0.759	0.352-1.639	0.4826	1.877	0.626-5.627	0.2609
Age, years	1.010	0.945-1.046	0.5818	0.920	0.840-1.007	0.0704
Concomitant amyloidosis(ref. no amyloidosis)			<0.0001			0.9531
Amyloidosis withoutkidney involvement	4.789	1.862-12.317	0.0012	1.149	0.148-8.924	0.8945
Amyloidosis withkidney involvement	11.174	3.974-31.420	<0.0001	1.416	0.157-12.796	0.7568
Any high riskchromosomes(more than 1)				0.115	0.0026-0.503	0.0041
Serum albumin, g/dL	0.491	0.287-0.868	0.0144	0.912	0.315-2.643	0.8653
β-2-microglobulin, mg/L				1.194	1.066-1.337	0.0021
eGFR categories,ml/min/1.73m^2 (ref. ≥60)			0.0033			
30~59	3.063	1.278-7.339	0.0121			
15~29	3.417	1.088-10.726	0.0353			
<15	10.080	2.677-37.951	0.0006			

**Variables with P-value less than 0.1 in univariate regression analyses were included in both multivariate models.*

P0569 **ACUTE KIDNEY INJURY AFTER LUNG TRANSPLANTATION: INCIDENCE, RISK FACTORS AND OUTCOMES IN A MONOCENTRIC RETROSPECTIVE COHORT STUDY**

Maria Teresa Gandolfo[1], Cecilia Bellincioni[1], Letizia Corinna Morlacchi[2], Valeria Rossetti[2], Francesco B. Blasi[2], Piergiorgio Messa[1]

[1]Ospedale Maggiore Policlinico Fondazione IRCCS Cà Granda, Medicine, Division of Nephrology Dialysis and Transplantation, Milano, Italy and [2]Ospedale Maggiore Policlinico Fondazione IRCCS Cà Granda, Medicine, Pneumology Division, Milano, Italy

Background and Aims: Acute kidney Injury (AKI) occurs in more than 50% of patients after lung transplantation (LTx). Our aim was to describe the incidence, risk factors and outcomes associated with AKI after LTx in a retrospective monocentric cohort study.

Method: We studied all recipients of LTx (> 16 years of age) occurring at Ospedale Maggiore Policlinico Milano between Jan 1st 2015 and Dec 31st 2017. AKI was defined according to KDIGO classification, eGFR was calculated according to CKD (Chronic Kidney Disease) Epidemiology Collaboration formula and CKD was defined by an eGFR< 60 ml/min per 1.73 m^2. Chi square, Fisher exact test, t.-test and logistic regression were used to define risk factors for AKI in the early post-surgical period and for CKD at 1 and 2 years after LTx. AKI-related survival was estimated using Kaplan Meyer model.

Results: Of 78 LTx patients enrolled in our Center, 50% of patients was affected by cystic fibrosis. Median age at transplant was 43 years (27-55); median follow- up was 31 months (20-40). Survival rate was 80.77% at 1 year, 69.23% at 2 years and 66.67% on Dec 31st 2019 (last follow-up).

AKI occurred in 42 (53.85%) patients within the first week after LTx, respectively grade I and II in 12 each (15.38%) and grade III in 18 (23.08%) patients.

Pre-transplant low albumin levels and hypertension were independently associated with AKI at univariate and multivariate (p= 0.0018 and 0.0004 respectively) analysis. Pre-transplant low albumin levels, pre-transplant ECMO-use, hypertension, ECMO-use during transplant surgery were associated with severe AKI in univariate analysis but only pre-transplant hypertension and ECMO-use during transplant surgery were independently associated in the multivariate one (p=0.0266 and 0.0463 respectively).

Survival was significantly reduced in patients affected by AKI (p=0.035); this observation became strongly significant when only mild and moderate (grade I and II) AKI was considered (p=0.0071).

CKD was diagnosed in 38.09% of patients at 1 year and 35.18% at 2 years.

While numerous risk factors were related to the occurrence of CKD at 1 and 2 years after LTx at univariate analysis, only grade III AKI remained independently associated with CKD at multivariate analysis (p= 0.0081 for 1 year-CKD, p=0.0154 for 2 year-CKD).

Conclusions: In our population, AKI after LTx occurred in about half of the patients and was predicted by history of hypertension, low albumin levels and hemodynamic instability during the surgery. Mild-moderate AKI, often clinically underestimated, was strongly associated with reduced survival. Severe forms of AKI were predictive of occurrence of CKD.

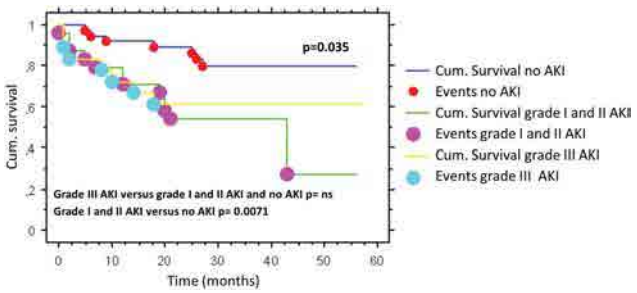


Figure: Kaplan Meyer survival curves stratified by presence and grade of AKI.

P0570

THE INCIDENCE, RISK FACTORS OF ACUTE KIDNEY DISEASES AND DISORDERS AND ITS IMPACT ON CHRONIC KIDNEY DISEASE IN PATIENTS AFTER RADICAL CYSTECTOMY

Shengnan Ge[1], Ying Tang[1], Junzhe Chen[1], Wenjuan Yu[1], Anping Xu[1]

[1] *Sun Yat-sen Memorial Hospital, Sun Yat-sen University, 107 Yan Jiang West Road, Guangzhou, China, Department of Nephrology, Guangzhou, P.R. China*

Background and Aims:

Acute kidney injury (AKI) is a widely-discussed complication associated with the radical cystectomy which is the gold standard for the management of invasive bladder cancer. Until now, few studies investigate the new criteria named Acute Kidney Diseases and Disorders(AKD) as the complication of radical cystectomy. In this study, we evaluated the incidence, risk factors of AKD and evaluate its impact on chronic kidney disease (CKD) in patients after radical cystectomy.

Method:

A total of 279 patients who underwent radical cystectomy at Sun Yat-sen Memorial Hospital, Guangzhou, China, from January 2006 to June 2019 were evaluated, including 168 patients for Robotic-assisted Laparoscopic Radical Cystectomy (RLRC) and 111 patients for Laparoscopic Radical Cystectomy(LRC). AKD was diagnosed according to the classification scheme proposed in the 2012 KDIGO guideline. Logistic regression modeling was used to explore risk factors of AKD, while risk factors associated with CKD in AKD patients were investigated using Kaplan-Meier analysis, respectively.

Results:

The overall incidence of AKD after radical cystectomy was 34.1% (95 out of 279) ,the incidences differ significantly between the RLRC and LRC groups (67 [39.9%] vs 28 [25.2%], *P*=0.011). Among 279 patients, risk factors associated with postoperative AKD included RLRC (OR 2.067, 95%CI 1.188 to 3.595, P=0.010), Age (years) (OR 1.046, 95%CI 1.018 to 1.074, *P*=0.001), baseline eGFR<60(ml/(min.1.73m^2) (OR 2.662, 95%CI 1.355 to 5.230, *P*=0.004), Further subgroup analysis identified age, operation time<250(min) as important risk factors of AKD in RLRC patients but not in LRC patients. Of 211 patients with a preoperative estimated glomerular filtration rate (eGFR) of > 60 ml/min/1.73 m2, CKD developed in 16.0% (21/ 131) of patients in the non-AKD group and 36.3% (29/ 80) of patients in the AKD group. Kaplan-Meier analysis(shown in figure 1) identified that AKD is associated with higher CKD rates in those patients (*P* <0.001).

Conclusion:

One-third of bladder cancer patients developed AKD after after radical cystectomy. RLRC, Age, baseline eGFR <60(ml/(min.1.73m^2) were independent risk factors for postoperative AKD in all patients. Occurance of AKD could increase the risk of new-onset CKD in the long run. Though the use of RLRC is now well established, we should be aware that it may increase the risk of postoperative AKD, especially for patients who are old and with lower eGFR .Besides, we should try to improve the management of those AKD patients with aim toward preventing further development of CKD.

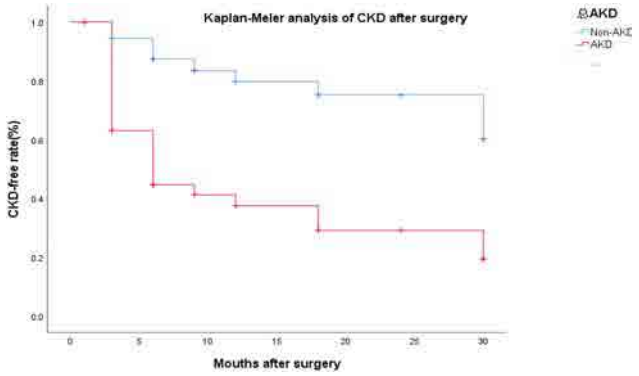


Figure 1.

P0571 EPIDEMIOLOGY AND OUTCOMES OF ACUTE KIDNEY INJURY IN CHILDREN IN UKRAINE

Svitlana Fomina[1], Olga Lavrenchuk[1], Ingretta Bagdasarova[1]

[1]*State Institution "Institute of Nephrology of National of Medical Science Academy of Ukraine", pediatric nephrology, Kyiv, Ukraine*

Background and Aims: The problem of acute kidney injury (AKI) in children continues to be relevant for pediatric nephrology and pediatrics due to the increasing frequency and the lack of a unified approach to management and further monitoring of these patients. The aim of our study was to determine the etiology and outcomes of acute kidney damage in children.

Method: 101 patients (aged from 3 months) were studied in referral center from early period after AKI (first month) to 18 years old. They were observed every 6 months during first year of disease course, and once per year till transfer to adult clinic. The outcomes were identified as complete recovery, isolated albuminuria and chronic kidney disease (CKD). The AKI outcomes were analyzed up to 1.5-3, 5-10 and 15 years of follow up (stage 1, 2 and 3, respectively).

Results: The predominant patients were males (72/71.3%). The most of the children were younger than 3 years old at the time of AKI (58/57.4%), and only a small part of patients were adolescents (7/6.9%).

The hemolytic uremic syndrome (HUS) related to diarrhea was the main cause of the AKI (64/63.4%), and children of the first years of life formed the basis of this clinical group (0-3 years old: 44/68.8%). Sepsis and complicated acute viral and bacterial infections have also been confirmed as common AKI causes (12/11.9% and 8/7.9%, respectively). In some cases AKI were associated with hemolytic anemia (5/5.0%), acute glomerulonephritis (5/5.0%), vaccination (1/1.0%), contrast nephrotoxicity (1/1.0%) or unknown cause (3/3.0%).

At stage 1 (1.5-3 years after event, n=60) complete remission were documented in 24/40.0%, albuminuria from 45 to 601 mg/day without other clinical signs – in 22/36.7%, and CKD 2-4 – in 12/23.3%.

At stage 2 (5-10 years after event, n=54) complete remission were confirmed in 29/53.7%, persisted albuminuria – in 6/14.8%, and CKD 2-4 – in 19/31.5%.

At stage 3 (15 years after event, n=12) CKD 2-4 were founded in all patients with arterial hypertension (n=7), focal-segmental glomerulosclerosis (n=2) and kidney cysts (n=3).

Conclusion: AKI was the most often in children of the first 3 years old, mainly in boys. The development of disease was firstly associated with HUS and severe infections. The long-term outcomes of AKI with distance from the event (AKI) to CKD even with recovery renal function and absence of clinical symptoms were difficult to predict. The prolongation of the observation period, the collaboration between the pediatric and adult centers, the widest usage of verified prognostic markers (i. g. albuminuria) and search for new ones are the most important options in post-AKI management.

P0572

ABSENCE OF RENAL FUNCTION RECOVERY AFTER AN ACUTE KIDNEY INJURY PREDICTS SHORT-TERM MORTALITY

Borja Quiroga[1], Marta Sanz Sainz[1], Begoña Santos Sánchez-Rey[1], Patricia Muñoz Ramos[1], Pablo Ruano[1]

[1]*Madrid, Nephrology, Madrid, Spain*

Background and Aims: The incidence of acute kidney injury (AKI) during a hospitalization is frequent and worsen the prognosis. Recovery of renal function after AKI has been lightly studied and cut-off for establishing full recovery has not been determined. The aim of the present study is to evaluate the association between different degrees of renal function recovery after AKI and short-term mortality post-discharge.

Method: This is a retrospective study that included all the AKI codified in the electronic records of our center in 2013 and 2014. We collect epidemiological data and comorbidities at baseline and laboratory values at admission and discharge. To analyze the impact of recovery of renal function after AKI we performed a univariate logistic regression with different cutoff of creatinine after 7 days of the AKI in comparison to baseline. We used the most sensitive cutoff to define recovery and evaluated associated factors (figure 1). Patients were followed during 30 days to assess associated factors to prognosis after AKI.

Results: We included 1720 patients in this study. After the hospitalization due to AKI, 1194 (69%) entered in the final analysis. Of them 869 (73%) recovered renal function. Factors associated to recovery were age (p=0.01), presence of CKD (p=0.04), basal renal function (p<0.001), history of heart failure (p=0.02), having cognitive impairment (p=0.01), dependence (using Barthel index, p=0.002), renal function at admission (p<0.001), severity of AKI (p<0.001), blood pressure at admission (p=0.02) and hemoglobin at admission (p=0.04). Independent predictors of recovery were basal CKD-EPI (p<0.001), CKD-EPI at admission (p<0.001), severity of AKI (p=0.037), hemoglobin at admission (p=0.016), blood pressure at admission (p<0.001) and history of heart failure (0.001). After discharge, 46 (3%) patients died in the first 30 days. Associated factors to mortality were history of neoplasia (p=0.02), cognitive impairment (p<0.001), Barthel index (p<0.001) and the absence of renal recovery after AKI (defined as reaching a creatinine above 1.2 times of the baseline) (p=0.01). In an adjusted model, renal function recovery independently predicted short term mortality (HR 2.6, 95%CI [1.2-5.4], p=0.01).

Conclusion: The absence of recovery after an AKI is an independent predictor of 30-day mortality.

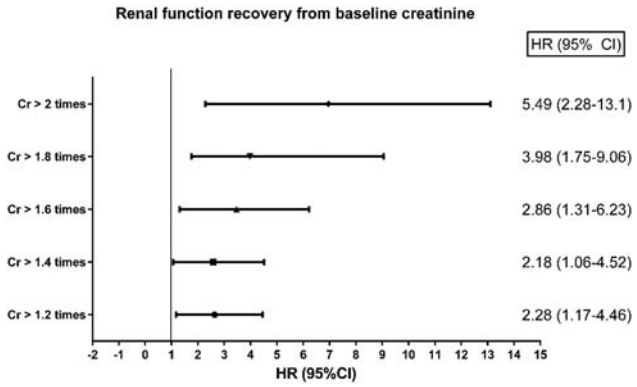


Figure: Forest plot for 30-day mortality regarding the renal function recovery after AKI.

P0573

CLINICAL PRESENTATION AND OUTCOMES OF ACUTE INTERSTITIAL NEPHRITIS: A TEN YEARS' EXPERIENCE FROM A TERTIARY CARE HOSPITAL IN KARACHI, PAKISTAN

Sonia Yaqub[1], Ayesha Aziz Rehman[1], Safia Awan[1]

[1]*Aga Khan University Hospital, Pakistan, Karachi, Pakistan*

Background and Aims: Acute interstitial nephritis (AIN) is a potentially reversible, but relatively under-diagnosed cause of acute kidney injury. The effectiveness of steroids for treatment of AIN is debated. Data is scarce regarding the clinical presentation, use of steroids and its impacts on outcomes in AIN in our part of the world. The objective of our study was to study the clinical features, causes and outcomes of AIN and to evaluate the role of steroids in the management.

Method: We performed a retrospective study of 48 patients with biopsy proven AIN. Exposure was defined as the use of steroids. The main outcomes were recovery of renal function (Early ($\leq$3 weeks) or Late ($>$3 weeks)) and hemodialysis dependence at 12 weeks

Results: 48 (4.9%) AIN cases were found among 978 renal biopsies performed from 2007-2018. Mean age was 47.6 $\pm$ 12.1 years. 56.3% were males. The offending agent was identified in 45.8% cases with NSAIDs (45.4%) being the most common, followed by antibiotics (22.7%), diuretics (9%), and PPI (4.5%). 75% presented with eGFR $<$15 ml/min/1.73m^2 (n=36) out of which 58.3 % (n=21) needed hemodialysis. Mean proteinuria was 2.28 $\pm$ 0.99 g/day. 81.3% (n=39) patients received steroids out of which 39.6% were started on steroids after an initial period of observation after stopping the offending agent. Mean dose of prednisone was 0.8 $\pm$ 0.2 mg/kg per day. Mean time to steroid commencement was 14 $\pm$ 17.39 days.

Early use of steroids ($\leq$11 days after presentation) was significantly associated with earlier recovery (p= 0.009) as compared to late steroids ($>$11 days). A non-significant trend towards complete recovery (within 25% of baseline Creatinine) was noted in early steroid group (52.9%, n=17) vs "no steroid" (33.3%, n=9) or "late steroids" (10.5%, n=19) groups (p=0.208). 47.4% remained dialysis dependent on follow up with no difference made by steroid use (p=0.971).

Conclusion: Our data showed the benefit of earlier use of steroids in achieving rapid and complete renal recovery. Late steroid use was not associated with any further recovery of renal function at an additional risk of exposing patients to undue adverse effects. This is the first report from Pakistan documenting the tendency of nephrologists towards use of steroids for AIN.

P0574

IS PERIPROCEDURAL BLOOD LOSS FOLLOWING PERCUTANEOUS CORONARY INTERVENTION A RISK FACTOR FOR CONTRAST-INDUCED ACUTE KIDNEY INJURY ?

Indu Ramachandra Rao[1], Ganesh Paramasivam[2], Ravindra Attur Prabhu[1], Shankar Prasad Nagaraju[1], Tom Devasia[2], Dharshan Rangaswamy[1], Srinivas Vinayak Shenoy[1], Mohan V B[1]

[1]Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Nephrology, India and [2]Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Cardiology, India

Background and Aims: Contrast-induced acute kidney injury (CI-AKI) is a significant concern with the use of intraarterial contrast agents, especially in percutaneous coronary interventions (PCI) in which higher contrast volumes are used. Presence of anemia is a risk factor for CI-AKI and is a component of various risk-prediction models. However, the impact of periprocedural hemoglobin (Hb) drop following PCI on CI-AKI is not known, despite the fact that significant blood loss is fairly common in patients undergoing PCI. The aim of this study was to examine whether periprocedural Hb drop is a risk factor for development of CI-AKI following PCI.

Method: This was a single-center, retrospective study of patients admitted for elective or primary PCI at our center between January 2015 and December 2018. Patients with baseline eGFR <15mL/min/1.73m^2 were excluded. CI-AKI was defined as per the KDIGO 2012 guidelines as an increase in serum creatinine by at least 0.3 mg/dl, or 1.5-1.9 times the baseline values within 48 hours after administration of contrast media. Periprocedural Hb drop was defined as fall in Hb by at least 1g/dL below baseline values within 48 hours following PCI.

Results: A total of 6418 patients were included. Baseline characteristics of the study population are shown in ***table 1***. Overall incidence of CI-AKI in our study was 7.6% (n=490), of which 3.9% (n=19) required dialysis. Higher incidence of CI-AKI was seen in those with baseline eGFR < 60 ml/min/1.73m^2 (16.4%) and a pre-procedural Mehran score >11 (33%). Peri-PCI Hb drop was seen in 49.9% (n=3203), with a drop >2g/dL in 18.5% (n=1185). On multivariate logistic regression analysis (***Table 2***), it was found that periprocedural Hb drop >2g/dL was independently associated with CI-AKI (OR 1.49, 95% CI 1.18-1.88, P=0.001). Furthermore, in those with periprocedural blood loss, the risk of CI-AKI was increased by 1.3 times for each 1g/dL drop in Hb (OR 1.30, 95% CI 1.14-1.49, P<0.001). Additionally, apart from traditional risk factors, hypertension was independently associated with development of CI-AKI (***Table 2***).

Conclusion: Periprocedural blood loss was associated with a higher risk of CI-AKI after PCI. Moreover, risk of CI-AKI increased with increasing severity of blood loss. Whether measures to minimize blood loss, like using a transradial approach, staging complex procedures and close monitoring of anticoagulation/antiplatelet regimens, will help reduce risk of CI-AKI needs to be studied.

Table 1. Baseline characteristics

	No CI-AKI (n=5928)	CI-AKI (n=490)	P value
Clinical			
Age (years)	60.3±10.8	64.2±10.4	**<0.001**
Male, n (%)	4439 (74.9%)	337 (68.8%)	**0.004**
Diabetes mellitus, n (%)	2542 (42.9%)	227 (46.3%)	0.141
Hypertension, n (%)	3074 (51.9%)	300 (61.2%)	**<0.001**
Primary PCI, n (%)	2325 (39.2%)	284 (58%)	**<0.001**
STEMI, n (%)	3012 (50.8%)	334 (68.2%)	**<0.001**
Pulmonary edema, n (%)	295 (5%)	120 (24.5%)	**<0.001**
Hypotension, n (%)	147 (2.5%)	55 (11.2%)	**<0.001**
IABP, n (%)	135 (2.3%)	48 (9.8%)	**<0.001**
Lab parameters			
Serum creatinine (mg/dL)	1.03±0.32	1.21±0.56	**<0.001**
eGFR (mL/min/1.73m^2)	79.6±21.5	69.8±27.2	**<0.001**
Baseline eGFR <60mL/min/1.73m^2, n (%)	1023 (17.3%)	200 (40.8%)	**<0.001**
Hb (g/dL)	13.4±2.0	12.9±2.4	**<0.001**
Anemia, n (%)	2021 (34.1%)	226 (46.1%)	**<0.001**
Peri-PCI Hb drop, n (%)	2925 (49.3%)	278 (56.7%)	**0.002**
>2g drop, n (%)	1043 (17.6%)	142 (29%)	**<0.001**
Risk score			
Pre-procedure Mehranscore >11, n (%)	193 (3.3%)	95 (19.4%)	**<0.001**

Table 2. Correlates of CI-AKI.

Variables	**Multivariate Analysis**			
	Odds ratio	Lower 95% CI	Upper 95% CI	P value
Peri-PCI Hb drop >2g/dL	1.49	1.18	1.88	**0.001**
Age >75 years	1.23	0.91	1.66	0.449
Male gender	0.96	0.77	1.19	0.734
Diabetes mellitus	1.01	0.83	1.24	0.859
Hypertension	1.41	1.15	1.73	**0.001**
Primary PCI	1.54	1.19	1.97	**0.001**
STEMI	1.50	1.16	1.93	**0.002**
Anemia	1.46	1.19	1.81	**<0.001**
eGFR<60 mL/min/1.73m^2	2.29	1.86	2.80	**<0.001**
Pulmonary edema	3.65	2.81	4.74	**<0.001**
Hypotension	2.17	1.48	3.17	**<0.001**
IABP	1.75	1.16	2.64	**0.007**

P0575 **TIME TO NEPHROLOGY CONSULTATION AND MORTALITY RISK IN COMMMUNITY ACQUIRED AKI**

Isabel Acosta-Ochoa[1], Armando Coca[1], Arturo Lorenzo[1], Alicia Mendiluce[1]

[1]*Hospital Clínico Universitario Valladolid, Nephrology, Valladolid, Spain*

Background and Aims: Acute Kidney Injury (AKI) is the most frequent cause of Nephrology consultation. Although time to nephrology consultation (TNC) has been object of study, few works focus on its influence on in-hospital mortality in patients with community acquired AKI (CA-AKI).

Method: We picked cases of CA-AKI, and divided individuals in dead in-hospital and survivors. We analyzed clinical and epidemiological variables, and categorized AKI with the KDIGO-2012 stages. We compared clinical outcomes and influence of TNC in mortality.

Results: We included 420 patients, 92 (22%) in the mortality group. These individuals were older, had higher Charlson's Index, were hospitalized in critical care units, and were classified in KDIGO-2012 Stage 3 more frequently (Table 1). TNC was higher in the dead patients and was significantly associated with mortality HR 1.28 (CI 95% 1.03-1.55, P=0,009). In KDIGO Stages 1 and 2 TNC was shorter in the survivors group, and in Stage 3 we found no differences. In general wards (medical and surgical), TNC was higher in the mortality group, with no differences in the consults from critical units (Table 1). In the survival curves we observe a decline in survival in patients with TNC ≥2 days since admission (Figure 1).

Conclusion: We found that a longer TNC was associated with a poorer survival. This finding would indicate that earlier nephrology attention could impact in-hospital mortality. We interpret the longer TNC in less severe AKI stages as a warning of the unawareness and late recognition of AKI in other specialties. More well designed and larger studies are needed to prove that electronic alerts offer a survival benefit.

Table 1.

Characteristic Value	Survivors n=328	Dead n=92	P
Masculine (%)	216 (66)	68 (74)	0,37
Age (SD)	**70 ± 15**	**76 ± 11**	**0,001**
HT (%)	296 (90)	74 (80)	0,08
DM (%)	142 (43)	40 (44)	0,99
CKD (%)	200 (61)	60 (65)	0,12
Charlson's Index (SD)	**4,1 ± 2,6**	**5,2 ± 2,2**	**0,01**
Time to Consultation			
KDIGO Stage at Admission			
1 (SD)	**3,9 ± 4,1**	**6,6 ± 4,3**	**0,01**
2 (SD)	**3,7 ± 5,1**	**10,4 ± 15,8**	**0,002**
3 (SD)	2,8 ± 3,5	3,0 ± 3,9	0,90
Medical Ward (SD)	**2,8 ± 3,2**	**5,2 ± 4,9**	**0,003**
Qx Ward (SD)	**5,1 ± 4,8**	**7,3 ± 6,5**	**0,01**
ICU (SD)	8,2 ± 6,5	6,8 ± 5,0	0,60
HD (SD)	4,6 ± 6,2	7,8 ± 7,7	0,26

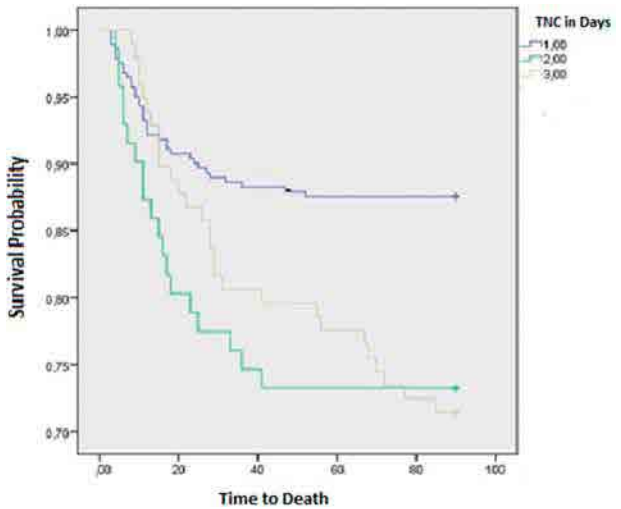


Figure 1.

P0576 **LEFT VENTRICULAR FUNCTION ON TISSUE PERFUSION AND RENAL OUTCOMES IN CRITICALLY ILL PATIENTS WITH SEPSIS**

Jungho Shin[1], Jin Ho Hwang[1], Su-Hyun Kim[1]

[1]*Chung ang University Hospital, Korea, Rep. of South*

Background and Aims: Left ventricular (LV) dysfunction has been regarded as a predictor of mortality in patients with sepsis. However, it remains uncertain whether LV dysfunction deteriorates multiple organ failure by impairing tissue perfusion or it has an independent impact. In this study, we investigated the association between LV dysfunction and tissue perfusion, and their impacts on renal outcomes in critically ill patients with sepsis.

Method: We retrospectively reviewed a total of 162 adult patients with sepsis who met the Sepsis-3 definition. Subjects included 83 (51.2%) with normal LV function, 39 (24.1%) with diastolic dysfunction defined as the septal E/e' ratio >15 among patients with ejection fraction $\geq 50\%$ and 40 (24.7%) with systolic dysfunction defined as an ejection fraction $<50\%$. Tissue perfusion was assessed by the levels of blood lactate.

Results: The initial and 24h levels of lactate, and lactate clearance did not differ regardless of the presence of LV dysfunction (P=0.861, 0.907 and 0.363). The incidence rate of acute kidney injury (AKI) among the patients with initial lactate <2 mmol/L was higher in those with LV dysfunction (P=0.044), conversely, the incidence rate was comparable in the patients with initial lactate ≥ 2 mmol/L (P=0.797). Risks of AKI and renal replacement therapy implementation increased if subjects had blood lactate levels ≥ 2 mmol/L (P=0.009 and 0.080), however, the impact of LV dysfunction on these outcomes depended on previous chronic kidney disease and lactate levels (diastolic dysfunction: P=0.449 and 0.663; systolic dysfunction: P=0.062 and 0.161). However, renal replacement therapy-free days were shorter in those with LV dysfunction, independent of previous chronic kidney disease (P=0.003). Renal function at discharge was not related to the lactate levels and LV function in this study (P=0.685 and 0.089)

Conclusion: LV dysfunction might not influence tissue perfusion in patients with sepsis, on the other hand, it could lengthen the duration of renal replacement therapy. Therapeutic options for preserving microcirculation should be warranted in patients with sepsis, in addition to individualized therapies tailored their LV function.

P0577 **CLINICAL CHARACTERISTICS AND IN-HOSPITAL OUTCOME FOR 1798 CONSECUTIVE PATIENTS WITH ACUTE KIDNEY INJURY**

Christina Montgomerie[1], Jonas Spaak[2], Marie Evans[3], Stefan H. Jacobson[1]

[1]Karolinska Institutet, Division of Nephrology, department of Clinical sciences, Stockholm, Sweden, [2]Karolinska Institutet, Division of Cardiology, department of Clinical sciences, Stockholm, Sweden and [3]Karolinska Institutet, Department of Clinical Science, Intervention and Technology, Solna, Sweden

Background and Aims: Acute kidney injury (AKI) is a common condition occurring in about 15% of all hospitalized patients. AKI have different pathophysiological etiologies; prerenal, renal or postrenal. Patients who recover from AKI have a higher long-term risk of end-stage kidney disease and death. However, most AKI studies include critically ill patients treated at intensive care units; less is known about general AKI patients treated at the nephrology ward. The aim of this large single center study was to report differences in laboratory findings and short-term hospital outcomes in relation to cause of AKI in consecutive patients admitted to a nephrology department.

Method: All patients diagnosed with AKI between 2009 and 2018 and admitted to the nephrology department at Danderyd University Hospital, Stockholm, Sweden, were included. Relevant laboratory and physiological measures were registered, including length of stay, procedures, etiology and level of AKI. AKI was defined as a first s-creatinine (sCr) >130 μmol/L (1.47 mg/dL) at admission, or an increase in sCr by 30% from previous stable out-patient value. These criteria were set at the beginning of the study based on clinical knowledge and clinical practice at the time. Patients on dialysis treatment were excluded. Patients were followed until either discharge or death, whichever came first.

Results: In 1798 patients with AKI, the majority (n=851) had combined type, followed by prerenal (n=668), renal (n=175), and postrenal (n=104) etiology. Patients with renal AKI were younger, had longer duration of stay, and had higher bicarbonate levels on admission (Table 1). The most common cause of renal AKI was interstitial nephritis. Patients with prerenal AKI had lower S-Cr, blood pressure and higher Hb upon admission. 58% of the patients recovered with an at least 30% decrease in sCr from baseline during their stay. Most of these were patients with prerenal AKI followed by combined AKI. There was no statistically significant difference in mortality between the four etiologies of AKI.

Conclusion: This study provides data from a large, contemporary AKI patient cohort under nephrology care. Both patient characteristics and short-term outcomes differ substantially in patients of variable AKI etiology. These findings have important implications for prognostic evaluation upon admission and further resource planning.

Table 1. Characteristics of AKI patients at admission and in-hospital outcomes

	Total	**Prerenal AKI**	**Postrenal AKI**	**Renal AKI**	**Combination**	**p<0.05**
Etiology (%)	*100*	37	5,8	9,7	47	-
At admission						
Age (years)	*74,9*	76,2	75,9	59,2	77	0.012[a]
Female (%)	*40,1*	49,7	21,2	43,4	34,2	<0.001[b]
Dehydration (%)	*58,4*	80,7	1,1	3,3	56,7	<0.001[b]
Urinary obstruction (%)	*14,1*	0,2	87,6	0,8	18,2	<0.001[b]
Interstitial nephritis (%)	*3,8*	0	0	25,4	3,6	<0.001[c]
sCr (μmol/l)	*394*	330	554	376	429	<0.001[a]
CRP (mg/dl)	*78,4*	78	94	73	78	0.403[a]
Hemoglobin (g/l)	*116*	121	113	113	112	<0.001[a]
Potassium (mmol/l)	*4,8*	4,8	4,9	4,4	4,9	0.668[a]
Bicarbonate (mmol/l)	*20,8*	21,1	20,1	23,5	20,2	<0.001[a]
Systolic BP (mmHg)	*131*	125	147	142	132	<0.001[a]
Length of stay (days)	*8,2*	7,1	7,1	9,7	8,9	<0.001[a]
Outcome						
Discharge sCr	*237*	170	218	296	280	<0.001[b]
Renal recovery (>30% sCr decrease) (%)	*57,8*	72,5	69,2	35,4	49,8	<0.001[b]
Deaths (%)	*4,5*	4,8	1,1	2,5	4,9	0.290[c]

a= ANOVA. b= Chi^2-test. c= Fisher-test. Values are presented as mean (SD).

P0578 **QUININE EXPOSURE AND THE RISK OF ACUTE KIDNEY INJURY: A POPULATION BASED OBSERVATIONAL STUDY OF OLDER PEOPLE**

Andrew Duncan[1], Simona Hapca[1,2], Nicosha De Souza[1], Daniel Morales[1,3], Samira Bell[1,4]

[1]University of Dundee, Division of Population Health and Genomics, School of Medicine, Dundee, United Kingdom, [2]University of Stirling, Division of Computing Science and Mathematics, Faculty of Natural Sciences, Stirling, United Kingdom, [3]Health Data Research U.K. Scotland and [4]NHS Tayside, Renal Unit, Dundee,

Background and Aims: Quinine can precipitate Acute Kidney Injury (AKI) by immune-mediated reactions. Cramps, for which quinine is traditionally prescribed, may be a symptom of conditions that are risk factors for AKI. The relationship between quinine and AKI at a population level is unclear. The aim of this study was to establish and quantify any observable association between the exposure to community prescriptions for quinine and AKI events in a population of older adults.

Method: We performed two observational studies of older adults (60+ years) who received quinine prescriptions in Tayside, Scotland, between January 2004 and December 2015. The first study was a retrospective longitudinal cohort study with the primary outcome AKI. Creatinine measurements less than seven days apart were grouped as episodes of care. Multivariable logistic regression was used to calculate odds ratios (OR) for AKI comparing between episodes with and without recent quinine exposure after adjustment for demographics, comorbidities and concomitant medications. A self-controlled case series (SCCS) was then conducted with follow-up divided into periods "on" and "off" quinine for the same individual, calculating incidence rate ratios (IRR) for AKI adjusting for age.

Results: The first study included 12,744 individuals who experienced 13,616 AKI events during cohort follow-up (crude incidence 12.5 per 100 person-years). Exposure to quinine before an episode of care was significantly associated with an increased probability of AKI (adjusted OR=1.27, 95% CI 1.21-1.33). The SCCS cohort included 5,907 people with quinine exposure with $\geq$1 AKI event. Exposure to quinine was associated with an increased relative incidence of AKI compared to unexposed periods (IRR=1.20, 95% CI 1.15-1.26), with the greatest risk observed within 30 days of quinine initiation (IRR=1.48, 95% CI 1.35-1.61).

Conclusion: Exposure to quinine in patients aged 60 years and over was associated with an increased risk of AKI, the incidence of which is unlikely to simply be explained be immune-mediated reactions only. Further research is required to determine exact reasons for the increased risk of AKI.

P0579

EVALUATION OF BIOMARKERS EFFICIENCY IN PREDICTIVE AND EARLY DIAGNOSTICS OF ACUTE KIDNEY INJURY IN ACUTE CORONARY SYNDROME

Eugene Vorobyev[1], Alexei Smirnov[1], Anatoly Kucher[1], Olga Galkina[1], Irina Zubina[1], Anastasia Anpilova[1], Evdokia Bogdanova[1], Elena Levykina[1]

[1]*First Pavlov St.-Petersburg State Medical University, Clinical Research Center, Institute of Nephrology, St-Petersburg, Russia*

Background and Aims: Acute Kidney Injury (AKI) is a common complication of acute coronary syndromes (ACS), and associated with higher mortality and adverse outcomes. Despite advances in research over the past years, effective treatments for current AKI are not available. Prevention and early intervention remain the most effective strategies for AKI of any entity. This study aimed to explore a risk factors and biomarkers for predictive and early diagnostic of AKI in ACS.

Method: Study was prospective and cohort, patients hospitalized with ACS in Pavlov First Saint Petersburg State Medical University were included. In case of exclusion of ACS, patients were determined in the comparison group, in case of confirmation of the diagnosis of ACS - in the study group. Biomaterial (blood and urine) was taken at admission (T1), 1 day after admission (T2) and 2 days after admission (T3). For the diagnosis of AKI, KDIGO 2012 criteria were used for the diagnosis of AKI. The measured biomarkers at each point were NGAL, KIM-1, cystatin C, sST2, troponin I.

Results: The study included 73 patients, the diagnosis of ACS was confirmed in 40 patients and AKI development was in 15 patients, all from the ACS group. The most significant for predictive diagnosis was the assessment of the parameters of systemic hemodynamics and the severity of acute heart failure (AHF): heart rate>90 (AUC=0,798, p=0,001), GRACE Risk Score>133 (AUC=0,926, p=0,005). In evaluation the suitability of biomarkers in terms of prognostic diagnosis of AKI, urine NGAL>32 ng/ml (AUC=0,814 p=0,04) and sST2>23.4 ng/ml (AUC=0,718, p=0,02) showed the best results.

Conclusion: In study of biomarkers efficiency, the use of urine sST2 and NGAL is most promising. Together with hemodynamic parameters, biomarkers have high predictive ability in the diagnosis of AKI in ACS.

P0580 ACUTE INTERSTITIAL NEPHRITIS RELATED TO EMPAGLIFLOZIN

Alon Bnaya[1], Eyal Itzkowitz[1], Jawad Atrash[1], Mohsen Abu-Alfeilat[1], Linda Shavit[1]
[1]*Shaare Zedek Medical Center, Nephrology Institute, Jerusalem, Israel*

Background and Aims: SGLT-2 inhibitors are effective anti-hyperglycemic agents with proved cardiovascular and renal benefits. However, there have been post marketing reports of episodes of acute kidney injury (AKI), some requiring hospitalization and even dialysis in patients receiving SGLT2 inhibitors. This phenomenon may be related to volume contraction and hemodynamic changes, particularly in patients with other risk factors (such as patients on RAAS blocking agents or NSAIDS, patients with CKD). We present a case of acute interstitial nephritis (AIN) and acute tubular necrosis related to an SGLT2-inhibitor.

Method: Case report description.

Results: A 67-year-old women was admitted with weakness, dizziness and abdominal pain. Her medical history was remarkable for hypertension, diabetes mellitus, ischemic heart disease and peripheral vascular disease. Her medications included bisoprolol, losartan, amlodipine, sitagliptin and aspirin. Two months prior the current presentation, empagliflozin was prescribed by her primary physician for her diabetes mellitus. However, several days after initiation of empgliflozin she felt weak and dizzy and empagliflozin was discontinued. A week before the current presentation, empagliflozin was re-initiated by her cardiologist.

The patient reported no recent illness, fevers, rash, arthralgias, respiratory symptoms or bone pain. She denied exposure to other new medications (including NSAIDS and antibiotics).

On admission, blood pressure was 165/76 mm Hg. The rest of the physical examination was unremarkable. Laboratory studies revealed acute kidney injury (creatinine 3.19 mg/dL, BUN 28 mg/dL, baseline creatinine 0.9 mg/dL). Complete blood count demonstrated no eosinophilia or thrombocytopenia.

Urinalysis showed a few leukocytes but no red cells or casts. The urine protein to creatinine ratio was 5160 mg of protein per gram creatinine. Abdominal ultrasonography showed normal-size kidneys and no hydronephrosis.

Immunologic and infectious serologies were unremarkable. over several days the patient became oligo-anuric and creatinine peaked to 9.22 mg/dL and hemodialysis was initiated. Empiric treatment with prednisone was given and a renal biopsy was performed. Four glomeruli were seen on light microscopy. The glomeruli were normocellular. An interstitial infiltrate of lymphocytes and small numbers of eosinophils were seen. Thining of the renal tubular brush border with intra-tubular necrotic content was a also seen. Immunofluorescence was negative. The findings were compatible with acute interstitial nephritis and acute tubular necrosis (Figure 1).

The patient was discharged with a regimen of intermittent hemodialysis and steroid therapy. Three months later, urine output and kidney function improved, and the patient was weaned off dialysis.

Conclusion: In this case report, we describe previously unreported histologically proven AIN likely related to empagliflozin exposure. Although SGLT2 inhibitors have been reported to be associated with AKI it has been supposed to be related to volume contraction and hemodynamic changes. As virtually any drug can cause AIN, further proof of the drug's causation in our case was an onset of renal dysfunction with re- institution of empagliflozin, biopsy-proven AIN and absence of other drugs, infection or systemic disease that might cause AIN. With the dramatic increase in use of SGLT-2 inhibitors worldwide, treating physicians should be aware of AIN as a possible cause of AKI in this context.

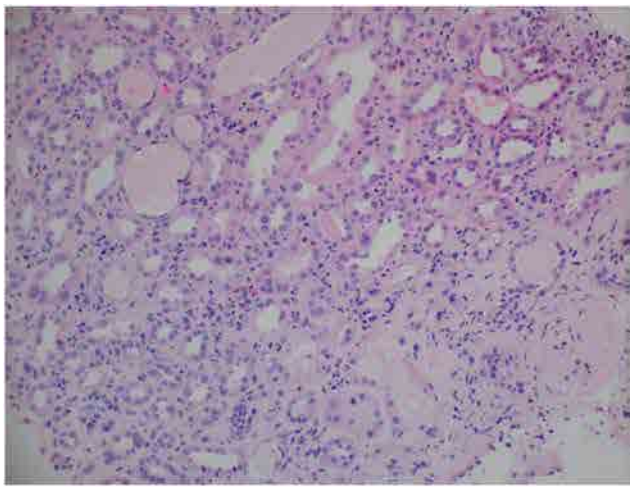


Figure 1. Kidney biopsy. Interstitial edema with lymphocytic and eosinophilic infiltrate. Dilated tubules with thinning of the brush border containing necrotic content is also demonstrated.

P0581 **HIPERKALEMIA IN COMMUNITY-ADQUIRED ACUTE KIDNEY INJURY. ASSOCIATED FACTORS AND CLINICAL CONSEQUENCES.**

Jose Maria Peña Porta[1], Almudena Castellano Calvo[1], Ana Coscojuela Otto[1], Alejandro Tomás Iatorre[1], José Antonio Ferreras Gascó[1], Rafael Alvarez Lipe[2]

[1]*Hospital Clinico Universitario Lozano Blesa, Nephrology, Zaragoza, Spain*

Introduction and Aims: Hyperkalemia (hyperK) is an analytical alteration that frequently occurs in the context of acute kidney injury (AKI) adding morbidity to the patient. We know little about the associated factors and the clinical consequences of this complication in patients with community-acquired acute kidney injury (CA-AKI). The aim of present study was to analyze the predisposing factors and the clinical consequences of the hiperK in patients with CA-AKI.

Method: The present study is based on a cohort of patients with CA-AKI admitted to the Nephology Service of a third level hospital from January 2010 to February 2015. Hyperkalemia was defined by the laboratory of our hospital as potassium levels above 5.1 meq / L

Results: A total of 308 patients were included in the final analyses. The mean age was 73,22±13,95 years. 58,4% were men. Charlson comorbidity index (CCI) was 7,16 ±2,7 points. The mean of drugs ingested daily was 7,81±3,66 and the length of stay 12,25±11,69 days. In view of the Etiology of AKI, 69,5% prerenal AKI and 30,5% non-prerenal ones. 212 patients had a history of previous chronic kidney disease (CKD) (68.8%). Hemodialysis (HD) was required in 54 patients (17.15%). 38 patients (12.3%) died during hospital stay. HyperK occurred in 173 cases (56,2 %). Mean potassium was 5,45±1,41 meq/L (95% IC 5,29-5,61) (range 2.65-9.70). There was a significant correlation between potassium and pH (r = - 0.328; p <0,001) as well as between K and CCI (r= 0,284; p <0,001). There was an association between hyperK and intake of potassium-sparing diuretics (p<0,001); ACEI/ARB (p=0,003) and beta blocker (p<0,001). There was no association with CKD nor NSAID intake. Using a multiple linear regression model the equation that predicted serum potassium level was: K = 36,44 – (4,4 x pH) + 0,98 (if intake of potassium-sparing diuretics) + (0.10 x CCI). Potassium level did not influence the length stay. Patients with HyperK required HD in a higher proportion (23.7 vs. 9.6%; p 0.01) and also had higher mortality during hospital stay (15.6 vs. 8.1%; p 0.048). After a follow-up of 971±702 days after hospital discharge, Kaplan-Meier survival curves showed a significant difference (Log Rank (Mantel-Cox): Chi-square 20,1; p< 0,001) between patients with hyperK and patients that did not present it.

Conclusion: HyperK occurred in just over half of our patients. The potassium level was significantly determined by the previous comorbidity, pH and the intake of potassium-sparing diuretics. HyperK patients required HD and died in a greater proportion during hospital stay than the others. Mortality after discharge was higher in patients who presented hyperK during hospital stay. Appropriate measures must be taken to correct hyperK early in patients with CA-AKI.

P0582 MAGNESIUM TREATMENT IN PREECLAMPSIA SHOULD BE TARGETED TO SERIC LEVELS TO AVOID TOXICITY

Afonso Santos[1], Eunice Cacheira[2], Sílvia Coelho[3], Paulo Telles Freitas[3]

[1]Hospital Fernando Fonseca, Nephrology Department, Lisboa, Portugal, [2]Hospital de Santa Cruz, Nephrology Department, Lisboa, Portugal and [3]Hospital Fernando Fonseca, Intensive Care Unit, Lisboa, Portugal

Background and Aims: Preeclampsia is potentially serious complication of pregnacy and frequently requires admission in ICU. Management of this condition involves treatment with magnesium sulfate to prevent progression to eclampsia or even more adverse outcomes such as maternal or fetal death. However the exact dose of magnesium needed is still to be determined and few studies have analyzed the impact of this therapheutic intervention in women admitted in intensive care units, in terms of outcomes and adverse effects. Herein, we present a series of patients diagnosed with preeclampsia, including its most severe presentations with eclampsia or HELLP syndrome, admitted in an intensive care unit.

Method: Demographic, clinical and laboratorial data of women admitted between January-2016 and December-2018 to the Polyvalent Intensive Care Unit (ICU) of Hospital Fernando Fonseca, a tertiary Hospital in Portugal, with the diagnosis of preeclampsia, were retrospectively collected. Diagnosis of preeclampsia, HELLP syndrome and eclampsia were performed according to the ISSHP criteria (2004). Acute Kidney Injury (AKI) was defined according to the KDIGO criteria. The study was approved by the Ethical Committee of the institution.

Results: 42 patients were included, 52.3% (n=22) diagnosed as non-severe preeclampsia; 31% (n=13) as HELLP syndrome and 16.7% (n=7) as eclampsia. Mean age at presentation was 29.6±6.6 years old, with 52,4% (n=22) caucasian and 47.6% (n=20) black. Most patients were admitted in ICU in post-partum period, after cesarian delivery in 95.2% (n=40). Seven patients (16.7%) had a previous diagnosis of hypertension; 11.9% (n=5) were obese; none has previous chronic kidney disease.

At presentation, most patients diagnosed with preeclampsia had three diagnostic criteria (28.6%, n=12), including hypertension. Renal dysfunction was found in 80.9% (n=34) of patients, with proteinuria >200mg/dL in 69% (n=29) and AKI in 19% (n=8). Mean Hb of 11.1±2.1g/dL, with median platelet count of 126000/uL (IQR 72000-201500) and median LDH of 388mg/dL (IQR 240-773).

Pre-partum magnesium sulfate treatment was initiated in 78.6% (n=33) of patients, but only 2.4% (n=1) had previous magnesemia levels determination. During the stay in ICU, daily levels of seric magnesium levels were obtained, with the highest median values found at day one after admission. Adverse events related to hypermagnesemia (bradipnea) occurred in 50% (n=21) of patients. In six patients (14.3%), treatment was stopped because of high levels of magnesemia or adverse events. 14.3% (n=6) progressed to eclampsia and fetal death occured also in 14.3% (n=6). Maternal deaths did not occur.

By logistic binary regression we found out that weight was an independent risk factor for the development of the composite outcome of eclampsia or fetal death, when adjusted to age, race, AKI, hemoglobin, platelet count, ALT, LDH, serum albumin and proteinuria. (p=0.04). However, when Magnesium was included in the analysis, all variables lost significance. An association between SOFA and SAPS scores and the occurrence of the composite outcome has been found (p= 0.03 and p=0.019, respectively).

Conclusion: Most patients with preeclampsia received treatment with magnesium sulfate without previous measurement of serum levels. Bradipnea occurred in 50% of cases and treatment had to be stooped in almost 15%. Nevertheless, magnesium levels were not independently associated with the composite outcome of fetal death or eclampsia. Future studies should evaluate if a dose adjusted to a specific target of magnesium seric level could be associated with less adverse effects while still reducing the risk associated with preeclampsia.

P0583 **RED CELL DISTRIBUTION WIDTH PREDICTS CONTRAST-INDUCED NEPHROPATHY IN PATIENTS UNDERGOING ENHANCED COMPUTED TOMOGRAPHY**

Youqi Li[1], Yongjun Shi[1], KeXuan Li[1], Jian Shen[1], ShaoBing Xiao[1]

[1] *Huizhou Municipal Central Hospital, Nephrology, Huizhou, P.R. China*

Introduction: Contrast-induced nephropathy (CIN) is an major complication of enhanced computed tomography(CT) procedures.Development of CIN after enhanced CT may lead to worse clinical outcomes. Thus, markers are used to identify the risk of patients ,who undergo enhanced CT with CIN.Red cell distribution width(RDW) is a measurement of erythrocyte variability and heterogeneity, and it is obtained routinely in standard complete blood cell counts.Current researches indicate that RDW is the independent predictor of AKI after patients receiving percutaneous coronary intervention (PCI).However, the correlation of RDW and CIN after enhanced CT are yet to be determined.In this study we investigated whether RDW levels correlate with development of CIN in patients after enhanced CT.

Method: A total of 633 patients undergoing enhanced CT from June 2015 to June 2018 at Huizhou Central Municipal Hospital were enrolled. Patients were divided into CIN group and no-CIN group. The diagnostic criteria for CIN is an increase in serum creatinine(Scr) more than 44.2μmol/L or 25% higher than the baseline value within 72 hours after contrast administration.

Results: The study population consisted of 633 patients ,25(3.95%) patients developed into CIN. Patients who got CIN were older and had a higher prevalence of active smoking compared with those were without CIN. The range of the baseline serum creatinine and red cell distribution width was significantly higher in CIN groups.However,baseline eGFR,red blood cell counts,hemoglobin and albumin levels were significantly lower in patients who developed CIN(all $P<0.05$).Multivariate logistic regression analysis revealed that baseline RDW level(OR=2.325,95% CI 1.521∼3.556,$P<0.001$),albumin(OR=0.888,95%CI 0.803∼0.982, P=0.021)and eGFR(OR=0.921,95%CI 0.849∼0.999,P=0.047)were independent risk factors in the development of CIN in patients after enhanced computed tomography.The area under the ROC curve for RDW was 0.803(95% CI 0.706∼0.900,$p<0.001$),and an RDW of 13.85% or higher predicted CIN with a sensitivity of 72% and specificity of 75.80%(Figure 1).

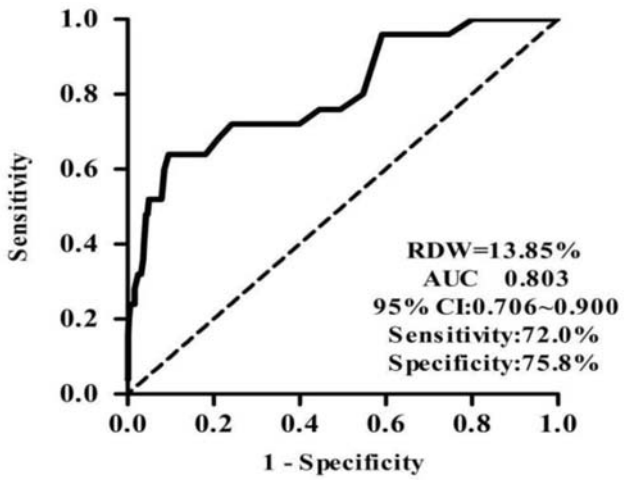


Figure 1 The ROC curve analysis for red cell distribution width(RDW)

levels in predicting of contrast-induced nephropathy(CIN)

Conclusion: Increased baseline of RDW, decreased eGFR and lower albumin are independently related with a higher risk of CIN in patients undergoing enhanced CT.RDW is possibly a predictive biomarker for the early diagnosis of CIN.

P0584 **A COMPARATIVE STUDY ON THE INCIDENCE OF CONTRAST INDUCED NEPHROPATHY FOLLOWING INTRA-ARTERIAL VERSUS INTRAVENOUS CONTRAST ADMINISTRATION**

Adel Moideen[1]

[1]*Dr. D.Y. Patil Medical College, NEPHROLOGY, Pimpri-Chinchwad, India*

BACKGROUND: Contrast-induced nephropathy (CIN) / Contrast induced-acute kidney injury (CI-AKI), defined as a relative increase of ≥25% or an absolute increase of ≥0.5 mg/dL in S.Cr levels assessed at 48 hours post procedure, is a well described following an administration of Intra-arterial (IA) iodinated contrast agent, but its occurrence after Intravenous (IV) contrast is being questioned.

AIMS: To compare the incidence of CIN following IV and IA contrast procedures and to identify its risk factors.

METHOD: This is a prospective, single center study of 774 patients (449 males and 325 females with mean age of 48.85 ± 14.05 years) who underwent contrast studies with nonionic, low-osmolar iodinated contrast agent (Iomeprol) via IV and IA routes were included in the study. We recorded baseline characteristics along with laboratory parameters; underlying renal injury risk factors; contrast administration volume, type, and route of administration; incidence of CIN and requirement of renal replacement therapy (RRT). Univariate and multivariate models were used to determine predictors of CIN.

RESULTS: The total incidence of CIN was 14.85% (115 patients). Baseline eGFR was lower for patients undergoing intra-arterial contrast procedures (66.02 ± 23.70 ml/min/1.73m^2 vs 71.31±24.07 ml/min/1.73m2, p=0.002). Simple logistic regression showed a statistically significant difference in the rate of CIN in patients who received IV vs. IA iomeprol (6.2% vs 25.1%). The total risk of RRT was 1.7% with the incidence being more in the IA group than the IV group (3.1% vs 0.5%, p=0.005). Advanced age, dehydration and hypotension, CCF, anemia, proteinuria, diabetes mellitus, preexisting renal disease (i.e. baseline serum creatinine>1.5mg/dl), baseline eGFR<60ml/min/1.73m^2), use of nephrotoxic antibiotics and route of contrast correlated significantly with CIN. Proteinuria ≥1 g/day and hypoalbuminemia was significantly higher in the intra-arterial group than the intravenous group (p=0.001).

CONCLUSION: We found that administration of both IV and IA iodinated contrast agents is associated with a risk of CIN with a significant higher risk of CIN as well as RRT following IA contrast. Proteinuria may be a new risk factor for the development of CIN.

Risk factor	Intra-arterial (n=354)	Intravenous (n=420)	p value
Mean age (yrs)	55.768±12.45	41.94±15.64	0.001
Female sex	143 (40.4%)	182 (43.3%)	0.49
CIN incidence	89 (25.1%)	26 (6.2%)	0.001
Mean volume of contrast (ml)	154.32±38.63	69.79±26.71	0.001
DM	154 (43.5%)	116 (27.6%)	0.001
Hypertension	140 (39.5%)	105 (25.0%)	0.001
Dyslipidemia	74 (20.9%)	48 (11.4%)	0.001
Hypotension	32 (9.0%)	12 (2.9%)	0.001
Dehydration	46 (13.0%)	23 (5.5%)	0.001
Coronary artery disease	118 (33.3%)	78 (18.6%)	0.001
Heart failure	82 (23.2%)	0 (0%)	0.001
Prior PCI	79 (22.3%)	50 (11.9%)	0.001
Smokers	160 (45.2%)	160 (38.1%)	0.04
Nephrotoxic antibiotics	189 (53.4%)	233 (55.5%)	0.56
ACEi/ARBs	58 (16.4%)	55 (13.1%)	0.19
Diuretics	62 (17.5%)	54 (12.9%)	0.07
NSAIDs	101 (28.5%)	72 (17.1%)	0.001
Statin use	132 (36.0%)	115 (28.3%)	0.02
Pre-existing renal disease (S.Cr>1.5mg/dl)	83 (23.4%)	84 (20.0%)	0.24
Prior renal surgery	10 (2.8%)	7 (1.7%)	0.27
High risk (eGFR <60ml/min/1.73m^2	146 (41.2%)	140 (33.3%)	0.02
Anemia	193 (54.5%)	223 (53.1%)	0.69
Hypoalbuminemia	122 (33.2%)	79 (19.4%)	0.001
Proteinuria (UPCR≥1)	95 (25.9%)	66 (16.2%)	0.001

Laboratory parameter	**Intra-arterial** (n=354)	**Intravenous** (n=420)	p value
Hb (g/dl)	12.105±2.42	12.24±2.28	0.4
HCT (%)	35.54±6.68	37.16±6.88	0.001
TLC (per cu.mm)	6901.72±1483.08	7352.19±1729.53	0.001
Platelet (lakhs per cu.mm)	2.85±0.84	2.98±0.89	0.05
Pre-procedure S.Creatinine (mg/dl)	1.18±0.46	1.16±0.51	0.61
Pre-procedure eGFR (ml/min/1.73m2)	66.02±23.703	71.31±24.07	0.002
Post-procedureS.Creatinine (mg/dl)	1.50±0.97	1.12±0.76	0.001
Uric acid (mg/dl)	3.87±1.21	3.79±1.17	0.38
Serum albumin	3.35±0.61	3.52±0.51	0.001
UPCR	0.71±0.72	0.55±0.62	0.001

P0585 **ANEMIA AS A PROGNOSTIC FACTOR IN CONTRAST-INDUCED ACUTE KIDNEY INJURY IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE.**

Olga Mironova[1], Olga Perekosova[1], Alina Ushanova[1], Georgy Isaev[1], Alexander Ermolaev[1], Ekaterina Schelkanovceva[1], Polina Lakotka[1], Victor Fomin[1]

[1]*Sechenov University, Internal Diseases, Moscow, Russia*

Background and Aims: Contrast-induced acute kidney injury (CI-AKI) remains one of the major obstacles to perform percutaneous coronary interventions (PCI), especially in older patients and in patients with comorbidities. The number of cases of stable coronary artery disease (CAD) requiring such kind of interventions, in spite of optimal medical treatment received, remains high. Diabetes, hyperuricemia and other components of metabolic syndrome, as well as heart failure, are well known risk factors predisposing to the development of CI-AKI after contrast exposure. Anaemia is diagnosed in a number of patients without underlying chronic kidney disease (CKD), when they seek for medical help due to CAD.

The aim of our study was to assess the prevalence of CI-AKI (primary outcome) and the prognostic significance of anaemia as a its possible risk factor (secondary outcome) in different groups of patients with stable CAD requiring PCI using the contrast media.

Method: We conducted a single-centre prospective observational cohort study. 561 patients aged 18-89 with stable CAD undergoing PCI were enrolled from June 2012 until October 2013. The CI-AKI was defined as a rise in serum creatinine of $\geq$0,5 mg/dl ($\geq$44μmol/l) or a 25% increase from baseline value, assessed at 48-72 hours after PCI. Anaemia was defined according to the WHO definition – haemoglobin level $<$12,0 g/dl in women and $<$13,0 g/dl in men. The contrast media used was either iodixanol (iso-osmolar contrast) or iopromide (low-osmolar contrast), which are both known to cause less adverse events than high-osmolar types of contrast. Nephrotoxic drugs were stopped 48 hours before PCI. The 5-year prognosis including all-cause and cardiovascular mortality, myocardial infarction, stroke, gastrointestinal bleeding, decompensation of chronic heart failure, repeat revascularizations (PCI and coronary artery bypass grafting), end-stage renal disease (ESRD) development, was assessed via phone calls and appointments according to the clinical situation and severity of the condition.

Results: The prevalence of CI-AKI in this group of patients was 104 cases (18,5%) (primary outcome). The number of patients with anaemia was higher in the group of patients who developed CI-AKI after PCI (6% [7/104] vs 4,4% [20/457]). The female patients with anaemia were more likely to develop CI-AKI (71% [5/7] vs 35% [7/20]). The number of patients who suffered from MI having anaemia at the inclusion date was 2 (28,6%) vs 6 (30%) in patients with and without CI-AKI respectively. Acute heart failure decompensation in patients with anaemia was significantly higher in patients with CI-AKI (43% [3/7] vs 10% [2/20]). This fact needs further evaluation in larger studies but anaemia may be one of the prognostic factors, worsening the kidney damage and leading to worse cardiorenal outcomes.

Conclusion: Patients with stable CAD suffering from anaemia are more likely to develop CI-AKI even without underlying CKD or ESRD. Female patients with anaemia and stable CAD have higher risk of development of CI-AKI. The combination of CI-AKI and anaemia may lead to a higher 5-year risk of acute heart failure decompensation.

P0586

ACUTE KIDNEY INJURY IN PATIENTS UNDERGOING CARDIAC SURGERY: A PROSPECTIVE, OBSERVATIONAL STUDY TO ASSESS INCIDENCE, SEVERITY, RISK FACTORS AND MORTALITY IN TERTIARY CARE HOSPITAL IN INDIA

Reetesh Sharma[1], Salil Jain[2], Naresh Trehan[3]

[1]Asian Institute of Medical Sciences, Nephrology and Kidney Transplant Medicine, Faridabad, India, [2]Fortis Institute of Medical Sciences, Nephrology and Kidney Transplant, Gurgaon, India and [3]Medanta-the Medicity, Cardiac Surgery, Gurgaon, India

Background and Aims: Acute kidney injury (AKI) occurs in up to 30% of patients undergoing cardiac surgeries and is associated with increased morbidity and mortality. There is paucity of such data in our country. Hence this study was done to assess the incidence of AKI following cardiac surgery and its associated risk factors along with outcomes, in the Indian context.

The incidence and severity of AKI in patients with normal renal parameters vs those with underlying CKD was studied. We also compared incidence and severity of AKI in patients undergoing surgery off pump vs on pump.

Method: All patients age>25yrs of either gender undergoing cardiac surgeries were enrolled prospectively from July to October 2018. Patients undergoing aortic surgeries or on dialysis, renal transplants or with pre-existing AKI were excluded. Incidence and severity of AKI was defined by the AKIN criteria. NKF/DOQI definition was used to define CKD. Prevalence of risk factors such as age, sex, BMI, diabetes mellitus, hypertension, dyslipidemia, CKD, CVA, peripheral vascular disease (PVD), prior myocardial infarction (MI), peri-operative acute myocardial infarction (AMI), use of cardiopulmonary bypass (CPB) and prolonged ventilation were assessed.

Results: 1,040 patients were enrolled with these baseline characteristics: 83.5% were males, mean age 58.2±10.4 years, mean BMI 25.6±4.3, diabetes in 48.2%, hypertension in 57.5%,dyslipidemia in 70%,CVA in 36%,CKD in 6.3%,PVD in 0.9%,peri-operative AMI in 0.6%,use of CPB in 24%. Overall incidence of AKI was 23.3% and was 71.2% in patients with underlying CKD. AKI was more severe in patients with higher CKD stages. Stage3 AKI occurred only in patients with CKD stage 3 and 4. Overall the need for dialysis was 1.1% and it was 4.9% in AKI group. 8.5% of patients with CKD needed dialysis as compared to 4.1% without CKD.In multivariate risk factor analysis hypertension (p=0.01),peri-operative AMI (p=0.03), prolonged ventilation (p=0.01), CVA (p=0.01) and CKD ($p<0.001$) were found to be significantly associated with AKI whereas diabetes (p =0.12), PVD (p=0.13), use of CPB (p=0.4), prior AMI (p=0.07) were not significant. Mean hospital stay was prolonged in those with AKI (8.33±4.06 vs 7.16±3.01 days ($p<0.001$)). Overall the mortality was 0.67% and it was 2.9% in AKI group. All mortalities were associated with AKI.

Conclusion: Incidence of AKI (23.3%) and mortality (0.67%) in cardiac surgery patients at our centre in India is similar to other reported studies. We found that underlying CKD is the most significant risk factor for AKI in these patients in addition to hypertension, CVA, prolonged ventilation and pre-operative AMI. Use of CPB did not increase the incidence of AKI. AKI significantly increases mean hospital stay and is also associated with increased in-hospital mortality.

P0587

CLINICAL PROFILE AND SHORT-TERM OUTCOMES OF ACUTE KIDNEY INJURY IN PATIENTS WITH PRE-ECLAMPSIA AND ECLAMPSIA

Manjuri Sharma[1], MASTAKIM AHMED MAZUMDER[1], Pranab Jyoti Mahanta[1], Prodip Kumar Doley[1], Gayatri Pegu[1], Shahzad Alam[1]

[1]*Gauhati Medical College & Hospital, Nephrology, Guwahati, India*

Background and Aims: Acute kidney injury (AKI) is rare in women during pregnancy and puerperium. Although sepsis remains the predominant cause of AKI in pregnancy in developing countries, pre-eclampsia and eclampsia are important causes and can be life threatening. The primary focus of this study was to analyze the clinical profile as well as maternal and fetal outcomes of AKI in pregnant females with pre-eclampsia and eclampsia.

Method: A prospective study of patients admitted with pre-eclampsia or eclampsia and AKI in Gauhati Medical College Hospital from June 2018 to June 2019. Clinical profiles and outcome data were recorded. AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria.

Results: A total of 26 cases were recorded. The mean maternal age at delivery was 27.5 ± 5.1 years. At least one recorded preexisting medical condition, including hypertension, diabetes mellitus, or chronic kidney disease was present in 5 cases (19.2%). Cesarean section was performed in 9 cases (34.6%). Eighteen patients (69.2%) developed AKI in third trimester and 6 (23.1%) within 12 weeks postpartum. Four patients (15.4%) were treated with dialysis. Four women (15.4%) died and 2 (7.7%) remained dialysis dependent 12 weeks after delivery. Low birth weight (<2500 g), small for gestational age or preterm birth (<37 weeks gestation) occurred in 11 pregnancies (42.3%). There were 2 (7.7%) neonatal deaths. AKI occurring before 34 weeks of gestation had worse fetal outcomes as compared to those after 34 weeks ($p<0.05$).

Conclusion: AKI in pregnancies with pre-eclampsia or eclampsia can not only lead to maternal mortality and morbidity but also poor perinatal outcomes. Preeclampsia or eclampsia presenting with AKI early during gestation had worse fetal outcomes.

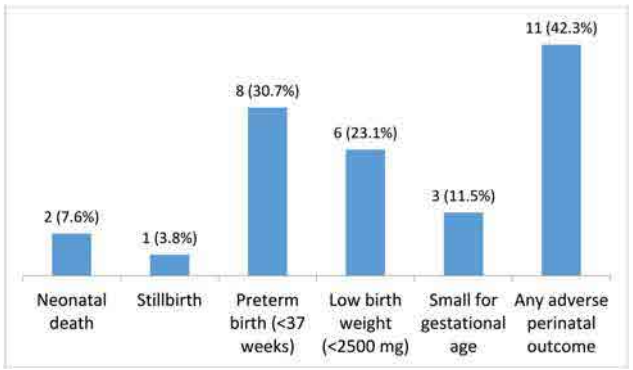


Fig 1. Adverse Perinatal Outcomes

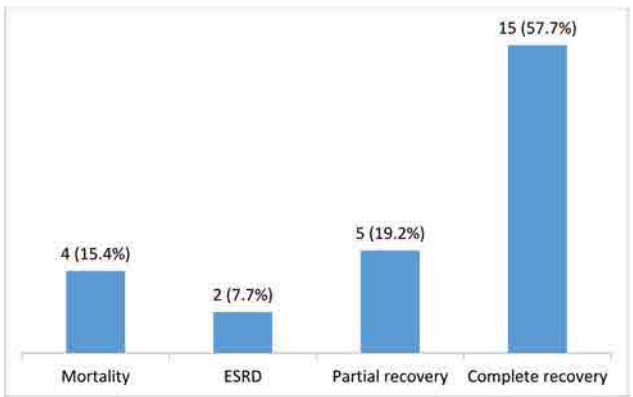


Fig 2. Maternal Renal Function at 3 months

P0588 **TUBULAR EPITHELIUM INJURY BIOMARKERS AND SURVIVAL AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION**

Kirill Smirnov[1], Vladimir Dobronravov[1], Alexei Smirnov[1]

[1]*Pavlov First Saint Petersburg Medical University, Nephrological department, Saint Petersburg, Russia*

Background and Aims: In our recent study we have shown, that some tubular epithelium injury molecular biomarkers (MBMs) may be used for acute kidney injury (AKI) prediction in a specific category of patients, receiving hematopoietic stem cell transplantation (HSCT). Here we aimed to determine the value of this MBMs for the evaluation of the mortality following HSCT.

Method: 90 HSCT recipients (46 males, 44 females) were enrolled. All-cause mortality was registered along 1 year of posttransplant period. MBM's (calbindin, clusterin, IL-18 (interleukin-18), KIM-1 (kidney injury molecule-1), GST-π (glutathione S-transferase- π), MCP-1 (monocyte chemoattractant protein-1)) relative concentration increase was determined in alive and deceased patients after HSCT. MBM's associations with death risk were estimated in multivariate models adjusted for clinical factors related to the prognosis (AKI, progression of the underlying disease, incomplete HLA compatibility, etc.).

Results: It was found that the relative increase in the concentrations of some MBMs was significantly higher in the group of deceased HSCT recipients (Figure). In multivariate models the associations of KIM-1, MCP-1, and calbindin with mortality were not reliable (data not shown). As for clusterin, this relationship was **reliable** and **independent** of other significant clinical factors, including overt AKI (HR=1,085 (1,034-1,139; p=0,001).

Conclusion: Urinary MBMs, taking into account their independent association with posttransplant all-cause mortality risk, may become a useful tool not only for AKI prediction, but also for HSCT prognosis evaluation.

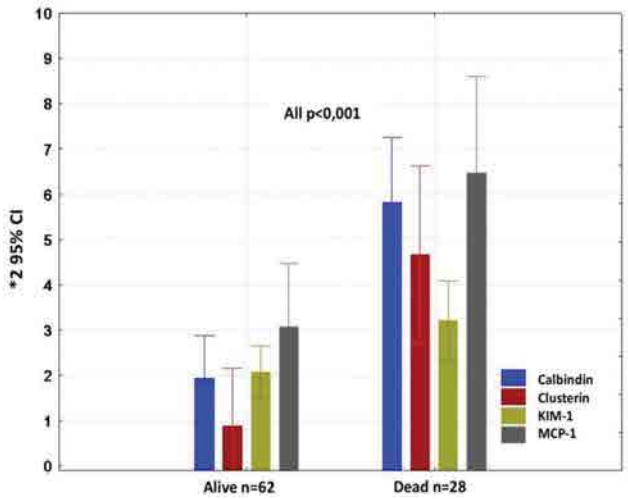


Figure:

P0589

ACUTE KIDNEY INJURY IN PATIENTS UNDERGOING LIVING DONOR LIVER TRANSPLANT-INCIDENCE ,RISK FACTORS AND SHORT TERM PATIENT OUTCOMES ,A PROSPECTIVE SINGLE CENTER STUDY

Abhyudaysingh Rana[1], Ashwini Gadde[1], Amit Mahapatra[1], Neeraj Saraf[2], Arvinder Soin[3], Shyam Bansal[1]

[1]Medanta-The Medicity, Department of Nephrology & Renal transplant, Gurugram, India, [2]Medanta-The Medicity, Department of Gastroenterology & Hepatobiliary science, Gurugram, India and [3]Medanta-The Medicity, Department of Liver transplant and Regenerative medicine, Gurugram, India

Background and Aims: AKI is a major concern in the management of candidates for liver transplantation. Post-LT AKI is associated with worse short- and long-term recipient and graft outcomes and the subsequent development of chronic kidney disease (CKD).Most of the studies done on this are on deceased donor Liver transplant ,or if done on Living donor are retrospective in nature & there is inconsistency in studies regarding definition of AKI

To assess incidence, risk factor and outcomes of patient developing acute kidney injury(AKI) in patients undergoing living donor liver transplant(LT).

Method: This is a single center prospective study. Patients over age of 18 years undergoing living donor liver transplant were selected consecutively from Jan 19 to April 19, prospectively followed for 1 month post op to assess incidence of AKI(Early-<=7,Late >7 to <30) & reassessed at 3 months for persistence of renal dysfunction .Patients with fulminant liver failure, those undergoing combined liver kidney transplant & who died within first 72 hour post-LT were excluded .AKI was defined by KDIGO criteria. Preoperative, Intraoperative & Post operative variables were analysed for risk factor & patient outcomes by regression analysis.

Results: 62 patients underwent LDLT between period of Jan 2019 to April 2019 .22(35%) patients developed AKI .15 (68%) had stage 1 AKI ,5 (23%) Stage 2 & 2(9%) had stage 3 AKI requiring CRRT.14 (64 %) patients had early AKI ,8 (36%) had late AKI.Acute CNI toxicity (3,14%) was most common cause of early AKI.Most common cause of Late AKI was Sepsis (7,11%).Use of vasopressors intra op & Past history of AKI (HRS) were the only statistically significant($p < 0.001$) risk factors for AKI .The mean ICU stay among patients with AKI was 7.2 $\pm$4.2 days vs 4.5$\pm$1.2 days in patients without AKI .Median days to normalization of liver enzymes in non AKI group was 10 days vs 20 days in AKI group.2 (3.2%)patient had persistence of renal dysfunction at 3 month. 7(11.2%) patients died during analysis period, 2(3%) of them from AKI group.

Conclusion: - Incidence of AKI (35%) was higher in our study as compared to other cohort but lead to CKD in 2 patients . Past history of AKI (HRS) was a significant risk factor for Post op AKI though pre transplant e GFR did not differ in both group. Although AKI was transient but it lead to increase ventilator stay ,ICU stay and prolonged normalization of graft function in patients undergoing Living donor liver transplant.

P0590

ADVERSE RENAL OUTCOME FOLLOWING ADMINISTRATION OF INTRAVITREAL ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR INHIBITORS IN A SINGLE TERTIARY CENTRE IN MALAYSIA

Maisarah Jalalonmuhali[1], Tengku Ain Fathlun Tengku Kamalden[2], Nurul 'Ain Sham Ismail[3], See Yen Yong[1], Wei Ting Teo[4], Soo Kun Lim[1]

[1]Pusat Perubatan Universiti Malaya, Department of Medicine, Kuala Lumpur, Malaysia, [2]Pusat Perubatan Universiti Malaya, Department of Ophthalmology, Kuala Lumpur, Malaysia, [3]Port Dickson Hospital, Department of Medicine, Port Dickson, Malaysia and [4]Queen Elizabeth Hospital, Department of Medicine, Kota Kinabalu, Malaysia

Background and Aims: Intravenous (IV) anti-vascular endothelial growth factor(VEGF) is a potent anti-angiogenic factor for the treatment of solid tumours. While, intravitreal anti-VEGF injection is used in the treatment for macular and retinal diseases. The effects of IV anti-VEGF agents are well documented to cause hypertension, renal impairment and proteinuria. However only few reports showed the significance of intravitreal anti-VEGF injection causing minimal change disease (MCD) and acute kidney injury (AKI). Hence, this study is to determine the outcome of renal function following intravitreal anti-VEGF injection.

Method: This is a prospective, cross sectional study recruiting patients from ophthalmology day-care operation theatre that were scheduled for intravitreal anti-VEGF injection in University Malaya Medical Centre (UMMC). On the day of the injection of anti-VEGF, patients' demographic data (age, gender, medical background, medications), blood pressure, height, weight and investigations for serum creatinine and urine protein creatinine ratio (PCR) were collected. Following these, they will receive the intravitreal anti-VEGF as per schedule. All these patients were given a follow-up within 72hours to reassess blood pressure, serum creatinine and urine PCR.

Results: A total of 90 patients were recruited. However, 15 patients were subsequently excluded as there was no repeated serum creatinine at 72-hours post treatment. Their mean age was 67.25 ± 10.41. Among all, 3 patients had significance increased in serum creatinine (4%) with significance changed of urine PCR post treatment. Table 1 showed baseline parameters prior to treatment and table 2 was post treatment parameters.

Higher serum creatinine and proteinuria pre intravitreal anti-VEGF were identified to have higher OR of 1.018 (95% CI 1.001-1.035) (p=0.043) and OR 1.004 (1.000-1.007) (p=0.025) respectively among those who developed AKI. In assessing the association between higher pre-treatment creatinine and proteinuria (independent variable) and development of AKI (dependent variable) estimated by logistic regression with no AKI as a reference group we found that there were no significance.

Conclusion: Following intravitreal anti-VEGF administration, there were no significant changes in blood pressure. However, 4% from our cohort had AKI and worsening proteinuria at 72 hours post treatment. These patients had higher serum creatinine and proteinuria prior to treatment. However, our study is underpowered to establish the relationship between intravitreal anti-VEGF and development of AKI. Further study with larger sample size and longer-term outcome is needed.

Variable	No AKI (n=72)	AKI (n=3)	p value (95% CI)
Underlying Diabetes Mellitus	56/72 (77.78%)	3/3 (100%)	0.598
Height	161.18 ± 8.38	164 ± 1.00	0.565 (-12.52-6.89)
Weight	69.92 ± 13.86	60.37 ± 5.29	0.241 (-6.54-25.63)
Systolic BP pre injection	142.01 ± 18.50	141.67 ± 9.29	0.974 (-21.15-21.85)
Diastolic BP pre- injection	71.58 ± 11.29	76.00 ± 7.21	0.505 (-17.56-8.73)
Creatinine pre-injection	91.92 ± 41.87	159.33 ± 123.62	0.015 (-121.54- -13.29)
uPCR pre injection	91.66 ± 176.81	437.30 ± 527.54	0.004 (-575.06- -116.22)

Table 1: Baseline parameters before intravitreal anti-VEGF injection among the patients that developed AKI vs no-AKI.

Variable	No AKI (n=72)	AKI (n=3)	p value (95% CI)
Systolic BP post injection	141.14 ± 21.53	139.67 ± 17.47	0.907 (-23.69-26.63)
Diastolic BP post injection	71.72 ± 10.51	70.33 ± 6.66	0.822 (6.14 - -10.86)
Creatinine post injection	90.56 ± 41.18	209.67 ± 159.66	<0.001 (28.55- -176.01)
uPCR post injection	97.16 ± 266.02	639.00 ± 795.88	0.003 (173.52- -887.83)

P0591 AKI TREATMENT WITH CVVH IN THE ICU: A FIFTEEN MONTH SINGLE-CENTER EXPERIENCE

Bernardo Lucca[1], Silvia Perletti[1], Gabriele Mortari[1], Paola Gaggia[1], Roberto Zubani[1], Chiara Manenti[1], Ezio Movilli[1], Francesco Scolari[1]

[1]*ASST Spedali Civili di Brescia, U.O. Nefrologia, Brescia, Italy*

Background and Aims: AKI (Acute Kidney Injury) is a condition associated with elevated morbility and mortality. It determines prolonged hospitalization and severe long-term complications. AKI often complicates the course of patients' stay in ICU (Intensive Care Units) sometimes requiring CRRT (Continuous Renal Replacement Therapy). Our aim was to prospectively analyze and report our experience on CRRT carried out in our hospital's ICUs, and to compare it with guideline recommendations and with other international experiences.

Method: This is a single-center prospective observational study. We collected epidemiologic, clinical and technical data regarding all CRRT treatments performed in the four ICUs (two general ICUs and two cardiological ICUs) at the ASST Spedali Civili of Brescia Italy, between 02/01/2018 and 05/31/2019. AKI was defined according to KDIGO guidelines. Exclusion criteria were: age less than 16 years, chronic dialysis treatment, functioning kidney transplantation. All CRRT were provided in the CVVH (Continuous Veno-Venous Hemofiltration) mode.

Results: We included 146 incident patients (M: 103; 70%), mean age 71 ± 15 years. Most treatments were performed in the cardiological ICUs (58%) as opposed to the general ICUs (42%). AKI was present at the moment of admission to the ICU in 67% of patients. 53% of patients had previous CKD. The most frequent comorbidities were: hypertension (73%), diabetes (45%), ischemic heart disease (38%). The most frequent reasons for starting CVVH were: severe oliguria (88%) and fluid overload (68%). 57% of patients had stage 3 AKI. At the time of treatment initiation 55% of patients also had congestive heart failure, 52% metabolic acidosis, and 51% sepsis. 23% were recovering from heart surgery and 10% from general surgery. Mechanic ventilation was performed in 40% of patients, non-invasive ventilation in 28%. 82% of patients required vasoactive treatment. The average SOFA score was 10 ± 2,9. Technical details of CVVH prescription are reported in Fig 1. The most common vascular access was a dual lumen femoral vein catheter in 96% of cases. Citrate anticoagulation was used in 32% of treatments, heparin in 27%. Circuit coagulation was the most frequent cause for set substitution (45%). Treatments using citrate had fewer set coagulations compared to heparin (18% vs 32%). The average dialysis dose was 31,2 ml/kg/h. Median treatment duration was 7,6 days, median stay in the ICU was 14,3 days, median global hospitalization lasted 30,9 days. Mortality rate was 47% in the ICU and 64% 90 days after discharge. The most frequent causes of death were MOF (33%), septic shock (20%) and cardiogenic shock (14%). As illustrated in figure 2, multivariate analysis showed that mortality was negatively influenced by the presence of liver cirrhosis, septic shock, cardiogenic shock and rhabdomyolysis. After hospital discharge, 14 patients continued to require chronic dialysis.

Conclusion: Our experience shows that in patients with AKI requiring CVVH, mortality rate is negatively influenced by the presence of septic and cardiogenic shock, liver cirrhosis and rhabdomyolysis. Treatment prescription respected clinical and technical guideline recommendations, and is mostly comparable to the related international literature.

Table 1 Technical details of CVVH prescriptions.

	Mean
Qb (ml/min)	143 (SD ± 19)
Reinfusion (ml/h)	1863 (SD ± 502)
Fluid removal (ml/h)	114 (SD ± 58)
Predilution (%)	75 (SD ± 11)
Patient weight (kg)	78 (SD ± 18)
Dialysis dose (ml/kg/h)	31,2 (SD ± 4,7)

Table 2 Technical details of CVVH prescriptions.

	Liver cirrhosis	Septic shock	Cardiogenic shock	Rhabdomyolysis
RR	4,4	2,2	2,3	2,9
CI 95%	2,02 – 9,46	1,38 – 3,67	1,38 – 3,85	1,13 – 7,39
P	<0,001	0,001	0,001	0,027

P0592 **RISK FACTORS FOR SEPSIS ASSCOCIATED-ACUTE KIDNEY INJURY IN INTENSIVE CARE UNIT PATIENTS**

Xin Wang[1], Jiaojiao Zhou[2], Jia Yang[1], Siwen Wang[1], Lichuan Yang[1]

[1]West China Hospital of Sichuan University, Division of Nephrology, Chengdu, P.R. China and [2]West China Hospital of Sichuan University, Division of Ultrasound, Chengdu, P.R. China

Background and Aims: To explore the risk factors of acute kidney injury in patients with sepsis in intensive care unit (ICU).

Method: The medical records of patients diagnosed with sepsis in ICU of west China hospital of Sichuan university from March 2009 to June 2016 were retrospectively analyzed. Differences between AKI group and Non-AKI group in general data, background disease, ICU entry and exit dates, complications, laboratory data and other related data were analyzed through univariate and multivariate statistical methods.

Results: A total of 2331 patients with sepsis were included in the study, including 626 patients in the AKI group and 1695 patients in the Non-AKI group. The multivariate logistic regression analysis confirmed that age >40 yr. [odds ratio (OR) =2.811], diabetes (OR=2.818), hypertension/coronary heart disease (OR=1.781), CKD (OR=13.221), the length of ICU stay ≥14 days (OR=3.327), heart failure (OR=2.316), ARDS (OR=2.105), SAP (OR=2.566), hypotension (OR=2.048), hypoproteinemia (OR=1.607), lactic acidosis (OR=2.380), hypoproteinemia (OR=1.607), organ failure >1 (OR=4.604),WBC > 10 $\times 10^9$/L (OR=4.197), serum creatinine (OR=4.535), PCT (OR=1.808), Cys-C (OR=7.066), mild anemia (OR=2.321), moderate anemia (OR=4.047), and severe anemia (OR=6.100) were all independent risk factors of SA-AKI.

Conclusion: A variety of risk factors are related to the occurrence of SA-AKI. Early identification and monitoring of risk factors for SA-AKI and early prevention of AKI can improve the prognosis of sepsis patients.

Table 1 Comparison of baseline characteristics between Non-AKI group and AKI group

Variables	Non-AKI n=1695	AKI n=636	t/x^2	*P*
Age (yr.)	57±13.09	63.35±12.40	-10.573	<0.001
Gender	-	-	1.219	0.270
Male (%)	1105 (65.19)	399 (62.74)		
Female (%)	590 (34.80)	237 (37.26)		
Hypertension/CHD (%)	440(25.96)	266(41.28)	55.132	<0.001
Diabetes (%)	325(19.17)	230(36.16)	73.586	<0.001
COPD (%)	591(34.87)	252(39.62)	4.53	0.033
CKD (%)	20(1.18)	100(15.72)	200.321	<0.001
LOS in ICU (d)	12.78±7.74	18.25±8.40	-14.286	<0.001
Heart failure (%)	389(22.59)	238(37.42)	49.256	<0.001
SAP (%)	134(7.91)	107(16.82)	39.68	<0.001
Hypotension (%)	628(37.05)	369(58.02)	83.073	<0.001
Hypoproteinemia (%)	551(32.51)	293(46.07)	36.826	<0.001
Lactic acidosis (%)	298(17.58)	190(29.87)	42.223	<0.001
Failed organ (%)	-	-	103.543	<0.001
0 failed organ	240(14.16)	22(3.46)		
1 failed organ	218(12.86)	26(4.09)		
2 failed organs	334(19.71)	160(25.16)		
3 failed organs	459(27.08)	216(35.96)		
≥ 4 failed organs	444(26.19)	212(33.33)		

Table 2 Multivariate logistic regression analysis of influencing factors of AKI for patients with sepsis

Variables	*B*	*SE*	Wald	*P*	*OR*	95%*CI*
Age (>40 yr.)	1.033	0.386	7.158	0.007	2.811	1.318-5.992
Diabetes (yes)	1.036	0.211	24.121	<0.001	2.818	1.864-4.261
Hypertension/CHD (yes)	0.577	0.202	8.174	0.004	1.781	1.199-2.645
CKD (yes)	2.582	0.465	30.805	<0.001	13.221	5.313-32.903
LOS in ICU (≥14 d)	1.202	0.193	38.76	<0.001	3.327	2.279-4.856
Heart failure (yes)	0.84	0.204	16.881	<0.001	2.316	1.551-3.457
ARDS (yes)	0.744	0.19	15.328	<0.001	2.105	1.450-3.055
SAP (yes)	0.942	0.275	11.715	0.001	2.566	1.496-4.403
Hypotension (yes)	0.717	0.192	13.93	<0.001	2.048	1.405-2.983
Hypoproteinemia (yes)	0.474	0.191	6.135	0.013	1.607	1.104-2.339
Lactic acidosis (yes)	0.867	0.215	16.328	<0.001	2.380	1.563-3.623
Failed organs (>1)	1.527	0.306	24.91	<0.001	4.604	2.528-8.385
Baseline Scr (mg/dL)	1.512	0.143	111.061	<0.001	4.535	3.423-6.007
HGB (g/L)	-	-	41.215	<0.001	-	-
Female: 90≤HGB<110	0.842	0.314	7.187	0.007	2.321	1.254-4.295
Male: 90≤HGB<120						
60≤HGB<90	1.398	0.277	25.553	<0.001	4.047	2.353-6.958
30≤HGB<60	1.808	0.297	37.12	<0.001	6.100	3.410-10.914
WBC (>10 $\times 10^9$/L)	1.434	0.25	32.798	<0.001	4.197	2.569-6.857
Cys-C (mg/L)	1.955	0.129	230.634	<0.001	7.066	5.490-9.094
PCT (μg/L)	0.592	0.074	64.254	<0.001	1.808	1.564-2.090

P0593 **INCIDENCE AND IMPACT OF ACUTE KIDNEY INJURY (AKI) IN A THIRD LEVEL HOSPITAL**

Wenceslao Aguilera Morales[1], Alfonso Lara Ruiz[1], Irene Díaz Díez[1], Marina Almenara Tejederas[1], Mercedes Salgueira Lazo[1]

[1]*Hospital Universitario Virgen Macarena, Nefrología, Sevilla, Spain*

Background and Aims: The AKI index is increasing, reaching 22% in hospitalized patients. Despite the negative impact it implies, in daily practice its management remains suboptimal and there is little awareness of the problem. Aims: Know the incidence of AKI in a Third-level hospital; its impact on mortality, average stay and associated costs.

Method: Descriptive cross-sectional study of data extracted from CMBDA corresponding to a third level hospital during 2016-17. We analyze: hospitalization episodes, referral assistance units, AKI episodes at discharge, stays and exitus. To calculate associated costs, we use as reference the costs/day-hospitalization per Healthcare Unit in SAS according to BOJA-Number 218 (14nov2016). We compare groups according to presence/no AKI. Limitations: These data may be underestimated since the diagnosis of AKI may be present and not reported upon discharge; Nor do we include dialysis costs.

Results: 56,816 revenues were produced; 3,589 reported AKI (incidence: 6.31%). Patients with AKI add 42,801 stays; Average stay of 18.4 days in 2016, 16.4 in 2017, compared to 6.6 and 8.7 days respectively when FRA is not associated ($p < 0.01$). The estimated costs associated with the FRA were 22,815,558 euros, with a cost / episode of 6023 euros, compared to 3523 euros in patients without FRA. The overall associated mortality AKI was 23.2% vs 11% in the rest ($p < 0.01$). Average stay, costs and mortality vary widely according to the Assistance Units, the impact being especially worrying in Surgical Units (table).

Conclusion: The incidence of AKI in our hospital lower than that referred to in the literature probably responds to inadequate registration in discharge reports. Despite the limitations, our data demonstrate the impact of the diagnosis of AKI in hospitalized patients, doubling the average stay, costs and mortality. These differences are accentuated in some Assistance Units, being especially alarming in Surgical Units.



Tabla comparativa por Unidades Asistenciales con mayor impacto.

Figure:

P0594 **USEFULNESS OF THE NEUTROPHIL-TO-LYMPHOCYTE AND PLATELET-TO-LYMPHOCYTE RATIOS IN THE COMMUNITY-ADQUIRED ACUTE KIDNEY INJURY.**

Jose Maria Peña Porta[1], Almudena Castellano Calvo[1], Ana Coscojuela Otto[1], Alejandro Tomás Iatorre[1], José Antonio Ferreras Gascó[1], Pilar Martín Azara[1], Rafael Alvarez Lipe[1]

[1]*Hospital Clinico Universitario Lozano Blesa, Nephrology, Zaragoza, Spain*

Introduction and Aims: The neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte (PLR) ratios have been identified as markers of inflammation and endothelial dysfunction in recent literature. Both are easily measured, reproducible and inexpensive, therefore cost-effective. To date, its usefulness as prognostic markers in community-acquired acute kidney injury (CA-AKI) has not been evaluated. The aim of this study was to analyze the usefulness of the NLR and PLR in terms of morbidity and mortality in community-acquired acute kidney injury.

Method: We established a cohort of 308 patients with community-acquired acute kidney injury (CA-AKI) admitted to the Nephrology service of a third level hospital from January 2010 to February 2015. NLR and PLR ratios were obtained with the levels of the first analysis performed at admission.

Results: We studied 308 patients with CA-AKI, 180 were men (58,4 %), mean age was 73.22 (±13,95). The mean length of stay was 12,25 days (±11,69). The etiology of CA-AKI was divided in prerenal 214 cases (69.5%); renal 71 cases (23.1%); obstructive 23 cases (7,5%). AKI KDIGO stages were stage I, 45 cases (14.6%); stage II, 34 cases (11%); stage III 229 cases (74.4%). Previous chronic kidney disease (CKD) was detected in 212 cases (68.8%). A total of 54 patients (17,15%) required hemodialysis and 38 patients died during admission (12.3%).

Mean NLR was 9.14 ± 8,47 (95% IC 8,2-10,1). Mean PLR was 236,99 ± 228,41 (95% IC 211,38-262,6). NLR according to etiology was: prerenal 8,55±6,8; renal 9,37±9,8; obstructive 13,99±14,82 (significant differences of the latter group compared to the prerenal group). PLR according to etiology: prerenal 228,31±216,34; renal 236,15±233,77; obstructive 320,37±304,89 (non-significant differences). Within the group of prerenal origin, 79 cases were complicated by the development of acute tubular necrosis (ATN). These cases presented a higher NLR (NLR of ATN 10,7±10,28 vs NLR of pure prerenal 7,8±5,6; p=0,026). There were no significant differences between the PLR of the pure prerenal group and the group with ATN (225,95±262,54 vs 285,78±278,61).

The NLR showed a significant correlation with the peak creatinine (r= 0,186; p = 0,001) and with the serum albumin (r= -0,237; p < 0,001). The PLR also showed correlation with the peak creatinine (r= 0,134, p = 0,018) and the serum albumin (r = 0,165, p= 0,07).The NLR, but not the PLR, was associated with the length of hospital stay (multiple linear regression analysis). Through a multivariate binary logistic regression analysis, the variables that were independently associated with mortality during admission were the Liaño individual severity index and the NLR (OR 1,060; IC 95 % 1.014 – 1,108). The variables that were ruled out by the model were sex, age, Charlson comorbidity index, peak creatinine, serum albumin, chronic kidney disease, etiology of AKI (prerenal vs. non prenal), potassium, KDIGO stage of AKI, need of hemodialysis and PLR.

The best cut-off point of the NLR to predict mortality was 6,68 (AUC 0,584; sensitivity 0.60; specificity 0.58; Youden index 0.178)

Conclusion: In our cohort of patients affected by CA-AKI, the NLR was associated with the morbidity and the mortality during admission. More studies are need to confirm this finding, but the easiness of obtaining it and its economic cost make it cost-effective, giving the NLR a leading role in assessing the risk of CA-AKI.

P0595

CHANGING EPIDEMIOLOGY AND OUTCOME OF AKI PATIENTS IN TEACHING HOSPITAL FROM A DEVELOPING COUNTRY: A POPULATION-BASED COHORT STUDY

Daniela Ponce[1,2], Welder Zamoner[1], Marci Batistoco[3], Andre Balbi[1]

[1]Clinical Hospital from Botucatu School of Medicine, Internal Medicine, Brazil, [2] and [3]Clinical Hospital from Botucatu School of Medicine, Brazil

Background and Aims: While considerable information is available on acute kidney injury (AKI) in North America and Europe, large comprehensive epidemiologic studies of AKI from Latin America and Asia are still lacking. The present study aimed to evaluate the epidemiology and outcome of AKI in patients evaluated by nephrologists in a teaching Brazilian hospital.

Method: We performed a large retrospective observational study that looked into epidemiology for AKI and its effect on patient outcome across time periods. For comparison purposes, patients were divided into two groups according to the year of follow up: 2011-2014 and 2015-2018.

Results: We enrolled 7,976 AKI patients and after excluding patients with Chronic Kidney Disease stages 3 to 5, kidney transplanted and those with incomplete data, 5,428 AKI patients were included (68%). The maximum AKI stage was 3 (50.6%) and mortality rate occurred in 1865 patients (34.3%). Dialysis treatment was indicated in 928 patients (17.1%). Patient survival improved along study periods: patients treated at 2015-2018 had a relative risk death reduction of 0.89 (95% CI 0.81–0.98, p=0.02). The independent risk factors for mortality were sepsis, older >65 anos, admission to ICU, AKI-KDIGO 3, recurrent AKI, no metabolic and fluid demand to capacity imbalance as dialysis indication and the period of treatment.

Conclusion: We observed an improvement in AKI patient survival along the years even after correction for several confounders and using a competing risk approach. Identification of risk factors for mortality can help in decision making for timely intervention, leading to better clinical outcomes.

P0596 LONG TERM FOLLOW UP OF CONTRAST INDUCED ACUTE KIDNEY INJURY IN A TERTIARY JORDANIAN HOSPITAL

Ashraf Oweis[1], Sameeha Alshelleh[2]

[1]Jordan University of Science and Technology, Internal Medicine, Jordan and [2]The University of Jordan, Internal Medicine, Jordan

Background and Aims: Contrast induced acute kidney injury (CI-AKI) is potentially preventable and reversable cause of acute kidney injury (AKI).

Multiple factors are associated with the development of CI-AKI, some are modifiable such as drugs, type and amount of contrast, others are not like preexisting chronic kidney disease (CKD), heart failure.

Though it's usually a reversable condition, there is increasing evidence of adverse long-term outcome (increasing morbidity and mortality).

The aim of this study to evaluate the long-term outcome of CI-AKI on mortality, the rate of re-catheterization and the development of CKD.

Method: In a prospective observational study design, we evaluated all patients admitted for cardiac catheterization between June 2015 and January 2016. A total of 326 patients signed the consent to participate in the study.

Patients had blood withdrawn 48 hours after the procedure for their creatinine level.

CI-AKI was defined as an increase in serum creatinine by >25% or 44 mmol/l from the baseline level (48-72) hours after contrast administration, without any other obvious cause.

We used only low osmolality contrast media (CM) (Lopamidol, Bayer, Germany).

Of the 326 patients included, 202 patients had their second sample taken, thus, were eligible to continue in the study.

Patients were followed for at least 3 years.

Results: The incidence of CI-AKI was 14.8% (30 patients), for baseline characteristics see table 1.

At the end of follow up; a total of 7 patients died; 6 in the non CI-AKI group vs. 1 in the CI-AKI group (p=), though the difference between the mean eGFR was not statistically significant by the end of the follow up (85.4ml/min for the CI-AKI vs. 79.2ml/min for the other group (P=0.31)), but the decline in eGFR for the CI-AKI was significant (a drop from 105.4 ml/min to 85.4ml/min vs. 85.2ml/min to 79.2ml/min, P=0.004).

The rate of re-catheterization was not statistically significant between the two groups (61 for the non CI-AKI vs. 12 for the other group; P=0.63).

Conclusion: CI-AKI carries a higher negative long-term effect on eGFR, while did not affect the mortality in our cohort.

P0597

TRAINING IS NOT ENOUGH: RESISTANCE TO THE APPLICATION OF THE AGREED CRITERIA (KDIGO) FOR THE DIAGNOSIS OF ACUTE KIDNEY INJURY IN INTENSIVE CARE UNITS IN EGYPT

Samar Abd ElHafeez[1], Yasmine Naga[2], Graziella D'arrigo[3], Giovanni Tripepi[3], Carmine Zoccali[3]

[1]High Institute of Public Health, Alexandria University, Epidemiology Department, Alexandria, Egypt, [2] Faculty of Medicine, Alexandria University, Internal Medicine Department (Nephrology Unit), Alexandria, Egypt and [3]Ospedali Riuniti, CNR-IFC Clinical Epidemiology and Pathophysiology of Renal Diseases and Hypertension Unit, Reggio Calabria, Italy

Background and Aims: Acute kidney injury (AKI) is one of the most serious complications of patients admitted to intensive care units (ICUs). It is associated with high short- and long-term mortality and resource utilization. The definition of AKI has been established by the KDIGO guidelines based on changes in serum creatinine, urine output or both. However, in clinical practice physicians may ignore the standard criteria and rely on clinical judgement. We therefore aimed to assess the degree of physicians' compliance with the KDIGO guidelines in diagnosis of AKI.

Method: We collected data (demographic, clinical, and biochemical) in a multicenter prospective cohort study from all adults admitted to ICUs (10 surgical and 8 medical) units at Alexandria University Teaching Hospitals from February 1st, 2016 till August 1st, 2016. Alexandria Teaching Hospitals cover four governorates of Northern Egypt and serve approximately 14 million people. Doctors were preliminarily instructed to apply KDIGO criteria for the diagnosis of AKI. Personal and clinical experience data were collected from the treating physicians. We followed patients for thirty days from study entry until discharge, death or study end. Written informed consent was obtained from all participants. AKI was defined and classified based on KDIGO 2012 criteria. In parallel, we registered the actual clinical diagnosis made by the treating physicians. We used frequencies and means for qualitative and quantitative variables as appropriate.

Results: The study included 532 patients who were on average 46 year old ($\pm$18), 41.7% were males, 23.5% with smoking, 23.1% had diabetes, 34.8%, were hypertensive, 11.3 % with pre-existing chronic kidney disease, and 30.1% had cardiovascular diseases. There were 140 physicians responsible for treating the enrolled subjects, with mean age 30 $\pm$3 years, 57% were males, 20% were nephrologists, and the median years of experience was 3 years (inter-quartile range: 2-4years). The AKI incidence was 62.2% according to KDIGO criteria versus 49.9% based on the clinical diagnosis of treating physicians. Among those not reported to have AKI by the treating physicians; 19.1% were in stage 1, 26.4% in stage 2, and 12.9% in stage 3 AKI based on KDIGO. About 24% of patients who had AKI at ICU admission and 15% of those who developed AKI after ICU admission were not appropriately identified as AKI patients according to the physicians. There was a significant association between the physician speciality (nephrology vs other specialties) and the correct AKI diagnosis based on KDIGO criteria (X^2=47.06, p<0.001).

Conclusion: To streamline a correct and timely identification of AKI, treating physicians in ICUs at a large hospital in North Africa, like the Alexandria University Teaching Hospitals in Egypt, need well focused training and knowledge verification post training on KDIGO guidelines for identifying AKI patients. Implementation of electronic alerts could help in proper diagnosis and management.

P0598

COMPARISION OF OUTCOMES ACCORDING TO URINE CHEMISTRY TESTING TIME FOR THE CAUSES OF ACUTE KIDNEY INJURY PATIENTS ADMITTED TO THE EMERGENCY ROOM.

Won Min Hwang[1], Sung Ro Yun[1], Se Hei Yoon[1]

[1]*Konyang University Hospital, Division of Nephrology, Department of Internal Medicine, Daejeon, Korea, Rep. of South*

Background and Aims: Rapid identification and treatment of acute kidney injury can help to restore kidney function. In order to differentiate between prerenal AKI and intrinsic AKI, we perform a urine chemistry test to determine the function of the renal tubule. However, there is no report that it is helpful to arrive at the hospital as early as possible and to perform these urine chemistry tests as soon as possible.

Method: We analyzed the timing of urinary chemistry in AKI patients who were admitted to our hospital through the emergency room for 3 years and divided into two groups. Early group was defined as patients who performed the test within 3 h of arrival in the emergency room. Late group was defined as patients who were late or not. The prognostic factors were change in 30 day eGFR and duration of hospital stay. We also compared the usefulness of urine chemistry test between pre renal AKI and intrinsic AKI in each group.

Results: The changes of eGFR after 30 days in each group are 41.6 ± 27.6 mL/min/1.73 m^2 (Early group, n = 92) vs 30.4 ± 26.8 mL/min/1.73 m^2 (Late group, n = 180) (P = 0.0013). Early group patients were discharged more quickly than patients in the late group (Hospital day: 11.5 ± 10.1 vs 13.8 ± 10.5, P = 0.0450). When analyzed according to the causes of AKI, these changes showed differences in prerenal AKI rather than intrinsic AKI(Figure).

Conclusion: A urine chemistry test is a test to help determine the cause of AKI. Based on the results of urine chemistry performed within 3 h after arrival at the hospital, patients with AKI who visited the emergency room had better improved kidney function and less hospitalization.

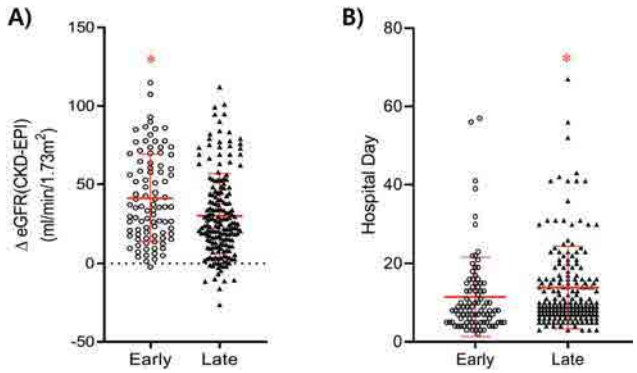


Figure:

P0599 THE LYSOSOMAL URINE ENZYMES ACTIVITY IN CHILDREN AFTER ACUTE KIDNEY INJURI

Olga Lavrenchuk[1], Lesya Korol[1], Ludmila Migal[1], Ingretta Bagdasarova[1]

[1]*State Institution "Institute of Nephrology of National of Medical Science Academy of Ukraine",, pediatric nephrology, Kyiv, Ukraine*

Background and Aims:

The urgency of the problem of acute kidney injury (AKI) in children is due to the high risk of chronic kidney disease (CKD) as an outcome. Lysosomal enzymes in urine are considered to be informative markers of renal parenchyma damage. The aim of study was to determine the activity of lysosomal enzymes β-galactosidase (GAL) and N-acetyl-β-D-glucosamynidase (NAG) in urine as markers of CKD progression in children after AKI.

Method:

41 children were examined after AKI with achieving self-diuresis and clinical improvement. The functional state of the kidneys was evaluated by the glomerular filtration rate (Schwartz GFR), the level of albuminuria. Urine enzyme activity was determined and cross-linked to mmol urinary creatinine. The control (reference) group consisted of 28 children who were conditionally healthy, without kidney disease.

Results:

The NAG activity was 8 times higher level than in the reference group of healthy children (87/46;193 vs. 15/11;18, $p<0.001$), and GAL was elevated in 3 times either (34/22;45 vs. 10/6;13, $p<0.001$) in patients with a disease period of up to 2 years after AKI. In patients with follow-up period 2 or more years enzyme activity levels decreased, but remained 4 times higher (NAG: 49/31;109, $p<0.001$ compared to control; GAL: 35/25;44, $p<0.001$ compared to control). The high levels of enzyme activity was documented in 73.2% of patients after one year of follow up, but the GFR decrease was found in 22.0%, and albuminuria - only in 34.1%.

Conclusion:

The urine activity of NAG and GAL in children is an informative marker for diagnosing recovery after AKI or CKD progression with renal function decline. This method is non-invasive, inexpensive, and simple to conduct.

P0600 **LONG-TERM PROGNOSIS OF PATIENTS WITH METFORMIN - ASSOCIATED LACTIC ACIDOSIS(MALA) AND ACUTE KIDNEY FAILURE**

Maria Rosa Melero Martin[1], Alejandra Muñoz de Morales[1], Alberto Tejedor Jorge[1], Rodriguez benitez Patrocinio[1], Arturo Bascuñana[1], Antonia Gueorguieva[1], Marian Goicoechea[1]

[1]*Hospital Universitario Gregorio Marañón, Nefrologia, Madrid, Spain*

Background and Aims: Although metformin-associated lactic acidosis (MALA) is a very rare event, is frequently seen in patients on metformin with risk factors for developing acute kidney injury (AKI). The long-term prognosis in patients with metformin-associated lactic acidosis (MALA) and renal failure remains unknown.

To describe the characteristics and prognosis of AKI in patients with MALA and investigate whether prescription of RRT and previous renal function are associated with long-term outcomes.

Method: A retrospective single-centre case series. One hundred and nine patients affected with MALA and AKI admitted between Marx 2007 and February 2019 were included. We analysed comorbidities, laboratory tests, clinical parameters and prescription pattern of RRT at admission. After discharging, renal outcomes (doubling serum creatinine or starting dialysis) and mortality were assessed in the long-term.

Results: We included 109 patients (59 males and 50 females), mean age of 74.2±8.6 years and mean Charlson comorbidity index of 8.0±2.4. 54 out of 109 patients had previous chronic kidney disease (eGFR $<$ 60 ml/min/1.72 m^2). Precipitating causes of AKI associated MALA included; acute dehydration (84.4%), exposure to iodinated contrast (7.3%) and non-specified causes (8.3%). During the admission, renal replacement therapy (RRT) was performed in 72 patients (continuous renal replacement therapy in 47 and dialysis in 25). RRT requirements was significantly associated with lactate, acidosis and serum creatinine levels, but not was associated with higher mortality rate during admission.

The patients were followed a median time of 33 (10-65) months after discharging. 33 patients had a renal event and 55 patients died. The patients with CKD before admission had higher number of renal events (log Rank 6.346, p=0.012) and higher mortality (log Rank 12.943, p$<$0.001). In a model adjusted by age and RRT at admission, women were less likely to develop (HR 0.315(0.136-0.730, p=0.007) long-term renal events and previous CKD increased this probability (HR 2,532 (1.190-5.385), p=0.016). Previous CKD and RRT during admission increased mortality in a model adjusted by age, gender and comorbidity (HR 2.315(1.177-4.553), p=0.015 and HR 1.895(1.003-3.580), p=0.049, respectively).

Conclusion: The renal function prior to the episode of AKI associated to MALA and the RRT at admission are the main factors related to renal outcomes and mortality in the long-term.

P0601

SAFETY AND EFFICACY OF INTRAVENOUS ADMINISTRATION OF RINGER'S LACTATE VERSUS NORMAL SALINE 0.9% SOLUTION IN PATIENTS WITH ACUTE KIDNEY INJURY AND ESTABLISHED CHRONIC KIDNEY DISEASE.

Marios Papasotiriou[1], Adamantia Mpratsiakou[1], Georgia Georgopoulou[1], Lamprini Balta[1], Paraskevi Pavlakou[1], Evangelos Papachristou[1], Dimitrios Goumenos[1]

[1]*University Hospital of Patras, Department of Nephrology, Patras, Greece*

Background and Aims: Crystalline solutions, such as normal saline 0.9% (N/S 0.9%) and Ringer's Lactate (L/R), are readily administered for increasing plasma volume. Despite the utility of administering N/S 0.9% to hypovolemic patients, the dose of 154 mmol of sodium (Na) contained in 1 L exceeds the recommended daily dose increasing the risk of sodium overload and hyperchloremic metabolic acidosis. In contrast, L/R solution has the advantage of lower Na content, significantly less chlorine and contains lactates which may be advantageous in patients with significant acidemia such as patients with acute kidney injury (AKI) and chronic kidney disease (CKD). The aim of the present study is to investigate the safety and efficacy of administration of L/R versus N/S 0.9% in patients with prerenal AKI and established CKD.

Method: The study included adult patients with known CKD stage II to V without need for dialysis, with prerenal AKI (AKIN Stage I to III Criteria). Patients with other forms of AKI as well as hypervolemia, heart congestion or hyperkalemia (serum K>5.5 meq/l) were excluded from the study. Patients were randomized in 1:1 ratio to receive intravenously either N/S 0.9% or L/R solution at a dose of 20 ml/kg body weight/day. We studied kidney function (eGFR: CKD-EPI) and response to treatment at discharge and at 30 days after discharge, duration of hospitalization, improvement in serum bicarbonate levels (HCO_3), acid-base balance, serum potassium levels and the need for dialysis.

Results: The study included 26 patients (17 males) with a mean age of 59.1 $\pm$ 16.1 years. Thirteen patients received treatment with N/S 0.9% and the rest with L/R solution. Baseline demographic and clinical characteristics at hospital admission and historical data did not show any significant differences in both groups of patients. Renal function at the onset of AKI did not show significant differences between the two groups (16.4 $\pm$ 5.8 vs 16.9 $\pm$ 5.7 ml/min/1.73 m^2, p=ns, treatment with N/S and L/R respectively). The mean volume of solutions received by the two groups (N/S 0.9% 1119 $\pm$ 374 vs L/R 1338 $\pm$ 364 ml/day, p=ns) as well as the mean total volume of liquids received per day, did not differ significantly (2888 $\pm$ 821 vs 3069 $\pm$ 728 ml/d, p=ns). Patients treated with L/R were discharged 1 day earlier than patients treated with N/S (5.2 $\pm$ 3.2 vs 6.2 $\pm$ 4.9 days of hospitalization, p=ns). Renal function improvement during hospitalization and 30 days after discharge did not differ significantly between the two groups. Patients that received L/R showed a higher increase in plasma HCO_3 (ΔHCO_3) concentration at discharge than those that received N/S 0.9% (4.9 $\pm$ 4.1 vs 2.46 $\pm$ 3.7 meq/l, p=ns) and pH increase (ΔpH) was slightly higher in those that received L/R solution (0.052 $\pm$ 0.066 vs 0.023 $\pm$ 0.071, p=ns). Patients treated with N/S 0.9% showed a greater decrease in serum potassium (ΔK) at discharge compared to those treated with L/R (-0.39 $\pm$ 1.03 vs -0.17 $\pm$ 0.43 meq/l, p=ns, respectively). No patient received acute dialysis treatment.

Conclusion: Administration of L/R solution as a hydration treatment to patients with prerenal AKI and established CKD is not inferior concerning safety and efficacy to N/S 0.9% solution. In addition, L/R administration seems to marginally improve acid-base balance in this specific group of patients.

P0602 CLINICAL PATTERN, RENAL RECOVERY AND PATIENT OUTCOMES AFTER ACUTE KIDNEY INJURY IN ADULTS IN AN EMERGING COUNTRY

Arunkumar Subbiah[1], Sanjay Kumar Agarwal[1]

[1]*All India Institute of Medical Sciences (AIIMS), Nephrology, New Delhi, India*

Background and Aims

Acute Kidney Injury (AKI) is an important determinant of outcome in hospitalized patients. Further, there is a risk for development of Chronic Kidney Disease (CKD) in the future. Though the long-term impact of AKI has been studied in developed countries, there is a paucity of data in this area from the Indian subcontinent. This single-centre study aimed to assess the pattern, clinical spectrum, short-term and long-term outcomes of AKI.

Method

In this prospective observational cohort study, detailed demographic and clinical data at presentation, during hospital stay and follow-up at 1, 3, 6 and 12 months after discharge were obtained prospectively for a cohort of patients with AKI. Both community (CAAKI) and hospital acquired AKI (HAAKI) were included. Patient with pre-existing CKD were excluded. Outcome variables examined were in-hospital mortality, renal function at discharge and on follow-up after discharge from hospital.

Results

In our study cohort with 476 patients, majority of the cases were CAAKI (395, 83%). The mean age at presentation was 44.8 $\pm$ 18.7 years. Medical causes (84%) contributed to the majority of AKI while the remaining were due to surgical (10%) and obstetrical (6%) causes. Sepsis (176/476; 36.9%) was the most common cause of AKI. The most common source for sepsis was respiratory (41%) followed by urological source (18.7%). The in-hospital mortality rate for patients with AKI was 38%. Age >60 years (HR = 1.51; 95% CI, 1.11 – 2.07), oliguria (HR = 1.48; 95% CI, 1.05 – 2.10), need for ventilator (HR = 2.45; 95% CI, 1.36 – 4.41) and/or inotropes (HR = 14.4; 95% CI, 6.28 – 33.05) were predictors of mortality. At discharge, 146 (30.7%) patients had complete renal recovery, while 149 (31.3%) had partial renal recovery. Oliguria ($p < 0.001$), hypoalbuminemia ($p = 0.001$) and need for renal replacement therapy (RRT) ($p = 0.01$) were significantly associated with partial recovery. Of the 295 patients on follow-up at discharge, 211 (71.5%) patients had normal renal function, 4 (1.4%) died and 33 (11.2%) were lost to follow up; 47(15.9%) patients developed CKD of which 6 (2%) were dialysis dependent. Elderly patients, higher AKIN stage with oliguria and those requiring RRT were more likely to develop CKD. Among these, the need for in-hospital RRT was the single most important factor predicting the risk of CKD (OR 1.77, 95% CI, 1.12-2.78).

Conclusion

In conclusion, our data shows that AKI in hospitalized patients still has high mortality in emerging countries like India. Though a fairly good percentage of cases recovered, there is a definite risk of CKD development, especially in patients who required RRT during hospitalization.

P0603 INFLUENCE OF FERRITIN VALUES IN THE PORGNOSIS OF ACUTE KIDNEY INJURY

Pablo Díez[1], Andres Fernández Ramos[1], Patricia Muñoz Ramos[1], Marta Sanz Sainz[1], Begoña Santos Sánchez-Rey[1], Pablo Ruano[1], Borja Quiroga[1]

[1]*Hospital de La Princesa, Nephrology, Madrid, Spain*

Background and Aims: Acute Kidney Injury (AKI) is one of the most frequent causes of hospitalization and many factors have been associated to its prognosis and recovery. The role of iron in AKI physiopathology and its influence is not well known. Recent studies have shown that elevated levels of catalytic iron are associated with higher mortality in patients with AKI, however, catalytic iron is not available in usual clinical practice. Ferritin, especially abundant in the liver, is the primary intracellular iron storage protein. A small amount is secreted to the circulation and is an indirect marker of total body iron deposits. In this study we analyze the influence of iron, with ferritin values, in the prognosis of AKI.

Method: We developed a retrospective, single-center study that enrolled patients with AKI, hospitalized in our center between 2013 and 2014 with iron metabolism values in the first 72 hours after admission. At baseline, we collected demographic information, comorbidities, reason for admission and iron metabolism values (ferritin, transferrin, transferrin saturation index and serum iron). We analyzed variables associated with low and high ferritin values and its impact in AKI long-term prognosis using univariate and multivariable Cox regression.

Results: Of the 1731 analyzed patients, 833 (48.1%) had ferritin records. The mean age was 78±14 years and 48% of the patients were women. The most frequent comorbidity was hypertension (76%), followed by chronic kidney disease (46%), dyslipidemia (44%), heart failure (31%), diabetes mellitus (29%) and atrial fibrillation (27%). The most frequent reason for admission was infection (35%) followed by AKI (19%). Ferritin values differed significantly according age ($p<0.0001$), sex ($p=0.024$), diabetes (0.012), hypertension ($p=0.002$), neoplasia ($p=0.016$), reason for admission ($p=0.018$), baseline CKD-EPI (0.012) and lactate at admission ($p<0.0001$). During the hospitalization, 165 (20%) patients died. Factor associated to mortality were ferritin>500 ng/ml ($p=0.013$), lactate at admission ($p<0.001$), age ($p=0.045$), hypertension ($p=0.014$), dyslipidemia ($p<0.001$), ischemic heart disease ($p=0.006$), chronic kidney disease ($p=0.001$), baseline CKD-EPI ($p=0.01$), atrial fibrillation ($p=0.005$), neoplasia ($p=0.023$), Barthel index ($p<0.001$) and hemoglobin ($p=0.006$) and bicarbonate ($p=0.012$) at admission. Multivariate logistic regression demonstrated that ferritin levels over 500 ng/mL was an independent predictor of mortality (1.6 [1,1-2,3] HR [CI 95%]) ($p=0.013$).

Conclusion: Ferritin values higher than 500 ng/mL independently predicts mortality in patients admitted with AKI.

P0604

IDENTIFICATION OF NOVEL ENDOTHELIAL ACTIVATION BIOMARKERS IN PATIENTS WITH LEPTOSPIROSIS AND ITS ASSOCIATION WITH ACUTE KIDNEY INJURY

Elizabeth De Francesco Daher[1], Pedro Eduardo Andrade de Carvalho Gomes[1], Gabriela Studart Galdino[1], Gdayllon Cavalcante Meneses[1], Alice Maria Costa Martins[1], Geraldo Bezerra da Silva Junior[1,2]

[1]Federal University of Ceará, School of Medicine and Farmacy, Fortaleza, Brazil and [2]Universidade de Fortaleza, Public Health and Medical Sciences Graduate Programs, Fortaleza, Brazil

Background and Aims: Leptospirosis has a broad clinical spectrum. Many patients present a severe disease, with potentially fatal outcomes. Novel biomarkers of endothelial activation are being studied in order to predict the severity of disease and to establish early assistance to the patients.

Method: For the analysis of biomarkers, blood samples were collected at hospital admission, in proper material for serum isolation. Aliquots were frozen at -80 °C until the analysis was done. To quantify the biomarkers, ELISA kits were used: Syndecan-1 (Abcam–ab47352), ICAM-1 (Abcam–ab47349) e VCAM-1 (Abcam–ab47355), Angiopoietin-2 (R&D Systems–Duoset DY623) e FGF-23 (R&D Systems–Duoset DY2604).

Results: A group of 27 patients was evaluated. 24 (88.9%) were males and 3 (11.1%) were females. Mean age was 39.1 ± 17.6 years. 14 (53.8%) required dialysis. Patients who required dialysis presented higher levels of syndecan-1 (572 [300-811] vs. 263 [106-421] ng/mL; p = 0.03), angiopoietin-2 (1.52 [0.72-2.72] vs. 0.63 [0.4-1.38] ng/mL; p = 0.01), and FGF-23 (291 [56-2,031] vs. 10 [10-806] pg/mL; p = 0.021). There were no significant differences in the levels of VCAM-1 and ICAM-1 between the two groups. Syndecan-1 showed significant correlation with the levels of creatinine at hospital admission (r = 0.546; p = 0.05) and total bilirubin at hospital admission (r = 0.534; p = 0.013). Angiopoietin-2 showed significant correlation with the levels of creatinine at hospital admission (r = 0.513; p = 0.009) and the number of hemodialysis sessions (r = 0.406; p = 0.049). No correlation was shown concerning FGF-23.

Conclusion: Novel biomarkers revealed leptospirosis-associated endothelial activation and were significantly increased in patients with renal involvement. Therefore, they may be useful for establishing early identification and assistance in those patients.

P0605 ACUTE KIDNEY INJURY AFTER MAJOR ABDOMINAL SURGERY

Marija Milinkovic[1,2]

[1]C, Clinic of nephrology, Belgrade, Serbia and [2], School of Medicine, Univerity of Belgrade, Serbia, Belgrade, Serbia

Background and Aims:

We analyzed the incidence of acute kidney injury (AKI) after major abdominal surgery, as well as demographic, clinical, laboratory and surgical factors that might have contributed in it's development.

Method:

Retrospective data analysis of 83 pts who underwent major abdominal surgery at the emergency surgery department (intraperitoneal approach, hospitalization longer than 48 hours, surgery duration over one hour). Demporaphic data, comorbidities, biochemical parameters (blood count, serum concentrations of nitrogenous substances, electolytes etc), type of surgery, intraoperative characteristics (duration of surgery, blood pressure, use of vasoactive substances), postoperative complications including AKI, defined as serum creatinine concentrations increase of 0.3mg/dl and more or reduction in diuresis, as well as intrahospital mortality.

Results:

The mean age of the patients was 60.9 $\pm$ 12.9 years. A total of 45 (54.2%) patients were male. AKI was registered in 15 (18.1%) patients with an average age of 69.5 $\pm$ 9.2 years, of which 8 (53.3%) were male. The average duration of surgery in the group of patients with AKI was 2.5 $\pm$ 0.8 hours, and the most common operations performed in this group involved reconstruction of the small and large intestine. The total intrahospital mortality was 10.8% and in the AKI group 33.3%.

Conclusion:

Patients with AKI were significantly older, with more comorbidities and more frequent surgery that involved resection of the small and large intestine. The development of AKI was accompanied by a higher mortality rate. Given the specific pathophysiological mechanisms in abdominal surgery, further study of the factors responsible for the development of AOB is required to contribute to the development of preventive protocols and to reduce the rate of this serious postoperative complication.

P0606 OUTCOME OF CANCER PATIENTS WITH ACUTE KIDNEY INJURY REQUIRING DIALYSIS

Suramath Isaranuwatchai[1], Supanat Worawichawong[1]

[1]*Chulabhorn Hospital, Internal Medicine, Bangkok, Thailand*

Background and Aims: Recent advances in treatment of cancer lead to improvement in mortality among cancer patients. However, data regarding outcomes of cancer patients with acute kidney injury (AKI) requiring dialysis were scarce. We conducted this study to see the difference in mortality and other outcomes between cancer and non-cancer patients who had AKI requiring dialysis.

Method: We reviewed medical record of previous 18 months in our institute. Patients with age at least 18 years with acute kidney injury requiring dialysis were included in our study. Primary outcome was mortality at 30 days. Renal recovery and chronic kidney disease (CKD) after AKI events were also recorded.

Results: A total of 61 patients were included in our study; 28 patients had no cancer and 33 patients had cancer. Of cancer patients, 81.8% had advanced stage cancer. Modality of dialysis was continuous renal replacement therapy in 36.1%. Mortality at day 30 was not significantly different between cancer patients and non-cancer patients (57.6% vs. 53.6%, P = 0.754). Of alive patients, renal recovery among cancer patients and non-cancer patients was also not significantly different (69.2% vs. 50.0%, P = 0.310). CKD after episodes of AKI was also not significantly different between cancer patients and non-cancer patients (42.8% vs. 77.8%, P = 0.302).

Conclusion: This is the first study to compare mortality between cancer and non-cancer patients who had AKI requiring dialysis. We found no significant difference regard to mortality between AKI patients requiring dialysis with and without cancer. Renal recovery and CKD development were also not significantly different between two groups. More studies in nephro-oncology field are required for better treatment in cancer patients.

P0607 CLINICAL SIGNIFICANCE OF HYPOALBUMINEMIA FOR ACUTE KIDNEY INJURY IN PATIENTS WITH SCRUB TYPHUS

Kwang Young Lee[1], In O Sun[1]

[1]*Presbyterian Medical Center, Internal Medicine, Korea, Rep. of South*

Background and Aims: The aim of this study is to investigate the clinical significance of hypoalbuminemia (HA) for acute kidney injury (AKI) in patients with scrub typhus.

Method: From 2010 to 2017, 449 patients were diagnosed with scrub typhus. We divided the patients into two groups [normoalbuminemia (NA) vs. hypoalbuminemia (HA)] based on the serum albumin level of 3.5 g/dL, and compared the incidence, clinical characteristics, and severity of AKI based on RIFLE classification between two groups.

Results: Of the total 449 patients, 52 (11.6%) were categrized as HA group. Compared with patients in NA group, patients in HA group were older (74 ± 8 vs. 63 ± 13, $P<0.01$) and had higher total leukocyte counts (10.4×10^3/ mL vs. 6.9×10^3/mL, $P<0.01$). HA group showed significantly longer hospital stay (10.1 ± 4.7 vs 8.8 ± 4.5, $p<0.01$) and higher incidence of acute kidney injury (56% vs. 19%, $p<0.01$). The overall incidence of AKI was 22.9%; of which, 12.2%, 10.0% and 0.7% were classified as Risk, Injury and Failure, respectively. In a multivariate logistic regression analysis for predciting AKI, age, presence of chronic kidney disease, leukocytosis and hypoalbuminemia were significant predictors of AKI. Most patients recovered baseline renal function without renal replacement therapy following antibiotics therapy and supportive care.

Conclusion: Hypoabluminemia was closely associated with scrub typhus associated with AKI.

P0608

TROPICAL FEVER ASSOCIATED ACUTE KIDNEY INJURY - RISK PREDICTION MODEL IN A RESOURCE LIMITED SETTING IN SOUTH INDIA

Rajesh Rajasekharan Nair[1], Venkatram Murugesan[1], George Kurian[1], Anil Mathew[1], Zachariah Paul Polachirakal[1], Sandeep Sreedharan[1]

[1]*Amrita Institute of Medical Science, Nephrology, Kochi, India*

Background and Aims: Acute kidney Injury (AKI) is a serious medical condition estimated to affect more than 10 million people around the world annually, resulting in a 1.7- to 6.9-fold increased risk of hospital mortality. Out of 1.7 million deaths per year caused by AKI globally, around 1.4 million occur in low- and middle-income countries, sepsis being the leading cause. AKI occurs in 40–50% of patients with sepsis and increases the mortality six- to eight-fold. By comparing the prevalence of potential risk factors in populations of patients who had developed AKI with control groups with no AKI, several risk assessment tools have been proposed and generated for specific clinical settings such as intensive care units, cardiac surgery, general surgery, those undergoing radiological investigations involving intravenous contrast and those presenting to the emergency department. The AKI Risk Assessment (ARA F4) model incorporated newer biomarkers of kidney injury (TIMP-2, IGFBP7) along with clinical parameters to detect patients at risk for AKI as fast as possible and to prevent further damage. However, they are yet to be available freely in our country. To the best of our knowledge, no risk assessment tool in the setting of tropical fever associated AKI has been proposed till date.

The aim of this study is to provide a practical model to identify patients at high risk for tropical fever associated AKI in a resource limited setting in the absence of newer biomarkers.

Method: Ours is a retrospective, single center study. Patients who had an increase in serum creatinine (S.Cr) $\geq$0.3 mg/dL within 48 hours; or an increase in S.Cr to $\geq$1.5 times baseline, which is known or presumed to have occurred within the prior 7 days or a urine volume of <0.5 mL/kg/h for 6 hours were included. We recruited 342 consecutive admissions with tropical fever associated AKI and evaluated them based on clinical and biochemical profiles.

Results: We analyzed data of 342 patients. Our population of patients had representation from all age groups, 72% were between 21 to 60 years, 20.4% were >60years and 34.7% were females. There was a clear relationship between age and the number of AKI risk factors. Baseline serum creatinine was available for 117 patients, the average S.cr was 0.9591mg/dL and the average rise in S.cr was 1.22mg/dL. Leptospirosis (11.98%), dengue (84.79%), malaria (2.63%) and complicated malaria (0.29%) were the etiologies for AKI.

19,21 and 2 patients with leptospirosis had <=5, 6 to 10 and >10 risk factors respectively. 258,32 and 0 patients with dengue had <=5, 6 to 10 and >10 risk factors respectively. 8,1 and 0 patients with malaria had <=5, 6 to 10 and >10 risk factors respectively. One patient with complicated malaria had <=5 risk factors.

15/42 with leptospirosis, 2/290 with dengue, none with malaria and 1/1 with complicated malaria required renal replacement therapy.

Five patients expired, out of which three were on renal replacement therapy. 3/286 with total risk score <5, 14/53 with total risk score between 6-10 and one out of two with total risk score >10 required renal replacement therapy.

Conclusion: Tropical fever associated AKI is a major public health burden in southern India. Our aim was to propose a risk stratification model to assess severity of tropical fever associated AKI and dialysis requirement in a resource limited setting.

In our study, the number of risk factors, incidence of AKI and dialysis requirement were more in people with leptospirosis. We also observed that as the risk scores went up, the need for hemodialysis increased irrespective of the etiology. In the absence of availability of newer biomarkers this risk prediction score is quite useful. Ours is the first risk assessment tool in tropical fever associated AKI in resource limited setting. We are planning on a prospective evaluation of the same in the near future to validate our Tropical fever associated Acute Kidney Injury Risk assessment (TAKIR) tool.

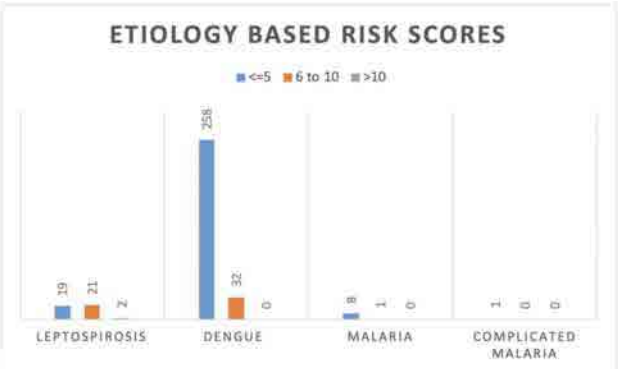


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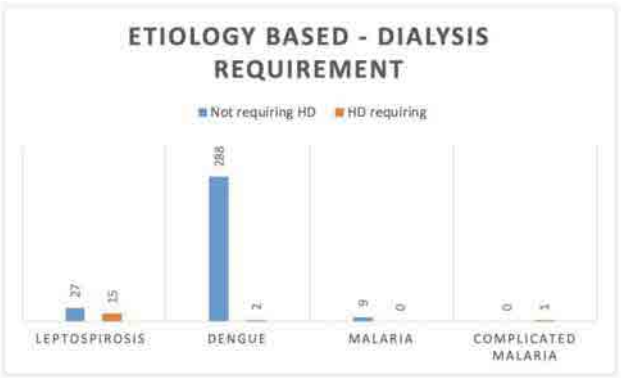


Figure 2:



Figure 3:

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P0609

THE INCIDENCE AND RISK OF CONTRAST INDUCED ACUTE KIDNEY INJURY IN THE ELDERLY UNDERGOING PULMONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY

Alrowaie Fadel[1], Khalid Almatham[1], Saud Almousa[1], Majed Abonab[1], Abdullah AlJaser[1], Ali Alqahtani[1], Said Alsaif[1], Ammar Alkadi[1], Khalid Alquefil[1]

[1]*King Fahad Medical City, Medical Speciality Department / Nephrology section, Riyadh, Saudi Arabia*

Background and Aims: Contrast-induced acute kidney injury nephropathy (CI-AKI) is a leading cause of acquired acute kidney injury and has been associated with prolonged hospitalization and adverse clinical outcomes. Advanced age has been reported as risk factor for CI-AKI. However, limited studies available to determine the exact incidence of CI-AKI in elderly patient. The aim of this study was to investigate the incidence of, risk factors for developing CI-AKI in patient above 65 years old who underwent Pulmonary Computed Tomography Angiography (PCTA).

Method: This single center retrospective study, performed in a large, tertiary care hospital in Riyadh, Saudi Arabia. It is a sub-study of (3 P-CIAKI) The Practice Pattern of Preventive Measures for Contrast Induced Acute Kidney Injury in Patients Undergoing Pulmonary Computed Tomography Angiography. Patients > 65 years of age, who underwent PCTA during a 5-year period (2014 to 2018) were included. Patients receiving long-term hemodialysis or peritoneal dialysis, and those without repeated serum creatinine 48-72 hours post procedure were excluded from the analysis. CI-AKI defined as raise of serum creatinine by 44 mmol/l 48-72 hours post PCTA.

Results: 272 out of 908 patients, with a mean age of 74.93 ± 7.09 years, 58.1% having diabetes mellitus (DM) and estimated GFR of 74.92 ± 23.57 ml/min per 1.73 m^2 were enrolled. 201 patients (73.9%) had eGFR > 60 ml/min. Diuretics was used by 37.1% of the patients, while 33.1 % of the patients on ACEI / ARBs. Prophylactic measures used in 35.7 % of the procedures. CI-AKI occurred in 19 cases (7.0 %) as compared with 4.7 % in the original 3 P-CIAKI study with mean age of 52 years and eGFR 97 ml/min. Renal replacement therapy required in 3 patients who had CI-AKI. DM status was only significant predictor for the development of CI-AKI.

Conclusion: Elderly patients are at greater risk for the development of CI-AKI even with eGFR above 60 ml/min specially in DM patient .The Incidence of CI-AKI in patients > 65 years of age is up to 7 %, that is less than the reported in the literature and this can be explained by higher base line eGFR in our study .

Table – 1: Basic demographic and clinical characteristics of study (N = 272)

Characteristics	N (%)	
GenderMale	110 (40.4%)	
Age, mean ± SD	74.93 ± 7.09	
Inpatient status	261 (96.0%)	
Comorbidities		
DM	158 (58.1%)	
HTN	182 (66.9%)	
CHF	56 (20.6%)	
PVD	14 (5.1%)	
Anemia	79 (29.0%)	
Medications		
NSAIDs	26 (9.6%)	
Diuretics	101 (37.1%)	
ACEI or ARB	90 (33.1%)	
CIAKI Prophylaxis use		
Any prophylaxis	97 (35.7%)	
NS only	65 (23.9%)	
NS + NAC	8 (2.9%)	
NAC + SB	28 (10.3%)	
SB only	13 (4.8%)	
Renal function (Mean ± SD)		
Cr (Baseline) mmol/l	79.56 ± 39.33	
Cr (48 - 72 hour) mmol/l	82.94 ± 52.28	
eGFR ml/min	74.92 ± 23.57	
eGFR ml/min	< 15	2 (0.7%)
	15 - 29	9 (3.3%)
	30 - 59	60 (22.1%)
	> 60	201 (73.9%)

Table – 2: Association between the Prophylaxis and Non-Prophylaxis patients with respect to study characteristics

Characteristics	CIAKI YES (n = 19)	CIAKI NO (n = 253)	OR [95% CI]	P – value
Gender, Male	7 (36.8%)	103 (40.7%)	0.85 [0.324 - 2.231]	0.740
Location, Inpatient	19 (100.0%)	242 (95.7%)	————	0.353
DM	17 (89.5%)	141 (55.7%)	6.75 [1.528 - 29.84]	*0.004
Diuretics	7 (36.8%)	94 (37.2%)	0.99 [0.375 - 2.594]	0.978
ACEI or ARB	10 (52.6%)	80 (31.6%)	2.4 [0.94 - 6.143]	0.109
Prophylaxis	10 (52.6%)	87 (34.4%)	2.12 [0.83 - 5.412]	0.798
Serum Creatinine >132 mmol/l	4 (21.1%)	16 (6.3%)	3.950 [1.174 - 13.294]	*0.018
eGFR <60 ml/min	9 (47.4%)	62 (24.5%)	2.773 [1.078 - 7.133]	*0.029
< 15	0 (0.0%)	2 (0.8%)	————	0.697
15 – 29	2 (10.5%)	7 (2.8%)	4.13 [0.797 - 21.454]	0.068
30 – 59	7 (36.8%)	53 (20.9%)	2.2 [0.826 - 5.866]	0.107
>60	10 (52.6%)	191 (75.5%)	0.36 [0.14 - 0.928]	* 0.029

Table – 3: Identification of most significant risk factors / predictors developing the risk of CIN by multiple logistics regression analysis

Characteristics	OR [95% C.I]	P value
DM	6.471 [1.457 – 28.737]	*0.014
eGFR	2.591 [0.992 – 6.798]	0.052



Figure 1: Incidence of CIAKI and Renal Replacement Therapy requirement

P0610 **ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS IN THE ICU**

Mira Markovic[1], Violeta Knezevic[2], Tijana Azasevac[1], Aleksandar Knezevic[3], Svetlana Stojkovic[3], Dejan Celic[2]

[1]Clinical center of Vojvodina, Novi Sad, Serbia, Department of Nephrology and clinical immunology, Novi Sad, Serbia, [2]University of Novi Sad, Faculty of Medicine Novi sad, Novi Sad, Serbia and [3]Clinical center of Vojvodina, Novi Sad, Serbia, Emergency center, Novi Sad, Serbia

Background and Aims:

Acute kidney injury (AKI) is common and serious complication in critically ill patients in intensive care unit (ICU). The rapid increase in aging populations with more comorbidities contribute to high incidence AKI in ICU. Incidence varies from 20% to as high as 70%. AKI in the ICU frequently requires costly supportive therapies, has high morbidity and it's associated with poor outcomes.

We aimed to determine incidence of AKI, causes, risk factors, treatment and outcomes of AKI in critically ill patients in ICU.

Method: We collected data prospectively from case records of adult patients (older than 18 years of age) admitted to the ICU at the Department of Internal medicine, Emergency Center, Clinical center of Vojvodina in Novi Sad, Serbia, during 3 months. We included patients who had at least two measurements of serum creatinine. Data on patient demographics, diagnosis at the time of ICU admission, complete blood count, biochemistry, comorbidities (diabetes mellitus, arterial hypertension, other cardiovascular diseases, renal disease, prostate diseases, dehydration, burns, gastrointestinal bleeding, pancreatitis, peritonitis, sepsis), use of nephrotoxic agents, radiological procedures and treatment of AKI were recorded. We excluded patients with chronic renal disease who were on hemodialysis. There were no interventions.

Results: Of the 44 patients included in the study, median age was 67+/-13,20 years (range: 21 to 88). Of those 44 patients 20% developed AKI. De novo AKI was diagnosed in 51,22% of those patients and 48,78% had chronic renal failure in acutisation. The most frequent etiology was pre-renal, in 80,95% of patients. Renal origin and obstructive (post-renal) causes were detected in the same number of patients, 9,52%. Comorbidities were present present in all patients. Most common comorbidity was arterial hypertension, in 52,4% of patients, other cardiovascular diseases in 47,6 % of patients, sepsis also in 47,6% of patients and gastrointestinal bleeding in 33,3% of patients. Complete recovery of kidney function was detected in 42,86% of patients. Mortality was 28,57%. During the hospitalisation 90,48% of patients were treated conservative and 9,52% of patients required renal replacement therapy.

Conclusion: De novo AKI occurred in approximately half of the critically ill patients in ICU. The most frequent etiology was pre-renal. AKI was mainly detected in older patients with comorbidities. Age and comorbidities were also associated with the poor outcome. Mortality was high.

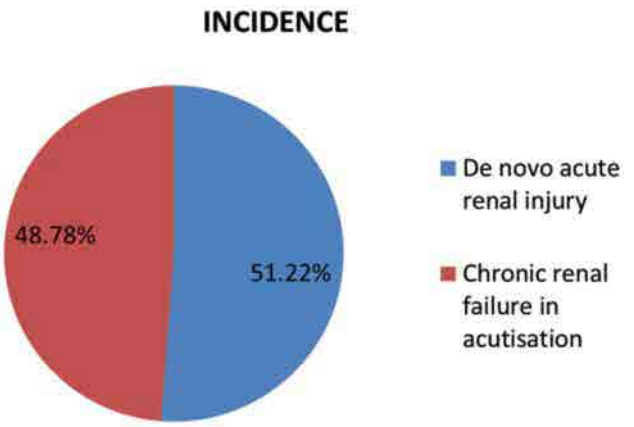


Figure 1. Incidence of de novo AKI and chronic renal failure in acutisation

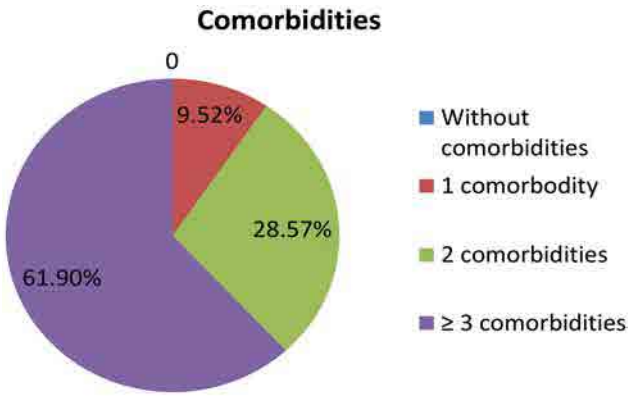


Figure 2. Number of comorbidities in patients with AKI

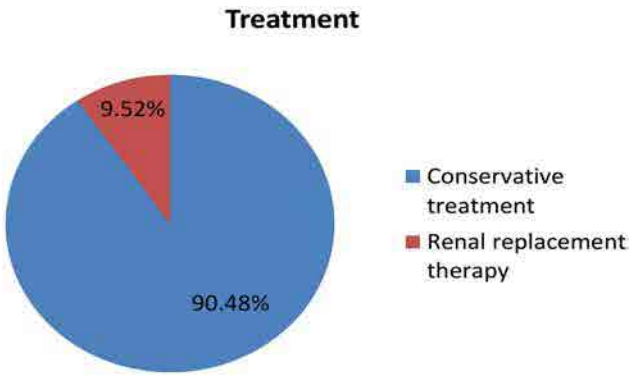


Figure 3. Treatment of AKI

P0611

COMPARISON OF FOUR PREDICTIVE SCORING MODELS AS ASSESSMENT TOOLS FOR CARDIAC SURGERY ASSOCIATED ACUTE KIDNEY INJURY IN POST CARDIAC SURGERY PATIENTS IN A PHILIPPINE LOCAL TERTIARY HOSPITAL FROM JANUARY 2010- JANUARY 2019

Cathleen Iway[1]

[1]*Perpetual Succour Hospital, Department of Internal Medicine, Cebu, Philippines, The*

Background and Aims: Cardiac surgery associated acute kidney injury is the most common cause of hospital acquired acute kidney injury in the intensive unit after sepsis. In Asia, incidence ranges from 17 to 49%, with 2 to 6 % of patients requiring dialysis after developing acute kidney injury. Its occurrence has shown increased morbidity, length of hospital stay, and utilization of resources which affect overall outcome of the patients. These patients face a combination of renal stressors and some patient populations deserve special consideration with regards to the risk factors identified preoperatively. Therefore, early prediction of cardiac surgery associated acute kidney injury is optimal.

This study aims to compare the clinical values of the Cleveland Clinical Score, Mehta Score, Simplified Renal Index and Acute Kidney Injury following Cardiac Surgery Score in predicting cardiac surgery-associated acute kidney injury among patients who underwent cardiac surgery in Perpetual Succour Hospital, Cebu City from January 2010- January 2019.

Method: A chart review was done to all patients who underwent open heart surgery during the time period of January 2010 to January 2019. The patients who developed cardiac surgery associated- acute kidney injuries were identified using the four different predictive scoring methods. Binary logistic regression was used to describe the relationship between the development of CSA- AKI and the four scoring methods as its predictors. Confidence interval is set at 95%, comparison significant at <0.05, hypotheses tested at 0.05 level of significance. Therefore, if the p-value is less than or equal to the significance level, it can be concluded that there is a statistically significant association between the response variable and the predictor.

Results: There were a total of 114 cases of open heart surgeries. A sample size population of 86 were reviewed, and was divided into 2 groups, there were 43 patients (50%) who developed cardiac surgery associated acute kidney injury and 43 patients (50%) who did not develop CSA- AKI. Patients with recorded variables useful in all scoring systems were included. The p- values for the Cleveland Clinical Score and Simplified Renal Index are greater than the significance level. With the p- values less than the significance level, there is statistically significant association between the Mehta (p value 0.019) and AKICS score (p value 0.011) and the development of CSA- AKI. The odds ratios for both Mehta Score (1.10) and AKICS Score (1.19) are also greater than 1, indicating that AKI is more likely to occur if the Mehta score or the AKICS Score increases.

Conclusion: In our single- center study, acute kidney injury was more likely if the scores for both Mehta and AKICS scoring system methods increase. This supports that either Mehta or the AKICS scoring systems are useful methods that can be employed to predict cardiac surgery-associated acute kidney injury among patients who underwent cardiac surgery.

P0612

UTILITY OF BODY COMPOSITION MONITORING (BCM) TO CORRELATE FLUID STATUS AND AKI IN PATIENTS UNDERGOING MAJOR CARDIAC SURGERY AND OUTCOMES

Rajeevalochana Parthasarathy[1], Madhusri Babu[1], Merina Alex[1], Preethi Nagesh[1], Milly Mathew[1], Georgi Abraham[1]

[1]*The Madras Medical Mission Hospital, Chennai, India*

Background and Aims: Technically assisted assessment of volume status before cardiac surgery may be useful to direct intraoperative fluid administration. Using a three-compartment physiologic tissue model, the body composition monitor (BCM, In Body) measures total body fluid volume, extracellular volume, intracellular volume and fluid overload as surplus or deficit of 'normal' extracellular volume. Fluid overload is a risk factor for infection, increased re intubation rates, pneumonia and acute kidney injury in these high risk patients. This study is planned to use BCM to assess fluid status in patients undergoing cardiac surgery and correlating it with the risk of AKI

AIMS: To do BCM analysis of patients undergoing major cardiac surgery to assess fluid status and renal outcomes

Primary Objective

To use BCM to assess fluid status in patients undergoing cardiac surgery and correlate it with the risk of acute kidney injury

Secondary Objectives

To assess the correlation of fluid status obtained by BCM to assess

1. In hospital mortality in patients with and without AKI

Method: The studyis being conducted at Madras Medical Mission, Chennai.

Time period : 1 year (June 1 2019- May 31 2020)

Inclusion criteria

All consecutive patients above 18 years of age undergoing cardiac surgery

Exclusion criteria

1. No informed consent

2. Patients having metal implants, pace makers

3. Pregnant and lactating mothers

After informed consent, all adult patients undergoing cardiac surgery will have a BCM analysis done by the dietician .(Free of Charge) The BCM analysisInbody S10) will be done on Day 0(preoperative), Day 2 and Day 5 . Data will be collected according to a set proforma (Attached) . Analysis will be performed using the SPSS platform.

Results: In this pilot study, 134 patients who underwent major cardiac surgery were enrolled. Of these 44 patients developed AKI as defined by KDIGO criteria(22 Stage 1, 15 stage 2, and 7 stage 3). There was no statistical significance in the baseline characteristics when compared to age, gender, htn, ckd between patients with and without aki. Overhydration as measured by ECW/TBW ration of > 0.38 was significantly higher on day 2 and 5 in patients who developed AKI .($P<0.00$, All 44 patients in aki versus 40 in the non aki group). The PBF, ICW, BMI nad overall BCM score was higher in patient with AKI ($p<0.00$). 7 patients required RRT(6 SLED and 1 Acute PD). There was 1 death in theAKI group. The mean duration of hospital stay was longer (14 +/- 5 vs 7 +/- 3.5) in the AKI grroup

Conclusion: There is not much data on BCM and fluid assessment in cardiac surgery patients. These patients have many risk factors and a failing heart and associated renal dysfunction in many makes it very difficult to guide volume therapy in these patients. Many of the so called standard objective measures in assessing volume are not foolproof . This study will be one of the firsts from India to assess fluid status in these patients and help in guiding therapy and also knowing the outcomes of such an objective measurement

P0613 **POSTPARTUM ACUTE RENAL FAILURE AND VITAMIN D STATUS A MULTICENTER STUDY OF RISK FACTORS**

Tehir Mohamed Cherif[1]

[1], *Annaba, Algeria*

Background and Aims: The postpartum AKI is a particular pathological and chronological entity, which remains a public health problem in Algeria.

The main objective was to describe the epidemiological, clinical and evolutionary profile of postpartum AKI and secondarily to evaluate the impact of Vit D status on: The severity of AKI (using AKIN Classification 2012), the use of the RRT and the Delays and quality of recovery of renal function.

Method: This is an observational, descriptive, prospective and multicentric study performed in two University hospital centers situated in East of Algeria (Annaba and Setif).

All patients admitted to ICU for postpartum complications over a 4 year (2014 to 2018) were included.

Results: Among the 538 pathological post partums identified in the two basins of life 179 (33.28%) presented AKI, the average age is 32.9 years and the average delivery time is 33.88 weeks.

AKI was defined by the KDIGO AKIN classification, the proportion of severe AKI requiring RRT was 34 (18.9%) and the incidence of CKD was 6.7 % with dialysis dependence for 1.11%.

Preeclamptic pathology is in the most commen cause of postpartum AKI (72.3%). However, it is not associated in univariate analysis with the occurrence and severity of AKI.

Associated factors ($p < 0.05$) in univariate and multivariate analysis are: the HELLP syndrome, especially when associated with postpartum hemorrhage (PPH) and acute fatty liver of Pregnancy.

Maternal mortality is dramatically high 20% especially in severe stage of AKI. Absolute deficiency of vitamin D (25OH D) $<$ 10ng/ml is correlated with the severity of the AKI.

Conclusion: The postpartum AKI is inexorably linked to pre-eclamptic pathology and its complications. The frequency of maternal and fetal deaths should prompt new strategies including early detection and closer surveillance, especially of women at risk. A particular attention should be given to vitamine D sttatut during Pregnancy

P0614 URINARY EXOSOMAL MICRORNA-21 AS A MARKER OF SCRUB TYPHUS-ASSOCIATED ACUTE KIDNEY INJURY

In O Sun[1], Kwang Young Lee[1], A Young Cho[1]

[1]*Presbyterian Medical Center, Internal Medicine, Jeonju, Korea, Rep. of South*

Background and Aims: Urinary microRNA (miRNA)-21 is reported to be a biomarker for detection of acute kidney injury (AKI). Analysis of urinary exsome may serve as a novel diagnostic approach in kidney disease. The aim of this study is to investigate the clinical significance of urinary exosomal miRNA-21 for AKI in patients with scrub typhus.

Method: In a cross-sectional study, we collected 138 urine samples at the time of admission from 145 patients with scrub typhus. For 25 patients with scrub typhus-associated AKI and 25 age, sex-matched scrub typhus patient without AKI, we measured miRNA-21 in urinary exosomal fraction and compared diagnostic value in predictiong AKI.

Results: Compared with patients in the non-AKI group, patients in the AKI group were more likely to have one or more comorbidity such as diabetes (50% vs. 5%, $P<0.01$) and chronic kidney disease (8% vs. 0%, $P<0.01$). Total leukocyte count were higher in patients with AKI than in those without AKI (10.40×10^3/ mL vs. 6.40×10^3/mL, $P<0.01$). The levels of urinary miRNA-21 were higher in the AKI group than in the non-AKI group. Urinary exosomal miRNA-21 levels correlated directly with serum neutrophil gelatinase-associated lipocalin values and total leukocyte counts and inversely with estimated glomerular filtration rate. The receiver operator characteristics curve analysis for urinary exosomal miRNA-21 showed good discriminative power for the diagnosis of scrub typhus-associated AKI, with area under the curve value of 0.907.

Conclusion: Urinary exosomal miRNA-21 could be a surrogate markers for the diagnosis of scrub typhus–associated AKI.

P0615 ACUTE KIDNEY INJURY CLASSIFICATION IN CRITICAL PATIENTS: COMPARISON OF THE THREE SYSTEMS

Carolina Ormonde[1], Ana Rita Leal[2], Joana Castro[3], Sara Ledo[4], Joana Costa[4], Anuschka Langner[4], Abel Alves[4], Manuela Henriques[4], Ana Magro[4], Humberto Costa[4]

[1]Hospital do Divino Espírito Santo, Nephrology, Ponta Delgada, Portugal, [2]Hospital do Divino Espírito Santo, Hemathology, Ponta Delgada, Portugal, [3]Hospital do Divino Espírito Santo, Internal Medicine, Ponta Delgada, Portugal and [4]Hospital do Divino Espírito Santo, Intensive Care, Ponta Delgada, Portugal

Background and Aims: Acute kidney injury (AKI) is one of the most common and severe complications in intensive care units' (ICU) patients. It is associated with worst outcomes, such as longer hospital stays and higher mortality. In the past years three consensus have been developed to provide uniform identification of AKI in clinical practice. An ideal classification should be sensitive but also correlate with the outcomes. RIFLE and AKIN have been exhaustively studied in critical patients. In the studies made until date, KDIGO classifications seems to be as sensitive as the other two. With this study the authors intend to compare the three systems of AKI classification in an ICU population.

Method: Retrospective observational study with descriptive and bivariate analysis using SPSS Statistics. Demographic and laboratory studies were collected from the patient's charts. The authors included patients who were admitted to a polyvalent ICU in the first six months of 2019. The exclusion criteria were patients under 18 years old, pregnant women, stage 5 chronic kidney disease and less than 24 hours ICU stays. Only the serum creatinine, and not urine output, was used as criteria to the three classifications.

Results: A total of 130 patients were studied. The mean age was 62.20±15.78 years (min 19; max 87) and 54.6% (n=71) were male. Medical causes were the most frequent type of admission (n=82; 63.1%). The median length of ICU and hospital stays were 6.50±9.19 days (min 2; max 48) and 23.00±25.68 days (min 2; max 126) respectively. The mortality rate in ICU and hospital were, respectively, 9.2% (n=12) and 20% (n=26). Eight patients (6.2%) needed renal replacement therapy. KDIGO classification identified more patients with AKI than RIFLE ($p<0.001$) and AKIN ($p<0.001$). There were no statistically differences between the median length of ICU ($p=0.191$ for KDIGO, $p=0.257$ for AKIN and $p=0.223$ for RIFLE) or hospital ($p=0.762$ for KDIGO, $p=0.096$ for AKIN and $p=0.105$ for RIFLE) stays between the patients with and without AKI by the 3 classifications. There was a significant statistically association between mortality in the ICU and AKI for KDIGO ($p=0.008$) and AKIN ($p=0.004$) classifications, but not for RIFLE ($p=0.167$). Likewise, there was also an association between mortality in the hospital and AKI patients identified by KDIGO ($p<0.0001$) and AKIN ($p=0.001$) classifications, but not with RIFLE ($p=0.054$). The AKI patients that were identified by KDIGO criteria but not by AKIN did not have and association with ICU mortality ($p=0.28$) but did have a statically significant association with hospital death ($p=0.026$) with an odds ratio of 4 (CI 95% [1.229-13.018]).

Conclusion: The authors concluded that KDIGO classification is the most sensitive of the three for AKI in critical patients. There were no differences in the length of ICU or hospital stays between the 3 classifications cases identified. On the other hand, there was a statistically association between KDIGO and AKIN cases with ICU and hospital mortality, but not with RIFLE. Still, patients who are identified by KDIGO but not by AKIN criteria have an odd 4 times higher to die in the hospital. This means that KDIGO classification is the most sensitive and correlates better with outcomes in critical patients with AKI than the other two.

AKI. CLINICAL. PREVENTION AND TREATMENT

P0618 **PREOPERATIVE LOW URINE SPECIFIC GRAVITY PREDICTS ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY**

Wonji Jo[1], Chan-Young Jung[1], Jaeyoung Kim[1], Jihye Kim[1], Sangmi Lee[1], Jung Tak Park[1]

[1]Institute of Kidney Disease Research, Yonsei University, Department of Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Acute kidney injury (AKI) is a common and serious complication following cardiac surgery. However, strategies that effectively predict AKI risk before cardiac surgery are scarce. Recent investigations identified urinary osmolality to be associated with non-glomerular kidney damage in normal kidney function individuals, suggesting urine concentration ability to be a surrogate of early kidney damage. Therefore, hypothesizing that urine specific gravity (SG) could reflect asymptomatic kidney damage, the clinical implication of preoperative urine specific gravity on AKI occurrence after cardiac surgery was investigated in subjects with normal kidney function.

Method: A total of 4135 patients who underwent coronary artery bypass or valve surgery at Yonsei University Health System from were enrolled. Patients whose eGFR was lower than 60mL/min/1.73m^2 were excluded. Fasting urinary SG was measured from the morning first void a day before the surgery. The patients were divided into tertiles based on urine SG. The primary outcome was occurrence of AKI within 48hours of cardiac surgery. AKI was defined according to Acute Kidney Injury Network criteria.

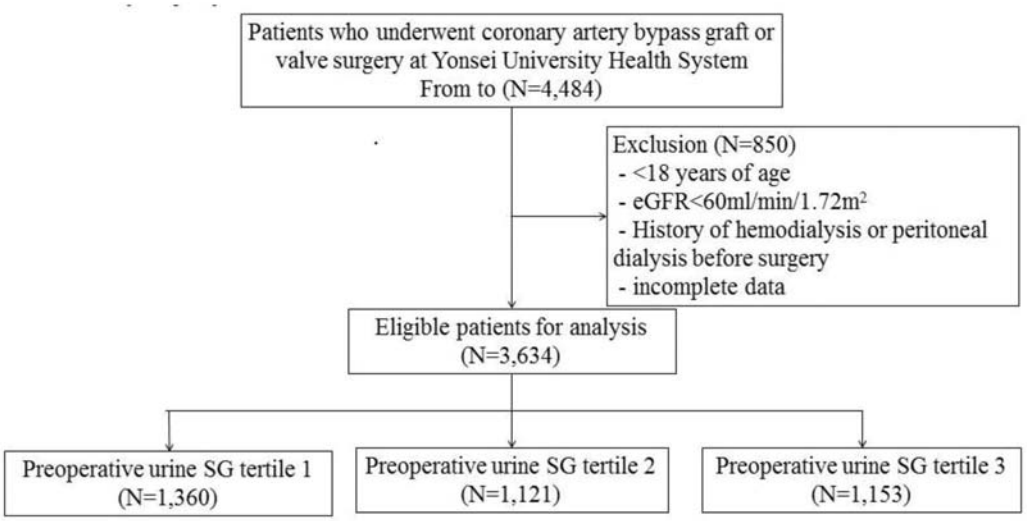


Figure 1. Flow chart of participants in the study

Table 1. Baseline characteristics of AKI patients and Non-AKI patients

	Total (N=3,634)	Non-AKI patients (N=2,430)	AKI patients (N=1,204)	*p*
Age (years)	60.4±13.5	58.5±13.8	64.1±12.0	<0.001
Male (%)	2,330 (64.1)	1,518 (62.5)	812 (67.4)	0.003
Hypertension (%)	1,678 (46.2)	1,095 (45.1)	583 (48.4)	0.056
Diabetes mellitus (%)	942 (25.9)	571 (23.5)	371 (30.8)	<0.001
Type of surgery (%)				0.002
CABG (%)	1,263 (34.8)	847 (34.9)	416 (34.6)	
Valve surgery (%)	2,214 (60.9)	1,498 (61.6)	716 (59.5)	
CABG + Valve surgery (%)	157 (4.3)	85 (3.5)	72 (6.0)	
eGFR (ml/min/1.73m^2)	98.4±15.2	100.6±14.3	94.1±16.0	<0.001
Hemoglobin	10.0±1.7	10.2±1.7	9.5±1.7	<0.001
Serum glucose (mg/dL)	205.5±57.1	203.3±55.6	209.9±59.9	0.001
Serum albumin (mg/dL)	2.7±0.4	2.8±0.4	2.6±0.4	<0.001

Data are expressed as mean±standard deviations or numbers (%), except where noted.
Abbreviation: AKI, acute kidney injury; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate.

Figure:

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Results: The mean age of the patients was 60 years and 60% were male. Diabetes consisted of 25.6% of the patients and 54.5% were hypertensive. The mean eGFR and urine SG was 98.8mL/min/1.73m^2 and 1.020, respectively. AKI developed in 1,089 (26.3%) patients. The incidence of AKI was highest in the lowest urine SG tertile group (410, 29.0%) and lowest in the highest tertile group (304, 23.5%) ($P < 0.001$). Multivariable logistic regression analysis revealed that being included in the lowest preoperative urine SG tertile group was significantly related with higher post cardiac surgery AKI incidence risk (odd ratio (OR), 1.33; CI, 1.12-1.57; $P = 0.001$). This association was significant even after adjustments were made for confounding factors.

Conclusion: Low urine SG was associated with increased risk of cardiac surgery associated AKI in patient with normal renal function. Evaluating preoperative urine SG may be useful in stratifying post cardiac surgery AKI risk.

P0619

POINT OF CARE CREATININE FOR EARLY DIAGNOSIS OF COMMUNITY ACQUIRED ACUTE KIDNEY INJURY IN NIGERIA. TECHNOLOGY EVALUATION AND DESIGN OF QUALITY IMPROVEMENT PROJECT

Dimitrios Poulikakos[1], Ibi Erekosima[1], Pedro Emem-Chioma[2], Prelador Fakrogha[2], RI Oko-Jaja[3], Nkoyo Utein[3], FS Wokoma[2], Manda David-West[2], Victor Ndu[2], Duru Stephen Ugochukwu[3], John Ohiri[3], Agba M Harry[4], Philip A. Kalra[1], David Lewis[1]

[1]Salford Royal NHS Foundation Trust, Renal, Manchester, United Kingdom, [2]Port Harcourt, Renal Department, University of Port Harcourt Rivers State Nigeria, Port Harcourt, Nigeria, [3]Port Harcourt, Chemical Pathology, University of Port Harcourt Rivers State Nigeria, Port Harcourt, Nigeria and [4]Port Harcourt, Primary Health Care Board Rivers State, Port Harcourt, Nigeria

Background and Aims: Acute Kidney Injury (AKI) in low- and middle-income countries is mostly a community-acquired potentially reversible syndrome and has high morbidity and mortality. Due to limited laboratory infrastructure diagnosis of AKI is often delayed until life threatening complications have developed and dialysis treatment is largely unavailable. Decisions for hospital referral from primary health care centers and triage decisions for hospital admission are not based on laboratory results in Port Harcourt Nigeria. To address the need for early diagnosis and treatment of AKI we established a collaboration between the Renal Unit of the University of Port Harcourt Teaching Hospital, Primary Health Care Board Rivers State and the Renal Department of Salford Royal NHS Foundation Trust, aiming at the evaluation of the use of point of care (POC) Creatinine (Cr) for early detection and management of community acquired AKI.

Method: The first stage of the project evaluated the accuracy of POC Cr technology. Following informed consent patients underwent concurrent measurement of Cr using the central laboratory (Lab) assay (Jaffe) from a venous sample and a point of care Cr measurement using a capillary sample (fingerstick) with the NOVA Stasensor Xpress Cr analyser. Pearson Correlation and Bland-Altman plots were used to assess correlation and agreement between the two methods. During the second stage, the results were discussed at a focused AKI workshop and guidance for the use of POC Cr was developed.

Results: During the first phase 96 concurrent POC Cr capillary and venous Lab Cr samples were analysed. Mean age was 49±14 years and 66 subjects were females. POC Cr values were 127±122 umol/l and Lab Cr values were 100 ±85 umol/L, mean positive bias of 27.2±47.94 umol/L. Overall, correlation between POC Cr and Lab Cr was very good, with Pearson correlation r=0.956) Figure 1A. All 4 out of 96 values that were outside the limits of agreement (set at mean ±2 standard deviations) were for Lab Cr values >200 umol/L. A Bland-Altman Plot is presented for paired samples with Lab Cr values <200 umol/L (Figure 1B).

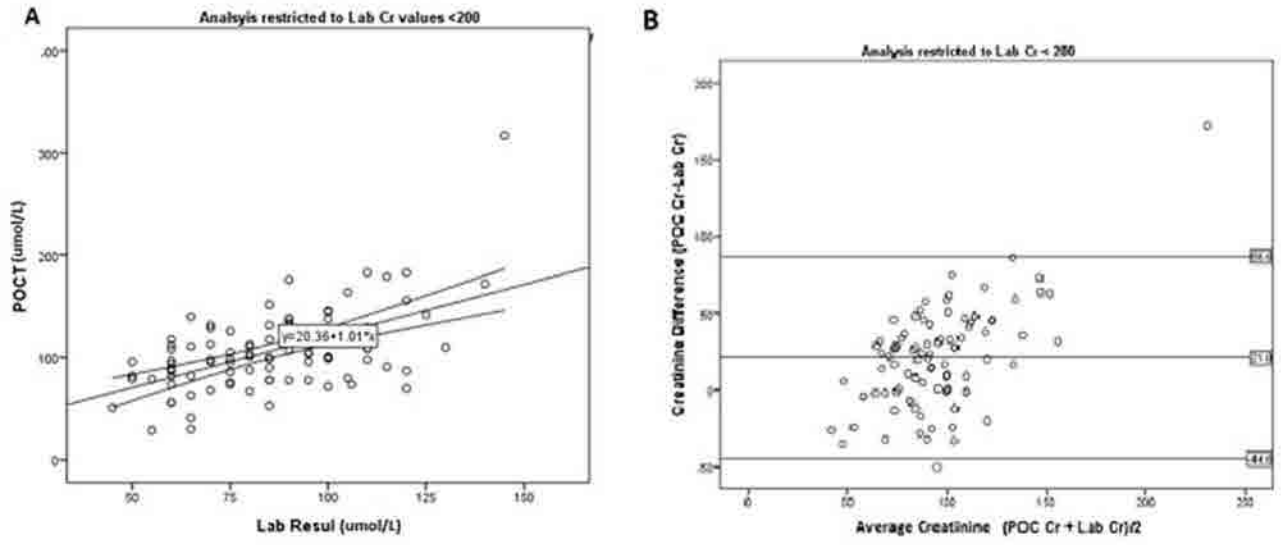


Figure 1: During the second phase 85 primary and secondary physicians participated in the AKI workshop in Port Harcourt. It was decided that possible AKI should be considered if the adjusted for positive bias result of POC Cr was > 1.5 times the upper limit of normal range of the Lab assay in the absence of baseline. A risk stratification algorithm based on history and clinical observations to identify high risk patients that the POC Cr should be tested and an AKI management algorithm was developed (Figure 2).

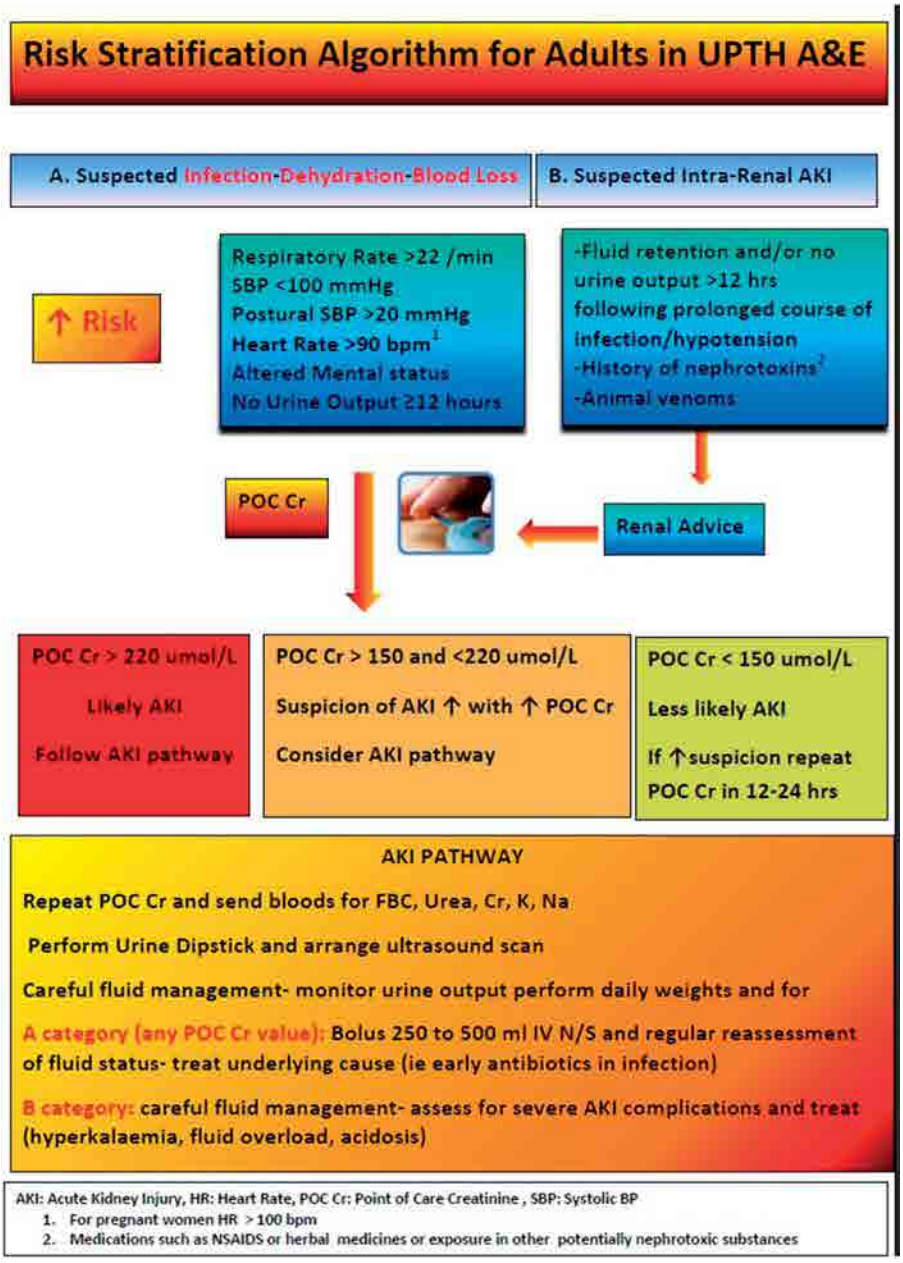


Figure 2: The project will start in the hospital emergency department and will roll out in 2 primary health care centres that will refer AKI cases to the renal team. Quality improvement methodology will be used.

P0620 **OXIDANT-INDUCED RENAL PRECONDITIONING BIOMARKERS FOR AKI PREVENTION WITH RBT-1**

Richard Zager[1], Ali Johnson[2], Stacey Ruiz[3], Alvaro Guillem[3], Jeff Keyser[3], Henrik Rasmussen[3], Bhupinder Singh[4]

[1]Fred Hutchinson Cancer Research Center, [2]University of Washington, [3]Renibus Therapeutics, Inc and [4]University of California, Irvine

Background and Aims: Ischemic preconditioning has shown tissue protective effects in various organs including kidneys in animal models. However, the translation of these findings to human acute kidney injury (AKI) has not been successful, at least partly because of difficulty in simulating an ischemic state, as attempted by remote ischemic preconditioning (RIPC). RBT-1 is a novel therapeutic composed of SnPP (tin protoporphyrin) and FeS (iron sucrose) and was designed to induce non-ischemic, oxidant renal preconditioning to prevent AKI. It has shown efficacy in various models of AKI: glycerol-induced (rhabdomyolysis), maleate (ATP depletion), ischemia/reperfusion (I/R), and post-AKI progression to CKD (long-term progression). This study investigated the mechanism of action of RBT-1 in mice, and its translation to the clinical setting.

Method: Male CD-1 mice were pretreated with control or RBT-1 for 18 hours; animals were then sacrificed for assessment of biomarkers of cytoprotection. Nrf2-/- mice were treated for 18 hours with RBT-1 prior to indication of ischemia/reperfusion (I/R); AKI was assessed by blood urea nitrogen (BUN) and plasma creatinine (PCr). Patients with CKD (Stage 3 and 4) were enrolled in Phase 1 studies of FeS and SnPP and cytoprotective biomarkers were assessed.

Results: In mice, RBT-1 significantly increased several Nrf2-dependent antioxidant, anti-inflammatory genes, such as HO-1, NQO1, SRXN1, and GCLC. RBT-1 also increased cytoprotective heavy chain ferritin (Fhc) levels. Nrf2-/- mice were resistant to RBT-1-mediated protection against AKI. At baseline, CKD patients had elevated plasma HO-1 and urinary NQO1 levels. Ferritin and hemopexin levels were also elevated at baseline. RBT-1 components were shown to further increase HO-1, NQO1, ferritin, and hemopexin in patients with CKD.

Conclusion: RBT-1 represents a novel therapeutic approach for the prevention of AKI. It mediates kidney protection by upregulating antioxidant and anti-inflammatory genes. Translation of RBT-1-mediated upregulation of cytoprotective markers has been demonstrated in the clinic in patients with CKD. These data, along with the broad range of RBT-1 activity previously shown in various models of AKI, highlight the potential of RBT-1 in AKI and suggest oxidant-induced renal preconditioning may be protective in preventing AKI.

P0621 IDENTIFYING PATIENTS WHO NEED LONG TERM FOLLOW UP AFTER RECEIVING RENAL SUPPORT ON ITU

Naomi Edney[1], Daniel Adlington[1], Coralie Bingham[1], Christopher Mulgrew[1], Richard Oram[2]

[1]Royal Devon and Exeter Hospital, Exeter Kidney Unit, Exeter, United Kingdom and [2]Institute of Biomedical and Clinical Sciences, University of Exeter Medical School, Exeter, United Kingdom

Background and Aims: The incidence of acute kidney injury (AKI) is between 20-50% in a critically ill population. AKI is associated with increased risk of chronic kidney disease (CKD), end stage kidney disease (ESKD) and death. 30% of patients on ICU with AKI will have pre-existing CKD1. Arrangements for renal follow up of patients who develop AKI whilst on ICU vary between centres.

We aimed to review the renal function pre admission and at one and two years after discharge for all patients who received renal replacement therapy (RRT) with haemofiltration or haemodialysis on ICU during 2016. We reviewed how many were under renal follow up and aimed to identify techniques to improve follow up if required.

Method: We reviewed electronic records of all patients who received RRT on the ICU during 2016. We assessed demographic details, renal function, details of ICU stay and co morbidities. We excluded patients who died on ICU or received RRT for non-renal indications. Patients who were not under renal follow up were offered a single renal clinic at 2 years (2018) after their ICU discharge.

In 2019 we set up a monthly electronic alert to the renal team for all patients who have received haemofiltration on ICU. Each patient's case was reviewed and either renal follow up arranged or letter sent to primary care and the patient to ensure a 1 year post discharge renal function check to risk stratify them.

Results: 64 patients received RRT therapy in ICU in 2016 of whom 20 died during their ICU stay and 4 received RRT for non-renal indications. 40 patients were included in further analysis. The median (IQR, range) age was 60(49.5-69.5, 20-87) years. 21/40(53%) were admitted to ICU for sepsis and 8/40(20%) had CKD (defined by eGFR<60), and 6/40(15%) had ESKD, (5 on haemodialysis, 1 transplanted) prior to admission. 33% had diabetes and 64% had vascular disease. 7 were known to the renal team prior to admission and 14/40 (35%) underwent renal follow up post discharge.

Excluding those on RRT prior to admission, median (IQR, range) pre-admission eGFR was 82 (55->90, 30->90). 3 patients were discharged on RRT. The majority of patients who were discharged from hospital off RRT met eGFR criteria for CKD stage 3, data available for 30, median eGFR 56 (range: 10->90, IQR: 26-83), N=16/30(54%), p=0.01 compared to pre ICU stay had CKD stage 3 by eGFR criteria.

By one year 2 of 3 patients were still on RRT. The majority of patients from hospital off RRT still met eGFR criteria for CKD stage 3, data available for 29, median eGFR 57 (range: 14->90, IQR: 39-77), N=15/29(52%) had CKD stage 3 by eGFR criteria.

By 2 years, data available for 19, median GFR was 51 (range: 12->90, IQR: 32-86) with 11/19 (57%) meeting CKD stage 3 eGFR.

Discharge eGFR was moderately correlated with 2 year follow up eGFR (r=0.49, p=0.03) and post discharge CKD stage 3 did not predict future CKD stage 3 (p=0.35) whereas eGFR at 1 year post discharge was much more strongly correlated with final follow up eGFR (spearman's r=0.95, p<0.0001) and CKD stage 3 at 1 year predicted CKD at 2 years (p=0.003). Of those with CKD stage 3 at 2 years 5/11 (45%) were followed up in a renal clinic.

In 2019, 34 electronic notifications were received. Primary care notified of 11 patients to ensure renal function measured at 1 year. 7 patients died, 8 patients already know to the renal team, 6 patients had new renal follow made at discharge and 2 patients had follow up under other medical specialities.

Conclusion: eGFR at 1 year post discharge from ICU is the best predictor of long term CKD and this could be used to target patients who need continued renal follow up. Electronic notifications from ICU can help accomplish this.

P0622

FIGHTING AGAINST PROXIMAL AND DISTAL TUBULAR DAMAGE BY REDUCING INFLAMMATORY BURDEN AFTER CARDIAC SURGERY

Nooshin Dalili[1]

[1]*Chronic Kidney Disease Research Center, Shahid Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Background and Aims: Going on cardiopulmonary bypass (CPB) during cardiac surgery causes systemic inflammatory response syndrome.

In different studies Pentoxifylline and Calcitriol have shown inhibitory effects on pro-inflammatory cytokines such as tumor necrosis factor (TNF) and interleukin-6 (IL-6) accompanying with production of free oxygen radicals in the ischemic reperfusion injury. On the other hand, they have positive effects on reducing oxidative stress. To investigate the effects of these drugs on reducing tubular injury after CABG surgery, by their anti-inflammatory properties we compared pre- and postoperative levels of urinary NGAL (as a proximal tubular damage marker), KIM-1 level (as a distal tubular damage marker), serum level of Malondialdehyde (MDA) (as an oxidative stress marker) and serum inflammatory markers such as IL-6, IL-8, and TNF levels in two groups of patients undergoing CABG, those who received Pentoxifylline and Calcitriol before surgery and those who didn't

Method: After signing an informed consent, 150 consecutive adult patients undergoing elective on-pump CABG were enrolled in a randomized control trial. Patients with collagen-vascular disease or having a history of treatment with immunosuppressive agents, corticosteroids ($>$ 3 days), Methylxantines, Diltiazem or sodium Nitroprusside and patients with a history of angiography in the past 7 days or hemorrhagic diathesis and coagulopathy, uncontrolled diabetes mellitus, sepsis, renal failure (sCr $>$ 2 mg/dl), hepatic failure (AST or ALT $>$ 40 U/L) or urinary tract infection were excluded. All patients received the same anesthetic regimen and routine CPB management.

The patients were randomly assigned to one of two groups:

Control group (placebo)
Intervention group (Pentoxifylline +Calcitriol)

PTX was administered as an oral 400 mg tab every 12hours plus IV Calcitriol (0.01 mcg/kg) daily starting from 3 days before surgery.

In the control group placebo tab and IV injection of normal saline were prescribed in the same direction.

Results: Results demonstrated that after three days prophylactic use of oral pentoxifylline plus IV Calcitriol there is improvement in selected checked inflammatory markers in the intervention group. Moreover Pentoxifylline+ Calcitriol showed beneficial effects by controlling the oxidative stress burden and reducing the mean serum MDA level in the patients undergoing CABG who are at risk of developing AKI as a post surgery complication. Probably by reducing inflammation and oxidative stress combination of these two drugs before CABG could decrease proximal and distal tubular damage which presented with significantly lower levels of uNGAL and KIM-1, as markers of tubular injury, in the intervention group.

Conclusion: Combination of Pentoxifylline and Calcitriol showed a promising prophylactic role in patients undergoing CABG with anti-inflammatory, anti-oxidant properties.

This study provided scope of add-on drug therapy for better prognosis in post CABG population, involving risk of endothelial dysfunction and renal tubular damage due to inflammatory milieu and renders support to future prospective clinical studies to demonstrate net control of inflammation and oxidative stress after cardiac surgery.

P0623 ACUTE RENAL FAILURE IN HAPOLIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION. TWO GRAFT VS HOST DISEASE (GVHD) PROFILAXIS PROTOCOL COMPARISON

Miguel Angel Solis[1], Aurora Pérez Ys[1], Ariadna Pérez[2], Juan Carlos Hernández-Boluda[2], Isabel Juan-Garcia[1], Elena Gimenez-Civera[1], Rafael Hernani-Morales[2], Carlos Solano-Vercet[2], Isidro Torregrosa Maicas[1], Jose Luis Gorriz[1]

[1]University Hospital Clinico. INCLIVA. Universidad de Valencia, Valencia. Spain, Nephrology, València, Spain and [2]University Hospital Clinico. INCLIVA. Valencia. Universidad de Valencia. Valencia. Spainencia, Hematology, València, Spain

Background and Aims: Haplo-hematopoietic cell transplantation (Haplo-HCT) assures a valid donor in short notice in over 95% of the patients with high risk haematological neoplasia. High doses of post-transplant cyclophosphamide, in combination with other inmunosupressive drugs like calcineurin inhibitors, rapamycine and micophenolate mofetil, is safe and useful in GVHD prevention.

The aim of the study was to analyze and compare acute kidney injury (AKI) in the first 100 days after transplantation, the characteristics of the patients who went on haplo-HCT, and prophylaxis for GVHD with cyclosporine (n=32) (group 1) or rapamycine (group 2), in combination with other immunossupresors.

Method: Fifty-two consecutive patients who recieved a Haplo-HCT at our institution between october/2012 and February/2019 were retrospectively reviewed.

Results: A total of 52 patients were included, 34 male (65.4%), with a median age median age of 52.8 years old (range 18-71). Co-morbidities: hypertension: 13 (25%), Diabetes: 13 (5.8%), previous neoplasia: 4(7.7%). 27 patients received previously platinum-based chemotherapy with and 50% had received a previous HCT. No chronic kidney disease (CKD) were present in any patient. Haematological diseases were :non Hodgkin lymphoma (28.8%), Hodgkin lymphoma (23.1%), acute myeloid leukemia (21.2%), myelodysplastic syndrome (13.5%), other (13.4%). 42 patients (80.8%) received reduced intensity conditioning. Major complications were: TMA: 7(13.5%), Sinusoidal Obstruction Syndrome: 3 (5.8%) and sepsis 27 (51.9%). During the first 100 days post-transplantation follow up, 26 patients (83.2%) in group 1 and 5 patients (25%) in group 2 developed AKI attending KDIGO classification ($p<0.0005$). At day 100 post-transplantation, 14.5% of survivors had renal failure, defined as increased of serum creatinine $\geq$ 0.3mg/dL with respect to their baseline. In group 2 none of the patients developed acute kidney injury (0%) at 100 days post-transplantation follow up.

Median serum Cr in survivors at day 100 was 0,65mg/dL in group 1 VS 0.62mg/dL in group 2, ($p<0.001$).

In the multivariate analysis, treatment with CI ($p<0.01$) and sepsis ($p<0.05$) were independent predictors of ARF.

Conclusion: Rapamycin use instead cyclosporine is associated with a significatively lower incidence of AKI in the first 100 days post-tansplantation in our group of patients. The findings of this study call for further research identifying if non cyclosporine group have similar results in term of prevention of GVHD and if this protocol has a better impact in renal function and surveillance in the follow up.

P0624

INCREASED URINARY BIOMARKERS OF KIDNEY INJURY IN PATIENTS AFTER ALLOGENETICHEMATOPOETIC STEM CELL TRANSPLANTATION REFLECT KIDNEY DAMAGE EVEN IN NORMALN KIDNEY FUNCTION.

Malgorzata Kepska[1], Inga Chomicka[1], Ewa Karakulska-Prystypiuk[2], Agnieszka Tomaszewska[2], Grzegorz Basak[2], Marcin Zorawski[3], Jolanta Malyszko[1]

[1]Medical University of Warsaw, Department of Nephrology, Dialysis and Internal Medicine, Warszawa, Poland, [2]Medical University of Warsaw, Department od Hematology, Oncology and Internal Diseases, Warszawa, Poland and [3]Medical University of Bialystok, Department of Clinical Medicine, Białystok, Poland

Background and Aims: Chronic kidney disease (CKD) and acute kidney injury (AKI) are common complications of hematopoietic stem cell transplantation (HSCT) associated with increased morbidity and mortality. On the other hand, presence of CKD is often used as an exclusion criterion when selecting patients who undergo HSCT, especially when fludarabine in conditioning or GVHD prophylaxis with a calcineurin inhibitor is contemplated. There is also no threshold (CKD stage, level of serum creatinine etc) below which patients should not undergo allogeneic HSCT. Kidney function in patients undergoing HSCT is frequently worsened by previous chemotherapy and exposure to a variety of nephrotoxic drugs. Several biomarkers were widely investigated for early diagnosis of acute kidney injury, including neutrophil gelatinase associated lipocalin (NGAL), urinary liver-type fatty acid-binding protein (uL-FABP) and others, however, in patients undergoing HSCT, the published literature is exceptionally scarce. A few studies with inconclusive results stress the knowledge gap and need for further research.

The aim of the study was to assess biomarkers of kidney injury in patients at least 3 months after HSCT (to avoid the effect of calcineurin inhibitors) under ambulatory care of Hematology, Oncology and Internal Medicine Department, University Teaching Hospital.

Method: We studied 80 prevalent patients after allogeneic HSCT and 32 healthy volunteers to obtained normal ranges for biomarkers. In this cross-sectional study following biomarkers of kidney injury in urine were evaluated: IGFBP-7/TIMP2 (insulin growth factor binding protein-7/, tissue inhibitor of metalloproteinases-2), netrin-1, semaphorin A2 using commercially available assays.

Results: All the biomarkers studied were significantly higher in patients after HSCT when compared to healthy volunteers (all $p<0.001$). When we divided patients according to kidney function (below and over 60 ml./min/1.72m^2), we found that only concentration of IGFBP-7 was significantly higher in 23 patients with CKD stage 3 (i.e. eGFR below 60ml.min/1.72m^2) relative to patients with eGFR over 60 ml.min.1.72m^2. All biomarkers in both subgroups of patients with eGFR below and over 60 ml./min/1.72m^2 were significantly higher relative to healthy volunteers. In univariate correlations sempahorinA2 was related to netrin 1 ($r=0.47$, $p<0.001$), IGFBP7 ($r=0.35$, $p<0.01$), TIMP2 ($r=0.32$, $p<0.01$), whereas IGFBP7 was positively related to serum creatinine ($r=0.38$, $p<0.001$) and inversely to eGFR ($r=-0.36$, $p<0.001$).

Conclusion: Concluding, patients after allogeneic HSCT despite normal or near normal kidney function show evidence of kidney injury, which might be due to comorbidities, previous chemotherapy, conditioning regimen,complement activation, calcineurin therapy after HSCT, other possible nephrotoxic drugs etc. Nephroprotective strategies are to be considered as chronic kidney disease is a risk factor for increased morbidity and mortality in this vulnerable population.

P0625

CONTINUOUS RENAL REPLACEMENT THERAPY WITHOUT ANTICOAGULATION IN CRITICALLY ILL PATIENTS AT HIGH RISK OF BLEEDING-A SYSTEMATIC REVIEW AND META-ANALYSIS

Shiren Sun[1], Wei Zhang[1], Ming Bai[1], Lijuan Zhao[1], Xiaolan Chen[1], Yan Yu[1]

[1]*Xijing Hospital, The Fourth Military Medical University, The Nephrology Department, Xi'an, P.R. China*

Background and Aims: Continuous renal replacement therapy (CRRT) has been widely used in the critical care setting and anticoagulation is usually necessitated. However, critically ill patients are commonly at incremental risk of bleeding, which contributed to the hesitation of anticoagulant use for CRRT in clinical practice. The current guideline recommended CRRT proceed without anticoagulation in patients with contraindication to citrate and increased bleeding risk. Nevertheless, the efficacy of anticoagulation-free CRRT remains inconsistent. Therefore, the purpose of our present systematic review is to evaluate the efficacy and safety of anticoagulant-free CRRT based on the current literatures.

Method: We conducted a comprehensive search of PubMed (US National Library of Medicine, Bethesda, MD, USA), Cochrane Library databases and EMBASE from database inception to January 12, 2019 for potential candidate studies. Studies included adult critically ill (age $>$ 18 years) patients with increased bleeding risk, and underwent CRRT without anticoagulation were considered for the inclusion.

Results: Finally, 17 observational studies and 3 randomized controlled trials with 1615 patients were included in our present meta-analysis. There was no significant difference in filter lifespan between the anticoagulation-free and systemic heparin group. The filter lifespan was significantly prolonged in the citrate (WMD -23.01, 95%CI [-28.62, -17.39], $P < 0.001$; $I2 = 0\%$, $P = 0.53$) and nafamostat (WMD -8.4, 95%CI [-9.9, -6.9], $P < 0.001$; $I2 = 33.7\%$, $P = 0.21$) groups, compared with anticoagulation-free group. The averaged filter lifespan of the anticoagulation-free CRRT ranged from 10.2 to 52.5 hours.

Conclusion: The filter lifespan in anticoagulation-free patients with increased bleeding risk was comparable to that in patients without increased bleeding risk underwent systemic heparin anticoagulation CRRT. Nafamostat was not recommended for CRRT anticoagulation due to its drawbacks. Currently, the optimal choice of anticoagulation strategy for critically ill patients without citrate contraindications at high risk of bleeding should be regional citrate anticoagulation. Further studies should focus on the special cut-off value of activated partial thromboplastin time (APTT), international normalized ratio (INR) and platelet (PLT) count, at which the anticoagulation-free CRRT would be beneficial.

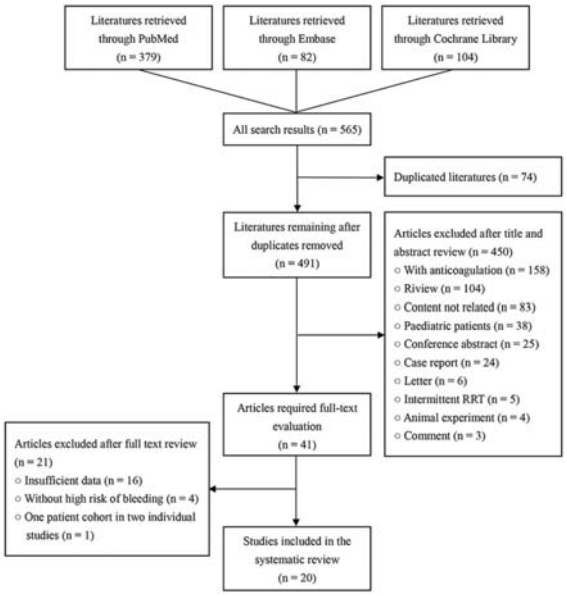


Figure 1: studies inclusion flow chart

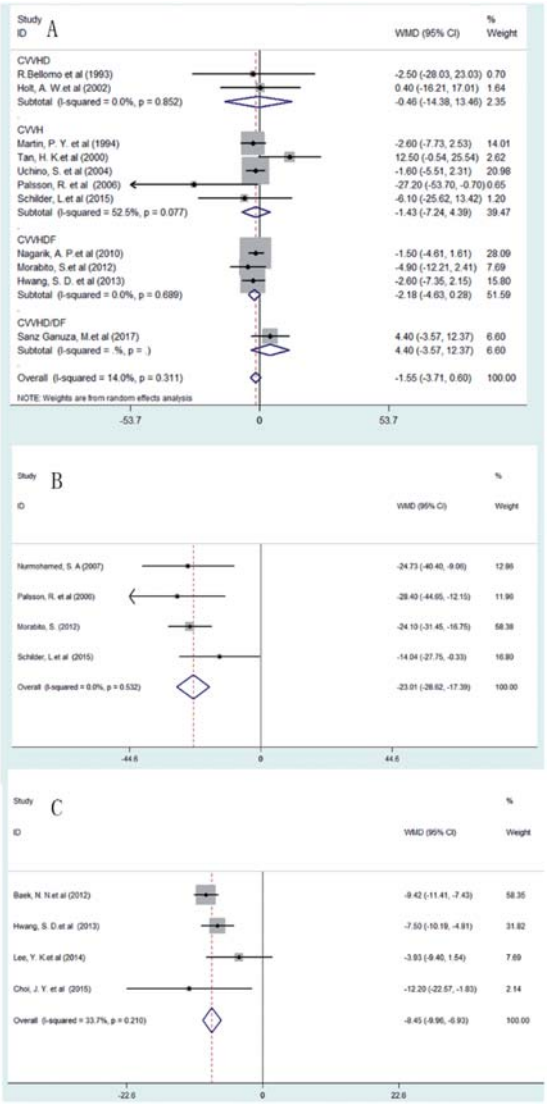


Figure 2: filter lifespan comparison between: A Heparin and anticoagulation-free, B citrate and anticoagulation-free, and C Nafamostat and anticoagulation-free

P0626 **THE RISK FACTORS OF ACUTE KIDNEY INJURY CAUSED BY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS**

Siwen Wang[1], Jiaojiao Zhou[1], Jia Yang[1], Lichuan Yang[1], Xin Wang[1]

[1]*Kidney Research, Division of Nephrology, Department of Medicine, Chengdu, P.R. China*

Background and Aims: Hemophagocytic lymphohistiocytosis (HLH) is a syndrome caused by uncontrolled natural killer (NK) cell and cytotoxic T cell activation, resulting in the overproduction of proinflammatory cytokines and hemophagocytosis. Acute kidney injury (AKI) characterized by rapid loss of renal excretion function is the most common complication of HLH in the kidney. In this retrospective study, we aimed to find the risk factors of AKI in patients with HLH.

Method: This study included adult patients with HLH admitted in West China Hospital of Sichuan University from January 2009 to June 2019. Patients with HLH were excluded from the study if they had a functioning kidney transplant, received renal replacement therapy (RRT) in the past month, suffered from end-stage renal disease (ESRD) or had the renal malignant tumor. The diagnosis of HLH was based on the HLH diagnostic criteria revised by the Histocyte Society in 2004 and AKI was defined according to the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) guideline. We collected basic information, clinical manifestations and laboratory data of patients from electronic medical records.

Results: We analyzed 294 patients this time, of whom 95 (32.3%) developed AKI. The patients were divided into two groups according to the occurrence of AKI. The mortality rate in the AKI group was significantly higher than that in the non-AKI group (40.0% VS 12.6%; $p<0.001$). The risk factors of AKI in patients with HLH were hyperphosphatemia [Odds Ratio (OR) 3.825; 95% Confidence Interval (CI) 1.647-8.886; p=0.002] ,heart failure (OR 2.972; 95% CI 1.029-8.584; p=0.044), increased heart rate (OR 1.025; 95% CI 1.008-1.043; p=0.004), prolonged prothrombin time (OR 1.025; 95% CI 1.001-1.049; p=0.041), elevated total bilirubin level (OR 1.003; 95% CI 1.000-1.007; p=0.030), and hypoproteinemia (OR 0.915; 95% CI 0.842-0.994; p=0.035).

Conclusion: The incidence of AKI in HLH patients is frequent, and the risk of death in HLH patients with AKI is significantly higher. The occurrence of AKI in patients with HLH is related to hyperphosphatemia, heart failure, increased heart rate, prolonged prothrombin time, elevated total bilirubin level, and hypoproteinemia.

	B	SE	Wald	P	OR	95% CI
Hypertension	0.668	0.551	1.472	0.225	1.951	0.663-5.746
Heart failure	1.089	0.541	4.053	0.044	2.972	1.029-8.584
platelet(×109/L)	-0.011	0.007	2.907	0.088	0.989	0.976-1.031
hemoglobin(g/L)	0.009	0.011	0.628	0.428	1.009	0.987-1.031
Baseline Scr(umol/L)	0.005	0.005	1.084	0.298	1.005	0.995-1.016
Serum phosphorus(mmol/L)	1.342	0.430	9.732	0.002	3.825	1.647-8.886
Total bilirubin(umol/L)	0.003	0.002	4.693	0.030	1.003	1.000-1.007
Serum albumin(g/L)	-0.089	0.042	4.465	0.035	0.915	0.842-0.994
Triglycerides(mmol/L)	0.051	0.048	1.127	0.288	1.053	0.957-1.158
aspartate aminotransferase(IU/L)	0.000	0.000	0.002	0.964	1.000	1.000-1.000
lactate dehydrogenase (IU/L)	0.000	0.000	3.907	0.048	1.000	1.000-1.000
Serum sodium(mmol/L)	0.006	0.034	0.027	0.869	1.006	0.941-1.075
Heart rate	0.025	0.009	8.301	0.004	1.025	1.008-1.043
prothrombin time(s)	0.024	0.012	4.165	0.041	1.025	1.001-1.049
procalcitonin(ng/ml)	0.014	0.013	1.198	0.274	1.014	0.989-1.039

P0627 INTRAOPERATIVE DIALYSIS DURING LIVER TRANSPLANTATION IS SAFE AND BENEFICIAL.

Małgorzata Kościelska[1], Joanna Matuszkiewicz-Rowińska[1], Krzysztof Zieniewicz[2], Marek Krawczyk[2], Dorota Gierczuszkiewicz[3], Janusz Sierdziński[4], Paweł Żebrowski[1], Jolanta Malyszko[1]

[1]Medical University of Warsaw, Department of Nephrology, Dialysis and Internal Diseases, Warsaw, Poland, [2]Medical University of Warsaw, Department of General, Liver and Transplantation Surgery, Warsaw, Poland, [3]Medical University of Warsaw, Department of Anaesthesiology and Intensive Care, Warsaw, Poland and [4]Medical University of Warsaw, Department of Medical Informatics and Telemedicine, Warsaw, Poland

Background and Aims: Orthotopic liver transplantation (OLt) is a technically complex surgical procedure associated with a major risk of hemodynamic instability and metabolic derangement, especially in patients with coexisting renal dysfunction. It remains uncertain if intraoperative renal replacement therapy (ioRRT) during OLt could be beneficial and in which subset of patients.

Method: A retrospective observational study of all adult patients undergoing intraoperative renal replacement therapy during OLt in our center from January 2010 till December 2018. IoRRT consisted of dialysis performed with the use of mobile Genius® single-pass batch dialysis system.

Results: 1319 OLts were conducted during the study period and 129 patients (9,8%) were treated with intraoperative dialysis. Seven patients with incomplete documentation were excluded from the study. The mean age of the cohort was 47,8±14,7 years, and 73 (60%) of patients were men. The mean calculated MELD score was 33,7±12,5. 41 procedures (33,6%) were retransplantations and 7 patients underwent simultaneous liver and kidney transplantation. 18 (14,7%) recipients had fulminant liver failure. 66 (54,1%) of patients were admitted to Intensive Care Unit before transplantation. The mean preoperative serum creatinine level was 2,95±1,15 mg/dl and 95 (78%) patients were undergoing renal replacement therapy or had creatinine level ≥2 mg/dl preoperatively. Others required emergent ioRRT due to intraoperative complications and development of significant hyperkalemia or acidosis. The mean preoperative serum potassium concentration was 4,23±0,68 mmol/l and the mean bicarbonate level was 19,8±4,5 mmol/l. Intraoperative dialysis was performed without anticoagulation. The mean surgical time was 400±90,6 minutes and the mean ioRRT duration remained 308 ±109 minutes. Dialysis circuit clotting occurred in 9 (7,3%) cases. There were no other adverse events of ioRRT. Achieved mean arterial bicarbonate and potassium levels after graft reperfusion were 18,5±3,6 and 3,8±0,95 mmol/l, respectively. In 111 cases dialysis was initiated at least 15 minutes before reperfusion. 13% of this subgroup (16 pts) experienced post-reperfusion syndrome (defined as a decrease in the mean arterial pressure of more than 30% of the baseline, occurring within first 5 minutes after the reperfusion of the graft and lasting at least 1 minute).

Conclusion: Our data suggests that intraoperative dialysis in severely ill patients with high MELD score is safe and effective. Lower than expected post-reperfusion syndrome occurrence needs to be confirmed in a study designed with appropriate control group.

P0628

CREATININE-CYSTATIN C RATIO IS ASSOCIATED WITH MORTALITY IN ICU PATIENTS UNDERGOING CONTINUOUS RENAL REPLACEMENT THERAPY

Chan-Young Jung[1], Wonji Jo[1], Jaeyoung Kim[1], Jung Tak Park[1]

[1]*Severance Hospital, Yonsei University Health System, Division of Nephrology, Seoul, Korea, Rep. of South*

Background and Aims: Development of acute kidney injury (AKI) in intensive care patients considerably increases the risk of mortality. Although several factors that are related to outcome have been recognized in this patient group, stratifying mortality risk still remains a challenge. While serum creatinine levels are confounded by muscle wasting in critical illness, cystatin C is expected to be less modulated by muscle mass. Speculating that the ratio between serum creatinine and cystatin C may reflect muscle mass in critically ill AKI patients, we evaluated the association between creatinine-cystatin C ratio and mortality in patients requiring continuous renal replacement therapy (CRRT) in the intensive care unit (ICU).

Method: Retrospective analyses were conducted on 443 ICU patients who underwent CRRT between August 2009 and October 2016 at Severance Hospital of Yonsei University Health System, Seoul, South Korea. The patients were divided into four groups based on creatinine-cystatin C ratio at the time of CRRT commencement. The primary outcome was 90-day mortality after CRRT initiation.

Results: The mean age was 64 ± 15 years, and 57.3% of patients were male. The most common cause of AKI was sepsis. The median and range of the creatinine-cystatin C ratio was 0.83 (0.13-6.20). The 90-day mortality rate for each creatinine-cystatin C ratio quartiles 1, 2, 3, and 4 were 76.6%, 73.9%, 61.3%, and 51.8%, respectively. Multiple Cox proportional hazard models revealed that the creatinine-cystatin C ratio was an independent predictor of 90-day mortality even after adjusting for confounding factors (Hazard ratio, 0.97; 95% confidence interval, 0.95-0.99, $P<0.01$). The prediction of mortality was significantly improved when creatinine-cystatin C ratio was considered compared to APACHE-II or SOFA scores alone.

Conclusion: Creatinine-cystatin C ratio is associated with mortality in ICU patients undergoing CRRT, and may be a practical marker in predicting survival among ICU patients with AKI.

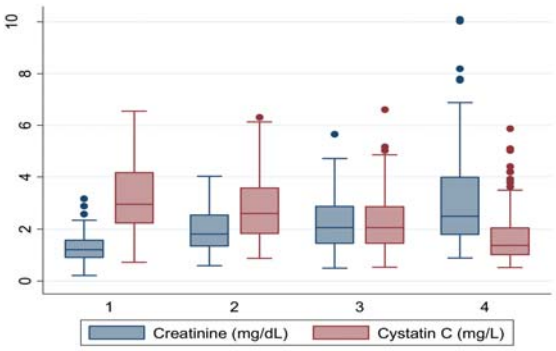


Figure 1. Boxplot for creatinine, cystatin C values according to creatinine-cystatin C groups

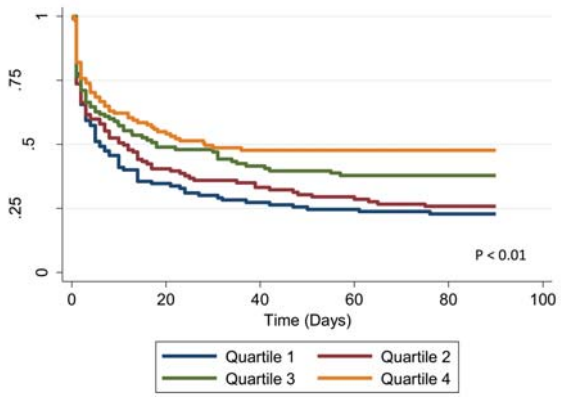


Figure 2. Kaplan-Meier estimates by groups of creatinine-cystatin C ratio

P0629

ESTABLISHING MORTALITY ASSOCIATED WITH AKI IN A DGH AND THEN TRYING TO DO SOMETHING ABOUT IT- INTRODUCTION AND AUDIT OF THE AKI7 CARE BUNDLE

Christopher Paisey[1], David Chapman[1], Kat Achilleos[1], Vivian Yiu[1]

[1]*West Suffolk Hospital, United Kingdom*

Background and Aims: Acute kidney injury (AKI) is a prevalent and treatable contributor to inpatient mortality. Simple management steps for AKI are frequently omitted or delayed in patient care due to its insidious onset and lack of symptoms. The NCEPOD report in 2009 found that only 50% of patients with AKI received good care. One response to this has been increased use across trusts of the electronic medical record for recognition and monitoring of AKI. Such systems also enable collection of reproducible datasets for audit as well as a platform for prompting the use of best practice guidelines.

We sought to establish mortality for patients with AKI and to audit the introduction of an electronic alert system and order set proforma for AKI: the AKI7 care bundle.

Method: We collated data from all inpatients in West Suffolk Hospital (WSH) flagged as developing AKI by the recording system 'eCare' over a 2-year period and present a mortality analysis for this cohort. Data was collected retrospectively from eCare and statistical analysis conducted in 'R'.

Results: Of 3527 individuals who developed AKI over a 2 year period in WSH; 79% did not progress beyond AKI stage 1, 13% stage 2 and 8% stage 3, the mean age was 74 years and mean length of stay 13 days. Across all stages of AKI, 75% were investigated with urinalysis, 94% received fluid balance monitoring, 5% were investigated with renal tract US and 58% were referred to a nephrologist for specialist input. Mortality analysis for this same cohort revealed an association between survival at 60 days and use of urinalysis p=<0.001, fluid balance monitoring p=<0.001 and investigation with renal tract US p=<0.001. The 1 year mortality associated with AKI increased significantly with severity; 29% for AKI stage 1, 51% for AKI stage 2 and 65% for AKI stage 3 (Figure.1). The all cause 1 year mortality for all stages of AKI combined was 39.1%. Following launch of the AKI7 care bundle we found that use of the document template promoted requests for renal tract US (20% versus 5%), urinalysis (83% versus 75%) and requests for input by renal physicians (75% versus 65%).

Conclusion: The AKI7 care bundle improves clinician awareness of AKI and promotes the use of important steps in AKI management. Since mortality increases with AKI stage, management targeted to ameliorate progression of AKI is vital and can be supported by well designed electronic care bundles. The association of improved survival with fluid balance monitoring and investigations for AKI further supports measures to promote the use of these steps. We intend to encourage use of the AKI7 care bundle during induction for junior doctors coupled with distribution of cards as an aide-memoire.

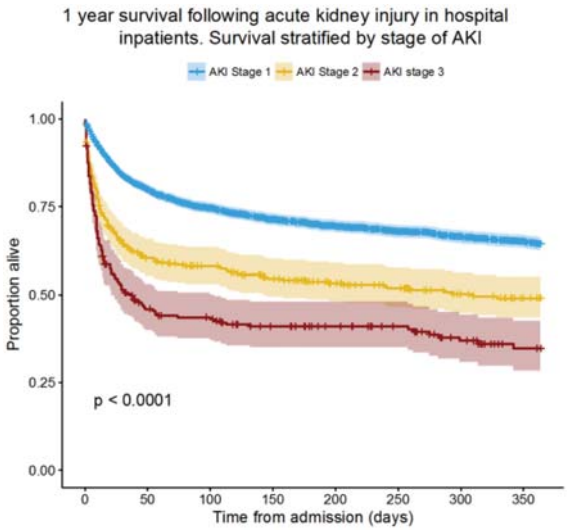


Figure:

P0630 EARLY CHANGES OF SEQUENTIAL URINE SEDIMENT ANALYSIS ARE INDICATIVE FOR DEVELOPMENT OF ACUTE KIDNEY INJURY AFER CARDIAC SURGERY

Moritz Schanz[1], Severin Schricker[1], Tina Oberacker[2], Nora Göbel[3], Dominik M. Alscher[1], Martin Kimmel[4], Markus Ketteler[1]

[1]Robert-Bosch-Hospital, Department of General Internal Medicine and Nephrology, Stuttgart, Germany, [2]Dr. Margarete Fischer-Bosch - Institut für Klinische Pharmakologie, Stuttgart, Germany, [3]Robert-Bosch-Hospital, Cardiac and Vascular Surgery, Stuttgart, Germany and [4]Alb Fils Kliniken - Clinic at Eichert, Department of General Internal Medicine and Nephrology, Göppingen, Germany

Background and Aims:

Microscopic examination of urine sediment is a well-established and inexpensive technique for differential diagnosis of acute kidney injury. Especially renal tubular epithelial cells (RTEC) and granular casts (GC) have been shown to be a strong predictor of acute tubule necrosis (ATN), the assumed most common cause for AKI in cardiac surgery patients. So far, no study evaluated urine sediment before manifest AKI is evident. Therefore, the aim of this prospective trial was to evaluate if early changes of urine sediment parameters are indicative for development of acute kidney injury.

Method:

Sequential urine sediment specimens were analyzed on day 0 (d0), day 1 (d1) and day 4 or 5 (d5) after cardiac surgery in n=37 patients. Urine analysis was conducted immediately after collection of urine specimens. Analysis includes detection of RTEC and GC as well as hyaline casts (HC), squamous epithelium (SE), erythrocyte count (EC) and leucocyte count (LC). Urine score (US) - consisting of RTEC and GC - which is described as indicative for ATN, was calculated as described previously. For detection of AKI, serum creatinine, serum cystatin c and urine output were recorded. Urine sediment changes over time were analyzed using differences between day of surgery (d0) and day 1 (d0-d1 = Δd1) or day 5 (d0-d5 = Δd5), respectively.

Results:

Of the 37 included patients n=10 (27%) developed AKI within 5 days. According to the definition of KDIGO 2012, two patients developed Stage 1 (20%), six patients Stage 2 (60%) and two patients Stage 3 (20%) AKI. Median age was 67 years (IQR: 63.5-73.0). Mean HC, GC, RTEC and US tended to be higher in AKI patients from day one after surgery. Looking at the urine sediment changes over time (Median; IQR), Δd1 of RTEC (AKI: 0.65; 0.00 – 1.15 vs. No AKI: 0.00; -0.03 – 0.03; p=0.010), GC (AKI: 0.25; 0.00 – 0.50; No AKI: 0.00; -0.20 – 0.00; p=0.002) and US (AKI: 0.00; -0.25 – 0.00 vs. No AKI: 0.00; 0.00 – 1.00; p=0.047) were significant higher in AKI group. Also HC (AKI: 1.00; 0.00 – 1.00; No AKI: 0.00; -1.25 – 1.00; p>0.05) tended to be higher in AKI on Δd1, whereas SE, EC and LC did not show any trend between both groups. Δd5 did not show any significant result between AKI and non-AKI. Because all of these patients were catheterised, the results on urinary erythrocyte count were interpreted with appropriate caution.

Conclusion:

This is the first study evaluating sequential urine sediment measurements for early detection of AKI in cardiac surgery. According to these preliminary data, Δd1 of RTEC, GC and US is significant higher in AKI, suggesting that an increase from day of surgery to day 1 may be indicative for the development of AKI right before manifest AKI is evident. Therefore sequential urine sediment measurements could be useful for early detection of AKI after cardiac surgery.

P0631 **COMPLICATIONS OF TREATMENT WITH HIGH CUT OFF FILTERS FOR ACUTE KIDNEY INJURY SECONDARY TO MULTIPLE MYELOMA**

ANA BERNI WENNEKERS[1], Ana Coscojuela Otto[1], MARIA VICTORIA DOURDIL[2], PABLO IÑIGO GIL[1], Rafael Alvarez Lipe[1]

[1]HOSPITAL UNIVERSITY LOZANO BLESA, NEPHROLOGY, Zaragoza, Spain and [2]HOSPITAL UNIVERSITY LOZANO BLESA, HEMATOLOGY, Zaragoza, Spain

Background and Aims: Acute kidney injury is a frequent complication of MM that can affect 18 to 56% of patients and more than 10% end up needing dialysis.

One of the drawbacks associated with the technique is attributed to the albumin loss. The other complications are related with the dialysis technique itself, especially infections, as highlighted by the Eulite study.

The objective of the study is to check that there are no more complications in dialysis with High Cut Off filters than in conventional Hemodialysis.

Method: We are the referral hospital in our community in the treatment of acute kidney injury secondary to myeloma. We have performed 28 treatments of hemodialysis with High cut off filters (HD-HCO).

The HD-HCO protocol includes daily dialysis session of 6 hours during the first 6 days to subsequently switch to dialysis every other dayuntil free light chains levels below 500 mg/L, or until the recovery of renal function allows the independence of dialysis.

All these patients have a chemotherapy regimen based on Bortezomib (25 of the 28 treatments) and Dexamethasone (28 treatments).

A retrospective analysis of the 28 treatments that are performed with HD-HCO after 8 years of experience (July 2011 to May 2019) to demostrate the presence of the same complications as the conventional Hemodialysis.

Results: Loss of albumin is one of the main drawbacks of the technique. Our patients had no changes in albumin levels due to the fact that our protocol includes the infusion of 2 vials of 20% albumin of 50 ml. at the end of each HD-HCO session. Figure 2

Another concern is intradialytic complications. We have reviewed this topic and our results show that patients in HD-HCO do not present a greater number of complications than those who dialyze with HD-HD or other conventional dialysis. The total number of sessions was 298. 21 patients developed hypotension (7%). The number of sessions in which the patient presented fever was 6 (2%), coagulation of the circuit occurred in 23 sessions (7,7%). The catheter dysfunction (when it does not allow to reach 250 ml/min of blood flow) in 26 times(8.7%) and only 13 times the replacement of the catheter (4.26%) was necessary, consequently, in those who required a greater number of dialysis sessions. In only 1 case (patient who required 27 sessions) to place a permanent Tesio catheter was necessary. Figure 1

In referring to complications of dialysis for AKI secondary to myeloma, few studies consider them. These studies focus on quantifying the reduction of light chains and the efficiency of the treatment, but don't keep in mind the record of the complications.

In the EuLITE study, authors observed a greater number of lung infections in the HD-HCO group (12 vs 3) $p = 0.014$ and attributed this difference to extended dialysis and albumin loss.We have not observed this problem. The levels of albumin are stable with our infusion protocol of 2 vials of 20% human albumin of 50 ml at the end of each HD-HCO.

There's no more complications than conventional dialysis, even infection ones. 13 febrile episodes occurred in 6 patients (more than 37,5°C). Blood cultures were collected in all patients, being positive in only 4 patients. Germs found were: Escherichia coli (treated with Amoxicilin/clavulanic), Staphylococcus aureus (treated with Daptomycin), Staphylococcus epidermidis (treated with Meropenem) and Klebsiella pneumoniae (treated with Meropenem too). This 4 patients were the ones who required the replacement of the catheter.

Conclusion:

1. - Our findings indicate that the HD-HCO has the same safety profile as the conventional Hemodialysis.

2.- There is no serious infectious complications in our patients despite of the fact that all of them are immunosuppressed patients (AKI secondary to Multiple Myeloma in patients treated with chemotherapy)

Figure 1.- Dialysis complications

No more complications than any other type of chronic and/or acute HD.

Dialysis complications	n/n total sessions*	%
Catheter change	13/288	4,5%
Catheter dysfunction	26/288	9,0%
Circuit coagulation	23/288	8,0%
Hypotension	21/288	7,3%
Fever	6/288	2,1%

* Number of total sessions of dialysis: 298

Figure:

P0632 RISK FACTORS FOR ACUTE KIDNEY INJURE AMONG PATIENTS WITH RHABDOMYOLYSIS

Jia Yang[1], Lichuan Yang[1], Xin Wang[1], Siwen Wang[2]

[1]West China Hospital of Sichuan University and [2]West China Hospital of Sichuan University, Chengdu,

Background and Aims: Rhabdomyolysis (RM) is a syndrome characterized by the abruption of the integrity of skeletal muscle cells with subsequent release of intracellular components into extracellular fluid and circulation. Acute kidney injury (AKI) is a life-threatening complication of rhabdomyolysis. The aim of this study was to assess patients at high risk for the occurrence of AKI defined by KDIGO criteria and in-hospital mortality.

Method: We performed a retrospective study of patients with creatine kinase levels in excess of 1000 U/L, admitted in West China Hospital of Sichuan University from January 2011 to march 2019. The sociodemographic, clinical and laboratory data of the patients were obtained in an electronic medical record database. Univariate and multiple regression analyses were conducted.

Results: 329 patients were included in our study. The incidence of AKI was 61.4%, the overall mortality was 19.8%, and patients with AKI tend to have higher mortality than those without AKI (24.8% versus 11.8%, $P < 0.01$). The clinical conditions most frequently associated with rhabdomyolysis were trauma (28.3%), infection (14.6%), bee stings (12.8%), thoracic and abdominal operations (11.2%) and exercise (7.0%). Patients resulted from sepsis, bee stings and acute alcoholism were susceptible to AKI. The risk factors for the occurrence of AKI among rhabdomyolysis patients included age≥60 (OR 3.070), chronic alcoholism (OR 3.256), hypertension (OR 4.252), multiple organ dysfunction syndrome (OR 7.244), elevated white blood cell counts (OR 1.047) and serum phosphorus (OR 5.526). Age≥60 (OR 3.188), multiple organ dysfunction syndrome (OR 2.262), diabetes (OR 2.746) and elevated prothrombin time (OR 1.079) were independent risk factors for in-hospital mortality of rhabdomyolysis patients with AKI.

Conclusion: AKI is independently associated with mortality in rhabdomyolysis patients. Several risk factors were found to be associated with the occurrence of AKI and in-hospital mortality. The findings aiming to suggest early prevention of AKI should target on patients with high risk and more effective management to improve the quality of medical care.

P0633

EFFECT OF DIPEPTIDYL PEPTIDASE-4 INHIBITORS ON CISPLATIN-INDUCED ACUTE NEPHROTOXICITY IN CANCER PATIENTS WITH DIABETES MELLITUS: A RETROSPECTIVE STUDY

Takamasa Iwakura[1,2], Hirotaka Fukasawa[1], Atsushi Kitamura[1], Kento Ishibuchi[1], Hideo Yasuda[2], Yoshihide Fujigaki[3], Ryuichi Furuya[1]

[1]Iwata City Hospital, Renal division, Iwata, Japan, [2]Hamamatsu University School of Medicine, Internal Medicine I, Division of Nephrology, Hamamatsu, Japan and [3]Teikyo University School of Medicine, Department of Medicine, Tokyo, Japan

Background and Aims: Cisplatin is a highly effective chemotherapeutic agent. However, acute kidney injury (AKI) limits its subsequent use, resulting in poor cancer prognosis. Dipeptidyl peptidase-4 (DPP-4) inhibitors have been reported to attenuate cisplatin-induced AKI in animal models, but the effect in human patients remains to be clarified. We hypothesized that DPP-4 inhibitors can prevent cisplatin-induced AKI in diabetic-cancer patients.

Method: We retrospectively reviewed all consecutive cancer patients who were treated with a first cycle of cisplatin-containing regimen between January 2011 and October 2019. We analysed data of diabetic-cancer patients treated with high-dose cisplatin (> 50 mg/m2)-containing regimens. The change of estimated glomerular filtration rate (eGFR) within 2 weeks after cisplatin treatment was compared between the patients treated with DPP-4 inhibitors and those treated without DPP-4 inhibitors.

Results: A total of 455 patients were treated with cisplatin during the period. Of these, 35 patients were eligible for the analysis. The change of eGFR was significantly less in the patients treated with DPP-4 inhibitors, compared to those without DPP-4 inhibitors [Fig.1; the percentages of eGFR decline (mean ± SD) was 23.6 ± 20.3% vs 41.2 ± 20.6%, respectively; P=0.016]. Furthermore, the incidence of AKI was significantly less in the patients treated with DPP-4 inhibitors (25% vs 60%, respectively; P=0.040).

Conclusion: DPP-4 inhibitors may decrease the risk of cisplatin-induced AKI in diabetic patients. Therefore, the use of DPP-4 inhibitors may be one of supportive therapies for cancer patients treated with high-dose cisplatin.

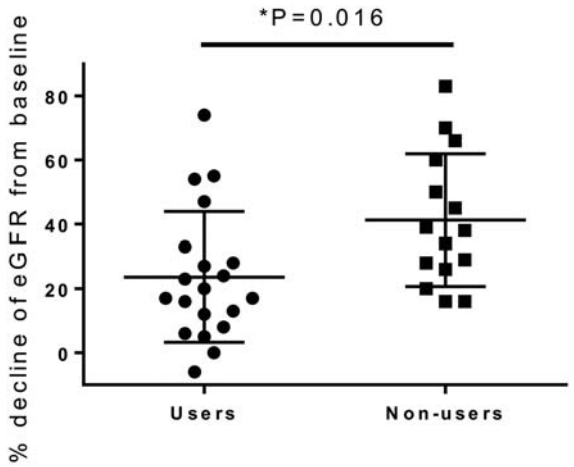


Figure:

P0634 **RISK OF HYDROELECTROLYTIC AND ACID-BASE DISORDERS INDUCED BY LIPOSOMAL AMPHOTERICIN B USE IN VISCERAL LEISHMANIASIS PATIENTS**

Gabriela Freire Bezerra[1], Gdayllon Cavalcante Meneses[1], Danya Bandeira Lima[1], Geraldo Bezerra da Silva Junior[1,2], Vittoria Nobre Jacinto[1], Emanuel Paula Magalhães[1], Thaiany Pereira da Rocha[1], Isabella Evelyn Prado de Azevedo[1], Elizabeth De Francesco Daher[1], Alice Maria Costa Martins[1]

[1]Federal University of Ceará, School of Medicine and Pharmacy, Fortaleza, Brazil and [2]Universidade de Fortaleza, Public Health and Medical Sciences Graduate Programs, Fortaleza, Brazil

Background and Aims: Visceral leishmaniasis (VL) is a serious illness if untreated. Liposomal Amphotericin B (L-AMB) is the more effectiveness treatment against LV and less nephrotoxic formulation. We aim to evaluate expression of kidney transporters in VL patients before and during L-AMB use.

Method: This is a prospective study with 9 selected VL patients that used only L-AMB during hospital stay. Renal transporter analyzes were from before and during the treatment and compared with a control group composed by healthy people. The urine transporters (AQP2, aquaporin 2; NKCC2, Na-K-2Cl cotransporter; NHE3, Na/H exchanger) and a constitutive exosome marker (TSG 101) expressions were measured after urinary exosomes isolation.

Results: No significant increase of TSG 101 was observed in all comparisons, including between both times and vs healthy controls. Additionally, were observed increased urinary protein expression in VL patients in both times (before and after L-AMB use) in comparison with healthy controls of the AQP2: (105.32 (22.90 – 140.27) vs 1362.97 (627.93-2620.09) or 846,20(552.60-1249.14) %, $p<0.01$); NHE3: (74.81 (57.17 – 126.33) vs 3373.36 (282.69-6877.97) or 462.67 (123.80-7280.21) %, $p<0.01$); and NKCC2: (90.98 (79.07 – 120.30) vs 634.45 (345.18-1588.41) or 545.74 (284.34-2183.87) %, p=0.03). Moreover, the patients treated with L-AMB showed a significant decrease in AQT2 (P=0.023) and NHE3 (P=0.008) expression.

Conclusion: We suggest that despite less nephrotoxic, the L-AMB use may be monitored to investigate patients at risk of hydroelectrolytic and acid-base disorders.

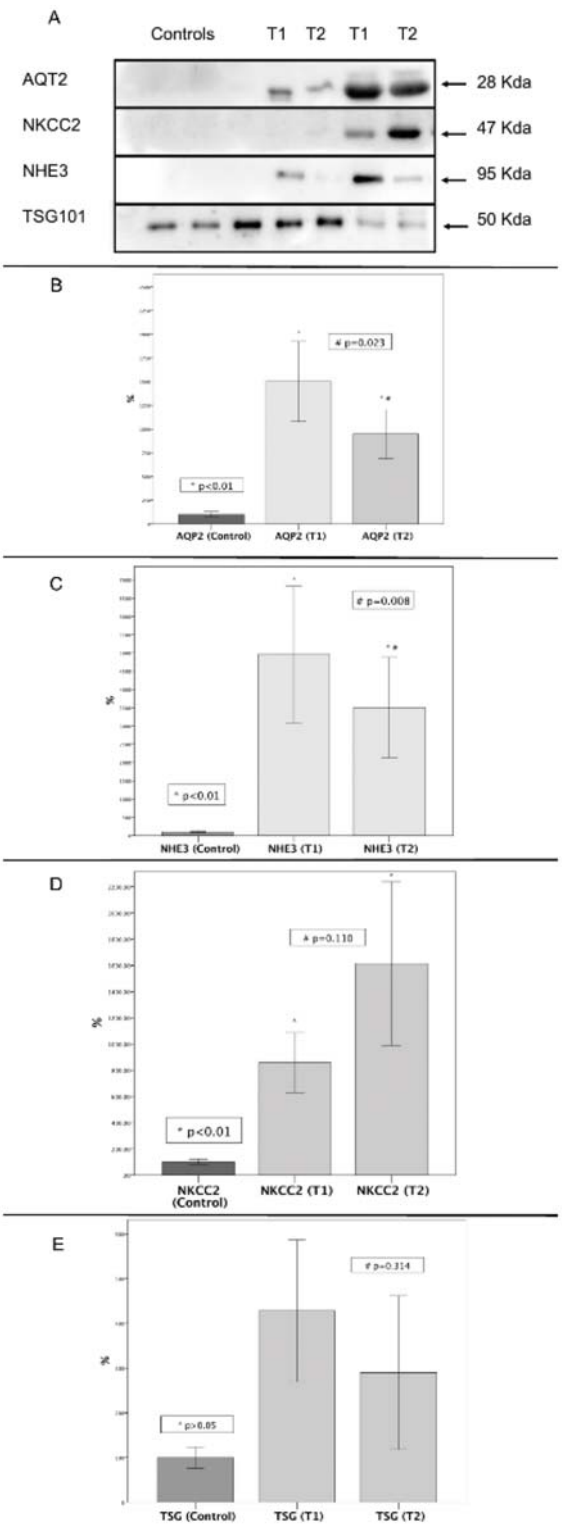


Figure:

P0635

MYOGLOBIN CLEARANCE IN CVVHD USING HIGH CUT-OFF FILTER VERSUS CVVHDF WITH REGIONAL CITRAT ANTICOAGULATION: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

Jonathan De Fallois[1], Lorenz Weidhase[2], Sirak Petros[2]

[1] Division of Nephrology, Medical Department III, University Hospital Leipzig,, Leipzig, Germany and [2]Medical Intensive Care Unit, University Hospital Leipzig, Leipzig, Germany

Background and Aims: Acute kidney injury (AKI) is frequent among critically ill patients and it is associated with high mortality. Rhabdomyolysis is a distinct cause of AKI. As myoglobin has renal toxic effects, clearance via continuous renal replacement therapy (CRRT) may be favourable. Current international guidelines recommend regional citrate anticoagulation (RCA).

Clinical data comparing different modalities of CRRT addressing myoglobin clearance are lacking. Hemofiltration is recommended to eliminate myoglobin, which requires systemic anticoagulation. RCA would be impractical due to the high citrate load as a result of the higher blood flow.

Continuous veno-venous hemodiafiltration (CVVHDF) is one opportunity to realize lower citrate load and maintain middle molecule clearance. Another approach may be the application of hemodialysis with high cut-off (HCO) membranes with a pore size larger than 0.01 µm in CVVHD (CVVHD-HCO). We have previously shown that CVVHD-HCO is superior to conventional high-flux dialyser regarding the clearance of β_2-microglobulin. Based on this finding, we analyzed of various etiologiesre Filter lilifespan mit dem efonnummer der Virologie zum Befunderfragenmyoglobin clearance with CVVHDF compared to CVVHD-HCO with RCA.

Method: The present study is a prospective, randomized, single-blinded, monocentric trial. We enrolled patients from May 2017 to September 2018 in our 28-bed medical ICU at the University Hospital Leipzig.

We screened 430 patients with AKI and indication for RRT for eligibility. A total of 70 patients underwent randomisation 1:1 into the intervention (CVVHD-HCO, high cut-off dialyzer Ultraflux EMiC2) and control group (CVVHDF, high-flux dialyzer Ultraflux AV1000S).

The concentrations of myoglobin (17053 Dalton (Da), urea (60 Da), creatinine (113 Da), β2-microglobulin 11800 Da), interleukin 6 (IL-6, 26000 Da) and albumin (66470 Da) were measured before (pre) and after (post) the dialyzer 1, 6, 12, 24 and 48 h after initiating CRRT.

We hypothesized non-inferiority of CVVHD-HCO versus CVVHDF regarding myoglobin clearance (primary end-point).

Results: Myoglobin clearance showed non-inferiority in the intervention group for all time points. The dialyzer in the intervention group resulted in even a better myoglobin clearance during the whole study period. (Table 1).

Clearance values for urea and creatinine were equal and there was no albumin loss in both groups.β_2-microglobulin clearance was significantly better in the intervention group than in the control group at all time points. The clearance of IL-6 was also better at T0 in the intervention group. The filter lifespan was 51.5 hours (CI: 44.24; 58.76) in the control group and 62.3 hours (CI 56.83; 67.7) in the intervention group (log-rank, p=0,029).

Conclusion: Myoglobin can be reliably cleared using both CVVHD-HCO and CVVHDF. Nevertheless, the plasma specific clearance rate of myoglobin was higher with CVVHD-HCO. High myoglobin levels are associated with AKI and higher mortality rates and on this account clearance of myoglobin represents a relevant clinical issue.

Table 1: Primary endpoint: Myoglobin plasma clearance (ml/min).

Time after starting treatment (hours)	*CVVHDF*	*CVVHD-HCO*	*P value*	*n*
1h	3.65±3.95 (2.26-5.13)	11.90±3.91 (10.57-13.08)	<0,001	66
6h	3.99±4.28 (2.72-5.68)	10.20±3.47 (8.99-11.41)	<0,001	65
12h	3.38±4.83 (1.66-5.21)	8.62±5.61 (6.77-10.41)	<0,001	62
24h	2.27±4.10 (0.83-3.91)	8.58±2.66 (7.69-9.52)	<0,001	57
48h	4.11±6.19 (1.57-7.01)	8.18±5,44 (2-8.42)	0,022	48

P0636

REMOVAL OF METHOTREXATE BY BLOOD PURIFICATION IN PATIENTS WITH ACUTE RENAL FAILURE DUE TO METHOTREXATE POISONING(A CASE REPORT)

Katsuji Otsuka[1], Toshikazu Harada[1], Miho Ishikawa[1], Daisuke Obara[1], Tatsuo Yamamoto[1], Youji Murakami[2], Kazuhiko Nishi[2], Asami Yamada[3], Daisuke Kadowaki[4]

[1]Kumamoto University Hospital, ME equipment technology section, Kumamoto, Japan, [2]Department of Blood Purification Therapy, Kumamoto University Hospital, Kumamoto, Japan, [3]Department of Hematology, Kumamoto University Hospital, Kumamoto, Japan and [4]Faculty of Pharmaceutical Sciences, Sojo University, Kumamoto, Japan

Background and Aims: High-dose methotrexate (MTX) chemotherapy is used to treat a variety of malignancies, including lymphoma, lymphoid leukemia, and sarcomas. Since MTX binds to proteins at a binding ratio of 50%, and nearly 90% of MTX in the blood is excreted via the kidneys, impaired kidney function would cause accumulation of MTX and result in complications. We encountered 4 patients who developed acute renal failure following high-dose MTX administration, but recovered after several modalities of blood purification therapies at our hospital. To clarify which blood purification method might be the most effective to remove accumulated MTX, we retrospectively investigated the removal rate of MTX by different modalities of blood purification therapy.

Four patients (3 males and 1 female) who developed acute renal failure immediately after the start of administration of high-dose MTX therapy received blood purification therapies, including hemodialysis (HD), hemodiafiltration (HDF), plasma exchange (HD + PE), direct hemoperfusion (DHP), or any combination of the above, from January 2010 to December 2015.

Methods: Case 1: Patient (female, 57 years old, weight 54 kg) received HD (9times) followed by HDF (5 times) for 4 h each using a cellulose triacetate (CTA) membrane. Case 2: Patient (male, 56 years old, weight 90.7 kg) received HD (8 times) with 2different membranes (polyethersulfone and polyarylate blended polymer (PEPA); CTA; polymethyl methacrylate (PMMA)) for 4 h each. Case 3: Patient (male, 79 years old, weight 56 kg) received HD (3 times) followed by HDF (6times), HD + PE (once) for 4 h each. Case 4: Patient (male, 23 years old, weight 104.6kg) received HDF using CTA (3 times) membranes, followed by HD + PE, HD + DHP (3 times) and DHP (once) for 4 h each. We retrospectively investigated the blood level of MTX before and after each of the blood purification therapies and compared the removal rate of MTX by the different modalities.

Results and discussion: The average dose of MTX prescribed was 1.1 g/m^2 (0.9-3.8). The blood levels of MTX reduced from 29.4 μM (9.8-57.8) to 0.06 μM (0.02-0.09) after several treatment sessions, and improvement of the renal function was observed in all cases. The highest removal rate was observed with HD + DHP (61.7%, n = 3), followed by DHP (50.0%, n = 1), HDF (44.1%, n = 19), HD (34.6%, n = 23) and HD + PE (30.3%, n = 2). As for the most effective membrane used for HD, the highest removal ratio was observed with PEPA (69.6%, n = 3), followed by PMMA (36.5%, n = 3) and CTA (28.2% %, n = 17). In regard to the most effective modality for removing accumulated MTX from the blood, high removal efficiencies were observed for HD + DHP and DHP. Therefore, it appears that use of these modalities would be the most desirable, as these appear to be highly capable of effectively removing accumulated MTX. Higher removal rates were observed with the use of the PEPA membranes than with that of the CTA and PMMA membrane, probably due to the better adsorption capacities of PEPA membrane. From these results, we conclude that HD or HDF with a high-adsorption characteristics (PEPA) combined with DHP might be the most effective method for removing accumulated MTX from the blood, as well as controlling water removal and correcting electrolyte concentrations.

Conclusion: Improvement of the renal function was observed after several sessions of blood purification therapy in all patients who developed acute renal failure after high-dose MTX therapy. The removal efficiency of MTX was sufficiently high when HD + DHP, HDF or HD was performed, especially with the use of a membrane with high adsorption characteristics.

P0637

SAFETY, EFFICACY AND OUTCOMES OF SLOW LOW EFFICIENCY DIALYSIS (SLED) IN CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY INJURY (AKI) IN MEDICAL INTENSIVE CARE UNITS (ICU)- A PROSPECTIVE STUDY IN A TERTIARY CARE HOSPITAL IN INDIA

Reetesh Sharma[1,2], Mayur Maksana[2]

[1]Asian Institute of Medical Sciences, Nephrology and Kidney Transplant, Faridabad, India and [2]Medanta the Medicity, Nephrology and Kidney Transplant Medicine, Gurgaon, India

Background and Aims: Slow low efficiency dialysis (SLED) is increasingly being used as a renal replacement therapy in hemodynamically unstable, critically ill patients with acute kidney injury (AKI). SLED may reduce intradialytic hemodynamic instability as compared with conventional intermittent haemodialysis, while reducing resource demands of continuous renal replacement therapies (CRRT). There are very few studies which have evaluated its safety, efficacy and outcome despite its increasing use, especially in Indian subcontinent.

Method: We conducted a single centre, prospective study to demonstrate safety, efficacy and outcome of SLED.. Net fluid removal and duration of SLED were based on need and hemodynamic status of the individual patient as decided by treating nephrologist. SOFA score was used as severity illness score. Efficacy of SLED was studied in terms of ability to achieve ultrafiltration goal, correction of acidosis and urea reduction ratio. Safety was studied in terms of hemodynamic and cardiovascular stability and complications during and after SLED. Outcomes were noted at time of discharge and six months later in terms of dialysis dependence, renal parameters (if dialysis independent) and mortality (In hospital and 6 months following discharge).

We included hemodynamically unstable patients with AKI from medical ICUs with age >18 years of either gender. We excluded patients with AKI who could tolerate conventional haemodialysis or ESRD on maintenance haemodialysis.

Results: We analysed 228 patients with AKI in medical ICUs who underwent 576 SLED sessions over period of six months. Mean age was 57.48 $\pm$ 15.67 years and 74% (n=169) were male. Comorbidities were hypertension (56%), diabetes mellitus (43%), CKD (33%) and cardiovascular diseases (28%). Sepsis (93%) and hypoperfusion (68%) were most common causes for AKI. Refractory fluid overload (91%) and refractory metabolic acidosis (79%) were most common indications for SLED. Mean SOFA score was 12.2 $\pm$ 7.75 with 61 % patients had SOFA score more than 11. 66% were on mechanical ventilator. Out of 576 sessions, 555 sessions (96%) completed the planned duration without any adverse event. Planned ultrafiltration goal was achieved in 94%. SLED was able to correct metabolic acidosis in majority (86.1%). 68% SLED sessions required a vasopressor support and 34.8 % of SLED sessions were associated with hemodynamic instability. Total 14(6.2 %) patients died during SLED session. No documented arrhythmias developed after starting SLED. In-hospital mortality occurred in 61% patients. At 6 months follow up, another 13% patients died. In subgroup analysis, mortality was significantly higher in patients with SOFA score more than 11 ($P<0.0001$). Ventilatory requirement was also significantly high in non-survivors($P<0.0001$). Univariate logistic regression analysis showed that inotropic requirement, higher SOFA severity score, acidosis with pH <7.25 and presence of underlying CKD were associated with significant mortality.

Conclusion: Our study demonstrated efficacy and safety of SLED in critically ill AKI patients in medical ICU. SLED was able to achieve planned ultrafiltration goal and correct metabolic acidosis in majority of patients. SLED had good hemodynamic tolerability. Mortality was noted in 61 % of patients (not attributable to SLED per se). High SOFA score, underlying co morbidities, vasopressor requirement and severe acidosis (pH <7.25) were associated with high mortality. SLED is a reasonable cost-effective option of RRT in hemodynamically unstable patients with AKI especially in developing countries.

P0638

COMPARISON OF CIRCUIT PATENCY AND EXCHANGE RATES BETWEEN THE ORIGINAL PRODUCTS AND THE GENERIC VERSIONS OF NAFAMOSTAT MESILATE IN ACUTE KIDNEY INJURY RECEIVING CONTINOUS RENAL REPLACEMENT THERAPY

Ho Sik Shin[1], Jisu Kim[1], Haesu Jeon[1], Ye Na Kim[1], Yeonsoon Jung[1], Hark Rim[1]

[1]*Gospel Hospital, Internal Medicine, Busan, Korea, Rep. of South*

Background and Aims: The generic versions have the same main component as the original products. But, due to the difference in additives or the level of impurities, it is questionable the the generic versions are completely identical to the original products. Nafamostat mesilate has been widely used as an anticoagulation in continuous renal replacement therapy (CRRT) with hemorrhagic diathesis. In this study, we performed comparison of circuit patency and exchange rates between the original products and the generic versions of Nafamostat mesilate in acute kidney injury patients receiving continuous renal replacement therapy

Method: We have conducted retrospective studies to compare the original product of nafamostat mesilate (n=732) with the generic version (n=328) on the CRRT running time.

Results: CRRT fiter life time of the generic version group was shorter than that of original product group although that was not significantly.

Conclusion: When generic versions of nafamostat mesilate are adopted in a hospital formulary, it must be emphasized that the effect these versions may be not completely identical to that of the original products.

P0639 COMPARISON OF SIRS AND QSOFA CRITERIAS IN RECOGNITION OF SEPSIS RELATED ACUTE KIDNEY INJURY

Özlem Alkan[1], İzzet Hakkı Arıkan[2]

[1]Marmara University, Internal Medicine, Istanbul, Turkey and [2]Marmara University, internal medicine, nephrology, Istanbul, Turkey

Background and Aims: Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection. Epidemiological studies have shown that the incidence of sepsis is increasing and therefore it is a public health problem. AKI is often associated with critical illnesses such as sepsis, and is associated with prolonged hospital stay, need for intensive care, increased morbidity and mortality. Although the mechanism of sepsis-induced AKI is not fully understood, it is thought that it has a different pathogenesis and requires a different approach and therefore it has been the focus of the studies. The aim of this study was to compare the criteria of SIRS and qSOFA in patients with suspected infection to determine which is more valuable in predicting sepsis associated AKI.

Method: SIRS and qSOFA scores of 120 patients with sepsis who were admitted to the Emergency Department of Marmara University Hospital were calculated at the time of admission. Age, gender and chronic diseases were recorded. The laboratory values at the time of admission and follow-up were recorded and the factors associated with the development of AKI were investigated by statistical analysis.

Results: Of the patients evaluated in the study, 60.8% (n = 73) were male and 39.2% (n = 47) were female. The median age was 66 (18-89) years. About 96% (n = 116) of the patients met the SIRS criteria, 54.2% (n = 65) met the qSOFA criteria, and 51.7% (n = 62) met both the SIRS and qSOFA criteria. AKI was found in 62.5% (n = 75) of the patients. According to AKIN staging, 40 (53.3%) patients had stage 1, 19 (25.3%) patients had stage 2 and 16 (21.4%) patients had stage 3 AKI. There was no correlation between SIRS criteria and development of AKI. However, all patients who received 3 points from qSOFA criteria developed AKI. According to the results of multivariate analysis, age, abnormal mental status and procalcitonin were associated with development of AKI.

Conclusion: Sepsis-associated AKI is related with deterioration in clinical outcomes, early diagnosis and treatment is important. According to our results, the risk of AKI is higher in patients with qSOFA score 3 but not SIRS criterias.

P0640 **DIAGNOSTIC AND TREATMENT OF THE SEVERE FORMS OF ACUTE RENAL FAILURE DURING MALARIA UNDER LIMITED CONDITIONS**

Dejan Pilcevic[1,1], Miroslav Kojic[2], Veljko Milic[3]

[1]Military Medical Academy, Clinic of nephrology, Belgrade, Serbia, [2]Military Medical Academy, Clinic for tropical and infectious disease, Belgrade, Serbia and [3]Military Medical Academy, Clinic for emergency, Belgrade, Serbia

Background and Aims: To explore clinical features and outcome of the most severe forms of acute renal failure (ARF) during Plasmodium falciparum malaria in United Nations personnel stationed in Central African Republic, during "MINUSCA " mission. ARF is one of the most important negative predictive criteria for outcome of malaria.Etiology is multifactorial, but most often is consequence of prerenal dehydration and tubular damages with hemoglobinuria during severe hemolysis

Method: We analyzed records of 54 inpatients with complicated forms of Plasmodium falciparum malaria who were treated in the Serbian level 2 hospital during 2017. Diagnosis of ARF was estimated based on RIFLE criteria. Having in mind the occasional lack of diagnostic kits for creatinine, at the almost one third of patients we used daily diuresis monitoring (with follow up of volume status) to diagnose this complication (according with RIFLE criteria).

Results: Total of 19 patients (35,19%) have developed ARF. Beside parenteral treatment with Artemisin, they were treated with parenteral solutions and diuretics. Despite therapy, 8 patients (14,81%) developed progressive and dialysis depended form of ARF (one had hemolytic-uremic syndrome) and they have been urgently evacuated accompanied by AMET into a senior medical institution. Based on provided back information, average creatinine on admission was 1242+/-342 µmol/l, Hb level 10,6 g/dl, potassium 6,8mmol/l. Six out of 8 patients completely recovered renal function (they needed average 7+/- 2 HD procedures; patient with HUS performed 5 plasma exchange sessions), one developed CRF grade 3 and one developed ESRD with necessity for chronic HD treatment. There were not lethal outcomes.

Conclusion: Early recognition of systemic complications including parameters of acute renal failure (decreasing urine output or changing of urine color could be useful markers under limited medical conditions)is necessaryin the purpose of timely recognition and promptly evacuation into higher medical facilities for further treatment.

P0641 ANALYSIS OF ACUTE KIDNEY INJURY PROGNOSTIC FACTORS IN SEVERELY BURNED PATIENTS (PRELIMINARY RESULTS)

Wojciech Klimm[1], Katarzyna Szamotulska[2], Zbigniew Bartoszewicz[3], Wojciech Witkowski[4], Stanisław Niemczyk[1]

[1]Military Institute of Medicine, Department of Internal Diseases, Nephrology and Dialysis, Warsaw, Poland, [2]Institute of Mother and Child, Department of Epidemiology and Biostatistic, Warsaw, Poland, [3]Medical University of Warsaw, Department of Internal Disease and Endocrynology, Warsaw, Poland and [4]Military Institute of Medicine, Department of Plastic and Reconstructive Surgery and Burs Management, Warsaw, Poland

Background and Aims:

AKI is one of the most common and severe complications in severely burned patients. However, it's aetiology, risk factors, clinic course, treatment and prognostic is still not very clear. The aim of the study was to analyse of incidence, clinic course and risk factors of the Acute Renal Injury (AKI) after massive burn injuries.

Method:

33 patients (pts); 11 (33,3%) females, 33 (66,7%) males; admitted to the hospital due to severe burn injury (total body surface area TBSA $\geq$15%) were involved in the study from 01.01.2017 till 30.06.2019. Mean age of the group was 48,3 ($\pm$18,8) years. Patients admitted to the hospital later than 72 hours after injury were excluded from the project. Mean time-period from the injury to the admission time was 2,1 ($\pm$0,9) hours. Mean injured skin surface was 42,2 ($\pm$18,1%) of the TBSA, the 3rd degree of burn was confirmed at 21 (63,6%) pts, respiratory tract was injured at 23 (69,7%) pts. None of the pts presented symptoms of chronic kidney disease before the injury. Basic life parameters, diuresis and chosen biochemical parameters (i.e. renal function) were measured at each patient once daily from admission till 7th day. Additionally the concentration of chosen novel AKI biomarkers (CystatinC, Neutrophil gelatinase-associated lipocalin, Kidney injury molecule-1, Interleukin-6 and 18, Insulin-like growth factor-binding protein 7, Tissue inhibitors of metalloproteinases 1$\div$4) were also measured in urine and blood sample during each first 3 day of hospitalisation and compared with the standard renal function parameters. Mean time of the 1st measurement was 44,7($\pm$17,7), the 2nd - 70,8 ($\pm$19,2) and 3rd - 94,8 ($\pm$19,2) hours after injury. AKI criteria were as follows: decrease in glomerular filtration rate (GFR) of less than 60 ml/min at admission, decrease in GFR of more than 75% compared to baseline, decrease in the daily diuresis of less than 500 ml/24 hours.

Results:

The medium hospitalisation time was 28,1($\pm$21,5) days. During observation time, clinical and biochemical symptoms of AKI were confirmed in 20 pts (60,6%). 8 (24,2% of all, 40,0% with AKI) required renal replacement therapy RRT: 37,5% (3 pts) - intermitted haemodialysis, 25,0% (2 pts) - continuous veno-venous haemodiafiltration and 37,5% (3 pts) – both methods. AKI developed usually in 3rd day of hospitalisation (maximum in 19th) and RRT usually started at the 8th day (maximum at 20th). The overall mortality was 48,5% (16 pts), 70,0% (14 pts) with AKI and 87,5% (7 patients) in RRT group. Death usually occurred at the 19($\pm$15) day after injury. 2 (12,5%) pts died from hemodynamic disorders in first 7 days, in 59 and 120 hour respectively. There were 14 (87,5%) pts in the group of late mortality (more than 7 days after injury), mean time of death was 24,5 ($\pm$15) days, in 57,1% connected with severe infection. The major causes of death in all were: cardiac arrest 14 (87,5%), cardiovascular failure 8 (50,0%), burn/septic shock 5 (37,5%), or respiratory failure 2 (12,5%) pts. The confirmed risk factors of AKI and mortality were injury more than 15% of TBSA, 3rd degree of burn injury age >65 years old, hemodynamic instability demanding catecholamine ($p<0,05$). AKI was also confirmed as an independent risk factor of mortality ($p=0,004$). The early analysis suggest potentially benefit of using novel biomarkers AKI in the clinic practise with superiority over standard AKI parameters (the final results of collected data analysis are still in progress).

Conclusion:

AKI is a frequent and important problem in severely burned patients. The occurrence of AKI significantly worsens the prognosis for survival. It is predicted by such factors as injury more than 15% of TBSA, 3rd degree of burn injury, older age and hemodynamic instability. Assessment of renal function, including novel AKI biomarkers, is an important prognostic factor after thermal injury and should be routine evaluated during treatment of burned patient.

P0642

EFFECTIVENESS OF HEMADSORPTION IN REDUCING FREE LIGHT CHAINS IN PATIENTS WITH MULTIPLE MYELOMA A.M.FOMIN, A.V.VATAZIN MOSCOW REGIONAL RESEARCH AND CLINICAL INSTITUTE. MOSCOW, RUSSIAN FEDERATION

Aleksandr Fomin[1], Andrey Vatasin[2]

[1]Moscow Regional Research and Clinical Institute ("MONIKI"), intensive therapy, Moscow, Russia and [2]Moscow Regional Research and Clinical Institute, nephrology, Moscow, Russia

Background and Aims: Acute kidney injury is a frequent complication of multiple myeloma with unfavorable prognostic significance. The aim of the present study is to evaluate the effectiveness of hemadsorption to reducing free light chains (FLCs) in patients with multiple myeloma without replacement kidney therapy.

Method: The research was conducted for 6 patients ages 65- 74 with multiple myeloma. All patients were already suffering from a mild degree of renal insufficiency and elevated free light chains (4 kappa, 2 lambda). All patients didn't have renal replacement therapy. Patients received VMP induction chemotherapy after two sessions of hemadsorption. The level of creatinine was from 198 μmol/l to 289 μmol/l. The glomerular filtration rate (eGFR) was from 34,8 to 21,3 mL/min/1,73 m2. The level of kappa FLC was 1714 – 5600 mg/L. The level of lambda FLC was 1575 – 3220 mg/L. In CytoSorb therapy, the blood is purified by adsorption in a procedure similar to hemoperfusion. The hemadsorption procedures were carried out on the AK10 device (Gambro, Sweden) with use of CytoSorb adsorbent cartridge. The content of the CytoSorb cartridge consists of a highly porous high-tech polymer. The patients were treated with 2 CytoSorb hemoadsorption treatments for 10 hours each separated and from one another by a pause interval of 12-14 hours. The blood flow rate was 130-160 ml/min. Anticoagulation was ensured by washing the bloodlines and a cartridge with a sorbent with normal saline with heparin – 4,000 units of activity per 1 L. 5,000 units of activity of heparin were injected intravenously at the beginning of the procedure. The FLCs, the level of creatinine and coagulogram test results of patients were studied prior to procedure and upon termination of procedure.

Results: An extracorporeal blood purification methods reduce elevated levels of FLCs. The cartridge with a total surface of>40,000 square meters, an adsorber is able to effectively and over time lower hydrophobic (water-insoluble) molecules that can be removed up to a size of 55kDa. FLC have high molecular weight (monomeric kappa of 22.5 kDa, dimeric lambda of 45 kDa). FLC removal, combined with chemotherapy may be associated with renal function recovery. As a result of hemadsorption after carrying out two procedures, there was a significant decrease in level kappa FLCs by 78.3 %, lambda FLCs by 64,0 %. All patients were dialysis independent. The level of creatinine decreased and the glomerular filtration rate increased. Other blood chemistry parameters did not show any changes. Throughout the treatment, the study did not show a decrease in dynamics of hemoglobin or platelets. There were not negative dynamics in change of INR (international normalized ratio), APTT (activated partial thromboplastin time), level of fibrinogen, prothrombin, or anti-thrombin III. No bleeding complication occurred in any patient during the procedure of hemadsorption. Other biochemical values did not change significantly.

Conclusion: The research showed that an extracorporeal blood purification method by CytoSorb therapy reduce elevated levels of FLCs in patients with multiple myeloma. The benefits of this modality need confirmation with a randomized controlled trial.

P0643

PROGNOSTIC IMPACT OF THROMBOCYTOPENIA IN THE RISK OF INTRAHOSPITAL BLEEDING IN ACUTE KIDNEY INJURY (AKI) PATIENTS

Zorica Dimitrijevic[1,2], Branka Mitic[1,2], Danijela Tasic[1], Goran Paunovic[1], Karolina Paunovic[1], Emina Kostic[1,2], Stevan Glogovac[1]

[1]*Clinical Centre of Niš, Clinic for nephrology, Niš, Serbia and* [2]*Медицински факултет Универзитета у Нишу, Ниш, Serbia*

Background and Aims: Low platelet count is a marker of adverse events in acute kidney injury (AKI) patients. Thrombocytopenia has often been reported as an indicator of underlying disease severity and worse patient outcomes; however, it's role in the prediction of the risk of bleeding is not well defined. Our study aimed to assess the prognostic impact of admission thrombocytopenia in the risk of major bleeding in non-septic, non-post surgery AKI patients.

Method: This retrospective study enrolled patients with AKI hospitalized at tertiary care hospital during the three years. Admission thrombocytopenia was defined as a platelet count < 150x103/mL. The primary endpoint was major bleeding, as defined by the International Society on Thrombosis and Haemostasis.

Results: Of 178 included patients (age 61.7±11.1 years; 68.3% males), 26 (14.6%) had thrombocytopenia. These patients had more comorbidities: cancer (19.4 vs 9.6%; p=0.05); previous ulcer disease (17.6 vs. 8.8; p=0.04) and bleeding history (7.4% vs. 2.0%;p=0.04). While in a hospital, there was a trend for the use of more blood transfusions (7.4% vs. 2.7%; p=0.03) and more concomitant medications (12.7 vs. 5.1; p<0.05) in patients with thrombocytopenia. During a hospital stay (IQR: 7-29 days), 19 patients (10.7%) died), 22 (12.35%) had major bleeding, and 5 (2.8%) intracranial bleeding. After adjusting for age, presence of cancer, and use of oral anticoagulant medications, patients with thrombocytopenia had a higher risk of major bleeding (HR 3.34 95%CI: 1.57-7.26; p < 0.001).

Conclusion: Thrombocytopenia is a predictor of major intrahospital bleeding in the non-septic, non-post surgery AKI patients. It should be regarded in bleeding risk estimation and therapeutic strategy decisions.

P0644

RELATIONSHIP BETWEEN THE PRESENCE OF INFECTION DISEASE AND CLINICAL OUTCOMES OF PATIENTS WITH CARDIORENAL SYNDROME TYPE 1

Jonathan Chávez[1], Adriana Valle-Rodríguez[1], Jorge Michell[1], Andres De la Torre-Quiroga[1], Andres Aranda-G de Quevedo[1], Ekhaterina Yanowski-Ortega[1], Jose Said Cabrera[1], Guillermo García-García[1]

[1]*Hospital Civil de Guadalajara Fray Antonio Alcalde, Nephrology, GUADALAJARA, Mexico*

Background and Aims: Introduction: Cardiorenal Syndrome type 1 (CRS-1) can be triggered by an infection. The pathophysiological basis is vascular congestion, which is why it has been treated with different strategies of diuretics, but in the presence of infection, the inflammatory, neurohormonal and hemodynamic effects can compromise the efficacy of the diuretic therapy and potentially worsen clinical evolution. Here we compare the clinical evolution during the hospitalization of CRS-1 patients with and without infection.

Method: This is a retrospective cohort study conducted in the Hospital Civil of Guadalajara "Fray Antonio Alcalde", from January 2015 to September 2018. Conducted in CRS-1 patients, we showed the clinical evolution and diuretic strategies analyzed according to the presence or absence of infection. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Results: We identified 63 patients classified as having CRS-1, 28 (44.4%) were classified as having an infectious disease. The mean age was 62 years (±14.6) and 58 (±12.4) in the group with infection and no infection, respectively. There were no statistically significant differences between the clinical outcomes of both groups. The median length of hospital stay was 8 days in the group with infection and 7 days in the group without infection (p=0.065). Three patients (10.7%) of the group with infection received renal replacement therapy and 1 patient (2.9%) in the group without infection (p=0.315). In the group with infection, 2 patients died (7.1%), whereas in the uninfected group there were no deaths (p=0.194). sCr values tend to diminish in a similar manner in both groups. Serum sodium tend to increase during the hospitalization but there was no significant difference between the groups. We found that all patients received furosemide at least during the first five days of hospitalization and the strategy of the diuretic chosen was similar between groups.

Conclusion: We showed that the clinical evolution of patients with CRS-1 is similar in the presence or absence of infection. We anticipate that this study may be a reason to expand knowledge in patients with CRS-1 and the presence of infection.

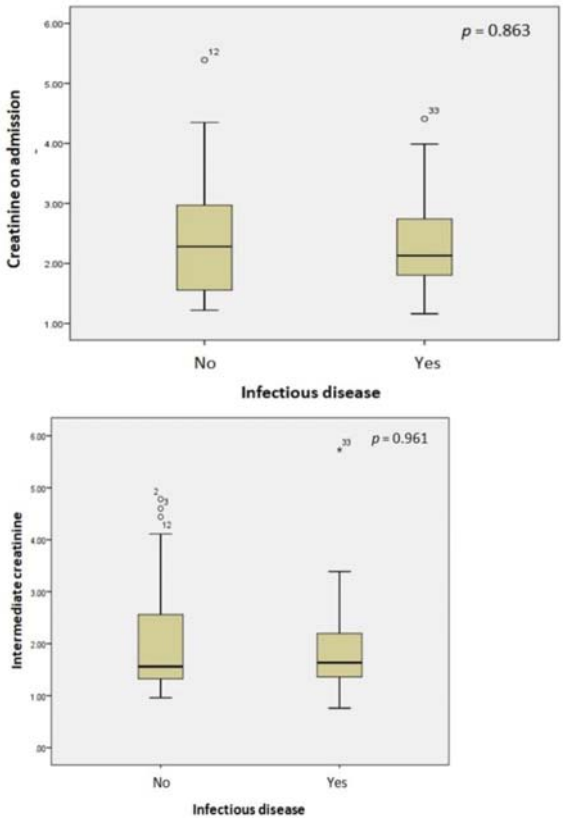


Figure 1 serum creatinine at admission, intermediate and at discharge between two goups.

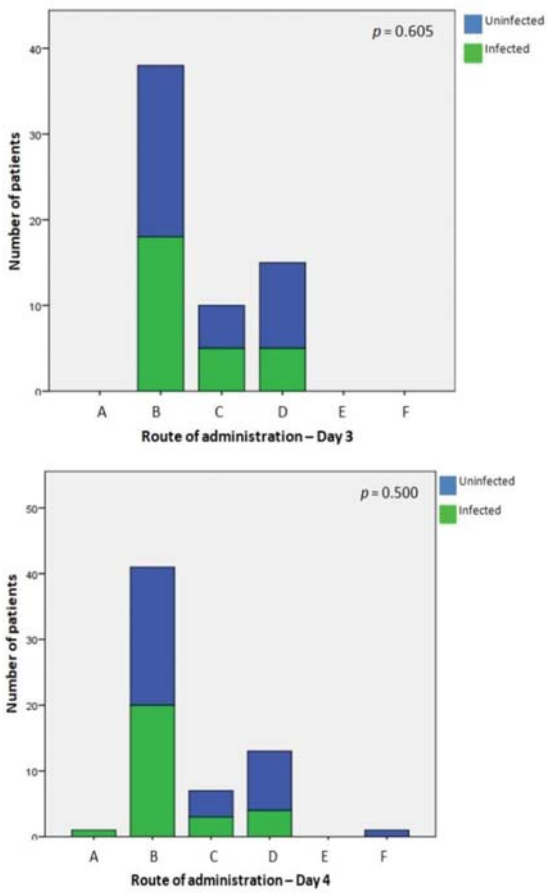


Figure 2 Route of administration of diuretic treatment in the first 3rd to 7th day between two goups.

P0645 EDARAVONE MAY DECREASE THE INCIDENCE OF CONTRAST INDUCED ACUTE KIDNEY INJURY (CI-AKI)

Dmytro Ivanov[1], Mariia Ivanova[2], Illia Burlachenko[3]

[1]National Medical Academy of Post-Graduate Education Named After P.L. Shupik, Nephrology and RRT, Kyiv, Ukraine, [2]Università Milano Bicocca, School of Medicine and Surgery, Milano, Italy and [3]Bogomolets National Medical University, Department of Internal Medicine #2, Kyiv, Ukraine

Background and Aims: Edaravone is a low-molecular-weight antioxidant drug targeting peroxyl radicals of reactive oxygen species and has shown clinical efficacy in patients with acute ischemic stroke.

We have conducted a multicenter open prospective randomized controlled study to evaluate the efficacy of edaravone in preventing AKI in patients with CKD 3b-4 stages.

Method: The study included 2 groups of patients aged 46 to 68 (55 ± 3): group A (n=16) with CKD stage 3b or 4 (eGFR EPI 32 ± 4 ml/min) that received intravenous edaravone 30 mg bid on 0,1,2 day of contrast media infusion and control group B (n=20) with CKD stage 3b or 4 (eGFR EPI 33 ± 3 ml/min) with no edaravone intervention during CT coronarography. Patients of both groups received intravenous hydration with 0.9% sodium before CT. Primary endpoint: CIN onset in 48 hours after contrast media infusion and need for RRT. Secondary endpoint: serum potassium level above 5.5 mmol/l.

Results: CIN onset was obtained in 4 patients of group A and 12 patients of group B (p>0,05, RR 0.417, RRR 0.583, RD 0.350, NNT 2.857). Other results are presented in table

Table 1. CIN onset in two patients' groups.

Parameter	Edaravone G roup A, n=16	Group B, n=20	Fisher's criterion	P
AKI	4	12	0,485	>0,05
Need to RRT	2	8	0,132	P=0,93
Hyperkaliemia	1	6	0,104	Nd

P0646 **PREDICTABLE CAPACITY OF ACUTE KIDNEY INJURY OF NEPHROCHECK TEST IN EMERGENCY ROOM PATIENTS**

Elena Gomá[1], Guillermo Gonzalez-Martin[1], Juan Alfredo López-López[2], Maria Vanessa Perez Gomez[1], Alberto Ortiz[1], Catalina Martin[1]

[1]*Hospital Universitario Fundación Jiménez Díaz, Nephrology, Madrid, Spain and*
[2]*Hospital Universitario Fundación Jiménez Díaz, Internal Medicine, Madrid, Spain*

Background and Aims: Acute kidney injury (AKI) is increasingly prevalent and it is associated to increased hospital stay and costs, higher risk of developing a chronic kidney disease, and also major morbidity and mortality. Prediction tools may identify patients at high risk of AKI, allowing early intervention. Nephrocheck quantifies biomarkers of AKI (TIMP-2 and IGFBP-7), providing results within 20 minutes. This may allow stratification of the risk of developing an AKI in the next 12 hours in critically cardiovascular or respiratory ill patients and therefore implement preventive measures. We aimed to assess Nephrocheck performance to predict AKI development within 12 hours to 5 days in incident Emergency Room (ER) patients.

Method: Prospective observational study of 52 incident ER patients. Data were collected from April 2017 to November 2018. Inclusion criteria: sepsis of any origin, or cardiopulmonary insufficiency without AKI at baseline. Nephrochek was performed at baseline, patients were stratified into low (Nephrocheck test < 0.3), moderate (Nephrocheck between 0.3-2) and high risk (Nephrocheck >2) of AKI and occurrence of AKI was assessed (diagnosed as an increase of 0.3 mg/dl of serum creatinine) at 12, 24, 48 h and 5 days.

Results: Mean age as 70±13 years, 22/52 (43%) were women, risk factors included hypertension (54%), DM (29%), Cirrhosis: 2/52 (4%), heat failure (27%), prior CKD (12%), nephrotoxic use (38%). 18/52 (35%) of patients were Nephrocheck low risk, 21/52 (40%) were intermediate risk and 13/52 (25%) were high risk. AKI developed in 7/18 (39%), 3/21 (14%) and 3/13 (23%) of low, intermediate and high risk, respectively. When comparing patients who developed AKI with those who did not, those who developed AKI had been exposed more frequently to nephrotoxins and had lower urinary osmolarity and higher MAP (Table 1). However, a high risk Nephrocheck score identified patients with significantly higher urine osmolality (672±139 vs 387±172 mOsm/L, P=0.005) and lower MAP (76.7 ± 18.4 vs 101.62±22.7 mmHg; P=0.002).

Conclusion: LIMITATIONS: knowledge of Nephrocheck results may have changed patient care. CONCLUSIONS: A high risk Nephrocheck score was not associated with a higher risk of AKI in a ER setting. More nephrotoxins were used in the AKI group. Presumabily, these were discontinued in the ER, thus lowering AKI risk. By contrast, a past history of nephrotoxin use and lower urine osmolarity were associated with a higher incidence of AKI.

Table 1. Clinical characteristics of patients who developed AKI

	AKI	Non AKI	P value
Age (years)	69 ±17	70 ± 12	0.17
Women, n (%)	6/13 (46.15%)	16/39 (41.02%)	0.53
Hypertension, n (%)	6/13 (46.15%)	22/39 (56,41%)	0.52
DM, n (%)	3/13 (23.08%)	12/39 (30.77%)	0.59
Cirrhosis, n (%)	0/13 (0%)	2/39 (5.13%)	0.4
NYHA I, n (%)	3/13 (23.07%)	6/39 (15.38%)	0.79
NYHA II, n (%)	2/13 (15.39%)	6/39 (15.38%)	
NYHA III, n (%)	2/13 (15.39%)	4/39 (10.26%)	
CKD, n (%)	3/13 (23.07%)	3/39 (7.69%)	0.13
Nephrotoxins, n (%)	8/13 (61.54%)	12/39 (30.77%)	**0.04**
Nephrocheck, n (%)			0.20
Low risk	7/13 (53,85%)	11/39 (28.20%)	
Moderate risk	3/13 (23.07%)	18/39 (46.15%)	
High risk	3/13 (23.07%)	10/39 (25.64%)	
Mean Nephrocheck score	0.21 (IQR 1.6)	0.76 (IQR 1.7)	0.45
MAP* (mmHg)	97.3 ± 21.3673	85.7 ± 23.4	**0.01**
$_pO_2$ (mmHg)	89.5 ± 57.1	83.4 ± 47.1	0.21
Bilirubin total (mg(dl)	1.3 ± 0.7	1.7 ± 1.9	0.42
Lactate (mg/dl)	40 ± 39.7	26.3 ± 16.3	0.19
Urinary osmolarity (Osm/L)	453 ± 192	543 ± 191	**0.02**
Platelets (x10^3 μL)	186 ± 81	257 ± 16	0.18
Proteinuria (mg/dl)	25 (IQR 38))	25 (IQR 61)	Wilcoxon (p_0.72)

*MAP: mean arterial pressure

P0647 ACUTE KIDNEY INJURY SECONDARY TO SUCROSE CONTAING INTAVENOUS IMMUNOGLOBULIN

Sadiq Al Lawati[1], Issa Al Salmi[1,2], SUAD Hannawi[3]

[1]..., [2]Oman Medical Specialty Board OMSB and [3]Ministry of Health Head Office, Dubai, United Arab Emirates

Background and Aims: Intravenous immunoglobulins (IVIG) are pooled polyvalent IgG antibodies extracted from the human plasma. While the initial indications were mainly immune deficiency states and some autoimmune diseases, the usage has been widened to include several immune mediated diseases, viral infections, and organ transplant rejection. Stabilizers in IVIG may include sugars, such as sucrose, glucose, or maltose. Sucrose in IVIG preparations may cause acute kidney injury. We report the case of a renal transplant patient who developed acute kidney injury due to sucrose nephropathy following the administration of sucrose containing IVIG.

Method: Four months after transplantation he was referred to our Hospital for deterioration of kidney function with eGFR (by MDRD formula) of 27ml/min. Cytomegalovirus virus (CMV) PCR turned positive (3300 copies/ml). Cyclosporine levels were high (C2: 2937 ng/ml) and hence, cyclosporine dose was adjusted. Induction therapy with Injection Ganciclovir for 2 weeks, followed by therapeutic dose of oral Valganciclovir was administered for the treatment of CMV infection. Skin examination revealed annular purple patches, suspicious of Kaposi Sarcoma, on the upper limbs. Skin biopsy confirmed the diagnosis.

It was planned to give total IVIG of 2 gm/ kg in four daily divided doses. After completion of the second dose, serum creatinine increased to 370 µmol/L. He was clinically asymptomatic, euvolumic, vital signs were stable, and his urine output remained normal and his urinalysis was inactive.

Results: The ultrasound of the transplant kidney was normal with normal resistivity index. IVIG was stopped. He was well hydrated and underwent ultrasound guided biopsy. The graft biopsy showed acute tubular injury with flattening and vacuolation of tubular epithelial cells. Mitosis indicating tubular regeneration was seen. There was mild focal interstitial inflammation (20%) with mild lymphocytic tubulitis not amounting to graft rejection. Immunohistochemistry for C4d and polyomavirus (BKV) were both negative. The features were most consistent with sucrose induced nephropathy (Figure 1).

Subsequent visits showed a decrease in BKV-PCR serum level and eventually undetected serum level of BKV-PCR at follow up about a month later.

Conclusion: In this paper, we presented a case of a living unrelated kidney transplant recipient who developed BKV nephropathy and developed impaired kidney function. The patient also had new onset diabetes mellitus after kidney transplantation (NODAT) but was otherwise in good general health. Treatment included sucrose containing IVIG. The patient subsequently developed acute kidney injury.

The outcome was favorable with recovery of filtration rate to the baseline within 21 days without the need for dialysis.

We conclude that the administration of sucrose containing IVIG may lead to acute kidney injury. We recommend the use of sucrose-free IVIG whenever possible. In all cases, caution is required when administrating IVIG.

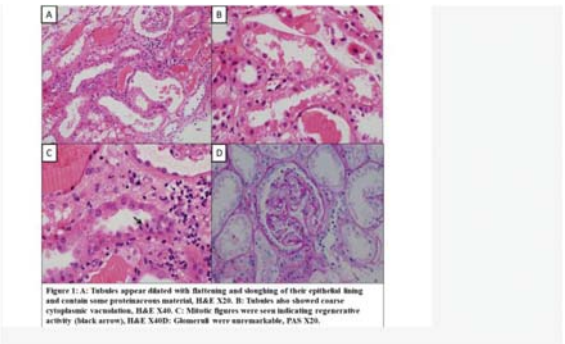


Figure 1: A: Tubules appear dilated with flattening and sloughing of their epithelial lining and contain some proteinaceous material, H&E X20. B: Tubules also showed coarse cytoplasmic vacuolation, H&E X40. C: Mitotic figures were seen indicating regenerative activity (black arrow), H&E X40D: Glomeruli were unremarkable, PAS X20.

P0648 LEVELS OF PHYSICAL ACTIVITY FOLLOWING AN EPISODE OF STAGE 3 AKI ARE ASSOCIATED WITH RENAL RECOVERY

Anam Asad[1], Maurice Dungey[1], Katherine Hull[1,2], James Burton[1,2,3], Daniel March[1,2]

[1]University of Leicester, Department of Cardiovascular Sciences, United Kingdom, [2]University Hospitals of Leicester NHS Trust, John Walls Renal Unit, Leicester, and [3]Loughborough University, School of Sport, Exercise and Health Sciences, United Kingdom

Background and Aims:

Acute kidney injury (AKI) is a known risk factor for the development of chronic kidney disease (CKD). Animal studies have demonstrated the potentially reno-protective effects of physical activity, both against the development of AKI and in promoting renal recovery. However, this has not been investigated in humans. The aim of the study was to investigate the association between physical activity levels and recovery in kidney function, measured by eGFR and creatinine, following an episode of stage 3 AKI.

Method:

Twelve hospitalised participants with non-obstructive stage 3 AKI (as per KDIGO criteria) were asked to complete two questionnaires; the General Practitioner Physical Activity Questionnaire (GPPAQ), a measure of physical activity and; the Duke Activity Status Index, a measure of functional capacity. Baseline questionnaires were completed whilst in hospital (where participants were asked to recall their physical activity and functional capacity levels before hospitalisation) and again at 6-months post discharge. In addition, participants wore a pedometer for 7 consecutive days following discharge to ascertain their daily step count. Baseline renal function was collected using eGFR and creatinine measurements within the 12-months prior to admission; further readings were collected 25 $\pm$ 46 days after discharge as a measure of renal recovery (referred to as recovered creatinine).

Results:

Data from the 12 participants who provided step count information were analysed. At diagnosis of stage 3 AKI, participants had a mean creatinine of 547 $\pm$ 280 with their mean baseline and recovered creatinine as follows; 95 $\pm$ 35 and 172 $\pm$ 83. A higher daily step count after discharge was associated with both a higher baseline eGFR ($r=0.73$, $p<0.01$) and significant improvements to their renal recovery ($r=0.69$, $p=0.01$). There were positive associations between renal recovery and physical activity levels measured using the GPPAQ ($r=0.55$, $p=0.06$) and functional capacity (0.17, $p=0.6$), although not to statistical significance. The participants were divided into two groups based on their recovered creatinine levels. Those who recovered renal function back to within 25% of baseline (n=5) had a higher mean step count compared to those whose renal recovery was less pronounced (n=7); (3712 $\pm$3960 vs 3334 $\pm$ 2254, respectively).

Conclusion:

These results show a positive association between physical activity levels and renal recovery following an episode of AKI. This suggests that higher levels of physical activity may be protective and promote recovery of renal function following an episode of AKI. Physical activity and exercise interventions should be tested in the setting of AKI to see whether they are efficacious in promoting renal recovery.

P0649

MAY HIGH CUT-OFF HAEMODIALYSIS STILL BE CONSIDERED BENEFICIAL IN THE TREATMENT OF ACUTE KIDNEY INJURY RELATED TO MULTIPLE MYELOMA?

SIMONA ALEXANDRU[1], Maria López Picasso[1], Laura García-Puente Suarez[1], Maria Soledad Pizarro Sanchez[1], Saul Pampa Saico[1], Marisol Poma Tapia[1], Raquel Barba[2]

[1]Hospital Universitario Rey Juan Carlos, Nephrology, Móstoles, Spain and [2]Hospital Universitario Rey Juan Carlos, Internal Medicine, Móstoles, Spain

Background and Aims:

Almost 20% of the patients with multiple myeloma (MM) associate renal involvement, and 5% need long-term haemodialysis treatment. Both plasmapheresis and high cut-off haemodialysis (HCO-HD) have been used to remove light chains from the blood and minimize the renal damage. In the largest study, plasmapheresis has been shown to be ineffective in the renal recovery. Furthermore, the most important trial, EuLITE II, concluded that HCO-HD did not improve renal recovery and independence from haemodialysis. The hypothesis of this work is that patients with an acute renal failure related to multiple myeloma undergoing early HCO-HD treatment, before being haemodialysis-dependent, may achieve better renal function in short and, perhaps, in long term.

Method:

We have studied five patients with multiple myeloma and acute renal failure who received treatment with HCO-HD in order to remove serum kappa or lambda light chains. The procedure was realized with Filtryzer BK2.1F dialyzer (Palex Medical) with an area of 2.1 m^2 at a blood flow of 250 ml/min and a dialysate flow of 500 ml/min, usually changing the dialyzer in the middle of the session. The sessions lasted between 6 and 8 hours, initially on successive days, and alternate days afterwards.

Results:

Between July 2016 and November 2019, five patients with a mean age of 67.8 years (2 women and 3 men) received HCO-HD. Three of them had MM with lambda light chains, and two of them had MM with kappa light chains. The average bone marrow plasmocytosis was 38.6 % (minimum 10% and maximum 90%). Two patients required treatment with haemodialysis for glomerular filtrate (FG) estimated by MDRD-4 formula of 4 and 5 ml/min, respectively. The other three had a GF (MDRD-4) between 19 and 30 ml/min. Initial hematological treatment included bortezomib, dexamethasone, and thalidomide. One patient was switched to carfilzomib. Only two patients underwent renal biopsy, both showing myeloma kidney with intratubular light chain casts. An average of 9.8 sessions has been administered (minimum 5, maximum 19). At the end of the treatment, serum kappa light chains decreased from a mean of 29461 mg/L to 1516.5 mg/L, and serum lambda chains decreased from a mean of 7245 mg/L to 1030.66 mg/L. At the beginning of the treatment the mean GF (MDRD-4) was 17.4 ml/min, 29.6 ml/min at the end of it, and 42.33 ml/min six months later (table 1). Only one patient became dependent of haemodialysis. This patient developed renal failure in context of a second relapse of a very aggressive myeloma. Another patient who presented 47900 mg/L of serum kappa light chains at diagnosis, 90% bone marrow plasmocytosis, and a GF (MDRD-4) of 30 ml/min when started HCO-HD, in the present and few days after 19 sessions has a GF (MDRD) of 43 ml/min.

Conclusion:

An early treatment with HCO-HD, before the patients need renal replacement therapy, may lead to a better renal outcome and independence from haemodialysis at least in the medium term. Largest studies are necessary to confirm this hypothesis.

Table 1. Light chain and renal function before and after HCO-HD treatment

Mean age (yr)	Mean number of HCO-HD sessions	Mean of serum lambda light chain (mg/L) before HCO-HD	Mean of serum lambda light chain (mg/L) after HCO-HD	Mean of serum kappa light chain (mg/L) before HCO-HD	Mean of serum kappa light chain (mg/L) after HCO-HD	GF (MDRD-4) before HCO-HD (ml/min)	GF (MDRD-4) after HCO-HD (ml/min)	GF (MDRD-4) six months after HCO-HD (ml/min)
67.8	9.8	7245±932	1030.66±576.7	29461±8774	1516.5±604.2	17.4±3.9	29.6±6.8	42.33±12.7

CKD. LAB METHODS, GFR MEASUREMENT, URINE PROTEOMICS

P0651 PROTEOMIC CHARACTERIZATION OF OBESITY-RELATED NEPHROPATHY

Tianlin He[1], Joachim Beige[2,3], Justyna Siwy[1], Ralph Wendt[4], Agnieszka Latosinska[1], Harald Mischak[1]

[1]Mosaiques Diagnostics & Therapeutics AG, Hannover, Germany, [2]Hospital St. Georg gGmbH, Leipzig, Germany, [3]Martin-Luther-University Halle-Wittenberg, Halle (Saale), Germany and [4]Hospital St. Georg, Nephrology, Leipzig, Germany

Background and Aims: During the last years, with the increase in secondary diseases following obesity the focus on the context of abnormally high body weight and chronic kidney disease (CKD) has changed. While in individual care, CKD along with obesity and improving renal function along with weight loss can be seen frequently and trials on obesity reduction yielded promising renal results, systematic insight into the pathogenesis and epidemiology of nephropathy related to obesity without diabetes (Obesity-related nephropathy, ORN) is rather limited. This work reaches out to investigate impact of BMI on urine peptides and to characterize yet non-specified peptide patterns in urine that may be indicative of ORN and may indicate possible molecular mechanisms of ORN pathophysiology. We used urine samples from earlier projects which could be characterized for presence of diabetes, BMI, eGFR, and age. By defining such urinary peptide patterns, pathophysiology-enlightening hypotheses should be stimulated and pathways suggested to enable specific future characterization of ORN.

Method: In this study we investigated the association of urinary peptides with body mass index (BMI), and renal function in proteome datasets from 4015 individuals. For this study urinary proteome data stored in the Human Urine Proteome Database obtained by capillary electrophoresis coupled to mass spectrometry (CE-MS) were assessed.

Results: 365 urinary peptides significantly associated with BMI could be identified. The majority of these peptides were collagen fragments. In addition, most of the peptides also demonstrated a significant concordant association with eGFR in the investigated cohort with diabetes exhibiting no significant association. A classifier based on 150 urine peptides enabled distinguishing non-obese subjects with preserved kidney function from obese, non-diabetic subjects with eGFR>45 mL/min/1.73㎡ in an independent cohort with an area under curve (AUC) of 0.93 (Fig.). The vast majority of significantly associated peptides are specific collagen fragments, most of them from collagen type I, and most of them (in fact all of the 10 most significant ones) are reduced with increasing BMI.

Conclusion: These analyses in a huge cohort of urine samples from patients with known eGFR, BMI and diabetes status showed a complex multi-level association between peptide fragments with renal risk in obesity. Of particular note, these relationships could be retrieved although the overall cohort inherited an almost negative eGFR – BMI gross correlation, presumably due to the origin of the dataset from a non-obesity-directed approach. Most peptides associated with GFR and BMI belonged to the collagen superfamily and were inversely associated with BMI but directly with eGFR.

This concordant observation indicates a reduction of collagen degradation with increasing BMI and/or reduced kidney function. It is tempting to speculate that collagen homeostasis along with body mass on one hand, and kidney function on the other, are substantially interconnected. The very strict association of BMI with collagen fragments was surprising, but also indicates specificity.

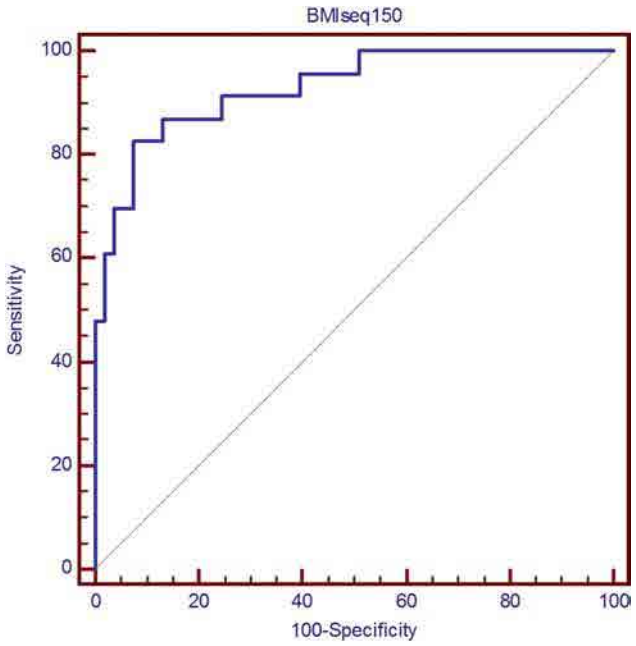


Figure:

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P0652 **THYMOSIN BETA 4 AND KIDNEY FUNCTION: AN INVERSE RELATIONSHIP?**

Tianlin He[1], Joost Schanstra[2], Justyna Siwy[1], Joachim Beige[3], Agnieszka Latosinska[1], Harald Mischak[1,4]

[1]Mosaiques Diagnostics GmbH, Hannover, Germany, [2]INSERM, Institute of Metabolic and Cardiovascular Research, Toulouse, France, [3]Hospital St. Georg, Department of Nephrology and Kuratorium for Dialysis and Transplantation Renal Unit, Leipzig, Germany and [4]University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom

Background and Aims: Thymosin β4 (Tβ4) is an abundant peptide in urine and plasma, involved in multiple processes including cell morphology, wound healing, and inflammation. A major, yet not well defined role of Tβ4 was described in the context of kidney and cardiovascular disease. Knock out of Tβ4 resulted, among others, in increased albuminuria in a nephrotoxic nephritis model. In animal models it has been shown that Tβ4 can modify renal and cardiovascular disease, fibrosis and inflammation. However, most of the data are derived from animal models and the relevance of Tβ4 in human is less clear. As a first step towards investigating the potential relevance of Tβ4 in chronic kidney disease (CKD) in human, we investigated the abundance of Tβ4 in human urine.

Method: We investigated human urine in 2240 subjects with a wide spread of kidney function for the presence of Tβ4 using capillary-electrophoresis coupled mass spectrometry (CE-MS) and tandem mass spectrometry. In addition, we evaluated the presence of Tβ4 abundance in hemodialysis fluid of 10 subjects.

Results: The full length acetylated Tβ4 peptide could be identified in human urine in high abundance (molecular mass 4960.485 Da). In addition, an oxidized isoform could also be observed at high abundance. When investigating the distribution of both isoforms in control subjects and patients at different stages of CKD, a highly significant inverse association of the abundance of Tβ4 with eGFR could be observed for both, with rho -0.388 for the non-oxidized and -0.387 for the oxidized isoform, $p<0.0001$ in each case. In hemodialysate, Tβ4 is found as the most abundant peptide in 2 of the 10 analyzed subjects, on average the second most abundant peptide, with β2 microglobuline being the most abundant one.

Conclusion: Tβ4 is highly significantly inversely associated with kidney function, suggesting a role of Tβ4 in kidney disease and/or its complications. Based on the experimental data published from animal models, the increase in Tβ4 may reflect a potential physiological mechanism to counteract CKD and its complications. Investigation of association of Tβ4 levels with progression in CKD, cardiovascular complications and death may inform on a potentially beneficial effect of Tβ4, is currently ongoing in longitudinal datasets and will be presented.

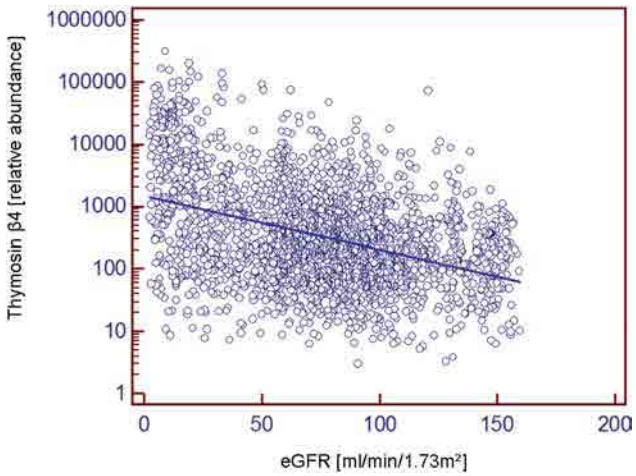


Figure:

P0653 **THE USE OF URINARY EPIDERMAL GROWTH FACTOR FOR EVALUATION OF KIDNEY GRAFT FUNCTION**

Joe Chan[1,2], Ivar Anders Eide[1,3], Trond Geir Jenssen[3], Bård Waldum-Grevbo[4], Tone Møller Tannæs[2,5], My Svensson[1,2]

[1]Akershus University Hospital, Department of Renal Medicine, Lørenskog, Norway, [2]Institute of Clinical Medicine, University of Oslo, Faculty of Medicine, Oslo, Norway, [3]Oslo University Hospital Rikshospitalet, Department of Transplantation Medicine, Oslo, Norway, [4]Oslo University Hospital Ullevål, Department of Nephrology, Oslo, Norway and [5]Akershus University Hospital, Department of Clinical Molecular Biology (EpiGen), Lørenskog, Norway

Background and Aims:

Follow-up after kidney transplantation requires repeated, reliable glomerular filtration rate (GFR) measurements. Measured GFR (mGFR), using urinary or plasma clearance of an exogenous filtration marker such as iohexol, provides precise measurements but are expensive and time consuming. Instead, estimated GFR (eGFR) based on serum creatinine is most commonly used in clinical practice. Epidermal growth factor is produced in the kidney and promotes tubular cell regeneration and recovery of kidney function after injury. Low levels of urinary epidermal growth factor (uEGF) are linked to progression of chronic kidney disease and increased risk of kidney graft failure. The aim of this study was to investigate uEGF as an additional marker to evaluate graft function in kidney transplant recipients (KTRs).

Method:

Participants in the Omega-3 fatty acids in Renal Transplantation (ORENTRA) trial were examined with mGFR by iohexol clearance at 1 year after kidney transplantation. The concentration of iohexol in serum was measured 3 and 4 hours after iv injection. On the same day, fasting blood and urine samples were obtained in the morning. Serum creatinine was measured and eGFR calculated with the MDRD formula. uEGF and a pre-specified selection of inflammation and fibrosis markers were measured with multiplex immunoassay technique and normalized with urinary creatinine. Principal component analysis (PCA) was used to explore clustering of markers. Correlations were calculated with Pearson's correlation coefficient R.

Results:

Fifty-nine participants had complete measurements of mGFR (57.2 ± 15.2 mL/min/1.73m^2), eGFR (68.6 ± 23.0 mL/min/1.73m^2) and uEGF. The correlation between mGFR and eGFR was strong (R=0.783, P<0.001). Measurements of uEGF had a coefficient of variation below 10% for all participants, with a mean value of 22.0 ± 12.1 µg/g creatinine. There was a significant correlation between mGFR and uEGF (R=0.678, P<0.001). The component score of uEGF and eGFR calculated with PCA (74% of variance) had the strongest correlation with mGFR (R=0.845, P<0.001).

Conclusion:

Combining uEGF with eGFR into one component score by PCA gives a greater correlation with mGFR compared to eGFR alone in this cohort of KTRs. These findings need to be validated in other patient populations.

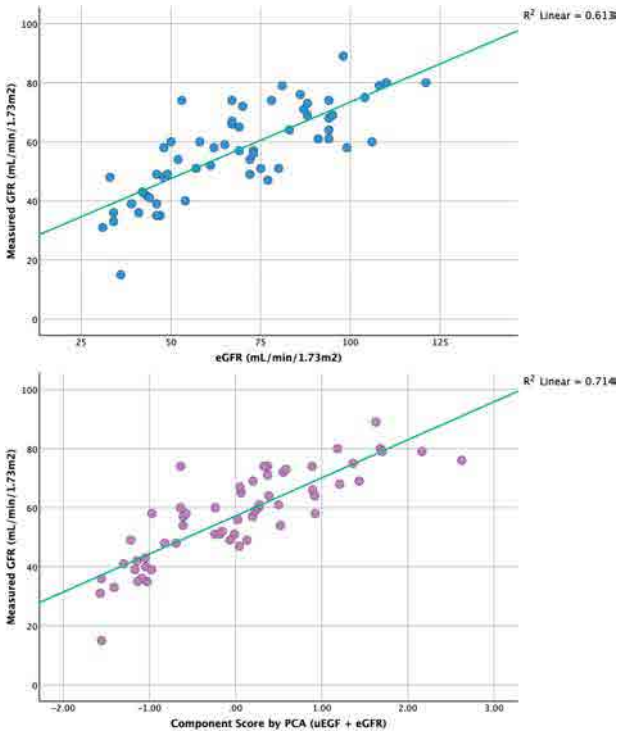


Figure:

P0654 INTEREST OF SCREENING FOR CKD AFTER AKI IN ICU AND THE PLACE OF CYSTATIN C IN THIS POPULATION.

Guillaume Claisse[1], Nicolas Maillard[1], Miriana Dinic[1], Christophe Mariat[1]
[1]University Hospital of Saint-Étienne, Saint-Priest-en-Jarez, France

Background and Aims: Acute Kidney Injury (AKI) is one of the most frequent complications in Intensive Care Unit (ICU). It's now clearly established that AKI may be associated with the installation and/or worsening of Chronic Kidney Disease (CKD). However, few patients are currently screened for CKD after hospitalization in the ICU. In addition, ICU patients often have changes in their volume of distribution and muscle mass that may interfere with plasma Creatinine (pCreat) dosing and thus the estimated GFR (eGFR) value using CKD-Epi equation.

Method: Since 2019, we are prospectively screening for CKD patients who developed moderate-to-severe AKI (KDIGO 2 and 3) in ICU. Patients are referred to Nephrology consultation within 2 to 3 months after discharge from the ICU. The screening for CKD is performed according to the GFR estimation using the CKD-Epi equation. In this cohort, we will assess the incidence of CKD after ICU discharge and factors associated with CKD installation and worsening (univariate and multivariate analysis). In addition, for some patients, we planned to measure GFR using Iohexol clearance to compare measured GFR (mGFR) to eGFR using both CKD-Epi equation and Cystatin C-based equations.

Results: So far, 43 patients have been referred in Nephrology consultation, 72% of male and a mean age of 62 (±16) years. The time between the ICU discharge and the consultation was 55 (±21) days. The main co-morbidities were diabetes (37%) and hypertension (58%). The mean eGFR before the ICU (basal renal function) was 78 (±24) ml/min/1.73m^2 and the pCreat was 89 (±21) µmol/l. At baseline, twenty-one percent of the patients had an eGFR $<$ 60 ml/min/1.73m^2. The length of stay in the ICU was 14 (±14) days. Nearly half of the patients (47%) were ventilated and 56% received vasopressive drugs. Most of the patients (74%) developed KDIGO Stage 3 AKI and 26% developed Stage 2 AKI. The mean entry pCreat was 252 (± 178) µmol/l, reaching a maximum of 382 (± 198) µmol/l during the hospitalization. Sixty percent of the patients underwent renal replacement therapy. The patients lost in average 10 kgs during the hospitalization. The pCreat at discharge was 175 µmol/l (± 175). At the time of the consultation, the eGFR was 70 (± 27) ml/min/1.73m^2 with 35% of the patients with an eGFR $<$ 60 ml/min/1.73m^2. Univariate and multivariate analysis will be performed to evaluate the mains factors associated with CKD.

At this time, 8 patients had a GFR measure using Iohexol. Mean mGFR was 32,8 (±14) ml/min/1,73m^2, lower than the CKD-Epi (57±19), the CKD-Epi Cystatin (35±13) and the CKD-Creatinine-Cystatin (43±14). Compared to the mGFR, the CKD-Epi Cystatin equation appears to perform better with a bias of 4 ml/min/1.73m^2 versus a bias of 24 ml/min/1.73m^2 for the CKD-Epi equation and 12.7 ml/min/1.73m^2 for the CKD-Epi Creatinine-Cystatin equation. Based on the Iohexol measure and the CKD-Epi Cystatin equation, all the patients (100%) had a GFR $<$ 60 ml/min/1,73m^2 against only 33% with the CKD-Epi equation.

Conclusion: In this analysis on the first 43 patients of our cohort, AKI seems to be associated with an increase of CKD 2 months after ICU discharge with 35% of patients with an eGFR below 60 ml/min/1,73m2. This proportion of CKD patients may be underestimated by the GFR estimation based on pCreat. Given the results of the analysis of our first 8 patients who have benefited from GFR measurement, Cystatin C-based equations may be an interesting tool to better assess renal function in this specific population.

P0655

CIRCULATING 1,25-DIHYDROXYVITAMIN D AND ITS RATIO WITH 1-84PTH ARE PREDICTORS OF WORSENING RENAL FUNCTION IN CKD3 PATIENTS

Andrea Galassi[1], Eliana Maria Fasulo[1], Douglas M Hawkins[2], Mario Gennaro Cozzolino[1]

[1]University of Milan, Renal Division, ASST Santi Paolo e Carlo, Dept. of Health Science, Milano, Italy and [2]Scottsdale Scientific LLC, Scottsdale, United States of America

Background and Aims: The variable deterioration of patients with chronic kidney disease poses an omnipresent need for improved renal care management. At present, renal function in CKD patients is measured or estimated using the glomerular filtration rate (mGFR and eGFR). While mGFR affords the most objective and accurate evaluation of kidney function, it is not routinely used for repeated assessment due to its expense and difficulty to execute. Although eGFR provides the most diffuse approach for the monitoring of renal function, its commonality does not come without limitations: above 60mL/min*1.73m^2, serum creatinine, and therefore eGFR variability are increasingly impacted by muscle metabolism/mass, age, gender, diet and fluid imbalances. eGFR can neither anticipate nor predict kidney damage.

In CKD, deficiency of 1,25-dihydroxyvitamin D (1,25(OH)$_2$D) develops during the progression of kidney failure, due to the decreased capability of renal proximal tubule cells to mediate the final hydroxylation step of 25-hydroxyvitamin D to 1,25(OH)$_2$D. While not measured routinely in the clinic, new methods make the measurement of 1,25(OH)$_2$D possible and reliable, and data on its performance as a biomarker are emerging.

The aim of this study is to describe the ability of the LIAISON® XL 1,25 Dihydroxyvitamin D measurement to predict worsening renal function in conjunction with other relevant analytes.

Method: This monocentric study was observational, prospective and descriptive, with a longitudinal approach. 71 patients were assessed for mGFR determination by ^{99m}Tc-diethylenetriamine-pentaacetic acid at baseline. Twenty percent worsening of renal function, based on eGFR, provided the primary endpoint which was evaluated at 3 and 6 months. In addition, serum levels of 1,25(OH)$_2$D, 25(OH)D, 1-84 PTH, intact FGF23, sclerostin, alkaline phosphatase (bone-specific and total) and calcium/phosphorus along with 24h urine levels of creatinine, phosphorus, calcium and sodium were measured. Endpoint analyses were performed by receiver operating characteristics, univariate, and multivariate logistic regressions.

Results: ROC analyses of 1,25(OH)$_2$D and the 1,25(OH)$_2$D/1-84PTH ratio for patients with early CKD (stage 3) showed very good performance in predicting worsening of renal function with AUCs of 0.916 ($p<0.0001$, criterion $\leq$29 pg/mL) and 0.791 ($p<0.0005$, criterion $\leq$0.844), respectively. Significance was lost for both markers' outcome prediction with CKD4 subjects. Of interest, endpoint prediction by 1,25(OH)$_2$D was also better in all patients <70 years old (AUC=0.883. $p<0.0001$). In univariate logistic regression analysis, 1,25(OH)$_2$D is the single and strongest predictor of WRF ($p=0.0029$) corroborating the ROC analysis. In backward-elimination multi-variate regression, the 1,25(OH)$_2$D/1-84PTH ratio and 1-84PTH are the final variables in the regression model ($p=0.00013$). Interestingly, while the ratio correlates well with mGFR ($R=0.541$), 1,25(OH)$_2$D does not ($R=0.116$).

Conclusion: 1,25(OH)$_2$D and the ratio of 1,25(OH)$_2$D/1-84PTH are strong predictors of outcome in CKD3 patients, and thus these measurements may indicate improved clinical care for this important class of patients. Further research of these biomarkers is needed to expand the observations to larger numbers and more diverse populations.

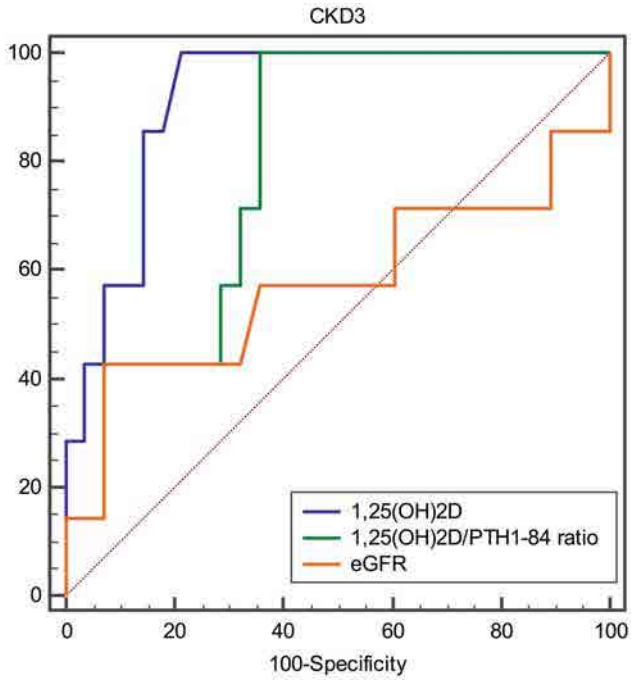


Figure:

P0656

FULL AGE SPECTRUM EQUATION IN THE ESTIMATION OF GLOMERULAR FILTRATION RATE IN RUSSIAN ADULT PATIENTS WITH CHRONIC KIDNEY DISEASE

Mokhamad Khasun[1,2], Ivan Kayukov,[3], Olga Beresneva[4], Marina Parastaeva[2], Anatoly Kucher[2], Alexei Smirnov[2]

[1]Pavlov First Saint Petersburg State Medical University, Department of Therapy, St.-Petersburg, Russia, [2]Pavlov First Saint Petersburg State Medical University, Institute of Nephrology, Sankt-Peterburg, Russia, [3]Pavlov First Saint Petersburg State Medical University, Institute of Nephrology, St.-Petersburg, Russia and [4]Pavlov First State Medical University of St. Petersburg, Institute of Nephrology, Sankt-Peterburg, Russia

Background and Aims: Glomerular filtration rate (GFR) is the most important and accurate parameter of kidney function in the course of chronic kidney disease (CKD). Renal or plasma inulin, diethylenetriaminepentaacetate (DTPA), ethylenediaminetetraacetate (EDTA), radiocontrast agents (iohexol, iothalamate) and some other substances clearances are the reference methods for determining GFR. However, these methods cannot be applied routinely because of the inconvenience. Several available methods have been developed to estimate GFR in a simpler manner and at low costs. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is widely used to evaluate the GFR in practice. However, this equation is not accurate for the full age spectrum. In 2016, the new equation, full age spectrum equation, based on the serum creatinine (FAScr), was developed and can be applicable to all ages. However, data on the benefits of using the FAScr-method in different populations are contradictory. In particular, it is unclear whether the FAScr provides any advantages over the CKD-EPI method in adults. In this regards, we attempted to compare data obtained FAScr method with results some non-reference and reference methods in adult Russian population.

Method: We examined 120 Caucasian patients (M:F - 52:68; age 18-76 year) with CKD 1 - 5 stages. Patients with nephrotic syndrome and congestive heart failure were excluded. GFR (reference method) measured by plasma clearance of ^{99m}Tc-DTPA (CDTPA). CDTPA determined by one- compartment model 2-4 h method using a Chantler-Barratt linear correction. Estimation GFRs (eGFR) were established by Cockcroft-Gault creatinine clearance (CG), CKD-EPI (creatinine), FAScr and Modification of Diet in Renal Disease (MDRD) methods. Also, renal creatinine clearance (Ccr; UV/P method) was measured. Only GFRs values corrected on 1.73 m^2 body surface area had been use.

Results: The values of GFR ($Mean_{(SEM)}$) are: CDTPA $67.0_{(2.46)}$; FAS $69.7_{(2.50)}$; CKD-EPI $64.3_{(2.54)}$; MDRD $60.9_{(2.62)}$; CG $77.6_{(3.31)}$; Ccr $85.2_{(3.40),}$ мл/мин/1.73 m^2. MDRD was significantly lower (paired Student t-test with correction on multiply comparison by Benjamini-Hochberg method) than CDTPA (P=0.0024), CG (P=0.0001) or Ccr (P<0.0001) were significantly higher. The bias (CDTPA minus non reference GFR) were: FAS $-2.67_{(1.71)}$; CKD-EPI $2.72_{(1.58)}$; MDRD $6.12_{(1.78)}$; CG $-10.57_{(2.51)}$; Ccr $-18.22_{(2.26),}$ ml/min. All biases are significantly differ between themselves (P from 0.00064 to <0.000001). The percentage of P_{30} of the FAS $81.6_{(3.5)}$ was not significant differ from P_{30} of CKD-EPI ($78.3_{(3.8)}$; P=0.524) or MDRD ($71.7_{(4.1)}$; P=0.071). However, P_{30} of CG ($67.5_{(4.3),}$%; P=0.01) or Ccr ($54.2_{(5.42),}$%; P<0,001) were significant lower, than P30 of FAS. There were significant comparable direct correlations between CDTPA and FAS (r=0.764), CKD-EPI (r=0.801), MDRD (r=0.756), CG (r=0.656), Ccr (r=0.749); P<0.00001 in all cases.

Conclusion: In adult Russian population FAScr-method of GFR estimation had not any advantage over CKD-EPIcr-method.

P0657 **CHANGES IN CREATININE MAY NO REFLECT MEASURED RENAL FUNCTION CHANGES IN PREDIALYSIS**

Escamilla Cabrera Beatriz[1], Nuria Victoria Sánchez Dorta[1], Natalia Negrã-n Mena[2], Sergio Luis-Lima[2], Federico Gonzalez Rinne[2], Esteban Porrini[2], Armando Torres Ramírez[1]

[1]HOSPITAL UNIVERSITARIO DE CANARIAS, SERVICIO DE NEFROLOGÍA, LA LAGUNA, Spain and [2]Universidad de La Laguna, Facultad de Medicina, La Laguna, Spain

Background and Aims: Serum creatinine is the most used biomarker of renal function in clinical practice. However, the correlation between creatinine and measured GFR is poor with a variability as wide as 200%. The causes of this phenomena are not clear. Some studies observed tubular handling (reabsorption and secretion) as well as intestinal secretion of creatinine, and depends of nutritional status . Importantly, these changes increased with the loss of renal function, masking changes in the evolution of real renal function. However, scarce evidence is available about the reliability of creatinine in reflecting the changes of renal function over the time in predialysis patients, compared to measured GFR. This information is relevant in the setting of clinical decisions.

Method: Spanish unicenter study developed at the Hospital Universitario de Canarias (Tenerife). In the pre-dialysis outpatient clinic, subjects are followed with measured GFR (clearance of iohexol by DBS). Measured GFR is performed at baseline and repeated as suggested by the clinical evolution. For this study we included all patients with repeated determinations of creatinine and measured GFR. The changes of creatinine in terms of increase (>10%), decrease (<10%) and stability (±10%) were compared with the changes in measured GFR.

Results: 89 cases with repeated measurement of GFR and creatinine were evaluated. In 61 cases (68.53%) discrepancies between changes in creatinine and measured GFR were evident. Graphic 1 shows differents discordancing cases with 39 cases (43.8%) overestimation, 7 (7.8%) of infraestimation and 15 cases (24.7%) not change of mGFR with changes on Cr.

Conclusion: Changes in creatinine do not reflect real changes in real renal function in about 70% of the cases. Whenever possible, the measurement of GFR by whichever method available should be considered in the renal care and follow-up of these patients.

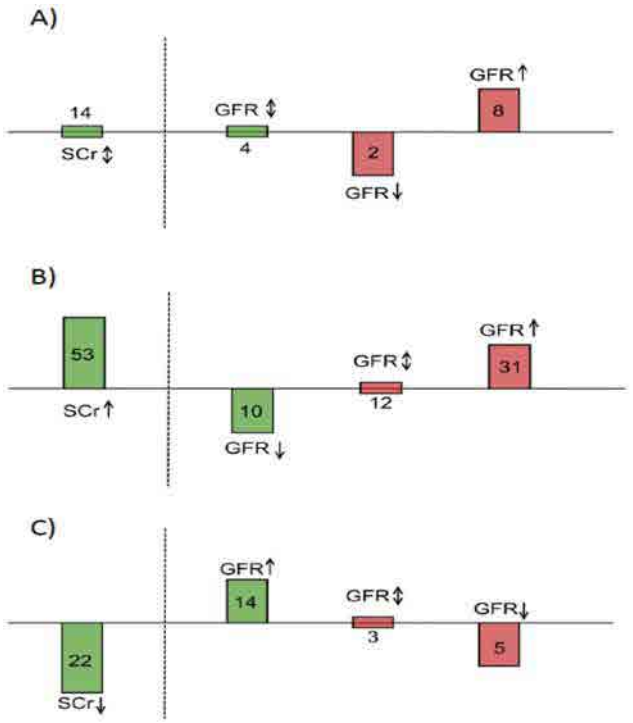


Figure:

P0658 MATRIX AND FLOW MODULATE GENE EXPRESSION IN A 3D VASCULARISED TUBULE MODEL

Julie Williams[1], Sanlin Robinson[2], Babak Alaei[3], Kimberly Homan[2], Maryam Clausen[4], Ryan Hicks[4], Graham Belfield[4], Lena William-Olsson[1], Annette Bak[5], Jennifer Lewis[2], Pernille Laerkegaard Hansen[1]

[1]AstraZeneca, Bioscience Renal, Research and Early Development Cardiovascular, Renal and Metabolism, BioPharmaceuticals R&D, Mölndal, Sweden, [2]Harvard, Wyss Institute, Boston, United States of America, [3]AstraZeneca, Quantitative Biology, Discovery Sciences, BioPharmaceuticals R&D, Mölndal, Sweden, [4]AstraZeneca, Discovery Biology, Discovery Sciences, BioPharmaceuticals R&D, Mölndal, Sweden and [5]AstraZeneca, Advanced Drug Delivery, Pharmaceutical Sciences, BioPharmaceuticals R&D, Mölndal, Sweden

Background and Aims: Questions abound regarding the translation of in vitro 2D cell culture systems to the human setting. This is especially true of the kidney in which there is a complex hierarchical structure and a multitude of cell types. While it is well accepted that extracellular matrix plays a large part in directing cellular physiology emerging research has highlighted the importance of shear stresses and flow rates too. To fully recapitulate the normal gene expression and function of a particular renal cell type how important is it to completely reconstitute their in vivo surroundings?

Method: To answer this question, we have cultured proximal tubular (PT) epithelial cells in a 3-dimensional channel embedded within an engineered extracellular matrix (ECM) under physiological flow that is colocalised with an adjacent channel lined with renal microvascular endothelial cells that mimic a peritubular capillary. Modifications to the system were made to allow up to 12 chips to be run in parallel in an easily handleable form. After a period of maturation under continuous flow, both cell types were harvested for RNAseq analyses. RNA expression data was compared with cells cultured under static 2-dimensional conditions on plastic or the engineered ECM. Additionally, the perfusion of glucose through this 3D vascularised PT model has been investigated in the presence and absence of known diabetes modulating agents.

Results: PCA of RNAseq data showed that a) static non-coated, b) static matrix-coated and c) flow matrix-coated conditions separated into 3 distinct groups, while cell co-culture had less impact. Analysis of transcriptomic signatures showed that many genes were modulated by the matrix with additional genes influenced under flow conditions. Several of these genes, classified as transporters, are of particular importance when using this model to assess drug uptake and safety implications. Co-culture regulated some interesting genes, but fewer than anticipated. Preliminary experiments are underway to monitor glucose uptake and transport between tubules under different conditions.

Conclusion: We have developed a medium throughput system in which matrix and flow modulate gene expression. This system can be used to study the physiology of molecular cross-talk between cells. Ongoing analysis will further consider relevance to human physiology.

P0659 MULTIMODAL IMAGING OF MALDI MSI DATA

Juliane Hermann[1], Kai Brehmer[2], Herbert Thiele[2], Vera Jankowski[1], Joachim Jankowski[1]

[1]Institute for molecular cardiovascular research (IMCAR), Germany and [2]Institute for Mathematics and Computing Imaging, Germany

Background and Aims:

MALDI mass spectrometric imaging (MALDI MSI) is a powerful histologic tool for the analysis of biomolecules in tissue samples. MALDI MSI measurements results in a high sensitivity and accuracy of spatial distribution of biomolecules in tissue samples The resolution information of MALDI MSI is in the range of 5-10 μm in the spatial distribution and has the ability to identify proteins, peptides, lipids and small biomolecules directly in tissue samples in one analytical step..For a more detailed analysis of MALDI MSI data and a correlation between the molecular and microscopic level, a combination of MALDI MSI data and histological staining is essential. By combining MALDI MSI data and histological data, much more information are obtained than from a single analysis of both methods. Therefore, MALDI MSI data sets and histological staining were fused to a 3D model presenting a biomolecule distribution of the whole organ and provide more information than a single tissue section. We developed, established and validate an algorithm for an automatic registration of MALDI data with different histological image data for the cross-process evaluation of multimodal data sets for creating 3D models. This multimodal image approach simplifies and improves molecular analyses of tissue samples clinical research and diagnosis.

Method:

The data sets for the fusion and creating of a 3D model consist of mass spectrometric data as well as histological and Immunohistochemical staining methods. Histological tissue sections of a whole mice kidney were prepared. For MALDI MSI data the organ sections were coated and incubated with a trypsin solution were performed by using a sprayer for MALDI imaging. As matrix, α-cyano-4-hydroxycinnamic acid was used. MALDI MSI was performed using the Rapiflex. For histological staining the hematoxylin-eosin and Gomori staining were chosen. For Immunohistochemical double staining and immunofluorescence, were used for the detection of Collagen type I, smooth muscle actin and the cell nuclei.

Results:

By using a mathematical registration, a perfect superposition of the individual histological sections mass spectrometric data was achieved. It is possible to combine mass spectrometric data, histological and Immunohistochemical data sets in a high number and to reconstruct the measured mice kidney. By using different imaging methods, a variety of information about tissue structure as well as tissue changes and protein distribution can be obtained. The fusion of the data also offers a virtual incision of the organ from any angle and level. The algorithms are adapted to take the data fusion automatically offering a high-throughput approach for clinical diagnostics and the possibility to involved artificial intelligence in its interpretation in research.

Conclusion:

There is a successful fusion of MALDI MSI data and different histological and Immunohistochemical staining data sets of a whole organ

P0660 **COMPARISON OF BIAS AND ACCURACY OF CREATININE AND CYSTATIN C-BASED CKD-EPI EQUATIONS FOR GFR ESTIMATION**

Ling Sun[1], Luxi Zou[2], Susanne B. Nicholas[3], Yan Lu[4], Satyesh Sinha K[5], Ruixue Hua[4]

[1]Xuzhou Central Hospital, Medical College of Southeast University, Division of Nephrology, Xuzhou, P.R. China, [2]Xuzhou Medical University, Xuzhou, P.R. China, [3]David Geffen School of Medicine at University of California, Divisions of Nephrology and Endocrinology, Department of Medicine, Los Angeles, United States of America, [4]Xuzhou Medical University, Department of Clinical Medicine, Xuzhou, P.R. China and [5]David Geffen School of Medicine at University of California, Division of Nephrology, Department of Medicine, Los Angeles, United States of America

Background and Aims: Glomerular filtrate rate (GFR) is a key index of kidney function, and directly measured GFR (mGFR) is the gold standard, but it is invasive and costly. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations have been widely used to estimate GFR with high accuracy. However, the comparative accuracy of estimated GFR (eGFR) using creatinine and cystatin C in CKD-EPI equations remains unclear. This study aimed to systematically assess the bias and accuracy of eGFR using equations of CKD-EPI$_{crea}$, CKD-EPI$_{cys}$, and CKD-EPI$_{crea/cys}$ in adult populations relevant to primary health care.

Method: Pubmed, Web of Science, EMBASE, and the Cochrane Library were searched from inception until December 2019 for studies comparing mGFR with simultaneous eGFR using CKD-EPI calculated from standardized serum creatinine and cystatin C. We pooled data on bias (difference between mGFR and eGFR), accuracy (P30; proportion of eGFR within 30% of mGFR), and correlation coefficient (R; between mGFR and eGFR), using random-effects models.

Results: A total of 35 studies with 23,667 participants, which reported the data on the bias, and/or P30, and/or R were included (Figure 1). The difference in the bias of eGFR using CKD-EPI$_{cys}$ was 4.84 mL/min/1.73 m^2 (95% CI, 1.88∼7.80) lower than using CKD-EPI$_{crea}$, and 1.50 mL/min/1.73 m^2 (95% CI, 0.05∼2.95) lower than using CKD-EPI$_{crea/cys}$. These gaps increased in subgroups of low mGFR (<60 mL/min/1.73 m^2) (Figure 2). CKD-EPI$_{crea/cys}$ eGFR achieved the highest accuracy (Figure 3), 7.50% higher than CKD-EPI$_{crea}$ (95% CI, 4.81∼10.18), and 3.21% higher than CKD-EPI$_{cys}$ (95% CI, -0.43∼6.85) (Figure 4); and the best correlation with mGFR, with Fisher's z transformed R of 1.20 (95% CI, 0.89-1.50) (Figure 5).

Conclusion: CKD-EPI$_{crea/cys}$ and CKD-EPI$_{cys}$ equations gave less bias and more accurate estimates of mGFR than CKD-EPI$_{crea}$ equation. Our findings validated and strengthened the use of cystatin C alone or in combination with creatinine in CKD-EPI equations. More variables and coefficients could be added in CKD-EPI equations to achieve less bias and more accuracy in future research.

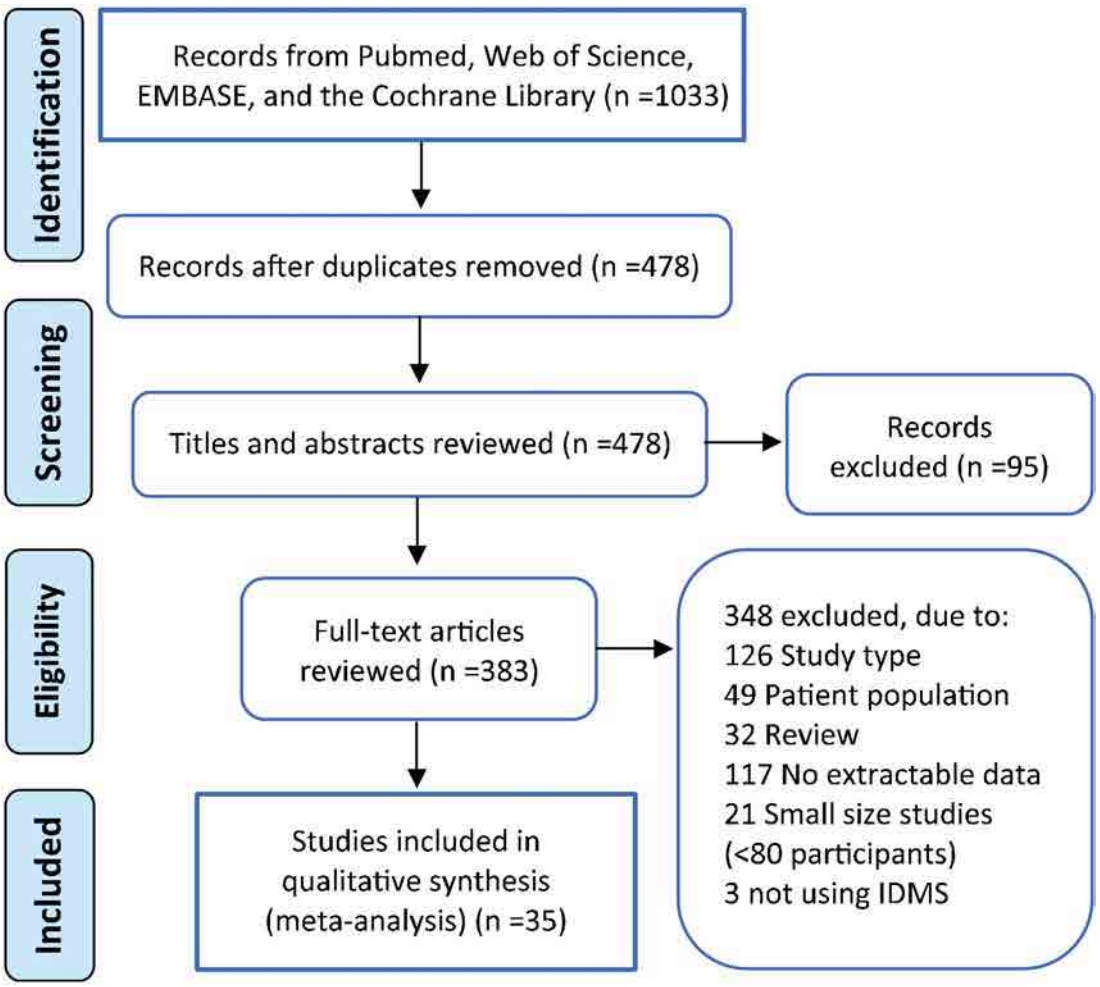


Fig. 1. Flowchart of study selection. IDMS, isotope dilution mass spectrometry.

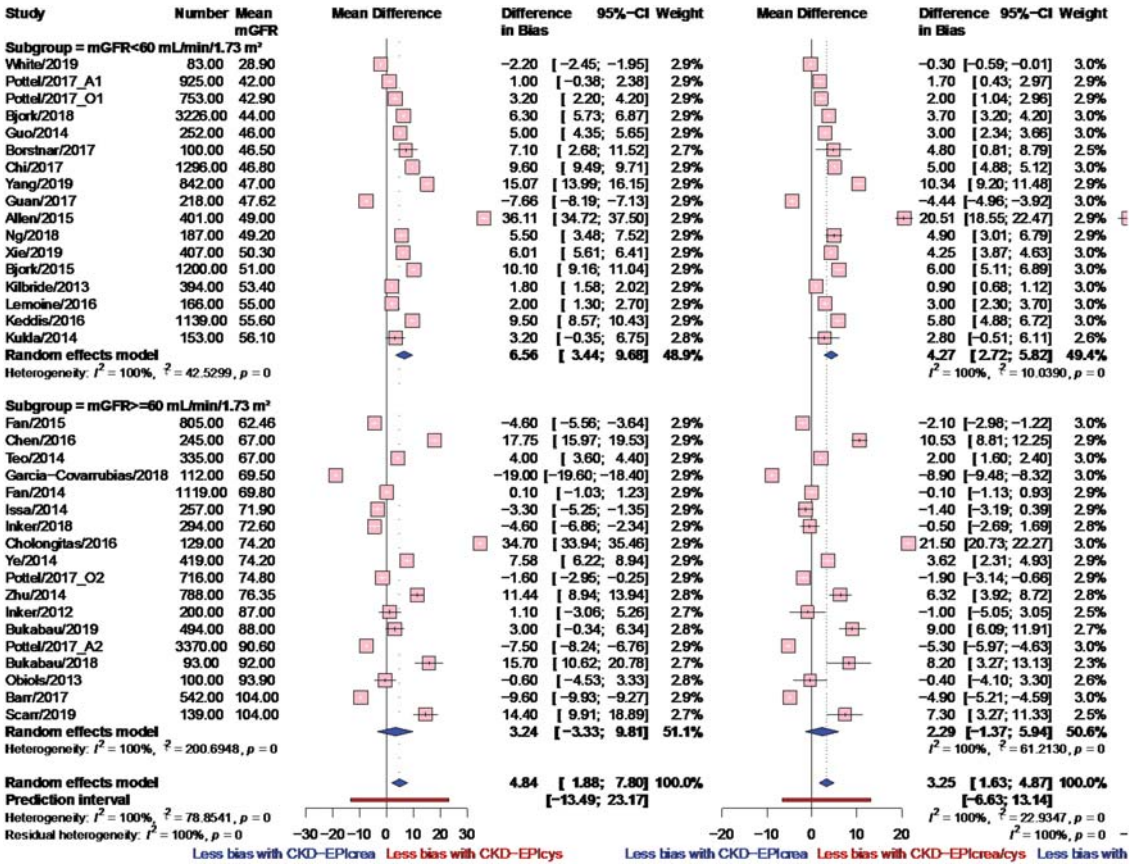


Fig. 2. Difference in mean bias from CKD-EPI$_{crea}$, CKD-EPI$_{cys}$, and CKD-EPI$_{crea/cys}$, and pooled estimate (diamond) stratified into subgroups of low and high mGFR using random-effects models. CKD-EPI$_{cys}$ had the lowest bias, and CKD-EPI$_{crea/cys}$ had lower bias than CKD-EPI$_{crea}$. CI, confidence interval.

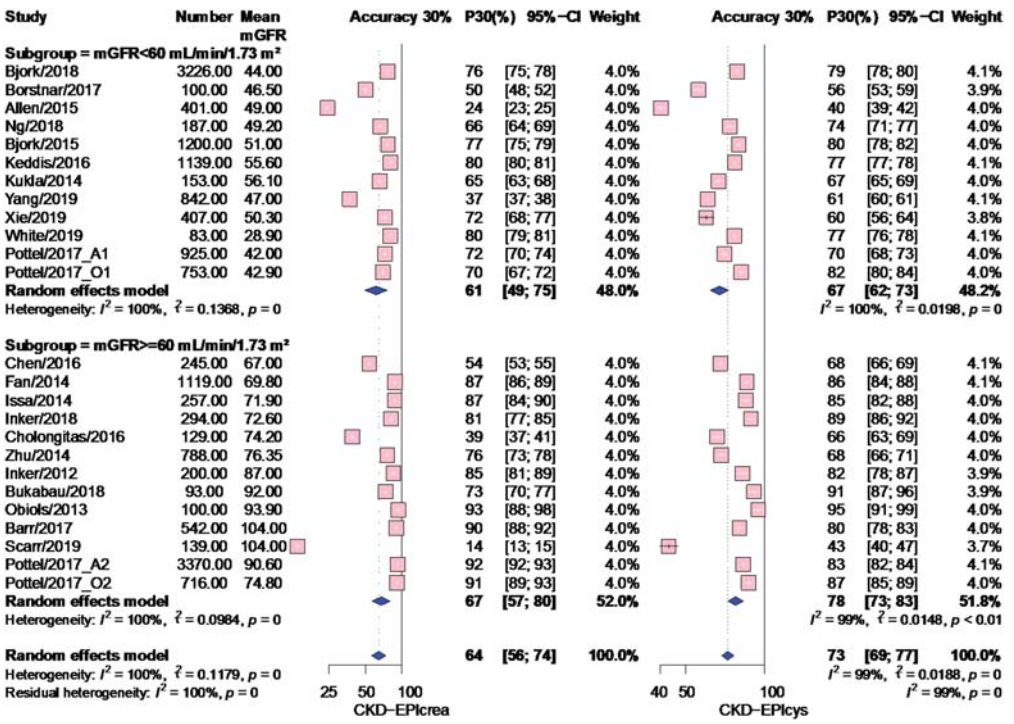


Fig. 3. Mean accuracy (P30) of eGFR using CKD-EPI$_{crea}$, CKD-EPI$_{cys}$, and CKD-EPI$_{crea/cys}$, stratified into subgroups of low and high mGFR using random-effects models. The mean P30 was 64%, 73%, and 73% in CKD-EPI$_{crea}$, CKD-EPI$_{cys}$, and CKD-EPI$_{crea/cys}$, respectively, and CKD-EPI$_{crea/cys}$ achieved highest P30 (80%) in the subgroup of mean mGFR $\geq$60 mL/min/1.73 m^2. P30, the proportion of eGFR results within 30% of mGFR result; CI, confidence interval.

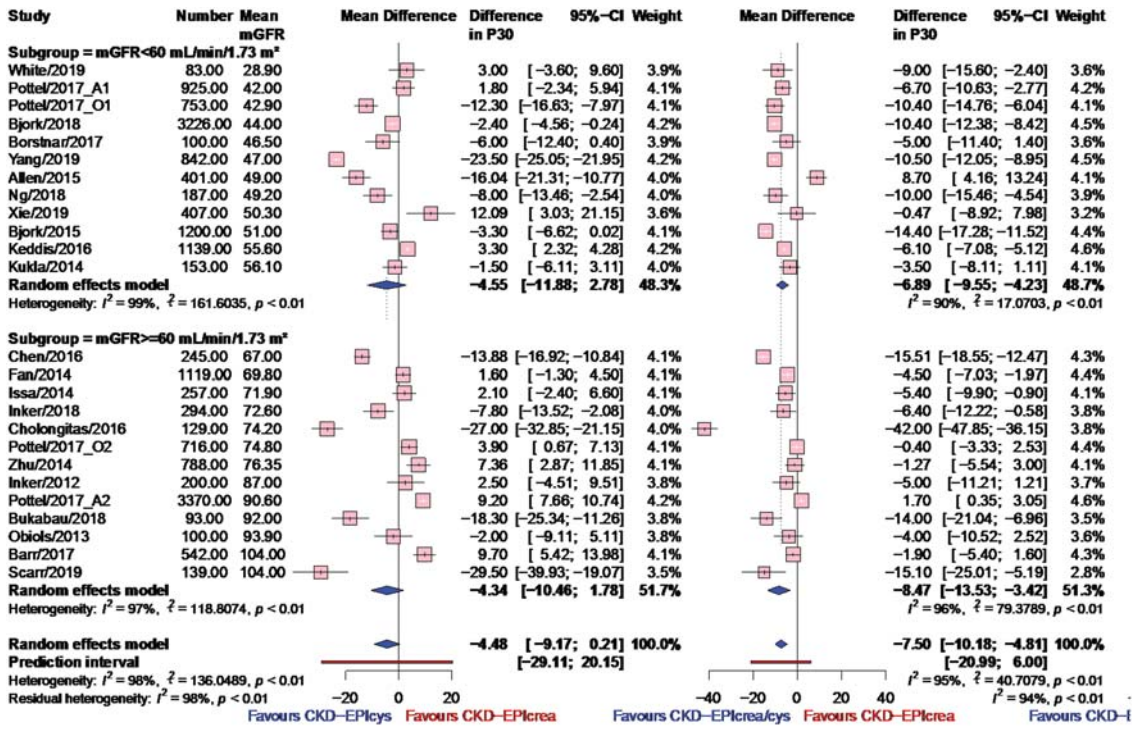


Fig. 4. Difference in mean accuracy (P30) from CKD-EPI$_{crea}$, CKD-EPI$_{cys}$, and CKD-EPI$_{crea/cys}$, stratified into subgroups of low and high mGFR using random-effects models. CKD-EPI$_{crea/cys}$ was the most accurate with the highest P30. P30, the proportion of eGFR results within 30% of mGFR result; CI, confidence interval.

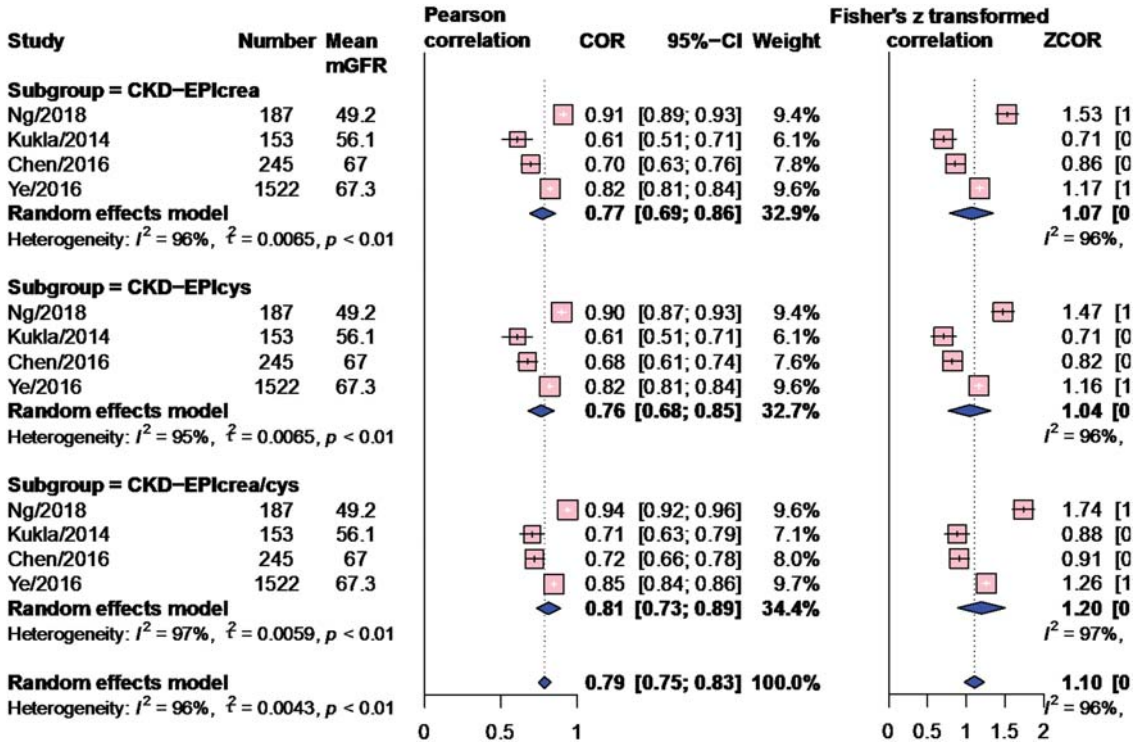


Fig. 5. Pearson correlation coefficient (R) and Fisher's z-transformed R between mGFR and eGFR using CKD-EPI$_{crea}$, CKD-EPI$_{cys}$, and CKD-EPI$_{crea/cys}$. CKD-EPI$_{crea/cys}$ performed better than CKD-EPI$_{crea}$ and CKD-EPI$_{cys}$, with the highest Pearson R and Fisher's z-transformed R. COR, correlation coefficient; ZCOR, Fisher's z-transformed correlation coefficient; CI, confidence interval.

P0661

DIAGNOSTIC VALUE OF FULL AGE SPECTRUM EQUATION AS A PREDICTOR OF MORPHOLOGICAL LESIONS IN PATIENTS WITH GLOMERULONEPHRITIS

Saganova Elena[1], Olga Galkina[1], Vasiliy Sipovskii[1], Ivan Kayukov,[1], Alexei Smirnov[1]

[1]*Pavlov First Saint Petersburg State Medical University, Research institute of Nephrology, Saint Petersburg, Russia*

Background and Aims: Glomerular filtration rate (GFR) is generally accepted as a best overall index of kidney function. However, it remains controversial to choose the optimal equation to estimate GFR in patients with glomerulonephritis (GN). Recent studies have reported that newly developed full age spectrum equation based on normalized serum creatinine (FASsCr) showed improved validity and was less biased, more accurate than currently recommended sCr-based eGFR equations. Our aim was to assess FASsCr equation as a predictor of various morphological lesions in patients with GN.

Method: 100 patients [48 female, age Me 39 (27; 54) years] with biopsy proven primary GN and without acute kidney injury, infectious diseases, severe heart failure, respiratory insufficiency, cancer were included in the study. Minimal change disease was diagnosed in 9% of cases based on the results of kidney biopsy, in 28% – focal segmental glomerulosclerosis, in 26% – membranous nephropathy and in 37% – IgA-nephropathy. Serum creatinine (sCr) level was measured by enzymatic method (Uni Cel DxC 800 PRO, «Beckman Coulter»,USA). eGFR was calculated using FASsCr equation. The extent of global glomerulosclerosis (GS) was assessed quantitatively as a sum of full and focal sclerotic glomeruli. Tubulo-interstitial fibrosis (TIF) and tubular atrophy (TA) were assessed semi-quantitatively (0-lesions absent; 1-mild focal tubular and interstitial lesions; 2-moderate tubular and interstitial lesions; 3 - diffuse tubular and interstitial lesions). All patients consistently were separated into 2 groups according to the degree of each morphological lesion (GS, TIF or TA): "mild" (GS$<$25% or TIF/TA grade 0 or 1) and "severe" (GS $\geq$ than 25% or TIF/TA grade 2-3).

Results: eGFR using FASsCr equation positively correlated ($p<0{,}001$ in all cases) with GS (r=0,44), TIF (r=0,64) and TA (r=0,61) and was significantly higher in patients with "mild" GS, TIF and TA ($p<0{,}001$) in comparison with "severe" group.

Using ROC-analysis all patients were separated ($p<0.001$) in 2 groups using FASsCr equation according to the degree of morphological lesions ("mild" or "severe"):

GS (Sn – 48.8%, Sp – 88.1%, ACC – 72.0%, AUC – 0.696, cut-off value – 47 ml/min/1.73m$^{2)}$, TIF (Sn - 75.4%, Sp – 76.9%, ACC – 76.0%, AUC – 0.815, cut-off value – 72 ml/min/1.73m$^{2)}$, TA (Sn – 65.9%, Sp – 88.8%, ACC – 70.0%, AUC – 0.798, cut-off value – 74 ml/min/1.73m$^{2)}$, (Figure).

Conclusion: Our results show that FASsCr equation is a significant marker of various morphological lesions in patients with GN. FASsCr equation predominantly can be used as a predictor of mild degree of interstitial sclerosis and tubular atrophy with high diagnostic value.

Figure: ROC curves with 95% CI of BM panel for A – GS; B – TIF; C – TA

P0662 A NOVEL NOMOGRAM TO PREDICT THE RELIABILITY OF ESTIMATED GLOMERULAR FILTRATION RATE FORMULA IN ONCOLOGY PATIETNS

Yichun Cheng[1], Liu Huang[1], Yunfeng Han[1], Chummun Vanisha[1], Shu-wang Ge[1], Gang Xu[1]

[1]*Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Department of Nephrology, Wuhan, P.R. China*

Background and Aims: Formulae of estimated glomerular filtration rate (eGFR) based on serum creatinine (Scr) are routinely used in oncology patients, however, they are inaccurate in some populations. Our aim was to identify population characteristics where eGFR formulae performed poorly and thereby build a nomogram to predict the reliability of estimates.

Method: Measured GFR (mGFR) using isotope from 444 oncology patients were compared with eGFR from four formulae (Cockcroft-Gault, Modification of Diet in Renal Disease (MDRD), Chronic Kidney Disease Epidemiology (CKD-EPI) Collaboration and Wright). Multivariate logistic regression was applied to identify characteristics associated with inaccurate eGFR and construct a predictive nomogram.

Results: The Cockcroft–Gault formula exhibited estimates with lowest bias and highest precision. Nonetheless, it was still unreliable in a relevant proportion of patients. The percentage of patients within 30%, 20%, and 10% of the accurate percentage error (APE) was seen in only 62.8%, 47.7% and 24.8% of patients respectively. Inaccuracy was found in overweight patients or in patients with BUN/Scr ratio greater than 20 or with eGFR greater than 120 ml/min. A novel nomogram was constructed to help oncologists to predict the risk of inaccuracy of eGFR. The calibration curve showed good agreement.

Conclusion: Our results suggest that all eGFR formulae tend to overestimate the eGFR in oncology patients. Our nomogram may assist oncologists in decision-making when mGFR is needed.

P0663

RELATIONSHIP BETWEEN ENDOTHELIAL LESION AND PULMONARY DYSFUNCTION AMONG HEMODIALYTIC CHRONIC KIDNEY DISEASE PATIENTS WITH AND WITHOUT DIABETES MELLITUS

Elizabeth De Francesco Daher[1], Debora Fortes Marizeiro[1], Daniela Gardano Bucharles Mont'alverne[1], Gdayllon Cavalcante Meneses[1], Taina Veras de Sandes Freitas[1], Alice Maria Costa Martins[1], Geraldo Bezerra da Silva Junior[1,2]

[1]Federal University of Ceará, School of Medicine, Farmacy and Physical Therapy, Fortaleza, Brazil and [2]Universidade de Fortaleza, Public Health and Medical Sciences Graduate Programs, Fortaleza, Brazil

Background and Aims: Patients with Chronic Kidney Disease (CKD) on dialysis and Diabetes Mellitus type 2 (DM2) may develop dysfunction in several systems, including the respiratory system. The aim of this study is to investigate if there is a relationship between endothelial lesion and pulmonary dysfunction in patients with CKD in hemodialysis with and without DM2.

Method: This is a cross-sectional study, from October 2017 to August 2018, including 60 patients divided into three groups: patients on hemodialysis (HD) without DM2 (HD in NDM = 30); HD with DM2 (HD in DM = 15); Non-hemodialysis with DM2 (DM without HD = 15) aged 40 to 60 years, regardless of gender. Analyzed pulmonary function were: maximal inspiratory and expiratory pressures (MIP and MEP) and measures of lung capacities and volumes: Forced Vital Capacity (FVC) and Forced Expiratory Volume in one second (FEV1).

Results: In the DM group in HD: MIP, MEP, FVC and FEV1 showed significant differences ($p = 0.008$; and $p = 0.000$; $p = 0.000$; $p = 0.000$), respectively. In the HD without NDM group: only the MIP parameter showed no significant difference ($p = 0.256$), MEP, FVC and FEV1 showed a statistically significant difference ($p = 0.001$; $p = 0.000$; $p = 0.000$), respectively. In the DM group without HD: only MIP showed no statistically significant difference ($p = 0.491$), MEP, FVC and FEV1 showed a statistically significant difference ($p = 0.000$; $p = 0.008$; $p = 0.000$), respectively when compared to their predicted value. Significant difference was detected between the groups regarding VCAM-1 only between DM in HD and DM without HD ($p = 0.040$). Syndecan-1 and Angiopoietin-2 plasma levels were statistically different when compared between the groups ($p = 0.000$) for the two biomarkers, this difference was observed only between the dialysis groups and the diabetic group without dialysis. In the multivariate regression analysis, when the fact that the individual had DM was also added, there was a greater association of VCAM-1 with the fact that the patient did not reach the predicted MEP, this value increased to OR = 8.762 (CI = 2.317 - 33.136) times of chance of not achieving the expected ($p = 0.001$). However, no statistically significant difference was found when the fact that the patient underwent hemodialysis was included ($p = 0.885$). Regarding Spearman correlation between MIP and VCAM-1 / Syndecan-1 / angiopoietin-2 there was no significant difference. However, in the correlation between MEP and endothelial lesion biomarkers, there was a significant difference only when compared with VCAM-1 ($r = -0.287$, $p = 0.036$). The FEV1 and FVC parameters obtained statistically significant results when correlated only with angiopoietin-2 ($r = -0.309$; -0.361), respectively.

Conclusion: Inspiratory muscle strength is reduced only when DM and HD are present when compared to their predicted. Expiratory muscle strength is reduced in all three groups and this parameter is most affected in diabetic individuals undergoing hemodialysis. Pulmonary function is compromised in all three groups equally. Endothelial glycocalyx lesion biomarkers (Angiopoietin-2 and Syndecan-1) are increased mainly in subjects on hemodialysis. Endothelial dysfunction is evidenced in HD group DM by increased VCAM-1 levels. There is a relationship between the lack of expected expiratory muscle strength with high values of VCAM-1 and when added the fact of having DM this relationship increases, however when added the fact of being dialytic there is no significant relationship. There is an inversely proportional correlation between expiratory muscle strength with the adhesion molecule marker (VCAM-1) and between pulmonary function with the endothelial lesion marker (Angiopoietin-2).

P0664 CKDSENS, A NOVEL HEALTHCARE PLATFORM FOR CHRONIC KIDNEY DISEASE

Marc Xipell Font[1,2], Elisenda Banon[2,3], Josep Lluís Falcó[2,4], Raphael Koster[2,5], Miguel Berenguel[2,6], Josep Joan Teruel[2,7], Cecilia Vera[2,8], Miquel Blasco[1,2], Francisco Maduell[1,2], Berta Borràs[2,4], Francisco Carrera[2,9], Marta Novell[2,9], Adrià Maceira[2,9], Josep Maria Campistol Plana[1,2]

[1]Hospital Clínic de Barcelona, Nephrology and Renal Transplantation, Barcelona, Spain, [2]CKDSens: a novel home healthcare platform for chronic kidney disease. ID Project 19579 of European Institute of Innovation & Technology (EIT) Health, [3]Fundació Privada Clínic per a la Recerca Biomèdica, Laboratori Experimental de Nefrologia i Transplantament (LENIT), Spain, [4]Genesis Biomed, Spain, [5]Madopa, France, [6]Eurecat Centro Tecnológico de Cataluña, Spain, [7]Universitat de Barcelona, Spain, [8]Universidad Politécnica de Madrid, Spain and [9]CreatSens Health, Spain

Background and Aims: The 10% of the global adult population, more than 730 million people, suffers from some degree of chronic kidney disease (CKD). From that population, a 30% is suffering from an advanced stage of the disease. Approximately 38 million of the European population is affected by an advanced stage renal disease with 1 million of new cases every year. These patients require close monitoring, which increase the burden of the disease. New tools and methods are required to improve the patients' well-being, the perception and management of their disease, decrease the impact of the complications, as well as to delay of the progression of the disease.

Method: Seven partners have joined in the CKDSens consortium and are contributing to the project with different expertise and technical resources (medical, technological, educational, business and management): CreatSens Health SL, Hospital Clínic de Barcelona – Fundació Privada Clínic per a la Recerca Biomèdica, Genesis Biomed, Eurecat, Universitat de Barcelona, Universidad Politécnica de Madrid, and Madopa. This consortium is a novel and unique technological platform, combining in vitro diagnostic devices and software components, that connects patients with CKD and healthcare professionals to improve the well-being of people and the efficiency of the healthcare system by monitoring relevant biomarkers out of the hospital in a simple and cost- effective connected paper-based sensors. The proposal aims to increase the quality of life of CKD patients through early diagnostics, real time monitoring and personalization of therapies.

Results: The CKDSens consortium is developing a novel technological platform for real-time and low-cost diagnostics for two key biomarkers in renal diseases (creatinine and potassium), which include a new point-of-care device that allows monitoring by remote control these biomarkers. The technology has been patented for both biomarkers, and it has been transferred to CreatSens, a spinoff from Universitat Rovira i Virgili. The product integrates paper-based sensors in a drop of blood analysis, wireless connectivity and a digital platform as data analytics. The aim of the consortium is to validate the use of a new medical device as a product that can fit and truly generate value and business. Through that perspective, the optimization, manufacturing and validation of the tool and the business case will be performed as a first step, while usability, end user interaction and regulatory pathway will be developed in the second step. CKDSens will afford a novel approach to embed healthcare in daily life and routine. This new strategy implies production and commercialization for prevention and diagnose where markets are well known and validated. The aim is to mimic a well-known business model such as glucometer, translating this one into renal diseases. CKDSens has risen funding for this purpose through a grant of the European Institute of Innovation and Technology (EIT Health, ID Project 19579), and it is working to have validated this device at the end of the year. This requires also a clinical validation, which will be performed in a clinical trial in the second half of the year.

Conclusion: CKDSens consortium has been created as a novel technological platform to develop and validate a new medical device for a remote control of patients with CKD, in order to increase the quality of life of CKD patients through early diagnostics, real time monitoring and personalization of therapies. It is expected to have this device designed and validated by the end of the year 2020 and ready for further commercialization.

P0665 RENAL FUNCTION ASSESSMENT IN A SMALL COHORT OF ADULT PROFESSIONAL SOCCER PLAYERS

Tatiana Kirsanova[1], Oleg Talibov[2,3], Eduard Bezuglov[3,4,5], Butovskiy Mikhail[3,4]

[1]Federal State Budget Institution "Research Center for Obstetrics, Gynecology and Perinatology", Senior researcher, Moscow, Russia, [2]Moscow State University of Medicine and Dentistry, Clinical Pharmacology, Moscow, Russia, [3]Moscow Witte University, High Performance Sport Laboratory, Moscow, Russia, [4]Federal Medical Biological Agency, Federal Research and Clinical Center of Sports Medicine and Rehabilitation, Moscow, Russia and [5]Sechenov First Moscow State Medical University (Sechenov University), Department of Sport Medicine and Medical Rehabilitation, Moscow, Russia

Background and Aims:

Signs of acute kidney injury (AKI) are registered in 10-60% of patients with exertional rhabdomyolysis. Most professional soccer players from the time to time meet the criteria for rhabdomyolysis in high season. Link between chronic high levels of myoglobin and AKI is well known, while 25% of people who had AKI subsequently develop chronic kidney disease (CKD) and in 0,3% end-stage renal disease is diagnosed over the next 3 years. Progression of renal decline depends on incomplete recovery and the amount of AKI episodes. In all studies renal function (estimated glomerular filtration rate - eGFR) was calculated by creatinine level (SCr), while usually sportsmen have greater body muscle proportion, which makes it difficult to assess eGFR by creatinine. Cystatin C level is relatively independent of body mass index and composition therefore this parameter more accurately represents kidney function

AIM: comparison of two different GFR evaluation methods, cystatin (GFRcys) and creatinine (GFRcr) in adult professional soccer players

Method:

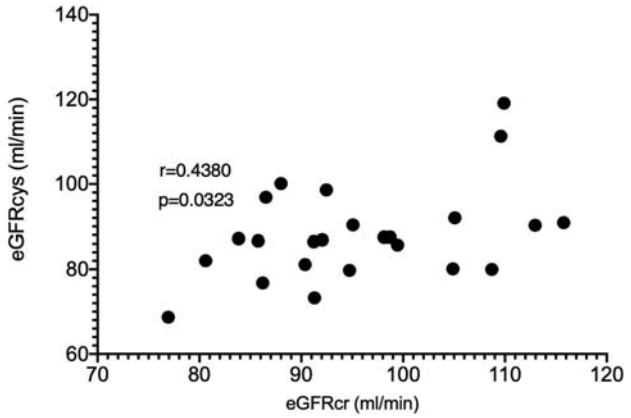
24 adult professional soccer players (age = 28±3.8 years, BMI=23±0.98) were included. Renal function was assessed by blood tests of serum creatinine (SCr) and serum cystatin C (SCys) performed on the next day of regular matches. Blood samples were collected fasting at 8:00 in the morning after 8-hour night sleep. eGFR levels was determined by CKD-EPI formula for SCr, and (eGFR=130xcystatin $C^{-1.069}$ x age $^{-0,117}$-7) for CysC.

Results:

Since data was distributed normally parametric tests were used. eGFRcr was significantly higher than eGFRcys : SCr 1.1±0.094 mg/dl, GFRcr 96±11 ml/min;CysC 0.94±0.093 mg/dl, eGFRcys 88±11 ml/min (p=0.0045, paired T-test). Both GFR methods and both indicators (SCr and CysC) have moderate weak statistically significant correlation. Pearson's r=0.438 (p=0.0323) for eGFR (Pic.) and 0.4047 (p=0.0498) for SCr vs Cys.

Conclusion:

In professional sportsmen cystatin C based eGFR evaluation has certain advantages in comparison to creatinine based method. Probably regular high-level physical exertions reduce kidney function.



Pic. eGFR evaluation: methods correlation plot.

Figure:

P0666

BRILLOUIN AND RAMAN SPECTROSCOPIES FOR NON-CONTACT ASSESSMENT OF MECHANO-CHEMICAL PROPORTIES OF URINARY PROTEINS: A PROOF OF CONCEPT STUDY

Abduzhappar Gaipov[1], Zhanatay Nurekeyev[2], Alisher Sultangaziyev[3], Duman Turebekov[4], Pavel Tarlykov[5], Rostislav Bukasov[3], Zhandos Utegulov[2]

[1]Nazarbayev University School of Medicine, Department of Clinical Sciences, Nur-Sultan, Kazakhstan, [2]Nazarbayev University School of Sciences and Humanities, Department of Physics, Nur-Sultan, Kazakhstan, [3]Nazarbayev University School of Sciences and Humanities, Department of Chemistry, Nur-Sultan, Kazakhstan, [4]Astana Medical University, Department of Internal Medicine, Nur-Sultan, Kazakhstan and [5]National Center for Biotechnology, Department of Proteomics and Mass Spectrometry, Nur-Sultan, Kazakhstan

Background and Aims: Proteinuria is a major marker of chronic kidney disease (CKD) severity, the predictor of renal function decline and cardiovascular mortality. The main pathway of CKD progressive is caused by tubular toxicity of filtering proteins, so more, the rapid development of renal failure is expected in those patients who have higher level of proteinuria. However, despite high level of proteinuria, paradoxically, some patients may have slow decline of renal function compared to those patients with lower level of urinary protein excretion. This may possibly due to their different mechanical (visco-elastic) and chemical properties, as well as the proteomics of excreting urinary proteins. Brillouin light scattering (BLS) and surface enhanced Raman scattering (SERS) spectroscopies are non-contact (laser optical-based) techniques providing visco-elastic and chemical property information of probed human biofluids. We aimed to study and compare the visco-elastic and chemical properties of urinary proteins using BLS and SERS spectroscopies in nephrotic patient with high protein excretion and healthy subject.

Method: Two urine samples from nephrotic patient (proteinuria>3.5 g/24h) and healthy subject (undetectable proteinuria) investigated using BLS and SERS spectroscopies. Brillouin spectroscopy performed using Torus single longitudinal mode laser in conjunction with high contrast JRS Instruments 6-pass tandem Fabry-Perot interferometer coupled with confocal microscope. Using Horiba LabRAM HR Raman microscope with 785 nm laser excitation andx100 microscope objective the SERS spectroscopy was performed on urine samples in contact 60 nm gold nanoparticles placed on gold film. Additionally, reversed-phase liquid chromatography-mass spectrometry (LC-MS) was conducted for profiling of urinary proteins LC-MS data was analysed by Mascot software using the SwissProt protein database.

Results: We found that elevated protein levels in urine alter the urine fluid elasticity sufficiently to be measurable by BLS spectroscopy, with urine from healthy and proteinuric subjects distinguishable to marked significance, which increases with sample concentration. BLS spectroscopy demonstrated that patients with High Protein Loss, characterized by stiffer urine (i.e. higher Brillouin shift and elastic modulus) and less viscous (i.e. less hypersound attenuation) compared to healthy subject. (Figure 1A). SERS measurements of two urine samples taken from patient with high protein loss in healthy subject (Figure 1B) showed the integrated Raman intensity ratio of 1338 cm^{-1} and 1002 cm^{-1} peaks is many times higher for the sample with high protein concentration vs sample with low protein concentration. Urinary protein sequencing and Mascot analysis (Table 1) demonstrated that proteinuric patient had different type of proteins with up to 187k Daltons of molecular weight.

Conclusion: In this proof of concept study, we demonstrated that laser-optical BLS and SERS techniques combined with LC-MS measurements revealed that human urine fluids of healthy and proteinuric subjects had strong variation in the visco-elastic and chemical properties coupled with various level of protein content.

Table 1: Human urine protein sequencing and Mascot analysis from proteinuric patient

Accession (HUMAN)	Score	Molecular mass (Dalton)	Num. of matches	Num. of sequences	Description
A1AT	733	46,707	47	9	Alpha-1-antitrypsin
CO3	296	187,030	14	4	Complement C3
HBB	137	15,988	8	4	Hemoglobin subunit beta
HBA	112	15,248	9	3	Hemoglobin subunit alpha
HEMO	54	51,643	1	1	Hemopexin
CERU	51	122,128	5	3	Ceruloplasmin
FETUA	42	39,300	3	1	Alpha-2-HS-glycoprotein
CNGB1	38	139,590	2	1	

Continued

Continued

Accession (HUMAN)	Score	Molecular mass (Dalton)	Num. of matches	Num. of sequences	Description
A1AT	733	46,707	47	9	Alpha-1-antitrypsin
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FETUA	42	39,300	3	1	Alpha-2-HS-glycoprotein
CNGB1	38	139,590	2	1	Cyclic nucleotide-gated cation channel beta-1
IGKC	36	11,602	1	1	Ig kappa chain C region
SUCO	36	139,343	1	1	SUN domain-containing ossification factor

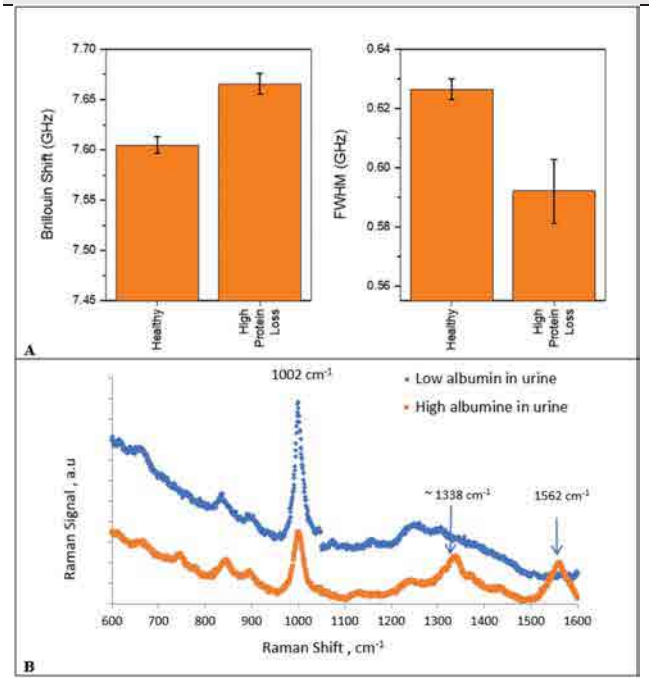


Figure 1: BLS (A) and SERS (B) spectroscopies of human urine from proteinuric patient and healthy subject

CKD. PATHOPHYSIOLOGY, PROGRESSION AND RISK FACTORS

P0668 UNILATERAL URETER OBSTRUCTION (UUO)-INDUCED RENAL FIBROSIS IS ATTENUATED BY SUPPRESSION OF INDOXYL SULFATE (IS) ACCUMULATION IN SULFOTRANSFERASE (SULT)1A1-DEFICIENT MICE

Huixian Hou[1], Nozomi Yabuuchi[1], Nao Gunda[1], Rika Fujino[2], Yuya Hayashi[2], Yuki Narita[2], Hirofumi Jono[2], HIDEYUKI SAITO[2]

[1]Kumamoto University Graduate School of Pharmaceutical Sciences, Clinical Pharmaceutical Sciences, Kumamoto, Japan and [2] Kumamoto University Hospital, Pharmacy, Kumamoto, Japan

Background and Aims: Obstructive nephropathy is the result of functional or anatomic lesions located in the urinary tract, and renal interstitial fibrosis is a common finding associated with long-term nephropathy. Many factors are suggested to be involved in the pathogenesis of renal fibrosis, such as infiltration of macrophages, growth factors, oxidative stress and cytokines. Indoxyl sulfate (IS), a typical sulfate-conjugated uremic solute, accumulates markedly in serum and renal tissue of cisplatin- or ischemia/reperfusion-induced acute kidney injury model animals, thereby inducing generation of oxidative stress. However, the relationship between IS and obstructive nephropathy or renal fibrosis remains unclear. IS is produced in the liver by CYP2A6/2E1-dependent oxidative metabolism of dietary protein-derived indole, followed by sulfotransferase 1a1 (SULT1A1)-mediated sulfate conjugation of indoxyl. IS in the blood circulation is efficiently taken up by renal proximal tubules via basolateral membrane-localized organic anion transporters, OAT1 and OAT3, and excreted into urine via unidentified apical membrane-located transporter. Thus, we established SULT1A1 gene-deficient (SULTKO) mice and developed UUO mice to investigate the pathological role of IS in UUO-induced renal fibrosis.

Method: The left ureter of C57BL/6J mice (wild type (WT), 8 weeks-old) and SULTKO mice (8 weeks-old) were obstructed last for 2 weeks. IS concentration in serum and kidney was determined by LC-MS/MS. Changes in histology and interstitial fibrosis were examined with PAS staining and Sirius red staining, respectively. Quantitative PCR was applied for determining expression levels of col1a1 encoding the major component of type I collagen, fibronectin, plasminogen activator inhibitor (PAI)-1, the activator of plasminogen and hence fibrinolysis, pro-inflammatory cytokine interleukin 6 (IL-6), Wnt4 encoding one protein of Wnt and Sfrp5, a gene that codes for antagonist of Wnt pathway. Renal fibrosis also evaluated through the expression of alpha smooth muscle actin (SMA) by Western blotting.

Results: By UUO treatment, the concentration of IS in serum, kidney and liver were elevated, which were suppressed in SULTKO mice. Ureter dilation was obviously observed in the obstructed kidney of WT mice, which was slightly prevented in SULTKO mice with UUO. Sirius red staining revealed that severe collagen deposition was found in the interstitium of WT kidney with UUO, but it was partly prevented in the kidney of KO mice with UUO along with the decrease in IS accumulation. The high expression of SMA, col1a1 and fibronectin in the kidney of WT mice with UUO were significantly suppressed in the kidney of SULTKO mice, 2.3-fold, 1.4-fold and 2.3-fold, respectively, suggesting that renal fibrotic responses were ameliorated in SULTKO mice. The expression of PAI-1, which was upregulated in WT mice with UUO, was also suppressed (1.8-fold) in SULTKO mice with UUO. The elevated expression of IL-6 in the kidney of WT mice with UUO was inhibited (1.8-fold) in SULTKO mice with UUO, indicating the possibility that inflammation-related signalling pathway also participated in the IS-exacerbated renal fibrosis. The enhanced expression of Wnt4 in the kidney of WT mice with UUO was suppressed (1.8-fold) in SULTKO mice with UUO, and the gene of Sfrp5 exhibited a higher expression level (3.2-fold) in the kidney of SULTKO mice with UUO compared with WT UUO mice.

Conclusion: Sult1a1-deficient mice showed the suppressed accumulation of IS in the kidney with UUO. Renal IS accumulation during pathological progression of obstructive nephropathy could enhance interstitial fibrosis through the activation of Wnt signalling pathway. Hepatic SULT1A1 could be a therapeutic target for preventing the progression of renal interstitial fibrosis by suppressing IS production during obstructive nephropathy.

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P0669

HIGH ESTIMATED PHENOTYPIC AGE ASSOCIATES WITH WORSE CLINICAL OUTCOME IN CHRONIC KIDNEY DISEASE PATIENTS

Hokuto Morohoshi[1,2], Ken Iseri[1,3], Lu Dai[1], Thomas Ebert[1], Anna Witasp[1], Bengt Lindholm[1], Olof Heimbürger[1], Franz Peter Barany[1], Louise Nordfors[1], Karolina Kublickiene[1], Abdul Rashid Tony Qureshi[1], Paul Shiels[4], Peter Stenvinkel[1]

[1]Karolinska Institutet, Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden, [2]Showa University, Clinical Research Institute for Clinical Pharmacology & Therapeutics, Tokyo, Japan, [3]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Tokyo, Japan and [4]Institute of Cancer Sciences, University of Glasgow, Wolfson Wohl Cancer Research Center, Glasgow, United Kingdom

Background and Aims: Ageing represents the greatest risk factor contributing to increased morbidity and mortality in most chronic diseases; it encompasses numerous biological changes resulting in declining physiological function and increasing burden of disease. Whether new biomarkers of ageing and risk scores for predicting physiological outcomes, including mortality, are applicable and more accurate than chronological age in patients with chronic kidney disease (CKD) is not clear. So far, the DNA methylation (DNAm) PhenoAge biomarker of ageing (Levine et al. Aging 2018) has not been tested in CKD. While we had no access to DNAm data, we applied the phenotypic age estimate proposed by Levine et al., which was included in their calculations of DNAm PhenoAge, and tested the relationship between estimated phenotypic age (ePhenoAge) and chronological age, respectively, with all-cause mortality in patients with CKD.

Method: In a cohort of 333 CKD patients (stage 1, n=78; stage 3-4, n=64; and stage 5, n=191) with median age 56 years, 43% females, 24% diabetes (DM), 25% cardiovascular disease (CVD), and 22% malnourished, we estimated age by ePhenoAge, using a formula with calculations based on nine biomarkers and chronological age, and compared this age index with chronological age. Framingham risk score, body composition, nutritional status, handgrip strength, and various biochemical markers (white blood cells, mean cell volume, hemoglobin, albumin, creatinine, glucose, calcium, alkaline phosphatase, intact-parathyroid hormone, triglyceride, cholesterol, HDL-cholesterol, high-sensitivity C-reactive protein (hsCRP), and interleukin (IL)-6) were recorded. During a median follow-up period of 52 months, 65 patients died, and 111 patients underwent renal transplantation. We used spline curve to illustrate sub-distribution hazard risk (sHR) for all-cause mortality versus increasing ePhenoAge and chronological age respectively as obtained by the Fine and Gray competing risk analysis.

Results: In univariate analyses, IL-6 (rho=0.49, $p<0.001$; n=268) and hsCRP (rho=0.37, $p<0.001$; n=333) were significantly correlated with ePhenoAge. The ePhenoAge remained significantly associated with hsCRP ($p=0.02$) when adjusted for sex, DM, CVD, nutritional status and CKD stages. The spline curves showing sHR for all-cause mortality derived from multivariate competing risk analysis and adjusted for sex, presence of DM and CVD, hsCRP, nutritional status and CKD stages, showed increased mortality risk with higher chronological age (sHR: 1.08, $p<0.001$). In contrast, the association of mortality with higher ePhenoAge (sHR: 1.04, $p=0.06$) was of borderline statistical significance.

Conclusion: All-cause mortality risk was associated with increasing chronological age in competing risk analysis with adjustments of confounders. A similar trend was observed for ePhenoAge, a finding which to a large extent may be explained by the inflammatory status of the study subjects. However, contrary to expectations, ePhenoAge was not as powerful as chronological age in predicting mortality, underlining that our knowledge about factors influencing phenotypic age in CKD patients is still limited. This should motivate further study of the potential role of other estimates of biological age in CKD.

P0670 DIFFUSIONAL KURTOSIS IMAGING PREDICTS THE PROGNOSIS OF CHRONIC KIDNEY DISEASE.

Yan Liu[1], Gu-mu-yang Zhang[2], Xiaoyan Peng[1], Xuemei Li[1], Hao Sun[2], Limeng Chen[1]

[1]Peking Union Medical College Hospital, Nephrology, Beijing, P.R. China and [2]Peking Union Medical College Hospital, Radiology, Beijing, P.R. China

Background and Aims: Renal fibrosis is the strongest prognosis predictor of ESRD in chronic kidney disease (CKD), but non-invasive and repeatable imaging markers are missing. Magnetic resonance imaging (MRI) has wide range of applications in renal parenchymal diseases, and diffusional kurtosis imaging (DKI) is a new promising non-invasive method of MRI which can provide more information about non-Gaussian diffusion using a polynomial model. We had successfully used DKI to assess renal fibrosis in IgA nephropathy in our previous work. This study aimed to evaluate the prognostic value of DKI in CKD.

Method: We prospectively enrolled forty-two CKD patients in our study in Jan. 2017. On recruitment, the basic clinical data were documented, and DKI was performed on a clinical 3T MR scanner. Region-of-interest (ROI) measurements were performed to determine apparent diffusion coefficient (ADC), kurtosis (K) and diffusivity (D) of the cortex of the kidneys. We had followed up these patients for 3 years, and collected all the clinical data and outcomes. The prognostic value of DKI metrics and clinical parameters were investigated.

Results: Forty-two patients consisted of 26 males and 16 females with mean age of 41.3±15.4 years. The most common etiology was IgA nephropathy (25/42, 59.5%). At baseline, the mean value of serum creatinine (SCr) was 224.4±156.2μmol/L. Among them, 18 patients had eGFR≥45ml/min and 24 patients had eGFR<45ml/min. According to the etiology and CKD classification, all the patients had received appropriate treatment. Besides supportive treatment and management of CKD complications, 21 patients (50%) had received corticosteroid and/or immunosuppressants treatment. After 36 months follow up, 12 patients had progressed to end stage renal disease (ESRD), and the mean value of SCr of the remaining 30 patients was 153.0±78.8umol/L. The Kaplan-Meyer survival regression showed that the patients with eGFR<45ml/min had worse clinical outcomes (p=0.0006). ROC analysis and Kaplan-Meyer survival regression showed that DKI metrics (K≥0.66 or ADC<1.35) not only predicted severe renal fibrosis, but also had worse clinical outcomes (p=0.01 and p<0.0001) (Figure 1). According to the COX regression analysis, both K (K≥0.66, HR 4.676, 95%CI 1.262-17.325) and ADC (ADC<1.35, HR 13.118, 95%CI 3.499-49.178) values, but not age, gender and eGFR group (cut-off value: 45ml/min), were the independent risk factors for the progression to ESRD.

Conclusion: Renal ADC and K values obtained from DKI showed significant predictive value for the prognosis of CKD, could be a promising non-invasive technique in patients follow-up.

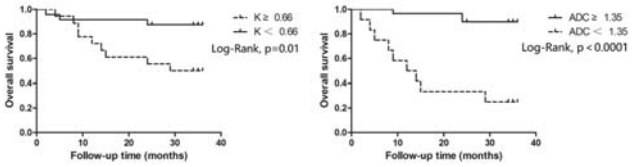


Figure 1. Kaplan-Meyer renal survival curve after 36 months follow-up based on DKI metrics.

P0671

THE ASSOCIATION BETWEEN HYPERKALAEMIA RISK AND CARDIOVASCULAR AND RENAL COMORBIDITIES IN A LARGE REAL-WORLD COHORT OF CKD PATIENTS

Louise Hoskin[1], Karolina Badora[1], Phil McEwan[1], Daniel Sugrue[1], Lei Qin[2], Glen James[3], Michael Hurst[1], Eskinder Tafesse[2]

[1]Health Economics & Outcomes Research Ltd, Cardiff, United Kingdom, [2]AstraZeneca Pharmaceuticals, Gaithersburg, MD, United States of America and [3]AstraZeneca Pharmaceuticals, Cambridge, United Kingdom

Background and Aims: Approximately 275.9 million people globally and 5.6 million people in the UK are living with chronic kidney disease (CKD). The risk of hyperkalaemia (HK) is elevated in CKD due to renal impairment and may increase further upon treatment with renin-angiotensin-aldosterone system inhibitors, which are commonly used in many cardiovascular and renal conditions. This study aimed to assess the relationship between comorbidity burden and HK risk in a large cohort of UK CKD patients.

Method: Primary and secondary care data from the UK Clinical Practice Research Datalink (CPRD) and linked Hospital Episode Statistics (HES) were used to identify patients aged ≥18 years who had a diagnosis of stage 3+ CKD (identified as either a READ code for non-dialysis CKD stage 3+ or an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m^2 without a prior READ code for dialysis) during the study period (2008–June 2018) or the five-year look-back period (2003–2007). Patient's index date was 1st January 2008 or the first date of CKD diagnosis, whichever occurred later. Diagnoses based on the presence of READ codes were used to define the accumulation of further cardiovascular or renal comorbidities of interest (resistant hypertension, heart failure, diabetes or dialysis-dependent CKD). The incidence of HK was defined as serum potassium (K^+) thresholds of ≥5.0, ≥5.5 and ≥6.0 mmol/L.

Results: In total, 297,702 eligible patients had a CKD diagnosis during the study or look back periods and their mean follow-up was 5.6 (SD 3.2) years from index date. At baseline, mean age was 74.7 (11.3) years, mean body mass index was 28.3 (5.9) kg/m^2, and 58.6% of patients were female.

CKD was the first diagnosis in 169,532 patients (56.9% of all CKD diagnoses), second diagnosis in 92,651 patients (31.1%), third in 32,606 patients (11.0%) and fourth or fifth in 2,913 patients (1.0%); however, only 11,129 CKD patients (3.74%) developed four or more comorbidities of interest. In total, 1.5% of the cohort (4,544 patients) progressed to dialysis and 29.6% (88,245 patients) died during the study period.

In general, the incidence of HK increased with the number of comorbidities of interest (Figure 1). At a K^+ threshold of ≥5.0 mmol/L, crude incidence rate of HK was 286.5 (95% CI: 285.2–287.8) per 1,000 patient-years in patients with CKD only; this increased 2.8-fold to 806.8 (741.5–876.4) in patients with five comorbidities of interest. A similar trend was observed at K^+ thresholds of ≥5.5 mmol/L and ≥6.0 mmol/L. A 5.9 fold increase was observed in crude incidence rate of HK (from 59.7 [59.1–60.3] with CKD only, to 350.3 [307.7–397.1] with all five comorbidities) at a threshold of ≥5.5 mmol/L and a 10.6-fold increase (from 9.1 [8.9–9.4] to 96.2 [74.6–122.2]) at the ≥6.0 mmol/L threshold.

Conclusion: This assessment of a large real-world patient cohort showed that the risk of HK in patients with CKD increases with the number of cardiovascular or renal comorbidities. Emphasis should be put on effective prevention and treatment of HK in CKD, especially in patients with high comorbidity burden.

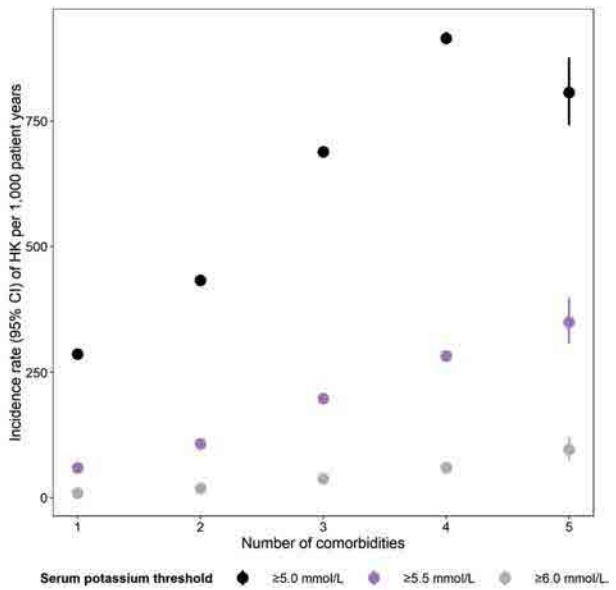


Figure: 1 Incidence rates of HK events by number of comorbidities in the CKD population

P0672

CALPAINS 1 AND 2 ARE INCREASED DURING THE DEVELOPMENT OF CHRONIC KIDNEY DAMAGE IN MICE FED WITH AN ADENINE RICH DIET

Elena Gutiérrez-Calabrés[1,2,3], Sofía Campillo de Blas[2,3], Lourdes Bohorquez Magro[2,3], Mercedes Griera-Merino[2,3], Diego García Ayuso[2,3], David Vaillo[1,2,3], Sergio De Frutos García[1,2,3], Manuel Rodríguez-Puyol[2,3], Laura Calleros[2,3], Diego Rodríguez-Puyol[1,2,4]

[1]Biomedical Research Foundation from Hospital Príncipe de Asturias, Alcalá de Henares, Madrid, Spain, [2]NOVELREN from Comunidad de Madrid, Madrid, Spain, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Fundación Renal Íñigo Álvarez de Toledo (FRIAT) and REDinREN from Instituto de Salud Carlos III, Madrid, Spain, [3]Universidad de Alcalá, Department of Systems Biology, Alcalá de Henares, Madrid, Spain and [4]Nephrology Unit from Hospital Príncipe de Asturias and Department of Medicine from Universidad de Alcalá, Alcalá de Henares, Madrid, Spain

Background and Aims: Calpains are intracellular cysteine proteases that play a critical role in cell remodeling, being involved in multiple biological processes linked to tissue damage and repair mechanisms. In addition, they are released into the circulation, being able to carry out systemic actions with pathological consequences. The aim of this study was to investigate the role of calpains in the progression of chronic kidney disease (CKD) in an experimental model of chronic renal damage induced by adenine.

Method: We induced an experimental model of CKD, in mice fed for 2 weeks with an adenine-supplemented diet (0.2% adenine) (A). Animals receiving this diet develop a tubulointerstitial damage resembling that is observed in human CKD. Mice with standard diet were used as controls (C). Renal function was assessed by measuring serum blood urea nitrogen (BUN) and creatinine (mg/dl). Fibrosis markers (collagen type I and fibronectin) were determined by RT-qPCR. Changes in the renal content of calpains 1 and 2 were analyzed by western blot (protein content), and RT-qPCR (mRNA expression).

Results: Our results show functional and structural changes at renal level in the adenine-fed mice, with increased BUN (A: 72 mg/dl, C: 28 mg/dl, $p < 0.05$), creatinine (A: 0.58 mg/dl, C: 0.25 mg/dl, $p < 0.05$), collagen type I mRNA expression (A: 12.9 units, C: 1.2 units, $p < 0.05$) and fibronectin mRNA expression (A: 3.46 units, C: 1.3 units, $p < 0.05$). Furthermore, protein content of calpains 1 (A: 1.27 units, C: 0.78 units, $p < 0.05$) and 2 (A: 1.30 units, C: 0.66 units, $p < 0.05$) was significantly higher in adenine-fed mice when compared to control. At the same time, we observed a significant increase in gene expression of both calpain 1 (A: 4.21 units, C: 0.51 units, $p < 0.05$) and 2 (A: 4.93 units, C: 0.56 units, $p < 0.05$) in the adenine model regarding to mice with standard diet. Our results demonstrate that calpain 1 and 2 expression in renal tissue increases as CKD progresses. Interestingly, we found statistically significant correlations between renal calpains 1 and 2 protein and mRNA content and plasma BUN and creatinine ($p < 0.05$, r between 0.79 and 0.92), as well as protein expression of calpain 2 and mRNA expression of collagen type I ($p < 0.05$, $r = 0.76$). These data suggest a potential direct relationship between renal calpain 1 and 2 content and loss of renal function, in part due probably to the modulation of the fibrotic changes, in adenine fed mice.

Conclusion: We suggest an implication of calpains 1 and 2 in the development of CKD. Thus, effective calpain blockade or downregulation could be useful as a therapeutic strategy to prevent CKD. Further experiments will be necessary to establish the relationship between these factors.

P0673

INVERSE ASSOCIATION OF TRANSFERRIN SATURATION WITH MORTALITY RISK IN CHRONIC KIDNEY DISEASE

Xin Li[1,1,2], Kristin Danielson[1], Innas Forsal[1], Ken Iseri[1], Lu Dai[1], Olof Heimbürger[1], Franz Peter Barany[1], Peter Stenvinkel[1], Abdul Rashid Tony Qureshi[1], Bengt Lindholm[1]

[1]Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden and [2]Tongji Hospital of Tongji University, Nephrology Department, Shanghai, P.R. China

Background and Aims: Transferrin saturation (TSAT) is an indicator of iron deficiency or overload, but its relationship with mortality in patients with different stages of chronic kidney disease (CKD) is unclear. We investigated the association of TSAT with mortality in CKD patients.

Method: In 479 CKD patients (97 CKD3-4 patients, 298 CKD5 non-dialysis patients and 84 peritoneal dialysis patients; median age 58 years, 67% males, 33% cardiovascular disease, CVD, and 29% diabetes), biomarkers of iron status (plasma iron, TSAT, transferrin and ferritin), systemic inflammation (high sensitivity C-reactive protein, hsCRP, and interleukin-6, IL-6) and nutritional status were assessed. During median follow-up of 35.6 months, 139 (29%) patients died, and 176 (37%) patients underwent renal transplantation. Patients were stratified into low (n=157) and high (n=322) TSAT tertile groups. All-cause and CVD mortality risk were analyzed with competing risk regression with renal transplantation as competing risk.

Results: TSAT [median 23% (IQR 17-30%)] was negatively associated with presence of DM and CVD, body mass index, hsCRP, IL-6, Framinghaḿs CVD risk score (FRS), erythropoietin resistance index (ERI) and iron supplementation, and positively associated with hemoglobin, ferritin and s-albumin. In competing risk analysis, low tertile of TSAT was independently associated with increased all-cause mortality risk (sHR=1.50, 95%CI 1.05-2.14) after adjusting for CKD stages, 1-SD of FRS, 1-SD of hemoglobin, 1-SD of hsCRP, 1-SD of ESA dose and iron supplementation (Figure 1).

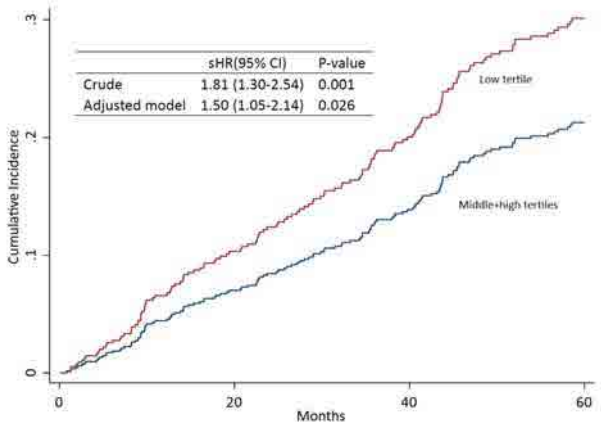


Figure 1. Cumulative incidence curves of 5-years all-cause mortality in relation to tertiles of TSAT levels (n=479). Figure inset show sHR for association of Low vs. Middle and high tertiles of TSAT with mortality in crude and adjusted model.

Conclusion: TSAT was inversely associated with mortality risk in CKD patients. When evaluating clinical outcomes of CKD patients, iron status using TSAT as a predictive marker, should be considered.

P0674

DCR2,AS A SENESCENCE MARKER,IS ASSOCIATED WITH DISEASE SEVERITY AND PROGRESSION IN IGA NEPHROPATHY PATIENTS

Huanzi Dai[1], Wei Hu[1], Jia Chen[1], Yani He[1]

[1]*Daping Hospital,Army Military Medical University, Nephrology, P.R. China*

Background and Aims: Accelerated senescence of renal tubular epithelial cells (RTECs) may contribute to the progression of IgA Nephropathy (IgAN). Our previous studies demonstrated that DcR2 may reflect senescence of RTECs in experimental models and patients with diabetic nephropathy. The objective of this study was to investigate the association of DCR2 with disease severity and progression in IgAN.

Method: We included a retrospective cohort of 105 patients with biopsy proven IgAN. 15 normal renal tissue specimens displaying insignificant alterations biopsied from patients with renal carcinoma were recruited as controls. Renal biopsies from all patients were scored according to Oxford classification (MEST-C score). We analysed the degree of expression and localization of DCR2 in biopsies from kidneys with IgAN, and correlated their immunostaining levels with various clinical and histological parameters at baseline. Cox regression was performed for the composite renal outcome defined as 30% reduction in initial estimated glomerular filtration rate (eGFR) and/or end-stage renal disease (ESRD), and for the individual components during a follow-up for 60 or more months.

Results: DCR2 was overexpressed in the cytoplasm of RTECs obtained from kidneys of patients with IgAN [male: 60.9%, age:39.5±13.0 years, mean arterial pressure (MAP): 95.2±18.0 mmHg, proteinuria: 1.9 (0.7, 3.7)g/day, Initial eGFR:89.8±37.2 ml/min/1.73 m2], and were elevated with the increasing T scores. At baseline, DCR2 protein levels in the RTECs was inversely correlated with eGFR (R=−0.597, P=0.000) and positively associated with 24h-proteinuria (R=0.379, P=0.000) and the T score (R=0.632, P = 0.000). During a median follow-up of 80 (60, 125) months, patients with ≥25% tubular DCR2 positive showed worse eGFR slopes (the rate of eGFR decline) than those<25% DCR2 positive group [4.35 (2.17, 5.53) versus 0.36 (-0.96, 1.19) ml/min per 1.73 m2 per year; P=0.000)]. Kaplan–Meier survival analysis revealed that renal survival for the composite outcome was significantly lower in the ≥25% DCR2 positive group than in the<25% DCR2 positive group (P=0.000). In Cox regression models, ≥25% tubular DCR2 positive expression independently associated with poor renal outcome (HR=2.02, P=0.001) after adjustment for multiple known risk factors for IgAN progression, including baseline proteinuria, hypertension, eGFR, Oxford scores, and steroids/immunosuppressive therapy. Moreover, tubular DCR2 expression showed the highest sensitivity and specificity (80.8% and 87.3%, respectively) at a cut-off value of 25.5% DCR2 positive expression over proteinuria and eGFR for the composite outcome. The area under the receiver operating characteristic curve (AUROC) of tubular DCR2 expression was 0.880.

Conclusion: DCR2 is associated with disease severity and prognosis in IgAN patients and may have additional prognostic value besides established risk markers.

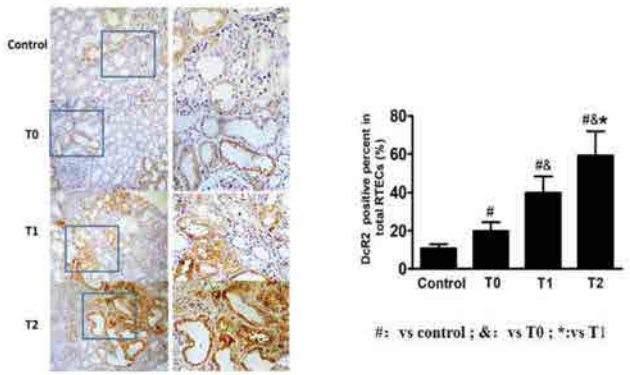


Figure: DCR2 expression levels in renal biopsies from patients with IgAN

P0675 **LEUCOCYTE PODOSOME FORMATION AND ADHESION TO ENDOTHELIUM IS MEDIATED BY INTEGRIN LINKED KINASE IN CHRONIC KIDNEY DISEASE (CKD)**

Sofía Campillo de Blas[1,2], Lourdes Bohorquez Magro[1,2], Elena Gutiérrez-Calabrés[1,2,3], Diego García Ayuso[1,2], David Vaillo[1,2,3], Mercedes Griera-Merino[1,2], Sergio De Frutos García[1,2,3], Manuel Rodríguez-Puyol[1,2], Diego Rodríguez-Puyol[2,3,4], Laura Calleros[1,2]

[1]Alcalá University, Department of Systems Biology, Physiology Unit, Alcalá de Henares, Spain, [2]Instituto Ramón y Cajal de Investigaciones Sanitarias (IRYCIS), Fundación Renal Iñigo Álvarez de Toledo (FRIAT), REDinREN from Instituto de Salud Carlos III, and NOVELREN from Comunidad de Madrid, Madrid, Spain, [3]Príncipe de Asturias University Hospital, Biomedical Research Foundation, Alcalá de Henares, Spain and [4]Nephrology Unit from Príncipe de Asturias University Hospital and Department of Medicine from Alcalá University, Alcalá de Henares, Spain

Background and Aims: Patients with CKD have a higher risk of developing cardiovascular diseases. Protein-bound uremic toxins, such as *p*-cresol (pc) and indoxyl-sulfate (IS), are retention solutes, poorly removed during hemodialysis. They lead to endothelial dysfunction inducing the expression of adhesion molecules and leucocyte adhesion to endothelium. Monocyte extravasation can be carried out by dynamic adhesion structures called podosomes. Integrin-linked kinase (ILK), a kinase and an intracellular scaffold protein, links the cell-adhesion receptors, integrins and growth factors to the actin cytoskeleton and to a range of signalling pathways. We demonstrate the role of ILK in the accumulation of integrin-associated proteins inside the podosomes. The aim of this study was to investigate if ILK is involved in uremic toxin-induced leucocyte podosome formation and adhesion under uremic conditions that simulate CKD.

Method: *In vitro* experiments were carried out in human cell line of leukemic monocytes, THP-1. We tested the effect of uremic toxins on cell viability and ILK expression levels or activation by performing dose and time-response experiments. Cells were exposed to IS (25-100 $\mu g\ ml^{-1}$) plus pc (10-100 $\mu g\ ml^{-1}$) both combined, for different times. ILK expression levels were determined by Western Blot and RT-qPCR and its kinase activity was tested by its downstream effector GSK-3β phosphorylated levels. Cell adhesion of THP-1 cells stained with cell tracker to a monolayer of human endothelial cells (EA.hy926) and podosome formation and cell adhesion of THP-1 cells stained with phalloidin to a fibronectin extracellular matrix, was determined by fluorescence confocal microscopy. ILK co-localization with podosome specific protein cortactin was assessed by fluorescence confocal microscopy. For *ex vivo* experiments in ILK conditional-knockdown mice (cKD-ILK), male CRE-LOX mice were injected with tamoxifen (cKD-ILK) or vehicle (wild-type, WT), to induce ILK deletion. Peripheral blood mononuclear cells (PBMCs) were obtained and treated with uremic toxins. Cell adhesion to a fibronectin extracellular matrix was determined by cell count of the percentage of attached cells against the total cells collected.

Results: Our data suggests that uremic toxins did not induce toxicity in THP-1 cells. Furthermore, ILK was activated by uremic toxins both at low and high concentrations, without changes in the protein expression. In the cell adhesion assay to the endothelium, uremic toxins induces an increase of THP-1 cells adhesion, which is completely abolished when ILK is knocked down by ILK siRNA, both at low and high toxins concentrations. Similar results were obtained from the cell adhesion assay to the fibronectin extracellular matrix. Moreover, uremic toxins induced podosome formation in THP-1 cells, even at low concentrations, compared to the control, while ILK knockdown abrogated almost completely fibronectin adhesion and podosome formation in uremic toxin-treated cells. Interestingly, we tested that ILK co-localize with cortactin in podosomes, which confirmed the implication of ILK in podosome structures formation induced by uremic toxins. In cKD-ILK PBMC mice the transgenic ILK depletion significantly decrease non-excised ILK mRNA levels. These cKD-ILK PBMC mice exhibited a lower adhesion to the fibronectin extracellular matrix compared to WT. By last, uremic toxins induced a significant increase of mice PBMCs adhesion in WT animals compared to the control that was significantly lower in PBMCs of cKD-ILK animals.

Conclusion: These data suggest that ILK plays a critical role in the required processes for leukocyte extravasation. ILK deletion may prevent podosome formation and adhesion of leucocytes, decreasing the endothelial and vascular damage caused by the accumulation of uremic toxins in CKD. Therefore, ILK could be a potential therapeutic target for the treatment of vascular damage associated with CKD.

P0676 CHOLESTEROL ABSORPTION JUGDED BY CAMPESTEROL / LATHOSTEROL RATIO AND OUTCOMES IN CHRONIC KIDNEY DISEASE

Insa Elena Emrich[1], Gunnar Henrik Heine[2], Schulze Christian[3], Kyrill S. Rogacev[4], Danilo Fliser[5], Wagenpfeil Stefan[6], Michael Böhm[7], Lütjohann Dieter[8], Weingärtner Oliver[3]

[1]Saarland University Hospital, Internal Medicine, Homburg, Germany, [2]AGAPLESION MARKUS KRANKENHAUS, Nephrology, Frankfurt am Main, Germany, [3]University of Jena, Cardiology, Jena, Germany, [4]Sanaa Klinikum Wismar, Cardiology, Wismar, Germany, [5]Saarland University Medical Center, Nephrology, Homburg, Germany, [6]Saarland University Medical Center, Statistics, Homburg, Germany, [7]Saarland University Medical Center, Cardiology, Homburg, Germany and [8]University of Bonn, Pharmacology, Bonn, Germany

Background and Aims: In dialysis patients, cholesterol-lowering therapy with statins is less effective than in other high-risk patients. This may partly be explained by a shift from cholesterol synthesis, which is inhibited by statin treatment, towards cholesterol absorption, which is inhibited by ezetimibe. In line, markers of cholesterol absorption – such as campesterol - better predict atherosclerotic cardiovascular events than markers of cholesterol synthesis – such as lathosterol - in dialysis patients. We now investigated in our CARE FOR HOMe study whether a similar shift towards cholesterol absorption occurs in non-dialysis chronic kidney disease (CKD), and whether the campesterol / lathosterol ratio predicts outcome in non-dialysis CKD patients.

Method: Since 2008, 599 participants suffering from chronic kidney disease have been included into the CARE FOR HOME study, an observational cohort study. 555 patients had baseline samples available for analyses of the lathosterol / cholesterol ratio as a marker for cholesterol synthesis, and the campesterol / cholesterol ratio as a marker for cholesterol absorption. We excluded those participants who were currently treated with statins or other lipid lowering drugs, leaving 251 patients for this analysis. Participants were followed annually for major atherosclerotic cardiovascular events (MACE), defined as non-fatal acute myocardial infarction, non-fatal ischemic stroke, cerebrovascular / peripheral arterial or coronary revascularization, major amputation above the ankle and cardiovascular death. Additionally, all-cause death and the composite endpoint MACE and all-cause death were explored. We performed univariate (Model 1) and multivariate Cox regression analysis, adjusting for age, gender (Model 2), estimated glomerular filtration rate (eGFR), log-transformed albuminuria (Model 3), prevalent cardiovascular disease, current smoking, diabetes mellitus, systolic blood pressure and body mass index (Model 4). The primary hypothesis was that patients with a high campesterol / lathosterol ratio had a higher event rate.

Results: Neither lathosterol / cholesterol ratio ($r = 0.022$, $p = 0.730$), nor campesterol / cholesterol ratio ($r = 0.042$; $p = 0.519$) nor the campesterol / lathosterol ratio ($r = -0.103$; $p = 0.105$) correlated significantly with eGFR. During follow-up of 5.1 ± 2.1 years, 47 participants suffered from MACE, 46 participants died and 61 participants reached the composite endpoint of MACE or all-cause death. In univariate Cox regression analysis, campesterol / lathosterol ratio did not significantly predict atherosclerotic cardiovascular events (HR 0.740; 0.368 – 1.487), all-cause death (HR 0.564; 0.277 – 1.145) or the composite endpoint (HR 0.652; 0.355 – 1.196). After full adjustment, results were not different: Campesterol / lathosterol ratio was not significantly associated with all three endpoints: MACE (HR 1.064; 0.507 – 2.231), all-cause death (HR 0.818; 0.420 – 1.594) and MACE and all-cause death (HR 0.956; 0.525 – 1.744).

Conclusion: We did not observe a shift from cholesterol synthesis to cholesterol absorption across the spectrum of non-dialysis CKD. Campesterol / lathosterol ratio did not predict future MACE or all-cause death in non-dialysis CKD. These findings do not support the concept that CKD patients may preferentially benefit from ezetimibe rather than from statin treatment.

P0677

CONTRAST-ENHANCED ULTRASOUND TO ASSESS RENAL MICROCIRCULATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Jonas Garessus[1], Wendy Brito[1], Nicolas Loncle[1], Anna Vannelli[1], Grégoire Wuerzner[1], Antoine Schneider[2], Menno Pruijm[1]

[1]University Hospital of Lausanne and University of Lausanne, Internal Medicine, Nephrology, Lausanne, Switzerland and [2]University Hospital of Lausanne and University of Lausanne, Intensive Care Unit, Lausanne, Switzerland

Background and Aims:

Vascular factors such as capillary rarefaction, increased vascular stiffness and reduced vasodilatation due to endothelial dysfunction probably play an important role in the pathophysiology of chronic kidney disease (CKD). However, our understanding of the underlying mechanisms is hampered by the lack of non-invasive techniques to quantify renal microvasculature in humans. The aim of this study was to assess whether contrast-enhanced ultrasonography (CEUS) can identify (1) differences in renal microcirculation and (2) the degree of nitroglycerin-induced vasodilatation (NIV) as a measure of renal flow reserve between CKD-patients and age-matched healthy volunteers.

Method:

All participants underwent CEUS under standardized conditions. Sonovue© (0.015 ml/kg/min) was perfused as contrast agent until a steady state was obtained, followed by four destruction-refilling sequences. Outcome measure of CEUS was the mean (change in) perfusion index (PI) of the outer renal cortex (see figure for an example). In a subgroup of participants, CEUS was repeated before and five minutes after the sublingual administration of nitroglycerin (0.2mg). Renal resistive index (RRI) as a measure of vascular stiffness was also measured at each time point with Doppler ultrasound.

Results:

A total of 38 healthy volunteers (aged 50±8 years, eGFR 95±13 ml/min/1.73 ṁ, 69% women) and 18 CKD stage 2-3 patients (aged 55±15 years, eGFR 64±32 ml/min/1.73ṁ, 56% women) were included. Renal PI was significantly lower in CKD patients (1304±762 vs 2989 ±2503 arbitrary units, p=0.034), whereas RRI did not differ (0.66± 0.07 vs 0.63± 0.04), p=0.10). PI was lower in CKD due to vascular nephropathy (n=3) or interstitial nephritis (n=4) than CKD due to diabetes (n=4) or other causes (7). In continuous analysis, PI correlated with eGFR (spearman's r=0.54, p=0.005) but not with blood pressure. Renal PI did not change after nitroglycerin in both groups; RRI decreased in healthy (from 0.64±0.03 to 0.61±0.02, p=0.01) but not in CKD patients.

Conclusion:

In this study, contrast-enhanced ultrasound identified important alterations in renal microperfusion in patients with moderate CKD. Whether a low perfusion index predicts renal function decline needs further study. Sublingual nitroglycerin seems to have limited potential as a new test of renal flow reserve.

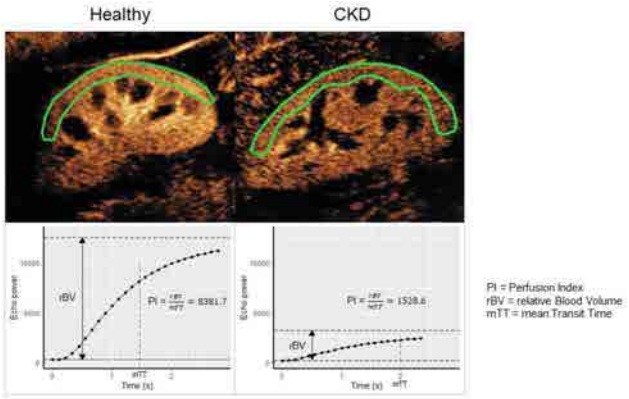


Figure:

P0678

RENAL SUBCAPSULAR ADMINISTRATION OF ADIPOSE DERIVED MESENCHYMAL STEM CELLS PREVENTED THE PROGRESSION OF RENAL DAMAGE IN AN EXPERIMENTAL MODEL OF CKD

Marina P Claro[1], Krislley R Pereira[1], Everidiene KVB Silva[1], Flavio Teles[3], Paulyana F Barbosa[4], Irene L Noronha[1], CAMILLA FANELLI[1]

[1]University of São Paulo, Medicine - Nephrology, São Paulo, Brazil, [3]UNICSAL, Medicine - Nephrology, Maceio - Alagoas, Brazil and [4]UNICSAL, Medicine - Nephrology, Alagoas - Maceio, Brazil

INTRODUCTION / AIMS

Chronic kidney disease (CKD) is a progressive, debilitating condition of high lethality, which prevalence have been increasing considerably in recent decades. CKD can be triggered by many different factors, such as genetic predisposition, systemic hypertension, diabetes mellitus and autoimmune diseases. It is characterized by the gradual loss of renal function, leading to kidney failure and the need for renal replacement therapy for the maintenance of life. Regardless of the etiology of CKD, the establishment of local renal inflammation, with leucocyte recruitment, cell proliferation, extracellular matrix accumulation, glomerular and tubulointerstitial fibrosis, contribute significantly to its establishment and evolution. Due to its known pathophysiology, the primary aim when clinically treating CKD is to slow the progression of renal function loss and the advance of inflammation. However, until the present moment, there is no efficient pharmacological treatment to completely arrest the aggravation of renal inflammation and, specially, renal fibrosis. This motivates the scientific community to develop experimental research in order to test new therapeutic approaches to stunt renal fibrosis. In this context, experimental application of mesenchymal stem cells (mSC) as a treatment to control renal inflammation have been showing promising results in studies with animal models of CKD. The aim of the present study was to analyze the renoprotective effects of subcapsular application of Adipose Tissue-derived mSC (ASC), in rats submitted to 5/6 nephrectomy, after the establishment of the disease (15 days after CKD induction), in order to more closely resemble the clinical settings in humans.

METHODS

ASC were obtained from gonadal adipose tissue from healthy male Wistar rats. These cells were cultured until P4 when characterization by flow cytometry and in vitro differentiation were performed. Male Wistar rats underwent 5/6 nephrectomy and were followed for 15 days until the complete establishment of CKD (group CKD 15d). At this time, animals underwent a new surgery in which they received a subcapsular injection of $2x10^6$ ASC diluted in 10 µL of sterile PBS (group CKD + ASC 30d), or only 10 µL of sterile PBS (group CKD 30d). Sham-operated rats, euthanized at day 15 (Sham 15d) and 30 (Sham 30d) were used as controls. Survival rate, body weight (BW), 24h urinary protein (24h UPE) and albumin (24h UAE) excretion serum creatinine (SCr) and blood urea nitrogen (BUN) concentration, percentage (GS%) and index (GSI) of glomerulosclerosis, tubulointerstitial fibrosis (INT%) and renal infiltration by macrophages (CD68) were studied at 15 and 30 days after 5/6 nephrectomy. Our results are presented as Mean ± SE. Differences among groups were analyzed by one-way ANOVA.

RESULTS

ASC injection significantly improved the survival rate of CKD + ASC 30d animals, compared to the observed in the untreated group. Moreover, ASC treatment markedly reduced protein and albumin urinary excretion, prevented the development of glomerulosclerosis, both the percentage of sclerotic glomeruli and the index of glomerular damage, numerically reduced interstitial fibrosis and significantly avoided renal inflammation by halting the progression of renal cortical macrophage infiltration.

CONCLUSIONS

According to our results, subcapsular ASC application promoted considerable renoprotection in the 5/6 renal ablation model, even after the complete establishment of severe CKD, suggesting that experimental therapy with these cells could be associated to the current pharmacological treatments employed to detain the progression of CKD.

	EXPERIMENTS AFTER ESTABLISHED CKD				
	15 days		30 days		
	Sham 15d (n=9)	CKD 15d (n=13)	Sham 30d (n=13)	CKD 30d (n=14)	CKD + ASC 30d (n=15)
Survival rate	100%	69%*	100%#	75%*a	93%#
BW (g)	315 ± 19	263 ± 10*	356 ±12 a	304 ± 6a	284 ± 12a
24h UPE (mg/24h)	22 ± 4	81 ± 20	22 ± 2	196 ± 41*#b	125 ± 32a
24h UAE (mg/24h)	1.0 ± 0.4	50.9 ± 19.0*	1.1 ± 0.4*#	121.8 ± 28.3*a	67.9 ± 20.6*a
SCr (mg/dL)	0.70 ± 0.06	0.91 ± 0.12	0.65 ± 0.04	0.97 ± 0.11	1.20 ± 0.17*a
BUN (mg/dL)	56 ± 5	105 ± 13*	51 ± 4*	88 ± 8a	106 ± 15*a
GS (%)	7 ± 3	28 ± 10*	7 ± 3*#	32 ± 6*a	23 ± 10*
GSI	1.7 ± 0.8	6.1 ± 1.7*	1.6 ± 0.6#	9.7 ± 2.5*a	7.7 ± 3.9
INT (%)	1.2 ± 0.2	3.2 ± 1.1	1.1 ± 0.2#	5.7 ± 1.5*a	3.3 ± 0.9*a
CD68 (cell/mm²)	38 ± 6	100 ± 17	39 ± 6	173 ± 39*a	105 ± 19

*: p<0.05 vs. Sham 15d; #: p<0.05 vs. CKD 15d; a: p<0.05 vs. Sham 30d; b: p<0.05 vs. CKD 30d

Figure

P0679

LOSARTAN REDUCES INFLAMMATION INDUCED BY TERTIARY LYMPHOID TISSUES IN ENSUING CKD AFTER ACUTE KIDNEY INJURY

YU-HAN SHAO[1], Yu-Hsiang Chou[1,2,3], SHUN-YANG CHENG[1], SHUEI-LIONG LIN[1,3]

[1]National Taiwan University, Graduate Institute of Physiology, College of Medicine, Taipei, Taiwan, R.O.C., [2]National Taiwan University Hospital, Jin-Shan Branch, Department of Internal Medicine, New Taipei City, Taiwan, R.O.C. and [3]National Taiwan University Hospital, Renal division, Department of Internal Medicine, Taipei, Taiwan, R.O.C.

Background and Aims: Chronic inflammation and renin-angiotensin system (RAS) overactivation have been demonstrated as a central mechanism that results in the development of progressive chronic kidney disease (CKD). Evidences have indicated that tertiary lymphoid tissues (TLT) form after acute kidney injury (AKI), especially in old-aged mice. Heterogeneous fibroblasts which appear and secret proinflammatory cytokines after AKI underlie TLT formation. There is an association between TLT sizes and impaired renal function along with increase of proinflammatory cytokines, suggesting a probable cause of persistent inflammation after AKI. In this study, we explored the relationship between TLT development and RAS activity. The phenotypes of heterogeneous fibroblasts diversified after AKI is also investigated.

Method: Here we utilized ischemia-reperfusion injury to cause ensuing CKD both in a CD-1 and C57BL6J mice model. We also used staining of CD3 and B220 to label and confirm multiple TLTs which represents T and B lymphocytes respectively.

Results: Administration of losartan, a kind of RAS inhibitor, offered protection against subsequent CKD development and attenuated number and size of TLT besides blood pressure reduction. Moreover, heterogeneous fibroblasts diminished and proinflammatory cytokines such as CXCL13, CCL21 and CCL19 which trigger the initiation of TLT were downregulated. In experiments of several fibroblast cell lines, angiotensin II (Ang II) administration could induce differentiation of fibroblasts with distinct phenotypes expressing p75 neurotrophin receptor and retinaldehyde dehydrogenase 2 which contribute to TLT formation. These fibroblasts expressing PDGFRβ stimulated production of aforementioned proinflammatory cytokines and expression of pro-fibrotic genes.

Conclusion: Our data demonstrates that TLT plays an important role in AKI-CKD transition. We also verify that Ang II causes phenotypic change of fibroblasts which constitute TLT. Losartan can ameliorate TLT formation through inhibition of these distinctive fibroblasts. It is a plausible mechanism to reduce ensuing CKD.

P0680

A POST-HOC ANALYSIS OF EFFICACY AND SAFETY OF TOLVAPTAN (TOL) IN DECREASING RATE OF RENAL FUNCTION DECLINE IN PATIENTS WITH VERY LATE-STAGE AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD)

Vicente Torres[1], Ronald Gansevoort[2], Ron Perrone[3], Arlene Chapman[4], John Ouyang[5], Jennifer Lee[5], Hina Japes[5], Tao Wang[5]

[1]Mayo Clinic, [2]University Medical Center Groningen, [3]Tufts Medical Center, [4]University of Chicago and [5]Otsuka Pharmaceutical Development & Commercialization, Inc

Background and Aims: ADPKD is a progressive inherited disease that causes end-stage renal disease (ESRD) in ∼50% of the affected individuals by 60 years of age. TOL, a selective vasopressin V_2-receptor antagonist, has been shown in randomized, placebo-controlled trials to slow the progression of renal function decline in ADPKD subjects with an eGFR of 25 mL/min/1.73m^2 or higher. The efficacy and safety of TOL in subjects with lower eGFR remain understudied. This post-hoc analysis evaluated the efficacy and safety of TOL in subjects with stage 4 ADPKD (eGFR of <30 mL/min/1.73m^2).

Method: This is a retrospective analysis of a subgroup of ADPKD subjects who enrolled in the TOL long-term open-label extension (OLE) trial (NCT02251275). Included subjects had a baseline eGFR of <30 mL/min/1.73m^2, received ≥ 1 TOL dose, and were randomized to the placebo group in the REPRISE trial (NCT02160145). Two subgroups of subjects were analyzed, one with baseline eGFR of 25-30 (Subgroup 1) and one with <25 (Subgroup 2). The variables evaluated included: 1) demographics, 2) adverse event (AE) profile, 3) intra-subject comparison of change in annualized eGFR decline during the open-label study (treatment period) to that during placebo use in the REPRISE trial (control period). Annualized eGFR change slopes in the treatment period were calculated using eGFR values between Month 1 and 12 visits to compensate for the acute hemodynamic effect of tolvaptan. Comparison was made by linear mixed model.

Results: Of the 1,803 subjects enrolled, 159 (8.8%) subjects (76 in Subgroup 1 and 83 in Subgroup 2) met the selection criteria for analysis. Annualized eGFR change slopes for all subjects (n=148) were -5.28 (SE 0.27) in the control period and -3.16 (SE 0.30) in the treatment period with a treatment effect of 2.11 mL/min/1.73m^2/year (95% CI 1.56, 2.66), p<0.0001). Demographic information, baseline eGFR, treatment duration and effects in the 2 subgroups are shown in the Table below. Treatment-emergent AEs were observed in 95% and 90% of the subjects in the 2 subgroups, respectively. Discontinuation due to AEs occurred in 15% and 17% of the 2 subgroups, respectively. The 5 most common AEs for all subjects were thirst (32%), polyuria (30%), renal pain (25%), blood creatinine increase (23%) and nocturia (22%); the rates were similar between the 2 subgroups. One incidence of hepatic enzyme increase, hemodialysis and death (unrelated to TOL) was observed in Subgroup 2, but not in Subgroup 1.

Conclusion: This post-hoc analysis demonstrated that TOL significantly decreases the rate of eGFR decline in ADPKD subjects with stage 4 CKD, including those with an eGFR of <25 mL/min/1.73m^2.

Table. De mographics, Treatment Information and Effects

	Subgroup 1 (Baseline eGFR 25-30)		Subgroup 2 (Baseline eGFR <25)	
n	76		83	
Mean Age	49.9		48.3	
% Male	61		50	
Mean Baseline eGFR (SD)	27.4 (1.5)		21.5 (2.8)	
Median Treatment Duration in Days (Inter-Quarter Range)	570 (385 – 736)		540 (333 – 632)	
Treatment and Study	Placebo REPRISE	Tolvaptan OLE	Placebo REPRISE	Tolvaptan OLE
Mean Change of Annualized eGFR Slope (SE)	-4.95 (0.42)	-2.95 (0.47)	-5.60 (0.33)	-3.43 (0.37)
Treatment Effect (95% CI)	1.99 (1.12, 2.86)		2.17 (1.50, 2.85)	
p Value	<0.0001		<0.0001	

P0681 **TIMP-1 DEFICIENCY DAMPENS RENAL GALECTIN-3 RESPONSE IN DIABETES**

Gabor Kokeny[1,2], Helga Popovics[1,2], Krisztina Mikone[1], Miklos Mozes[1,2]

[1]Semmelweis University, Dept of Translational Medicine, Budapest, Hungary and [2]Semmelweis University, International Nephrology Research and Training Center, Budapest, Hungary

Background and Aims: Overexpression of tissue inhibitors of metalloproteases (TIMPs) are a hallmark of renal fibrosis, and elevated TIMP-1 has been reported in experimental and human diabetes. Also, renal galectin-3 (Lgals3) overproduction might link macrophages to fibrosis progression. However, the possible association of renal Lgals3 with TIMP-1 in diabetes is still unclear. Thus, we investigated nephropathy and renal Lgals3 in type-1 diabetic wild type and TIMP-1 knockout (KO) mice.

Method: Type-1 diabetes was induced in 6 week-old male TIMP-1 KO (DM KO, n=7) and wild type (DM, n=6) mice with daily intraperitoneal streptozotocin (50 mg/kg/day) injections for 5 consecutive days. Non-diabetic controls (CTL, n=5) were injected with vehicle. Fasting blood glucose was monitored, and after 8 weeks kidneys were analyzed for histology and mRNA expression.

Results: Both diabetic groups developed similar hyperglycemia (CTL: 6±2, DM: 29±5, DM KO: 33±7 mmol/l, $p<0.01$). However, serum creatinine was elevated only in wild type diabetic mice (CTL: 9±2, DM: 47±28, DM KO: 11±2 ug/dl, $p<0.001$). Histology revealed significant tubular damage in DM mice (score: CTL: 0.4±0.1, DM: 2.3±0.2, DM KO: 1.6±0.2, $p<0.05$), accompanied by 10-fold lipocalin-2 (CTL: 1.0±0.3, DM: 10.9±6.2, DM KO: 3.3±1.7, $p<0.05$) and 2-fold collagen-1 overexpression (CTL: 1.0±0.2, DM: 1.9±0.7, DM KO: 1.2±0.4, $p<0.05$), practically absent in diabetic KO kidneys. Similarly, TIMP-1 deficiency was associated with twofold decrease in renal Lgal3 (CTL: 1.0±0.6, DM: 2.0±1.1, DM KO: 0.8±0.3, $p<0.05$) and tenfold decrease in CCL2 expression levels (CTL: 1.0±0.3, DM: 20.2±4.2, DM KO: 2.3±1.5, $p<0.01$) as compared to DM.

Conclusion: In our model of type-1 diabetes, TIMP-1 deficiency attenuated the development of renal fibrotic and inflammatory response by reducing galectin-3 and CCL2 (MCP-1), preserved tubular integrity and renal function. This might implicate TIMP-1 to be a possible therapeutic target in the future.

P0682 PSYCHOLOGICAL STRESS AS A RISK FACTOR FOR RENAL FUNCTION DECLINE

Jaeyoung Kim[1], Jihye Kim[1], Chan-Young Jung[1], Wonji Jo[1], Jung Tak Park[1]

[1]*Severance Hospital, Internal Medicine, Seoul, Korea, Rep. of South*

Background and Aims: Accumulating evidences propose that psychological stress leads to changes in biological processes or behavioral patterns that effects disease risks. Supporting this possibility, recent animal experiments and population studies show a probable link between psychological stress and cardiovascular and metabolic diseases. However, the association between psychological stress and kidney function is not well elucidated yet.

Method: Data were retrieved from a prospective community-based cohort study (Korean Genome and Epidemiology Study). Psychological distress was assessed as the primary exposure using PWI-SF (psychosocial well-being index short form) scores. The decline rate of estimated glomerular filtration rate (eGFR) over time was calculated using linear regression analysis of serial eGFR measurements for each subject. Rapid eGFR decline was defined as an average decline in eGFR $\geq$3 ml/min/1.73 m2 per year.

Results: In total, 6,968 participants were analyzed. During a median follow-up of 10.49 years, rapid eGFR decline was observed in 886 (12.7%) participants. When the participants were categorized into tertiles according to PWI-SF score, rapid eGFR decline was more prevalent in the highest PWI-SF score group (14.0%) compared to the lowest PWI-SF score group (11.1%). Multivariate logistic regression analyses revealed that the risk of rapid eGFR decline was significantly increased in the highest PWI-SF score group compared to the lowest group (odds ratio, 2.04; 95% confidence interval 1.27-3.27). When PWI-SF score was treated as a continuous variable, each 1 standard deviation increase in PWI-SF was associated with a 12% increased risk of rapid eGFR decline.

Conclusion: The amount of psychological stress was significantly associated with an increased risk of rapid renal function decline in participants with normal renal function.

Table 1. Baseline characteristics between groups assorted by the level of psychological distress

	Total (n=6968)	PWI groups			P
		Healthy group (n=3992)	Potentially stressful group (n=2866)	High-risk group (n=110)	
Male (%)	3384 (48.6)	2148 (53.8)	1205 (42.0)	31 (28.2)	<0.001
Age (y)	52.20 ± 8.83	52.17 ± 8.70	52.02 ± 8.95	57.87 ± 8.59	<0.001
Educational attainments lower th an high school graduates (%)	5979 (85.8)	3335 (83.5)	2540 (88.6)	104 (94.5)	<0.001
Income groups					<0.001
High income (%)	137 (2.0)	98 (2.5)	39 (1.4)	0 (0.0)	
Middle income (%)	2364 (33.9)	1423 (35.6)	928 (32.4)	13 (11.8)	
Low income (%)	4467 (64.1)	2471 (61.9)	1899 (66.3)	97 (70.5)	
Married (%)	6289 (90.3)	3637 (91.1)	2563 (89.4)	89 (80.9)	<0.001
BMI (kg/m^2)	24.60 ± 3.13	24.73 ± 3.07	24.44 ± 3.18	24.22 ± 3.89	<0.001
History of alcohol ingestion					<0.001
None (%)	3197 (45.9)	1758 (44.0)	1368 (47.7)	71 (64.5)	
Past drinker (%)	413 (5.9)	264 (6.6)	143 (5.0)	6 (5.5)	
Current drinker (%)	3358 (48.2)	1970 (49.3)	1355 (47.3)	33 (30.0)	
History of smoking					<0.001
None (%)	4110 (59.0)	2268 (56.8)	1769 (61.7)	73 (66.4)	
Past smoker (%)	1139 (16.3)	752 (18.8)	374 (13.0)	13 (11.8)	
Current smoker (%)	1719 (24.7)	972 (24.3)	723 (25.2)	24 (21.8)	
Hypertension (%)	1087 (15.6)	591 (14.8)	466 (16.3)	30 (17.2)	0.001
Diabetes mellitus (%)	447 (6.4)	239 (6.0)	197 (6.9)	11 (10.0)	0.101
Cerebrovascular accident (%)	74 (1.1)	33 (0.8)	37 (1.3)	4 (3.6)	0.005
Baseline eGFR (mL/min/1.73 m^2)	92.07 ± 14.01	92.09 ± 14.05	92.15 ± 13.98	89.23 ± 13.16	0.099
PWI score	17.27 ± 8.69	11.17 ± 4.92	24.95 ± 4.62	38.71 ± 1.91	<0.001
Rapid decline in renal function	886 (12.7)	443 (11.1)	416 (14.5)	27 (14.0)	<0.001
Hemoglobin (g/dL)	13.62 ± 1.56	13.74 ± 1.56	13.48 ± 1.55	13.14 ± 1.41	<0.001
Total cholesterol (mg/dL)	191.04 ± 34.93	190.85 ± 34.79	191.28 ± 35.19	191.38 ± 33.77	0.877
Serum total protein (mg/dL)	7.30 ± 0.45	7.30 ± 0.44	7.29 ± 0.45	7.23 ± 0.42	0.102
BUN (mg/dL)	13.95 ± 3.71	14.08 ± 3.70	13.77 ± 3.71	14.00 ± 3.90	0.003
Serum sodium (mmol/L)	142.57 ± 2.17	142.58 ± 2.19	142.54 ± 2.15	142.90 ± 2.12	0.213
Serum potassium (mmol/L)	4.49 ± 0.41	4.51 ± 0.42	4.47 ± 0.39	4.51 ± 0.50	<0.001

Note: Data are expressed as either mean ± standard deviations or numbers (%), except where noted.
It is defined as rapid decline in renal function if the annual decrease in eGFR of a subject is above -3 mL/min/1.73 m2.
Income groups are sorted according to classification criteria made by OECD; high income as an income level above 150% of a median income of a population, low income as an income level below 50% of a median income, and middle income as the rest.
PWI groups are sorted as follows; PWI score of more than 27 as high-risk group, PWI score of less than 8 as healthy group, and the rest as potentially stressful group.
Abbreviations: eGFR, estimated glomerular filtration rate; BMI, body mass index; PWI, psychosocial well-being index; OECD, Organization for Economic Cooperation and Development.

Figure:

P0683

PATTERNS OF HYPERKALAEMIA RECURRENCE AMONG CHRONIC KIDNEY DISEASE PATIENTS IN UK CLINICAL PRACTICE

Michael Hurst[1], Louise Hoskin[1], Karolina Badora[1], Eskinder Tafesse[2], Daniel Sugrue[1], Lei Qin[2], Glen James[3], Phil McEwan[1]

[1]Health Economics and Outcomes Research Ltd, Cardiff, United Kingdom, [2]AstraZeneca Pharmaceuticals, Gaithersburg, MD, United States of America and [3]AstraZeneca Pharmaceuticals, Cambridge, United Kingdom

Background and Aims: Patients with chronic kidney disease (CKD) are at increased risk of hyperkalaemia, HK (high serum potassium concentration) due to impaired renal function. This medical condition is potentially life threatening if untreated or poorly managed. This study describes the characteristics of CKD patients in the UK who experience HK and assessed the frequency of recurrent HK and time between first (index) and subsequent events.

Method: A retrospective cohort study was conducted using linked Clinical Practice Research Datalink (CPRD) and Hospital Episode Statistics (HES) data from 01 January 2008 to 30 June 2018, with a five-year lookback period (2003-2007).

Patients were included if they were diagnosed with CKD stage 3+ (READ code or eGFR $<$60 mL/min/1.73m^2 without prior dialysis) during the study or lookback periods and aged $>$18 years at diagnosis (index).

Patient demographics, clinical history and baseline medication use were described. HK was defined as serum K+ $\geq$5.0 mmol/L. HK events occurring during the study period, but after diagnosis of CKD, were assessed. Recurrent HK was defined as any event subsequent to the first event. Time to recurrence was calculated using Kaplan-Meier.

Results: In total, 297,702 CKD patients (mean age 74.7 years [standard deviation: 11.3], male [41.4%]) met eligibility criteria. At time of CKD diagnosis, 30.6% of the population had resistant hypertension. Other prominent comorbidities included diabetes (22.24%), CKD (7.9%) and cancer (7.8%). Approximately half of patients were in receipt of diuretics at baseline (49.2%), while 32.5% and 32.0% were in receipt of beta blockers and calcium channel blockers, respectively. During follow up, 67.0% of patients received a renin-angiotensin aldosterone system inhibitor (RAASi).

147,215 patients (49.5%) experienced at least one HK event, of which 53,695 (36.5%) had only one HK event, 93,250 (63.5%) had two or more HK events and 29,413 (20.0%) had six or more events. HK event incidence was predictive of subsequent events, with the probability of experiencing a HK event increasing from 49.5% to 63.5%, 70.7%, 74.1%, 76.5% and 78.6% for patients experiencing 2-6 events, respectively. There was an inverse relationship between the number of recurrent events and time to next event, with less time between the next event for those experiencing multiple events (Figure 1).

Conclusion: This study shows that approximately half of CKD patients experienced a HK event. Furthermore, patients who experienced a HK event were at increased risk of subsequent events. Frequent monitoring of serum potassium may help reduce the burden of HK in patients with CKD.

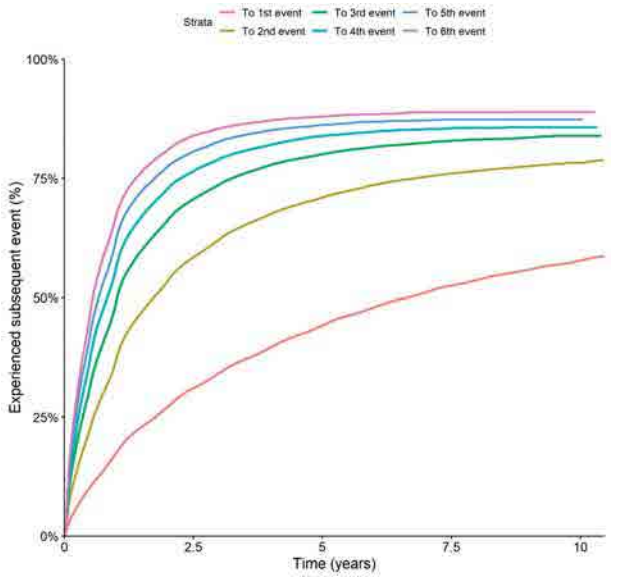


Figure 1. Time (years) to recurrent hyperkalaemia event

P0684 HDAC5/KLF2 AXIS REGULATES NLRP3 MEDIATED RENAL INFLAMMATION AND FIBROSIS ASSOCIATED WITH NEPHROCALCINOSIS-RELATED CHRONIC KIDNEY DISEASE

Sharma Pravesh[1], Kalyani Karnam[1], Kavita Sedmaki[1], Kirti Hira[1], Onkar Prakash Kulkarni[1]

[1]*Birla Institute of Technology & Science, Pilani - Hyderabad, Deparment of Pharmacy, Hyderabad, India*

Background and Aims: Role of epigenetic factors like histone deacetylases (HDACs) is largely unexplored in the pathogenesis of Nephrocalcinosis-related chronic kidney disease. The present study was performed to evaluate the functional role of HDAC5 in fibroblast activation in *in-vitro* and in a mouse model of Nephrocalcinosis-related chronic kidney disease.

Method: C57BL/6 male mice (6-7weeks old) were procured from registered CPCSEA breeder (Hyderabad, India), NRK49F cell line were generously provided by NCCS (Pune, India). All experimental procedures were approved by the animal ethics committee of the institute. Nephrolithiasis (oxalate nephropathy) was induced by feeding oxalate rich diet (Ssniff, Soest, Germany) to C57/BL6 mice for 10 days. NRK49F cells were stimulated with LPS (1µg/ml) for 2hrs followed by TGF-β (25ng/ml) for 24hrs. To achieve HDAC5 knockdown, the cells were pre-incubated with HDAC5 specific siRNA for 24hrs before stimulating with LPS. In another set of experiment, cells were incubated with 4-sodium phenyl butyrate(PBA) a non-selective HDAC5 and HDAC4 inhibitor at a dose of 1mM. 24 hrs after LPS stimulation cell lysates were analysed for protein expression of α-SMA, Collagen1a, KLF2, NLRP3, HDAC5 and β-actin. Mice fed with high oxalate diet were treated with PBA (500mg/kg) twice a day and on day 10 mice were sacrificed to analyse renal function and fibrosis parameters. Mice kidney tissues were analysed for crystal deposition (pizaalato staining), renal fibrosis (Picrosirius staining), and renal histology (H&E staining). The fibrosis markers were analysed by RT-PCR and immunoblotting. Renal function was determined by plasma BUN and creatinine analysis. Diet containing high oxalate with calcium was provided to mice in the control diet group (negative diet control).

Results: Renal fibroblasts (NRK 49F) stimulated with LPS and TGF-β showed upregulation of HDAC5, NLRP3, α-SMA, and Collagen-1a. Depletion of HDAC5 expression with HDAC5 siRNA significantly reduced expression of NLRP-3, α-SMA, and Collagen-1 in stimulated NRK49F cells. The expression of KLF2 in HDAC5 depleted cells was found to be upregulated. PBA treatment also reduced the expression of HDAC5 in NRK49F cells and had significant reduction in the expression of NLRP3 along with fibroblast activation markers, while KLF-2 expression was found to be upregulated. Similar to our observation in stimulated renal fibroblasts, the expression of HDAC5 was found to be upregulated in mouse model of oxalate nephropathy. Treatment with PBA showed significant downregulation of HDAC5 in kidneys of the mice fed with high oxalate diet. Mice treated with PBA showed down regulated renal expression of NLRP3, Collagen1a, α-SMA, TGF-β in comparison to vehicle treated mice. Treatment with PBA showed significant upregulation of KLF2 expression in kidney. PBA treated mice showed significant renal protection during nephrolithiasis as indicated by reduced plasma BUN and creatinine levels. Oxalate crystal deposition index was similar in all high oxalate diet groups. PBA treatment showed overall better renal histological protection observed through H&E (reduced tubular injury score) and picrosirius staining (reduced collagen deposition).

Conclusion: HDAC5 knockdown or HDAC5 inhibition with PBA attenuates fibroblasts activation by inhibiting NLRP3 expression. Treatment with PBA in mice with Nephrocalcinosis-related chronic kidney disease showed significant protection against renal fibrosis with downregulation of NLRP3 expression. We propose HDAC5 as a novel regulator of fibroblast activation in Nephrocalcinosis-related chronic kidney disease.

P0685

RENAL SUBCAPSULAR ADIPOSE-DERIVED MESENCHYMAL STEM CELLS (ASC) ADMINISTRATION, ASSOCIATED TO LOSARTAN TREATMENT, PREVENTED THE PROGRESSION OF RENAL DAMAGE IN AN EXPERIMENTAL MODEL OF CHRONIC KIDNEY DISEASE (CKD)

Marina P Claro[1], Krislley R Pereira[1], Everidiene KVB Silva[1], Flavio Teles[2], Paulyana F Barbosa[2], Irene L Noronha[1], CAMILLA FANELLI[1]

[1]University of Sao Paulo, Medicine - Nephrology, São Paulo, Brazil and [2]UNCISAL, Medicine - Nephrology, Maceio - Alagoas, Brazil

INTRODUCTION / AIMS: Chronic kidney disease (CKD) is considered a public health problem with epidemic proportions worldwide. Overactivity of the renin-angiotensin-aldosterone system (RAAS), associated to the establishment of a chronic self-sustained renal inflammation, are the main factors which contribute to the progression of CKD, leading to tissue fibrosis and loss of function. Consequently, RAAS inhibitors, such as the AT-1 receptor antagonist, Losartan, are among the most currently employed therapeutic strategies to slow down CKD progression, although the renoprotection afforded by these drugs is not complete. The association of anti-inflammatory and immunosuppressive drugs to RAAS inhibition is limited to the treatment of specific nephropathies, and its safety is still not entirely known. In this context, experimental application of mesenchymal stem cells (mSC) as a treatment to control renal inflammation and fibrosis have been showing promising results in studies with animal models of CKD. The aim of the present study was to analyze the renoprotective effects of subcapsular application of adipose-tissue derived mSC (ASC), associated to Losartan treatment, in rats submitted to 5/6 nephrectomy, after the establishment of CKD.

METHODS: ASC were isolated from gonadal adipose tissue from male Wistar rats, cultured until P4 and characterized by flow cytometry and in vitro differentiation. Male Wistar rats underwent 5/6 nephrectomy and were followed for 15 days to confirm the establishment of the nephropathy (CKD 15d). After this period, animals underwent a new surgery in which they received a subcapsular injection of 10 µL of sterile PBS (vehicle), or $2x10^6$ ASC diluted in 10 µL of sterile PBS. Part of these animals were than treated orally with 50 mg/kg/day of Losartan (LOS) for further 15 days (groups CKD + LOS 30d and CKD + LOS + ASC 30d). A group of animals that received only subcapsular vehicle were kept untreated for the same period (CKD 30d). Sham-operated rats, euthanized at days 15 (Sham 15d) and 30 (Sham 30d), were used as controls. Survival rate, body weight (BW), systolic blood pressure (BP), 24h urinary protein (24h UPE) and albumin (24h UAE) excretion, serum creatinine (SCr) and blood urea nitrogen (BUN) concentrations, percentage (GS%) and index (GSI) of glomerulosclerosis, percentage of tubulointerstitial fibrosis (INT%) and renal infiltration by macrophages (CD68) were assessed 15 and 30 days after 5/6 nephrectomy. The obtained results are presented as Mean ± SE. Differences among groups were analyzed by one-way ANOVA.

RESULTS: The renal subcapsular application of ASC after the establishment of severe CKD improved the renoprotection obtained with the classic treatment with LOS. The association of LOS + ASC significantly improved animal's survival, reduced blood pressure, proteinuria and albuminuria, prevented the development of glomerular structural damage and interstitial fibrosis, and inhibited renal inflammation by normalizing renal macrophage infiltration in the CKD + LOS + ASC group.

CONCLUSIONS: Our preliminary results demonstrate that the application of ASC, associated to the oral administration of LOS exerted additional renoprotection in the 5/6 renal ablation model, compared to LOS monotherapy. These findings suggest that ASC therapy could be employed as a therapeutic additive together with the traditional RAAS blockade, to detain the progression of CKD.

	EXPERIMENTS AFTER ESTABLISHED CKD					
	15 days		30 days			
	Sham 15d (n=9)	CKD 15d (n=13)	Sham 30d (n=13)	CKD 30d (n=14)	CKD + LOS 30d (n=12)	CKD + LOS + ASC 30d (n=15)
Survival rate	100%	69%*	100%#	75%*a	100%#b	100%#b
BW (g)	315 ± 19	264 ± 10*	356 ±12#	304 ± 6a	289 ± 9a	296 ± 5a
BP (mmHg)	155 ± 2	200 ± 9*	155 ± 2#	228 ± 7*a	190 ± 10*ab	181 ± 10b
24h UPE (mg/24h)	22 ± 4	81 ± 20*	22 ± 2#	196 ± 41*a	110 ± 46*a	47 ± 10b
24h UAE (mg/24h)	1.0 ± 0.4	50.9 ± 19.0*	1.1 ± 0.4#	121.8 ± 28.3*a	70.7 ± 36.7*a	19.2 ± 7.0*ab
SCr (mg/dL)	0.70 ± 0.06	0.91 ± 0.12	0.65 ± 0.04	0.97 ± 0.11	0.82 ± 0.06	0.83 ± 0.06
BUN (mg/dL)	56 ± 5	105 ± 13*	51 ± 4#	88 ± 8a	84 ± 7*a	82 ± 4*a
GS (%)	7 ± 3	28 ± 10*	7 ± 3#	32 ± 6*a	32 ± 5*a	15 ± 4
GSI	1.7 ± 0.8	6.1 ± 1.7	1.6 ± 0.6#	9.7 ± 2.5*a	7.6 ± 1.7*a	3.8 ± 1.2
INT (%)	1.2 ± 0.2	3.2 ± 1.1	1.1 ± 0.2#	5.8 ± 1.4*a	2.4 ± 0.4	2.5 ± 0.5a
CD68 (cell/mm²)	38 ± 6	90 ± 19	39 ± 6	153 ± 35*a	110 ± 22*a	56 ± 7b

*: p<0.05 vs. Sham 15d; #: p<0.05 vs. CKD 15d; a: p<0.05 vs. Sham 30d; b: p<0.05 vs. CKD 30d; c: p<0.05 vs. CKD + LOS 30d

Figure:

P0686 THE CIRCADIAN RHYTHM IN CKD PATIENTS

Jie Yang[1], Gong Xiao[1], Xiangcheng Xiao[1]

[1]*Xiangya Hospital, Department of Nephrology, Changsha, P.R. China*

Background and Aims: It is common to see that patients with chronic kidney disease CKD are complaint with sleep disorders. The data reveal that lymphocytes are under the regulation of circadian rhythm in the peripheral blood of humans. CKD patients have shown to stay up in a low-grade inflammatory status. And these patients are associated with systemic inflammation and acquired immune deficiency. In this condition, there are disorders of expression of chemokine receptors and function of lymphocytes in patients with CKD. Since the disorders of circadian rhythm have been reported, it is supposed that some proteins regulating circadian rhythm of lymphocytes may involve in sleep disorders. It is reported that circadian clock gene edcoded proteins, nuclear PER and CRY ptochrome (CRY), play an important role in the regulation of circadian rhythm. Therefore, we designed a questionnaire to patients with CKD stages 1-5 and investigated the levels of CRY mRNA and protein in PB lymphocytes.

Method: This research enrolled 101 patients (52 male and 49 female) with CKD stages 1-5, who were admitted to Xiangya Hospital, Changsha, China from August 2017 to August 2018. CKD was defined as the reduced level of eGFR when they received the Pittsburgh Sleep Quality-Index (PSOI) questionnaire. Patients were screened by strict exclusion criteria. The clinical files included general information of patients and blood biochemical test data. Subjective sleep quality was assessed in all patients using the Pittsburgh Sleep Quality-Index (PSQI). The expression of circadian clock genes PER1 and CRY1 in peripheral blood leukocytes using quantitative RT-PCR and Western blotting.

Results: Sleep questionnaires were obtained from the 101 patients from CKD stage 1 to 5. There were significant differences between the group of PSQI $\leq$ 5 and PSQI $>$ 5 in aging, Hb, HCT, Alb, ALT and CRP (Table1). The six valuables were chosen with Scr, eGFR, Ca, P, Hb and Anxiety/Depression score with logistic anlaysis. It was found that the values of Aging and Scr were significantly increased in high PSQI (Table 2). It also found that the PSQI score was negative correlated with the stage of CKD (Table 3). The higher level of PER1 and CRY1 in PBMC of CKD stage 1 patients was confirmed by Western blot and qRT-PCR. It was also found that the expression of PER1 and CRY1 significantly down regulated in the PBMC of CKD stage 5 patients. However, the expression of PER1 and CRY1 was no obviously differences of in the patients with CKD stage 2 to CKD stage 4 (Figure 1 and Figure 2).

Conclusion: It was found that the progress of CKD was associated with the degree of sleep disorders in our research. The score of PSQI was negativly correlated with the lower eGFR. It indicated that there is association between sleep quality and eGFR. It also found that Hb, HCT, Alb and ALT were significantly better in the group whose PSQI score was lower than 5. CRP is a hallmark of inflammations a close relation with sleep disorders. There is correlation between decreased sleep quality and elevated CRP level. It also found that the more aging and CRP, the higher PSQI score with logistical analysis in our research. It suggested that there is a chronic inflammation are associated with the sleep of the patients with CKD. PBMCs are invloved in status of inflammation. It indicated that the PBMCs of patients with CKD may be affected by the sleep disorders. The circadian rhythm can be also shown in human's PBMCs. The proteins of Per and CRY were two of period circadian clock proteins. In our research, we test that the expression of PER1 and CRY1 in PBMCs of patients with CKD. It found that PER1 and CRY1 were higher expressed in patients with CKD stage 1 and lowest in patients with CKD stage 5. It suggested that the circadian rhythm of PBMCs was associated with the stage of CKD. It was said that the function of PBMCs also are affected in CKD, such as the regulation of cellular calcium homeostasis, which can influence the circadian rhythm.

Table1: Age, Hb, Anxiety and depression were significant different in two group.*P<0.05

Item	Good sleep（PSQI≤5）	Poor sleep（PSQI>5）	P
	n=41	n=60	
Age	46.22±11.79	52.53±14.78	0.025
Sex（M/F）	17/24	35/25	0.096
Hb	107.41±19.95	93.83±24.33	0.004
SCr	277.25±196.21	352.67±300.50	0.254
BUN	11.75±6.64	12.81±8.39	0.688
Ca	2.16±0.23	2.10±0.22	0.149
P	1.34±0.31	1.39±0.45	0.537
eGFR	41.93±34.19	39.60±35.08	0.363
Anxiety/Depression（n）	27	54	0.003
Smoking（Yes/No）	14/27	12/48	0.110
HCT	32.62±6.26	31.37±7.94	0.123
Alb	34.88±8.14	34.00±6.33	0.545
ALT	20.87±18.71	45.60±169.49	0.276
AST	21.60±13.56	36.17±95.34	0.201
TC	5.11±1.41	4.99±1.52	0.687
CRP	4.68±6.38	8.46±17.12	0.001
UA	376.78±91.11	411.81±132.09	0.144
TG	1.02±0.28	1.09±0.26	0.199

Table2: There is positive association between the score of sleep and age/Scr. P<0.05

				95%CI	
	Wald	P	OR	down	up
Sex	-0.92	0.36	0.60	0.20	1.78
Sex（M/F）	-0.56	0.57	0.69	0.19	2.49
Age	2.10	0.04	1.04	1.00	1.09
TC	0.87	0.38	2.41	0.33	17.50
Hb	-0.99	0.32	0.99	0.96	1.01
Alb	0.79	0.43	1.03	0.95	1.12
SCr	2.45	0.01	1.00	1.00	1.01

Table3: The PSQI score was negative correlated with the stage of CKD.

	n	Grades	*F*	*P*
eGFR≥90ml/min*1.73m2	11	5.73±1.90		
60≤eGFR<90	20	6.75±2.34		
30≤eGFR<60	14	7.36±3.15	2.62	0.0398
15≤eGFR<30	24	7.54±3.39		
eGFR<15ml/min*1.73m2	32	8.63±2.90		

Figure:

P0687 DO ALL PATIENTS BENEFIT FROM MULTIDISCIPLINARY CHRONIC KIDNEY DISEASE CLINICS?

Bhanu Prasad[1], Maryam Jafari[2], Lexis Gordon[3], Navdeep Tangri[4], Joanne Kappel[5]

[1]Regina General Hospital, Saskatchewan Health Authority, Medicine, Regina, Canada, [2]Dr. T Bhanu Prasad Medical Prof Corp, Regina, Canada, [3]College of Medicine, University of Saskatchewan, Medicine, Saskatoon, , [4]Seven Oaks Hospital, Medicine, Winnipeg, Canada and [5]St. Paul's Hospital, Saskatchewan Health Authority, Medicine, Saskatoon, Canada

Background and Aims: Multidisciplinary clinics (MDC's) were established in Canada to offer a variety of support systems (diabetes care, social support, easy access to pharmacists, dietitians, specialty trained nurses), to monitor and delay progression through timed lab investigations and visits in conjunction with the Nephrologist. The reasons for better outcomes have been identified as better education, focus on self-care, dietary interventions, timely transplant referrals, modality education, lower hospitalizations and mortality. Treating all patients with chronic kidney disease (CKD) as part of a multidisciplinary care team runs the risk of adding unwarranted labs, interventions, polypharmacy and costs. Kidney Failure Risk Equation (KFRE) uses routine laboratory and clinical data, to stratify patients into three risk categories (low, medium, and high risk) of progression. KFRE has been shown to accurately estimate progression to kidney failure in adults with CKD. The objectives of the study were to i) validate the KFRE in our CKD patients, ii) evaluate health care utilization of patients based on the risk of progression in our province, Saskatchewan. iii) identify the subgroup of patients that benefit most from follow up in MDC.

Methods: We conducted a retrospective study on 1007 patients with CKD stages G3 and G4 in two CKD multidisciplinary clinics in the province of Saskatchewan, Canada (January 2004-December 2012). The predicted risk of kidney failure (low, medium high) for each patient was calculated using the 8-variable KFRE. Patients were followed for five years to validate the KFRE; data on initiation of dialysis or death was collected. Cost of delivery of care per patient per year in the CKD clinic was determined. Health care utilization was evaluated by measuring the number/cost of hospital admissions, cardiovascular and thoracic (CVT) surgery, non-nephrology specialist appointments, and medications.

Results: There were more patients in G 3 (n= 533) than in G 4 (n=474). 313 (59%), 150 (28%), and 70 (13%) were in low, medium and high-risk categories for G 3 CKD. 275 (58%), 86 (18%), and 113 (24%) were in similar categories for G 4. The mean age (SD) was 71 (12.8) years. The number of patients > 65 years of age was 75%. 57% were men, mean GFR (mls/min/1.73m^2) for G3 was 40 (7.8) and 23 (4) for G4. Of the G3 patients, 4% of low risk, 11% of the medium risk and 26% of the high risk progressed to dialysis by 5 years. In G 4 patients, 7% of low risk, 17% of medium risk and 48% of high risk progressed to dialysis over 2 years. These results validate the KFRE in our population. The cost of care per patient in MDC was $ 3800 (CAD) per year. There was a difference in the cost of medications, number and cost of (inpatient hospitalizations, cardiovascular surgeries, non-Nephrology specialist visits, and day surgeries) between low risk patients vs high risk patients in G4 patients.

Conclusion: We performed a cost-effectiveness analysis of our MDC's and show that very few patients at low-risk of progression advance to ESRD. They are also unlikely to benefit from intensive care management and better managed in primary care with advice from tertiary centres. Individual programs have significant opportunity to improve health care delivery by identifying the sub- groups that benefit the most from MDC based on the risk of progression to allow optimal utilization of resources. At $ 3800 (CAD) per patient, we suggest that MDC's are best utilized by patients with medium and high risk of progression. Further, we show that patients that the low-risk patients were older, had fewer inpatient visits, had lesser drug costs, underwent fewer cardiovascular surgeries, had fewer day surgery visits, and fewer non-nephrology specialist visits. This is the first study to our knowledge that focuses on health care utilization based on the risk of disease progression rather than the stage of CKD.

P0688 **GREATER MUSCLE STRENGTH IS ASSOCIATED WITH LOWER RISK OF CHRONIC KIDNEY DISEASE**

Jong Hyun Jhee[1], Gang Yoon Lee[1], Songuk Yoon[1], Hoon Young Choi[1], Hyeong Cheon Park[1]

[1]Gangnam Severance Hospital, Yonsei University College of Medicine, Division of Nephrology, Department of Internal Medicine, Korea, Rep. of South

Background and Aims: Frailty is a known risk factor for chronic disease and mortality. However, the association between frailty assessed by hand grip strength (HGS) and chronic kidney disease (CKD) among adults has not been elucidated. This study evaluated the association between muscle strength and the risk of CKD.

Method: Data were retrieved from a nationwide cohort study (Korean National Health and Nutrition Examination Surveys VI-VII, 2014-2017) and participants aged 40 to 80 years were included in the study analysis (male=6,660, female=8,195). HGS was measured using digital hand dynamometer and normalized to body mass index (BMI). The association between the risk of CKD (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m2 or the presence of proteinuria) and quartile of HGS per BMI was evaluated among male and female subjects.

Results: The mean age was 58.8 ± 11.6 years and mean eGFR level was 88.2 ± 18.7 mL/min/1.73 m2. The mean levels of HGS per BMI were 1.5 ± 0.3 and 0.9 ± 0.2 in male and female subjects, respectively. Those in higher quartile of HGS per BMI showed lower prevalences of advanced CKD stages than lowest quartile among both male and female subjects. When univariable logistic regression analysis for the risk of CKD was performed, higher quartile of HGS per BMI was significantly associated with lower risk of CKD in both male and female subjects. After adjustment for confounding factors including age, systolic blood pressure, smoking and alcohol intake, education and income levels, history of hypertension, diabetes, or arthritis, physical activity, baseline eGFR, total cholesterol, hemoglobin, and daily protein intake, the higher quartile of HGS per BMI were associated with lower risk of CKD in both male and female subjects (odds ratio [OR], 0.66; 95% confidence interval [CI], 0.49-0.88 in Q4; OR, 0.64; 95% CI 0.49-0.83 in Q3 in male; OR, 0.59; 95% CI, 0.43-0.81 in Q4; OR, 0.61; 95% CI, 0.47-0.80 in Q3; OR, 0.70;95% CI, 0.55-0.90 in Q2 in female, Q1 as reference group). These associations were consistent when the HGS per BMI was treated as continuous variable that 34% and 54% of risk was reduced as 1 m2 increase in male and female subjects.

Conclusion: Greater muscle strength normalized to BMI is associated with lower risk of CKD in adults. These findings suggest that frailty in adults is an important risk factor for CKD development.

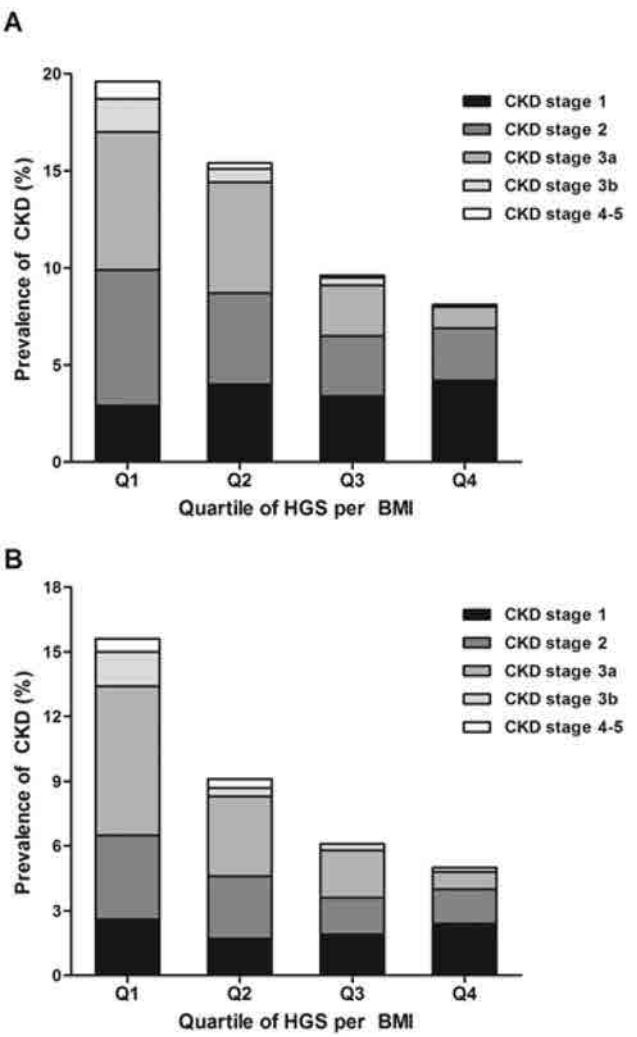


Figure: Prevalence of CKD stages according to quartile of HGS per BMI among male and female subjects.

P0689

LINACLOTIDE, THE GUANYLATE CYCLASE C AGONIST LIMITS CARDIAC FIBROSIS FORMATION IN MICE WITH CHRONIC KIDNEY DISEASE AFTER ISCHEMIA-REPERFUSION INJURY

Naohito Isoyama[1], Yuki Nakayama[1], Kimihiko Nakamura[1], Toshiya Hiroyoshi[1], Kouki Fujikawa[1], Hideyasu Matsuyama[1]

[1]*Yamaguchi university, urology, Ube, Yamaguchi, Japan*

Background and Aims: Cardiovascular disease (CVD) is a major cause of mortality in patients with chronic kidney disease (CKD). Renal ischemia-reperfusion injury (IRI) is a clinically significant condition that progress to CKD after acute kidney injury (AKI). We have reported that the suppression of Trimethylamine-N-oxide (TMAO), a hepatic metabolic product of trimethylamine generated from dietary phosphatidylcholine, by linaclotide could prevent renal fibrosis and improve renal function in the chronic phase after renal IRI.

TMAO has been linked directly with progression of CVD too. We investigated whether the reduction of TMAO by linaclotide limits cardiac fibrosis in mouse model of CKD after IRI.

Method: Linaclotide (100μg/kg) was administered for 2weeks before IRI and continued for 2weeks after IRI. After 2weeks since IRI, removed hearts sections were performed Azan stain to evaluate the level of fibrosis and western blotting to evaluate the expression level of fibronectin.

Results: The administration of linaclotide significantly improved cardiac fibrosis area (Fig1). Additionally, western blotting showed linaclotide suppress the expression level of fibronectin (Fig2).

Conclusion: The reduction of TMAO by linaclotide could prevent cardiac fibrosis in the chronic phase after renal IRI. Linaclotide may be a powerful tool for prevention of the cardiorenal syndrome after renal IRI.

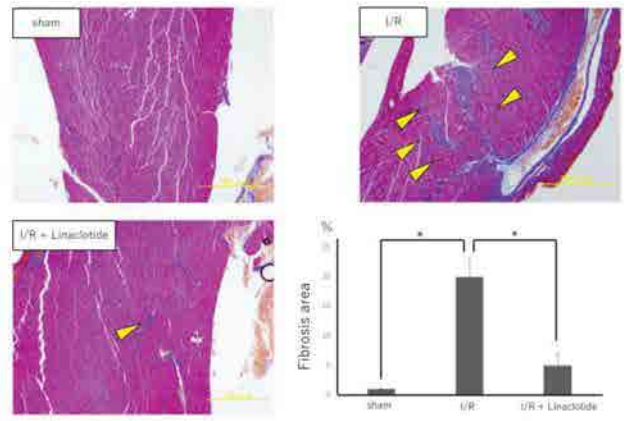


Fig 1

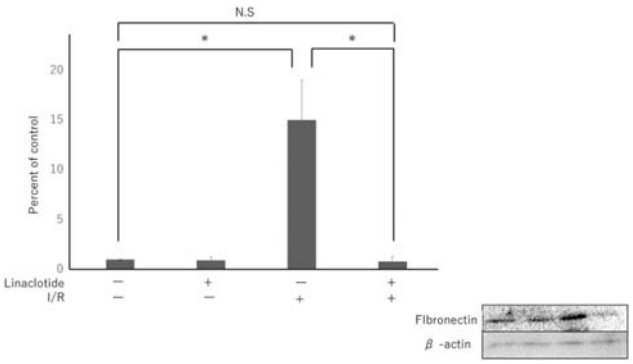


Fig 2

P0690

CORRELATIONS BETWEEN OPG/RANKL/RANK AXIS, VITAMIN D STATUS, PTH AND VASCULAR CALCIFICATION IN AN ADENINE-INDUCED MODEL OF CHRONIC KIDNEY DISEASE.

Beata Sieklucka[1], Tomasz Domaniewski[2], Marta Zieminska[2], Malgorzata Galazyn-Sidorczuk[3], Anna Pawlak[4], Dariusz Pawlak[1], Krystyna Pawlak[2]

[1]Medical University o Bialystok, Department of Pharmacodynamics, Poland, [2]Medical University of Bialystok, Department of Monitored Pharmacotherapy, Białystok, Poland, [3]Medical University of Bialystok, Department of Toxicology, Białystok, Poland and [4]Medical University of Bialystok, Department of Internal Medicine and Metabolic Diseases, Białystok, Poland

Background and Aims: Chronic kidney disease (CKD) is a major public health problem worldwide and refers to a wide range of disorders in bone and mineral metabolism, abnormalities of biochemical parameters and pathological calcification of the blood vessels. Vascular calcification (VC) is a common complication in CKD patients, contributes to cardiovascular disease (CVD), and associates with increased mortality and morbidity. The precise mechanism of VC in CKD is not yet fully understood. Recently discovered molecules such as osteoprotegerin (OPG), its ligand receptor activator of nuclear factor NF-κB ligand (RANKL) and RANK are not only well-known to play a crucial role in bone homeostasis, but they has also been implicated in the process of development of vascular complications However the exact role of OPG/RANKL/RANK axis in the process of VC has not been yet fully assessed. Thus, the aim of this work is to evaluate the role of OPG/RANKL/RANK axis in the process of calcification in CKD.

Method: Seventy two male Wistar rats weighing 260-290 g (8-weeks old) were initially divided into 6 groups containing 12 animals in each group. Rats were divided into six groups: control rats (K4, K6, K8) and CKD rats (B4, B6, B8). Control group rats received standard diet, whereas CKD rats were fed a low adenine – diet containing 0.3 % adenine, 1.0 % Ca, 1.2 % Pi through 4 (K4, B4), 6 (K6, B6) and 8 (K8, B8) weeks. Subsequently, CKD and control rats were sacrificed at weeks 4 (n=24), 6 (n=24) and 8 (n=24). One day before being killed, the rats were placed in metabolic cages for 24-hour urine collection. Thereafter, the rats were anesthetized and samples of blood, as well as aortas were collected. Next, the OPG, RANKL, parathyroid hormone (PTH), 25-hydroxyvitamin D (25(OH)D) and 1,25-dihydroxy vitamin D_3 1,25$(OH)_2D_3$ concentrations were determined using appropriate ELISA kits. Then the sRANKL/OPG ratio was calculated. The OPG, RANK and RANKL gene expression was assessed using real-time PCR (RT-PCR). The VC was quantified by measurement of the arterial calcium (Ca) and phosphate (Pi) content using flame atomic absorption. Serum levels of urea nitrogen, creatinine, uric acid, Ca, Pi and urinary levels of creatinine, Ca and Pi were measured.

Results: There was a progressive increase in serum urea nitrogen, creatinine, uric acid and PTH of CKD rats in comparison to control values. We also observed significantly decreased levels of 25(OH)D, 1,25$(OH)_2$D and serum Ca. Total Ca content in the aorta was significantly increased in CKD rats in comparison with control group, whereas total Pi content in the aorta was significantly increased only in B8 group in comparison to appropriate controls. There were no differences in serum OPG and sRANKL levels between CKD and control rats. In contrast, we observed decreased OPG, RANKL and RANK gene expression in a B4 group in comparison to appropriate controls, whereas in a B6 group we noticed increased OPG, RANKL and decreased RANK gene expression. B8 group revealed increased RANKL and RANK gene expression, but there were no differences in OPG gene expression between CKD rats and control group. Furthermore, we observed positive correlations between serum sRANKL and OPG and RANK gene expression. Ca and P content in the aorta inversely corelated with RANKL gene expression, whereas positively with OPG gene expression. Serum 25(OH)D concentrations correlated inversely with Ca in aorta. PTH was positively correlated with serum RANKL and OPG and gene expression these cytokines.

Conclusion: Our results suggest that OPG/RANK/RANKL axis may be involved in the process of vascular calcification in chronic kidney disease. However, its role and evaluation of precise mechanism in this field requires further evaluation.

P0691

LIPOPROTEIN(A) AS A POTENTIAL RISK FACTOR FOR CARDIOVASCULAR (CV) AND THROMBOTIC EVENTS IN CHRONIC KIDNEY DISEASE (CKD) AND TRANSPLANTED PATIENTS.

Simona Simone[1], Francesca Cianciotta[1], Fabio Sallustio[2], Francesco Pesce[1], Giuseppe Grandaliano[3], Loreto Gesualdo[1], Pertosa Giovanni[1]

[1]University of Bari Aldo Moro, Nephrology Unit, DETO, Bari, Italy, [2]University of Bari Aldo Moro, Department of Interdisciplinary medicine, Bari, Italy and [3]Catholic University of Sacred Heart, Rome, Italy

Background and Aims: Several studies suggested an independent association between elevated Lipoprotein (a) [Lp(a)] levels and the incidence of CV events in the normal population. Lp(a) levels start to rise with decreasing glomerular filtration rate. Whether high Lp(a) serum levels may contribute to the pathogenesis of atherosclerosis or thrombosis in CKD and, particularly, in transplanted (Tx) patients is largely unclear. Furthermore, it is still uncertain to which extent very high Lp(a) levels might influence CV events in this population. Aims: 1. To evaluate Lp(a) serum concentrations and lipid profile in CKD, dialysis and Tx patients. 2. To investigate the relationship between Lp(a) serum levels and atherosclerotic cardiovascular disease (ASCVD), including myocardial infarction, coronary revascularization, cerebrovascular accident, carotid endarterectomy, peripheral revascularization, gangrene, or limb amputation. 3. To assess whether Lp(a) may have a role in thrombotic events (failure of vascular access in HD or early renal allograft thrombosis after transplantation) in these patients.

Method: Serum Lp(a) levels and lipid profile were assessed in 295 patients (M 172, F 123; mean age 57.3, range 19-85 years): 23 with CKD stage I-III, 76 with CKD stage IV-V, 128 on dialysis (68 hemodialysis (HD), 60 peritoneal dialysis) and 68 were kidney Tx recipients (eGFR>30 ml/min). In the latter group, Lp(a) values were assayed before and after transplantation. Lp(a) levels were determined using the Macra® Lp(a) ELISA kit (Trinity Biotech, USA). Values are expressed as median and interquartile range. Logistic regression analysis was used to determine whether Lp(a) is a risk factor for CV and thrombosis disease. The cut-off value was identified according to maximum Youden index by receiver operating characteristic (ROC) curve.

Results: Increased mean serum levels of LDL-C (93.85 mg/d; normal values=<70 mg/dl) were observed in all groups of patients, while HDL-C and triglycerides serum levels were in the normal range. Serum Lp(a) levels (nv=14-31 mg/dl) were significantly ($p<0.001$) increased in advanced CKD group (stage IV-V) (45.5, 1.5-216.5 mg/dl) and, mostly, in patients on dialysis treatment (63.2, 2.0-216.6 mg/dl, $p=0.001$) compared to mild-moderate CKD group (stage I-III) (32, 1.3-149 mg/dl). Lp(a) serum levels correlated significantly with age ($r=0.11$, $p<0.05$) and, inversely, with eGFR only in advanced CKD group ($r=-0.21$ $p<0.05$). A significant (-56%; $p<0.001$) decrease of serum Lp(a) was observed after renal Tx, while staying in HD for another year resulted in an increase in serum Lp (a) levels of about 23.7% ($p<0.003$). No significant relationship was found between Lp(a) values and gender, inflammation (as assessed by serum C-reactive protein levels), or diabetes. By logistic regression analysis, Lp(a) values were found to be a risk factors for ASCVD in the whole population (No events 246 pts: Lp(a) 47.8 mg/dl; Yes events 49 pts: Lp(a) 53.8 mg/dl; $p=0.049$) and for thrombotic events in HD group (vascular access thrombosis: 4 events) and Tx patients (early acute renal vein thrombosis after Tx: 4 events) ($p=0.028$). The ROC curve (AUC 0.7829, 95% CI 0.5751-0.9907) allowed us to define the cut-off value for serum Lp(a) (82.45 mg/dl) (sensitivity of 87%; specificity of 73%) as a thrombotic risk factor in HD and Tx patients.

Conclusion: The study confirms the relevance of Lp(a) as non-traditional CV risk factor in CKD and Tx patients predicting both, the development of ASCVD and thrombosis. Serum Lp(a) levels higher than 82.45 mg/dl are potential thrombotic risk factors for vascular access failure in HD patients or early acute renal allograft thrombosis in Tx patients, suggesting more aggressive strategies to lower Lp(a) serum levels in this patient setting.

P0692 **NON-PROTEINURIC DIABETIC NEPHROPATHY AND THE RISK OF MORTALITY IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD)**

Antonio Santoro[1], Dino Gibertoni[2], Marcora Mandreoli[3]

[1]Alma Mater Studiorum - Università di Bologna, Specialty School in Nephrology, Bologna, Italy, [2]Alma Mater Studiorum - Università di Bologna, Department of Biomedical and Neuromotor Sciences, Bologna, Italy and [3]Ospedale S.Maria della Scaletta, Nephrology and Dialysis Unit, Imola, Italy

Background and Aims: Diabetes (DM) is considered one of the major causes of progressive CKD even when it does not induce proteinuria. However, the condition of diabetes without proteinuria is not universally considered to be accompanied by a reduced survival of the patient.

The aim of the study was to verify whether non-proteinuric diabetic CKD patients presented a different risk of mortality compared to non-diabetic and non-proteinuric CKD patients.

Method: Two matched cohorts of CKD patients were obtained from the PIRP database, that contains clinical and laboratory data from about 30,000 patients who have been followed since 2005 in the Emilia-Romagna Region (Italy). In the period 2005-2017, 2651 subjects with DM2 in CKD-EPI stages 3a to 5 and without evidence of proteinuria that entered the PIRP register surveillance were matched with as many non-diabetics patients without proteinuria by gender, age class, CKD stage. To assess the presence of a differential mortality risk in diabetic patients, a multivariable Cox regression model was fit, adjusted for several potential clinical confounders, using multiple imputation to estimate missing data and taking into account patients' clusterization into nephrology units to correct standard error estimates.

Results: In the 13 years examined, deaths were more frequent in patients with DM2 (38.7% vs 30.7%, $p<0.001$) as well as CV events before and after PIRP enrolment (52.2% vs. 42.9%, $p<0.001$), while dialysis initiation rate was lower (Fig.1). Furthermore, in diabetics there was a higher percentage of overweight or obese patients (38.9% vs 19.7%, $p<0.001$), lower levels of hemoglobin (12.3 g/dl vs 12.7 g/dl, $p<0.001$) and higher values of triglycerides 163 mg/dl vs 132 mg/dl, $p<0.001$). 10-year survival was significantly lower in diabetics (22.9% vs 36.4%, log-rank test: $p<0.001$, Fig.1). Multiple Cox regression identified a higher mortality risk for diabetics (HR = 1.326, $p<0.001$) after adjusting for sex, age, baseline eGFR, hemoglobin level, BMI, smoking status, presence of tumors or cardio-vascular comorbidities and cohort effect (5-years period indicator).

Conclusion: In patients with CKD and non-proteinuric nephropathy, concurrent diabetes was associated to a higher frequency of CV events and represented an independent risk factor for overall mortality. Thus, in diabetic patients, even in absence of proteinuria, we have to intensify therapeutic strategies to control the so-called CV intermediate risk factors (tobacco use, low-density lipoprotein cholesterol, hypertension, hypercoagulable states, obesity, etc.)



Figure:

P0693

THE MATRIX PROTEIN THROMBOSPONDIN-1 CONTRIBUTES TO THE DEVELOPMENT OF CARDIOVASCULAR PATHOLOGY IN CHRONIC KIDNEY DISEASE.

Natasha Rogers[1,2,3], Sohel Julovi[1], Kedar Ghimire[1], Nikita Minhas[1]

[1]The Westmead Institute for Medical Research, Centre for Transplant and Renal Research, Westmead, Australia, [2]Westmead Hospital, Westmead, Australia and [3]The University of Sydney, Camperdown, Australia

Background and Aims: Patients with chronic kidney disease (CKD) are at significantly greater risk of cardiovascular disease (CVD), which remains the leading cause of hospitalisation and mortality. Cardiovascular complications are 20-30 times more likely to occur in these patients than progression to end-stage kidney disease. Traditional cardiovascular risk factors are prevalent in patients with CKD, but clinical trials targeting standard cardiovascular risks have failed to improve outcomes in patients with CKD. This has led to the investigation of non-traditional pathways that drive the development of the CVD in CKD. The matrix protein thrombospondin-1 (TSP1), and its receptor CD47, regulates cell responses and we recently identified their role in acute kidney injury. We now investigate this pathway in vascular changes in CKD.

Method: Human plasma TSP1 was collected from n=120 patients attending outpatient clinics and measured by ELISA. Age matched male C57BL/6 (WT) and TSP1KO mice (on a C57BL/6 background) were used to develop a model of CKD employing a 5/6 nephrectomy technique (5/6Nx). Blood pressure and weight were checked weekly, and echocardiography analysed cardiac function at baseline. After 12 weeks, we performed echocardiography and biomolecular phenotyping on tissues. Human cardiomyocytes were used to assess the effect of TSP1 and the uremic toxin indoxyl sulfate on cell proliferation and senescence.

Results: Linear regression analysis demonstrate that plasma TSP1 correlated inversely with eGFR (r^2=-0.556, $p<0.001$). WT mice undergoing 5/6Nx developed renal interstitial fibrosis, hypertension, and left ventricular (LV) hypertrophy after 12 weeks. Echocardiography confirmed LV thickness with a concurrent reduction in LV ejection fraction compared to baseline. Histologic examination of WT myocardium revealed interstitial and perivascular fibrosis, and increased myocardial TSP1 expression. These findings were mitigated in TSP1KO mice who had preserved LV function, reduced LV hypertrophy and reduced cardiac fibrosis despite equivalent changes in renal mass and blood pressure. mRNA levels of cardiac-based TNF-α, IL-6, collagen-1, fibronectin and α-smooth muscle actin were increased in WT 5/6Nx mice compared to sham-operated controls, and transcript expression was robustly reduced in TSP1KO mice.

In vitro, the addition of uremic toxin (indoxyl sulfate) to cardiomyocytes robustly upregulated expression of TSP1, and this was dependent upon activation of the aryl hydrocarbon receptor. TSP1 significantly down-regulated cardiomyocte proliferation and increased β-galactosidase activity. Pre-incubation with a blocking antibody reversed the proliferative and senescent effects of indoxyl sulfate and TSP1.

Conclusion: Our findings show that TSP1 is elevated in CKD and may drive the cardiovascular manifestations of uremia. TSP1KO mice were protected from disease, suggestion this protein has a crucial role in the development of CVD. Manipulation of TSP1 signaling is an attractive target to potentially reduce the excessive burden of CVD seen in the CKD population.

P0694

ALTERATION OF PHYSICAL ACTIVITY AND ITS ASSOCIATION WITH CARDIOVASCULAR OUTCOMES AMONG PRE-DIALYSIS CKD PATIENTS

Soojin Lee[1], Yeonhee Lee[1], Sehoon Park[2], Yaerim Kim[3], Kyungdo Han[4], Jung-Hyun Kim[5], Kwon Wook Joo[1,2], Dong Ki Kim[1,2]

[1]Seoul national university hospital, Internal medicine, Seoul, Korea, Rep. of South, [2]Seoul National University College of Medicine, Seoul, Korea, Rep. of South, [3]Keimyung University Dongsan Hospital, Internal medicine, Daegu, Korea, Rep. of South, [4]Catholic University of Korea, Department of Biostatistics, Seoul, Korea, Rep. of South and [5]PaiChai University, Department of Home Economics Education, Daejeon, Korea, Rep. of South

Background and Aims: Cardiovascular disease is major cause of mortality among chronic kidney disease (CKD) patients, and it is fundamental to focus on reducing the potential risk factors. Regular physical activity is known to reduce the risk of cardiovascular disease in general population. However, whether the change of physical activity habits is beneficial for pre-dialysis CKD patients had not been examined thoroughly.

Method: We performed a nationwide population based cohort study using the database of Korean National Health Insurance System. Among adult patients who received national health screening program $\geq$2 times between 2012 and 2016, CKD patients were identified using the serum creatinine and dipstick albuminuria measurements. Those who previously underwent dialysis or diagnosed cardiovascular disease were excluded. The frequency and the intensity of the physical activity were obtained at least twice, from self-reported questionnaire during the health examination. The study groups were divided according to the status of physical activity habit alteration; active, quit exercise, start exercise, and inactive group. Then, the development of myocardial infarction (MI), stroke or death was assessed using the multivariate Cox regression analysis.

Results: During the median follow up of 3.18 years, 549,187 CKD patients were examined for adverse outcomes. Compared to those who remained inactive, the active group patients who consistently continued physical activity exhibited lower risk of MI (hazard ratio (HR); 0.76, 95% confidence interval (95% CI); 0.69-0.85), stroke (HR (95%CI) 0.69 (0.62-0.78)), and death (HR (95%CI) 0.62 (0.57-0.67)). Moreover, those who newly started physical activity also showed lower risk of adverse outcomes, compared to the inactive group (HR (95%CI) 0.83 (0.76-0.89)).

Conclusion: Continuation of physical activity in pre-dialysis CKD patients is beneficial to reduce the risk of cardiovascular disease development. Therefore, clinicians should encourage even mild intensity of physical activity to CKD patients.

P0695 **ANALYSIS OF HOSPITALIZATION EVENTS IN NON-DIALYSIS CKD PATIENTS**

Marcora Mandreoli[1], Dino Gibertoni[2], Antonio Santoro[3]

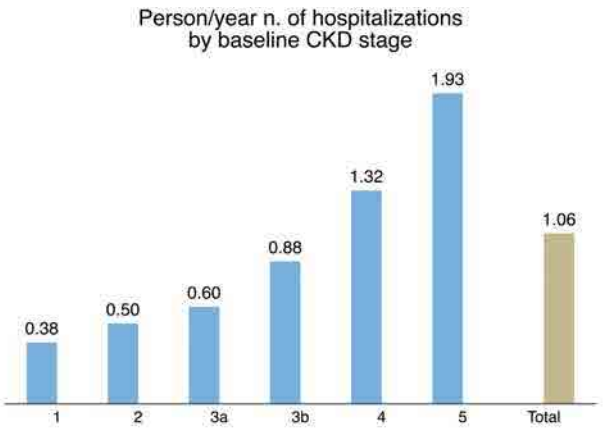
[1]Ospedale S.Maria della Scaletta, Nephrology and Dialysis Unit, Imola, Italy, [2]Alma Mater Studiorum - Università di Bologna, Department of Biomedical and Neuromotor Sciences, Bologna, Italy and [3]Alma Mater Studiorum - Università di Bologna, Specialty School in Nephrology, Bologna, Italy

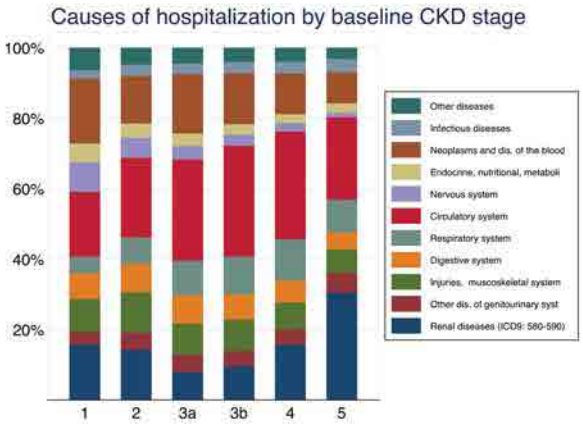
Background and Aims: Data are limited about rates and causes of hospitalization in patients with Chronic Kidney Disease (CKD) during maintenance period. In the present study, we investigate the amount, characteristics and trends of hospital admissions in a large cohort of pre-dialysis CKD patients followed within the Emilia-Romagna Region (Italy) PIRP project.

Method: Patients who were enrolled in the PIRP project in the period 1.4.2004-31.12.2018 constitute the study population. The PIRP database contains clinical and laboratory data collected at each follow-up visit. Hospitalization data regarding admissions occurred during patients' follow-up in PIRP were obtained from the regional hospital discharges database through unique individual linkage. Day-hospital admissions and hospitalizations aimed at arteriovenous fistula creation and peritoneal catheter placement were excluded.

Results: In almost 15 years of observation, 27,886 patients were enrolled in PIRP, mostly males (65,3%) with baseline median age of 75 years and baseline median eGFR=32.3 mL/min/1.73m2. Among them, 19,288 (69.2%) generated 72,432 hospitalizations during their follow-up in the project. The number of hospitalizations per person/year was 1.06 overall, increasing from 0.38 for stage CKD 1 to 1.93 for stage CKD 5 (Fig.1). The median length of stay was 9 days. Overall, cardio-vascular diseases were the main cause of hospitalization (30.0% of admissions), with renal diseases, tumors and respiratory diseases each accounting for over 10% of admissions, although the distribution of causes of hospitalization varies according to CKD stage (Fig.2). About one fifth of patients had one or more hospitalizations for acute kidney injury. The trend analysis revealed a steadily decreasing hospitalization rate for patients that were on CKD stage 4 and 5 at baseline, a constant hospitalization trend over time for patients who began their follow-up in stages 1 to 3a, while hospitalization rate of patients in CKD 3b stage declined after 9 years (Fig 3).

Conclusion: The study broadens our knowledge on the hospitalizations "consumption" by the population with CKD in the non-dialysis phase. It confirms that patients with CKD represent a vulnerable population, needing about 1 hospitalization / year / patient. The trend towards a reduction in hospitalizations during the follow-up period could be traced back to the specific care model, which encourages a more frequent management of patients in the Nephrology clinics.





P0696

CHARACTERIZATION OF A DAPA-CKD-LIKE POPULATION USING A CONTEMPORARY US HEALTHCARE SYSTEM: COHORT CHARACTERISTICS AND CLINICAL OUTCOMES.

Tope Olufade[1], Lois Lamerato[2], Juan Jose Garcia Sanchez[3], Like Jiang[1], Joanna Huang[1], Stephen Nolan[3]

[1]AstraZeneca, Wilmington, United States of America, [2]Henry Ford Health System, Detroit, United States of America and [3]AstraZeneca, Cambridge, United Kingdom

Background and Aims:

The Sodium Glucose Co-Transporter 2 inhibitor (SGLT-2i) class of drugs have demonstrated significant cardiorenal benefits in patients with type 2 diabetes (T2D), including reducing the composite renal outcome of significant eGFR decline, End Stage Kidney Disease (ESKD) or renal death in patients with T2D and preserved renal function and also in patients with overt Diabetic Kidney Disease. In addition, SGLT-2i have proven to have beneficial effects on cardiovascular (CV) outcomes in patients with heart failure with reduced ejection fraction (HFrEF) independent of glycaemic status. The DAPA-CKD Trial (A study to evaluate the effect of dapagliflozin on renal outcomes and CV mortality in patients with CKD) is the first SGLT-2i renal outcome trial to test the efficacy and safety of an SGLT-2i, dapagliflozin, in patients with diagnosed CKD with and without T2D.

In order to appropriately evaluate the future results and aid clinical interpretation of the DAPA-CKD trial, the present study assessed the renal and CV outcomes of a "DAPA-CKD-like population" (eGFR 25-75ml/min/1.73m2 and UACR 200-5000mg/g) in a contemporary US real healthcare system.

Method:

Administrative data from the Henry Ford Health System was used to identify persons with CKD stages 2 through 4 between 2006 and 2016 based on eGFR lab reading (n=38,376). Exclusions included no confirmatory eGFR > 90 days from index date, death within 30 days, history of renal transplant, and evidence of renal replacement therapy, or progression to CKD stage 5 during the baseline period (6 months pre or post index date). Within that cohort, 17,742 had eGFR (25-75ml/min/1.73m2) and 9,177 had a UACR (0-5000 mg/g) within 12 months of index date. Additional exclusions included type 1 diabetes (n=2,546), lupus nephritis (n=1) and polycystic kidney disease (n=20). Patients were followed through December 31st, 2018.

Results:

Of the 6,557 patients that met the eligibility criteria and were included in the study cohort, the mean age was 62.9 years and 46.2% were male. The population was stratified by UACR (0-<30, 30–199, 200–5,000mg/g). Across all outcomes assessed, the clinical outcomes were highest in the DAPA-CKD-like cohort (UACR 200-5000mg/g) (HF 36.1%; MI 11.3%, Stroke 8.9%; ESKD 18.6%; Mortality 18.5%; see Figure 1). The greatest increase was observed for renal outcomes particularly ESKD, increasing from 0.9% (UACR 0-<30mg/g) to 3.4% (UACR 30-199mg/g) to 18.6% (UACR 200-5000mg/g).

Conclusion:

In a contemporary US healthcare system, there remains significant adverse renal, CV and mortality outcomes among patients fitting the DAPA-CKD study inclusion criteria. These results highlight the unmet need existing for additional therapies to delay disease progression and improve patient outcomes and survival in this population.

	UACR 0-<30mg/g N= 4331		UACR 30-199mg/g N = 1354		UACR 200-5000mg/g N= 873		Total		p - value
	n	%	n	%	n	%	n	%	
All-cause mortality	243	6.0	146	11.7	139	18.5	528	8.7	< 0.0001
Renal outcomes									
ESKD (composite of 3 below)	37	0.9	42	3.4	140	18.6	219	3.6	< 0.0001
Progression to CKD stage 5	28	0.7	38	3.0	118	15.7	184	3.0	< 0.0001
Dialysis onset	7	0.2	16	1.3	83	11.0	106	1.8	< 0.0001
Renal transplant	9	0.2	3	0.2	7	0.9	19	0.3	< 0.001
CV Outcomes									
Myocardial infarction (MI)	191	4.7	92	7.4	85	11.3	368	6.1	< 0.0001
Stroke	161	4.0	71	5.7	67	8.9	299	4.9	< 0.0001
Heart failure (HF)	561	13.9	307	24.6	272	36.1	1140	18.9	< 0.0001

Figure: 5-year CV, renal and mortality outcomes across the 3 UACR categories analyzed.

P0697 **IDENTIFYING PATIENTS SUITABLE FOR PRIMARY CARE FOLLOW-UP IN A LARGE NON-DIALYSIS CKD COHORT**

Sophia Mohammed[1], Philip A. Kalra[2], Rajkumar Chinnadurai[2]

[1]University Of Manchester, Manchester, United Kingdom and [2]Salford Royal NHS Foundation Trust, Department of Renal Medicine, United Kingdom

Background and Aims: Chronic Kidney Disease (CKD) is a growing public health concern, affecting approximately 13.4% of the global population. Due to the rising burden of CKD and its economic cost, there is a pressing need to identify the risk factors which can predict CKD progression and thereby enable us to manage these patients in the community under primary care follow-up. Our study aimed to identify risk factors that can predict outcomes in patients with stable CKD.

Method: The study was conducted on patients recruited in the Salford Kidney Study, (a large prospective CKD database recruiting patients since 2002). From a total of 2952 recruited between 2002 and the year 2016, 1023 patients with a diagnosis of hypertension, diabetes or pyelonephritis were sampled for this study. Based on the annual rate of progression of estimated glomerular filtration rate (delta eGFR), 140 patients were identified as stable CKD patients (delta eGFR -0.50 and 0.50 ml/min/1.73m^2/year). The characteristics of this group was compared with 277 rapid progressors (RP) (delta eGFR<-3) and 212 patients in the improved group (delta eGFR>0.50).

Negative predictive value analysis was performed on all patients with an outcome of a GFR < 30ml/min/1.73m^2.

Results: Stable CKD patients had a significantly higher age compared to RP (69 vs 62, p<0.001). Further patients in the stable CKD group had a comparatively lower median blood pressure (141.5 vs 137, p<0.001). Other factors which were identified as risk factors for rapid progression included history of diabetes (177 vs 73, p=0.021), low albumin (41 vs 44, p<0.001), raised urine protein creatinine ratio (154.6 vs 18.8, p<0.001) and phosphate (1.24 vs 1.12, p<0.001) (Table-1). Comparing outcomes showed rapid progression reached ESRD (172 vs 18, p<0.001) but no significant difference in mortality (93 vs 55, p=0.25). Characteristics that were statistically different for stable CKD patients in this large cohort were identified: age, systolic blood pressure, diastolic blood pressure, diabetes, albumin, UPCR and phosphate. NPV analysis did not identify reveal any clear predictors for progression in stable CKD patients.

Conclusion: Several risk factors were identified to distinguish between stable, rapid and improved group. NPV did not identify any predictors in stable group. Further risk prediction models incorporating biomarkers are warranted to identify factors that can guide prognosis thereby stable CKD patients can be managed in the community.

Table 1 – Comparison of Characteristics, Bloods, Outcomes

Variable	Fast Progressors n = 277		Stable CKD n = 140		Improved n = 212		P-value Fast/Slow	P value Slow/ Improved	Anova All 3 groups
Age (years)	61.8	37 - 86.6	69.4	49.8 - 86	71.7	57.3 - 86.6	0.001	0.052	<0.001
SBP[b], mmHg	141.5	109.5 - 173.5	137	116 - 158	136.5	108.5 - 164.5	0.001	0.847	<0.001
DBP, mmHg	76	65 - 87	71	53 - 89	70	50 - 90	0.044	0.177	<0.001
Diabetes n(%)	177	63.9	73	52.1	98	46.2	0.021	0.278	<0.001
Albumin (g/l)	41	36 - 46	44	38 - 50	43	39 - 47	<0.001	0.157	<0.001
Phosphate (mmol/l)	1.24	0.87 - 1.61	1.12	0.82 - 1.42	1.13	0.83 - 1.43	<0.001	0.508	<0.001
UPCR (g/mol)	154.6	0 - 437.9	18.8	0 -59.5	14.3	0 - 39.8	<0.001	0.327	<0.001
ESRD	172	62.1	18	12.9	15	7.1	<0.001	0.069	<0.001
Death	93	33.6	55	39.3	91	42.9	0.25	0.498	0.101

P-value with 2 samples using Mann-Whitney U Test. Anova p-value using Kruskal – Wallis H test.

Age, SBP, DBP, Albumin, Phosphate, UPCR presented as median (interquartile range). Diabetes, ESRD, Death presented as number (percentage).

P0698

STRESS RELATED DISORDERS AND THE RISK OF KIDNEY DISEASE: A MATCHED COHORT STUDY BASED ON THE STOCKHOLM CREATININE MEASUREMENTS (SCREAM) PROJECT

Guobin Su[1,2,3], Huan Song[1], Vivekananda Lanka[1], Xusheng Liu[3], Fang Fang[4], Unnur A Valdimarsdóttir[5], Juan Jesus Carrero[1]

[1]Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden, [2]Nanfang Hospital, Southern Medical University, National Clinical Research Center for Kidney Disease, State Key Laboratory of Organ Failure Research, Department of Nephrology, Guangzhou, P.R. China, [3]Guangdong Provincial Hospital of Chinese Medicine, The Second Affiliated Hospital, Guangzhou University of Chinese Medicine, Department of Nephrology, Guangzhou, P.R. China, [4]Karolinska Institutet, Institute of Environmental Medicine, Stockholm, Sweden and [5]University of Iceland, Center of Public Health Sciences, Faculty of Medicine, Reykjavík, Iceland

Background and Aims: Psychiatric reactions to life stressors are common in the general population and may increase the risk of acute (AKI) and chronic kidney disease (CKD). The aim of this study is to evaluate the association between stress related disorders and subsequent risk of AKI or CKD progression.

Method: Population-matched retrospective cohort study conducted in the Stockholm CREAtinine Measurement project (SCREAM), Sweden from 2006 to 2012. The cohort included 31,137 exposed patients with stress related disorders (ie, posttraumatic stress disorder, acute stress reaction, adjustment disorder, and other stress reactions, defined by 10th international Classification of diseases, ICD-10: F43) and known kidney function (estimated glomerular filtration rate, eGFR), and 117,144 unexposed matched by age, sex and eGFR category. The primary outcome was CKD progression, defined as a sustained relative decline in eGFR of more than 40% or commencement of kidney replacement therapy. The secondary outcome was acute kidney injury (AKI), defined by death or hospitalization attributed to AKI or detected transient plasma creatinine elevations (KDIGO classification). Conditional Cox models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: During a medium follow-up of 3.3 years and compared with the unexposed population, patients with stress related disorders were at increased risk of CKD progression (HR 1.16, 95% CI 1.04-1.30) and AKI (HR 1.17, 95% CI 1.01-1.37). While the relative risk of CKD progression remained constant over follow-up, the association with AKI was most evident during the first year after stress diagnosis (HR: 1.31, 95% CI 1.04-1.66), disappearing thereafter. Among 9 prespecified subgroups, there was suggestion of heterogeneity with possible lack of association in patients with psychiatric comorbidity.

Conclusion: Exposure to a stress related disorder was associated with the long-term risk of CKD progression and the short-term risk of AKI. Studies are needed to better understand underlying mechanisms.

P0699 EVALUATION OF CALCIUM/MAGNESIUM RATE AND OTHER PREDICTORS OF CARDIOVASCULAR MORTALITY IN CHRONIC KIDNEY DISEASE

Eduarda Carias[1], Filipa Mendes[1], André Fragoso[1], Pedro Leão Neves[1], Ana Silva[1]

[1]*Centro Hospitalar Universitário do Algarve, Nefrologia, Faro, Portugal*

Background and Aims:

Cardiovascular disease (CVD) is the main cause of death in chronic kidney patient. The interaction between calcium and magnesium and mineral metabolism have been identified as risk markers for CVD.

The main objective was to identify the variables associated with cardiovascular and other causes of mortality in a group of patients with stage 4 of chronic kidney disease (CKD).

Method:

This was a prospective analysis conducted in an outpatient nephropathy clinic between 2005-2018, enrolling 692 patients with stage 4 CKD. Based on the calcium/magnesium ratio (rCaMg) the subjects were divided into 4 risk groups according to the following criteria: <25th percentile (rCaMg < 3.8mg/dl; n=168) – G1; 25-50th percentile (rCaMg: 3.8-4.7; n=171) – G2; 50-75th percentile (rCaMg: 4.7-8.6; n=188) – G3; and >75th percentile (rCaMg: > 8.6; n=165) - G4.

Descriptive statistics, ANOVA, chi-square and Log Rank test were used for comparison between groups. Bonferroni test was used as a post-hoc test. Kaplan-Meier analysis was used to evaluate mortality. The Kaplan-Meier method for measuring patient survival rate was applied and a comparison between the four percentiles was based on the log rank test

The multinomial regression models were used to assess predictive factors for cardiovascular mortality. CHAID analysis was used to assign patients to risk groups.

Results:

The mean age was 70 years, 53.5% women, with an eGFR of 19.9 ml/min (sd 8.1).

Differences among groups were evaluated with the use of an analysis of variance (ANOVA) model. Age ($p<0.001$), hemoglobin ($p<0.001$), phosphorous ($p<0.001$), pulse pressure ($p<0.001$), parathormone ($p<0.001$), estimated glomerular filtration rate ($p<0.001$) showed significant differences between groups. A post HOC analysis showed that G4 (rCaMg: > 8.6) were older ($p<0.001$), had lower hemoglobin levels ($p<0.001$), increased pulse pressure ($p<0.001$), higher phosphorus ($p<0.001$) and parathormone levels ($p<0.001$) and lower eGFR ($p<0.001$), than groups 1 and 2.

Survival at 84 months was progressively shorter with higher rCaMg (G- 1=81.4%, G-2:70.7, G- 3=60.5%, G- 4=28.4%. log Rank =xxx, p=0.004)

Multinomial regression analysis showed that Phosphorus; ORa: 1.946 (CI 1.194-3.169), p=0.007, rCaMg; ORa: 1.106 (CI 1.071-1.261) p=0.031, Age: ORa; 1.032 (CI 1.007-1.058) p=0.013, Pulse pressure: ORa; 1.033 (CI 1.007-1.060) p=0.011 were linked to increased cardiovascular mortality.

CHAID analysis identified that in 43.7% of patients with P> 4.1 mg/dl, 15.5% were associated with cardiovascular mortality ($p<0.001$), the model correctly classified 84.1% of patients and the estimate of the risk misclassification of events was 0.159 ± 0.014.

Conclusion:

The calcium/magnesium ratio was shown to be a strong predictor of cardiovascular mortality in patients with stage 4 chronic kidney disease.

After CHAID analysis the phosphorus level was assumed to be strongest predictor of cardiovascular mortality in this group of patients.

P0700 **FLAVONOID FISETIN ALLEVIETES RENAL DYSFUNCTION IN A SEVERE MOUSE MODEL OF HYPERURECEMIC NEPHROPATHY**

Qian Ren[1], Liang Ma[1], Ping Fu[1]

[1]Division of Nephrology, Kidney Research Institute, West China Hospital of Sichuan University, Chengdu, P.R. China

Background and Aims:

Flavonoid Fisetin is a natural product that has a wide distribution in many fruits and vegetables and exerts anti-cancer, anti-oxidant, anti-inflammatory and anti-mitotic effects. The renal protective effects of fisetin have been confirmed in models of diabetic nephropathy, cisplatin-induced AKI, ischemia reperfusion kidney injury and lupus nephritis. The current study instigates the protective effect of fisetin in a severe mouse model of hyperuricemic nephropathy (HN) and explores its underlying mechanisms.

Method:

Twenty-four C57BL6 mice were randomly divided into four groups: Control, Model, Allopurinol and fisetin. HN was established by oral administration of mixture of adenine (160 mg/kg/d)/potassium oxonate (2400 mg/kg/d) every other day for 28 days. Fisetin (100 mg/kg/d) and allopurinol (10 mg/kg/d) was given by gavage simultaneously. At the end of the treatment, serum uric acid, kidney functions (serum creatinine and BUN) kidney pathological changes, as well as underlying mechanisms were investigated by biochemical assay, histopathological score, RT-PCR, and western blotting analysis.

Results:

Oral administration of fisetin to HN mice lowered serum uric acid and improved renal functions. Renal fibrosis and inflammation in HN mice were attenuated by fisetin treatment. fisetin alleviated extracellular matrix deposition and reduced the release of pro-inflammatory cytokine IL-6, IL-1β, TNF-α and in the kidneys of HN mice. Furthermore, fisetin inhibited the activation of TGF-β and STAT3 signaling pathways in the kidneys of HN mice

Conclusion:

These data demonstrated that fiseitn exhibited renoprotective effect in a severe mouse model of hyperuricemic nephropathy (HN). Fisetin exerted anti-inflammatory and antifibrotic effects in HN mice, which might be associated with its inhibition on TGF-β /Smad3 and STAT3 pathways.

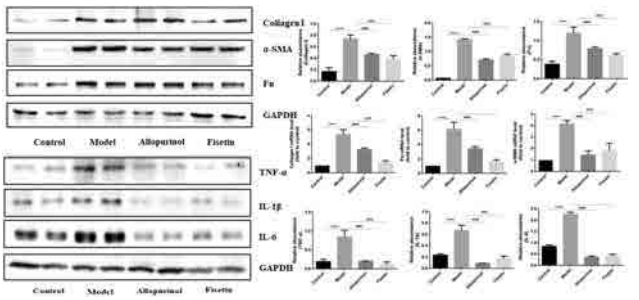


Figure2. Fisetin alleviated extracellular matrix deposition and inflammation in the kidneys of hyperuricemic nephropathy mice

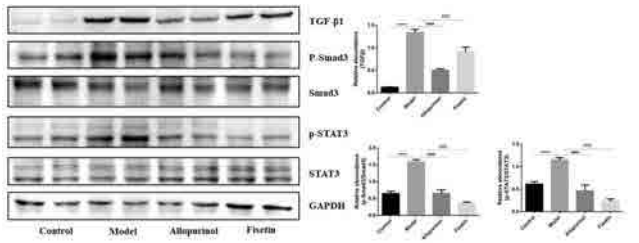


Figure3. Fisetin suppressed TGF-β1/Smad3 signaling and downregulated p-STAT3 in the kidneys hyperuricemic nephropathy mice

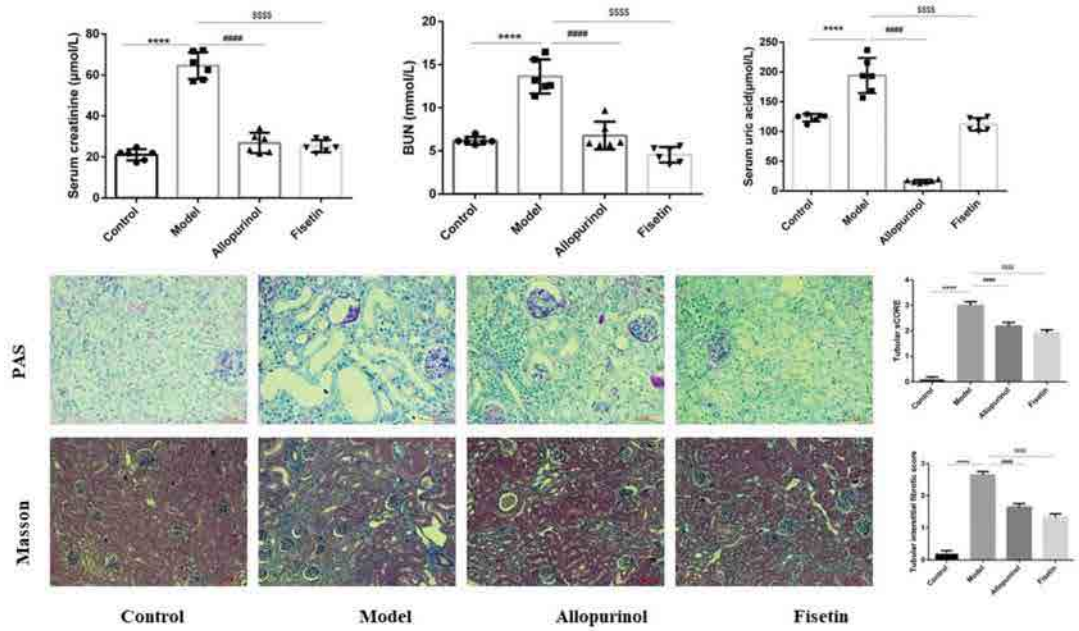


Figure1. Fisetin alleviates renal dysfunction in hyperuricemic nephropathy mice

P0701

LONG-TERM RETROSPECTIVE OBSERVATION STUDY TO EVALUATE EFFECTS OF ADIPONECTIN ON SKELETAL MUSCLE IN KIDNEY TRANSPLANT RECIPIENTS

Hiroki Adachi[1], Keiji Fujimoto[1], Yu Kagaya[1], Syo Kumano[1], Ai Fujii[1], Kazutoshi Matsuura[1], Keiichiro Okada[1], Kazuaki Okino[1], Furuichi Kengo[1], Hitoshi Yokoyama[1]

[1]*Kanazawa Medical University, nephrology, Kahokugun, Japan*

Background and Aims: Although it is reported that chronic kidney disease participates some roles in progression of sarcopenia, mechanisms of the progression of sarcopenia are unclear so far. In this observational study, we focused on serum adiponectin levels, that is a marker of metabolic syndrome, cardiovascular disease, and skeletal muscle mass in patients with kidney transplantation.

Method: Fifty-one patients who underwent renal transplantation at our hospital in and after 1998 (31 males and 20 females; aged 29-52 years at the time of transplantation) were retrospectively examined the relationships between the psoas muscle index (PMI), intramuscular adipose tissue content (IMAC), serum adiponectin fractions (high-/low-molecular-weight), and new-onset diabetes after transplantation (NODAT).

Results: Age at kidney transplantation negatively correlated with PMI before transplantation and positively correlated with IMAC before transplantation (rS=-0.427, $p<0.01$; rS=0.501, $p<0.01$, respectively). Both in one and five years after transplantation, PMI was higher than before transplantation ($p<0.01$). In contrast, IMAC transiently decreased one year after kidney transplantation, but subsequently recovered five years after kidney transplantation. Multivariate analyses identified that the mean increases of high-molecular-weight adiponectin concentrations was exacerbating factor for the mean change in PMI ($p=0.003$). Moreover, the mean increases of PMI and IMAC were exacerbating factors for the newly development of post-transplantation diabetes mellitus.

Conclusion: PMI increased associated with high-molecular-weight adiponectin levels after renal transplantation. In addition, PMI increased suppressed the development of NODAT.

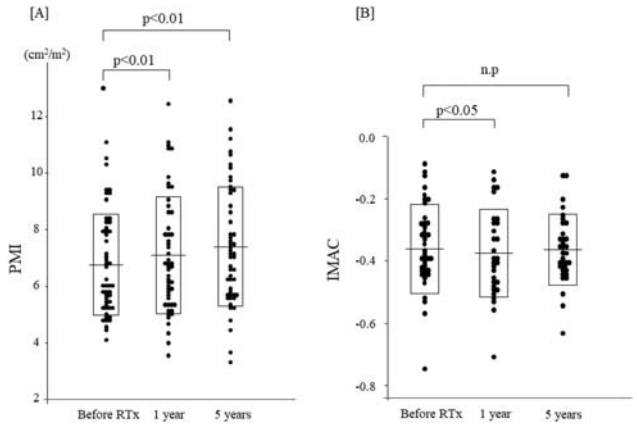


Figure: The change in PMI and IMAC in before and after RTx

P0702

IMPAIRED MYOCARDIAL MICROCIRCULATION PERFUSION IN ASYMPTOMATIC STAGE 1-4 CHRONIC KIDNEY DISEASE PATIENTS WITH INTRARENAL ARTERIAL LESIONS

Huanzi Dai[1], Fei Xiao[1], Weiwei Zhang[1], Yani He[1]

[1]*Daping Hospital,Army Military Medical University, Nephrology, P.R. China*

Background and Aims: Even mild renal disease is a powerful cardiovascular (CV) risk factor. However, the association between these pathophysiological processes, especially in the early asymptomatic stage, remains unclear. This study aimed to explore the relationship of cardio-renal microvascular disease in asymptomatic stage 1-4 chronic kidney disease (CKD) patients without obstructive coronary artery disease (CAD).

Method: This study consisted of 243 asymptomatic patients with stage 1-4 CKD who had no obstructive CAD. We distinguished different degrees of severity of intrarenal arterial lesions according to Oxford classification. Myocardial microcirculation perfusion was measured using single-photon emission computed tomography (SPECT). The summed stress score (SSS), summed rest score (SRS), and summed difference score (SDS) were estimated with the standard 17-segment, 5-point scoring model. Coronary microvascular disease (CMD) was defined as abnormal SPECT MPI (SSS $\geq$4 or SDS$\geq$2 on SPECT images) in the absence of obstructive CAD.

Results: The study subjects showed a stepwise increase in CMD severity with the aggravation of intrarenal arterial lesions; The SSS of no/mild/moderate/severe arterial lesions were 1.64$\pm$1.08, 2.56$\pm$1.35, 4.42$\pm$2.17, 6.48$\pm$3.52, respectively (all P$<$0.05); The SDS of no/mild/moderate/severe arterial lesions were 1.29$\pm$0.49, 1.75$\pm$0.56, 3.06$\pm$1.12, 4.16$\pm$1.85, respectively (all P$<$0.05). The percentage of subclinical CMD in CKD patients with intrarenal arterial lesions was significantly higher than those without arterial lesions (69.57% vs. 14.71%; P=0.01). Vice versa, the scores of intrarenal arterial lesions were significantly higher in patients who had myocardial perfusion defect (4.79$\pm$2.01 vs. 2.22$\pm$2.07, P=0.000), myocardial ischemia (3.69$\pm$2.16 vs. 2.35$\pm$1.69, P=0.001) compared to those without arterial lesions. Multiple regression analysis further supported renal arterioles hyalinization (OR=1.109, P=0.027) were independently associated with subclinical CMD in stage 1-4 CKD patients with no obstructive CAD.

Conclusion: This study demonstrated for the first time impaired myocardial microcirculation perfusion in asymptomatic stage 1-4 CKD patients with intrarenal arterial lesions. Renal arteriolar hyalinization may be a useful marker of the presence of CMD in CKD.

	Multivariable Model							
	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
	OR(95%CI)	P-value	OR(95%CI)	P-value	OR(95%CI)	P-value	OR(95%CI)	P-value
Intrarenal arterial lesion score	1.245 (0.765-1.715)	0.019	1.142(0.747-1.748)	0.040	1.219(0.841-1.707)	0.035	1.109(.711-1.750)	
Arcuate artery lesion score	0.747 (0.345-1.616)	0.150	0.724(0.298-1.757)	0.175	0.751(0.345-1.543)	0.081	0.739(.304-1.800)	0.106
Interlobular artery lesion score	1.498 (0.602-3.727)	0.085	1.373(.474-3.975)	0.059	1.176(0.495-2.794)	0.097	1.421(.488-4.141)	0.119
Arteriolar hyalinosis score	1.478 (1.099-2.164)	0.004	1.574(.944-2.626)	0.008	1.470 (1.062-2.627)	0.016	1.578(.946-2.636)	0.009

[a]Model 1 was adjusted for hypertension and diabetes;
[b]Model 2 was adjusted for eGFR, urinary ACR, 24-h UP, hemoglobin, hsCRP;
[c]Model 3 was adjusted for glomerular collapse/ischemia and tubular atrophy/interstitial fibrosis;
[d]Model 4 was adjusted for Model 1+Model 2+Model 3.

Figure: Multivariate logistic regression models testing associations of intrarenal arterial lesion with subclinical CMD.

P0703

IDENTIFICATION AND QUANTIFICATION OF UREMIC TOXIN PRECURSORS-GENERATING GUT BACTERIA IN CHRONIC KIDNEY DISEASE

Tessa Gryp[1,2,3], Mario Vaneechoutte[2], Marie Joossens[3], Wim Van Biesen[1], Griet Glorieux[1]

[1]Ghent University Hospital, Department of Internal Medicine and Pediatrics, Ghent, Belgium, [2]Ghent University, Department of Diagnostic Sciences, Ghent, Belgium and [3]KU Leuven, Department of Microbiology, Immunology and Transplantation, Leuven, Belgium

Background and Aims: In chronic kidney disease (CKD), impaired kidney function results in the accumulation of uremic toxins, which exert deleterious biological effects, contributing to cardiovascular morbidity and mortality. Protein-bound uremic toxins (PBUTs), such as *p*-cresyl sulfate, indoxyl sulfate and indole-3-acetic acid (IAA), originate from phenolic and indolic compounds, which are end products of the gut bacterial metabolization of aromatic amino acids (AAA). This study investigated the microbial composition in different stages of CKD by isolating, identifying and quantifying PBUT precursor-generating bacteria from fecal samples.

Method: Using fecal samples from patients in CKD stage 1 (n=6) and stage 5 (n=6), bacteria were cultured in a yeast casitone fatty acid glucose broth medium supplemented with AAA under aerobic (2d at 37°C) and anaerobic conditions (7d at 37°C), and confirmed as PBUT precursor-generating bacteria based on their generation capacity of phenolic and indolic compounds, measured with (U)HPLC.

Next, fecal DNA from 14 controls, 111 non-dialyzed and 27 dialyzed CKD patients was used to quantify the total bacterial number but also of 11 of the identified PBUT precursor-generating bacteria with qPCR. Using a Kruskal-Wallis test, bacterial loads were compared between the different CKD stages and control. Correlations between disease stages (control and CKD 1-5) and the abundance of bacterial species were assessed with the Spearman's rank test.

Results: In total, 150 different bacterial species were isolated from the CKD fecal samples, of which 101 were identified and 92 classified as PBUT precursor-generating bacteria. In general, *p*-cresol and phenol were mainly generated under anaerobic conditions, while indole and IAA were generated under both aerobic and anaerobic conditions. Phenolic compounds and IAA were predominantly generated by bacterial species belonging to the *Bacteroidaceae*, *Clostridiaceae*, *Enterococcaceae* and *Tannerellaceae*, while indolic compounds were mainly generated by *Bifidobacteriaceae* and *Enterobacteriaceae*.

Quantitative analysis of 11 confirmed PBUT precursor-generating bacteria revealed a higher abundance of *Streptococcus* spp. and *Enterobacteriaceae* in fecal samples from HD patients compared to controls and early CKD stages, and for *Roseburia* spp. compared to CKD 5. Moreover, in HD, the abundance of *Clostridioides difficile* and *Lactobacillus* spp. was increased compared to CKD 1-5, and of *Escherichia coli* compared to control (all $p>0.05$). The abundance of *Bacteroides* spp., *Faecalibacterium prausnitzii, Akkermansia muciniphila* and *Bifidobacterium* spp. as well as the total number of bacteria was comparable among the different CKD stages and controls. Finally, decrease in kidney function (ranging from control to CKD 5) positively correlated with the abundance of *Enterobacteriaceae* (r_s=0.210), and *E. coli* (r_s=0.286), while an inverse correlation was found with *Streptococcus* spp. (r_s=-0.255), *Butyricoccus* spp. (r_s=-0.326), *F. prausnitzii* (r_s=-0.250), *Roseburia* spp. (r_s=-0.342) and *Bifidobacterium* spp. (r_s=-0.303) (all $p>0.05$).

Conclusion: The identified PBUT precursor-generating bacteria are potential targets to reduce the plasma PBUT levels in CKD. In addition, in this CKD cohort, based on qPCR, an altered gut microbial composition with the progression of CKD could be established/confirmed.

P0704 **PROTECTIVE EFFECT OF DUAL ACTING LIGAND TARGETING A2A AND A3 ADENOSINE RECEPTOR ON OBSTRUCTION-INDUCED KIDNEY INJURY IN MICE**

Eun Seon Pak[1], Jiyoun Lee[2], Hunjoo Ha[1]

[1]Ewha Womans University, Graduate School of Pharmaceutical Sciences, College of Pharmacy, Seoul, Korea, Rep. of South and [2]Future Medicine Co., Ltd, Gyeonggi-do, Korea, Rep. of South

Background and Aims: Chronic kidney disease (CKD) has been a worldwide public health problem, and the current therapeutic strategies against CKD are limited. Adenosine plays a significant role in protection against cellular damage in the regions with high metabolism. All 4 known subtypes of adenosine receptors such as A_1AR, $A_{2A}AR$, $A_{2B}AR$, and A_3AR are expressed in the kidney. While $A_{2A}AR$ agonists protect the kidney against inflammation, our previous study has demonstrated that an A_3AR regulator effectively prevented diabetic kidney injury. The present study examined the preventive effect of LJ-4459, a newly synthesized dual acting ligand targeting $A_{2A}AR$ and A_3AR, on unilateral ureteral obstruction (UUO)-induced kidney injury in mice.

Method: UUO surgery was performed in 6-week-old male C57BL/6 mice. LJ-4459 was administered by oral gavage at dose of either 1 or 10 mg/kg per day. The control group was administered an equal volume of vehicle (0.25% carboxymethyl cellulose).

Results: LJ-4459 effectively prevented tubular damage presented by significantly reduced NGAL expression and tubular necrosis in the obstructed kidney. LJ-4459 effectively inhibited elevation of a-SMA, collagen I, and collagen IV protein expression as well as picro sirius red staining in the obstructed kidney, suggesting antifibrotic effect of LJ-4459. LJ-4459 also inhibited inflammation as estimated by significantly reduced F4/80 positive-stained area and protein expression of p-NF-kB and ICAM1.

Conclusion: The results suggest that LJ-4459 may become a potential therapeutic agent against interstitial fibrosis, a common feature of CKD.

P0705

MULTIPARAMETRIC RENAL MRI IN CHRONIC KIDNEY DISEASE: CHANGES IN CLINICAL AND MRI MEASURES OVER TWO YEARS

Rebecca Noble[1], Charlotte Buchanan[2], Huda Mahmoud[1], Isma Kazmi[1], Eleanor F Cox[2], Benjamin Prestwich[2], Nicholas Selby[1], Susan Francis[2], Maarten Taal[1]

[1]The University of Nottingham, Centre for Kidney Research and Innovation, Derby, United Kingdom and [2]The University of Nottingham, Department of Physics, United Kingdom

Background and Aims: Chronic kidney disease (CKD) progression is currently monitored using estimated GFR (eGFR) and albuminuria but these are relatively crude measures with multiple limitations. Multiparametric renal magnetic resonance imaging (MRI) combines several MR measures into a single scan session, offering the potential to assess severity, progression and response to therapy in CKD in a novel, non-invasive way. Previous studies have focussed on cross-sectional comparisons of MRI and clinical measures. In this study we sought to investigate the ability of MRI variables to predict and monitor progression of CKD over two years.

Method: Persons with CKD stage 3-4 (eGFR 15-59ml/min/1.73^2) who had undergone renal biopsy were recruited. Participants underwent multiparametric renal MRI scans on a 3T Philips Ingenia scanner at baseline, one and two years. In addition demographic data, medical history, eGFR and urine protein:creatinine ratio (uPCR) was collected. Multiparametric renal MRI comprised longitudinal relaxation time (T1 using SE-EPI and bFFE readouts), Diffusion Weighted Imaging, renal blood flow (Phase Contrast MRI), renal cortex perfusion (Arterial Spin Labelling), and Blood Oxygen Level Dependent (BOLD) relaxation rate (R2*). CKD progression was defined as participants having a slope in eGFR of -5ml/min/yr or greater over 2 years. Interstitial fibrosis was quantified on renal biopsy samples.

Results: 22 participants underwent MRI scanning at baseline (7 participants were classified as 'progressors' and 15 as 'stable'), while 13 completed all three scans (4 of whom were 'progressors'). At baseline, cortex T1 was significantly higher for 'progressors' compared to 'stable' participants (p=0.02), and renal cortex perfusion was significantly lower (p=0.03). There was no significant difference in total kidney volume (TKV), ADC, renal cortex or medulla R2*, or renal biopsy measures of interstitial fibrosis between 'progressor' and 'stable' CKD participants.

At Year 1 and Year 2 compared to baseline, a decrease in total kidney volume (TKV) was found, with a significantly greater decrease in TKV in the 'progressor' group (p=0.04). Over time, T1 increased in the 'progressor' group versus baseline, particularly in the cortex which showed a significant difference at year 1 (p=0.034) and year 2 (p=0.053). There was a trend for a reduction in ADC in 'progressors' versus stable participants over time. There was no significant change over time or between groups in renal cortex perfusion, renal cortex or medulla T2*, or renal biopsy measures of interstitial fibrosis.

Conclusion: Our results show that at baseline lower renal cortex perfusion and higher renal cortex T1 were associated with progression of CKD over 2 years suggesting that these MRI parameters may be a predictors of progression. On the other hand, cortex T1, TKV and ADC changed more in 'progressors' than in 'stable' participants over time (TKV and ADC decreased, T1 increased), suggesting that they may be useful MRI measures to monitor progression. Further studies are required to confirm these findings in a larger cohort of patients before renal MRI can be recommended for clinical use.

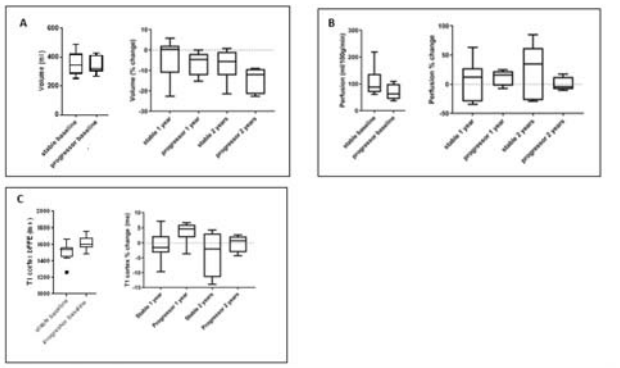


Figure 1: Multiparametric renal MRI measures shown comparing 'stable' and progressor' participants at baseline and % change over 2 years for (A) total kidney volume, (B) perfusion and (C) T1 cortex assessed using a bFFE readout.

Figure:

P0706 **THE EFFECT OF NON-VITAMIN K ANTAGONIST ORAL ANTICOAGULANTS ON RENAL OUTCOMES IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION.**

Siwaporn Deeprom[1,2], Thanit Chirananthavat[2]

[1]San Pa Tong Hospital, Medicine, Chiangmai, Thailand and [2]Police General Hospital, Nephrology, Bangkok, Thailand

Background and Aims: Lifelong oral anticoagulation (either with warfarin or a non–vitamin K antagonist oral anticoagulant (NOACs)) is indicated for stroke prevention in most patients with atrial fibrillation (AF). NOACs has been recommended for thromboembolism prophylaxis of nonvalvular AF. However, studies on the impact of NOACs on renal outcomes has been inconclusive.

Method: This retrospective cohort study compared 3 NOACs: apixaban, dabigatran and rivaroxaban to warfarin for their effects on renal outcomes in patients with non-valvular AF who had been using these medications for at least 2 years as of 2017-2018. The primary outcome was either the incidence of $>$ 30% decline in estimated glomerular filtration rate (eGFR) or doubling of the serum creatinine levels compare to baseline values at 24 months, and the secondary outcome was the incident of primary outcomes in different baseline eGFR subgroups ($>$ 60 vs $<$ 60 ml/min/1.73 m^2) and major bleeding as an adverse event.

Results: 90 patients were enrolled in each group, totaling to 360 patients. The incidence of $>$ 30% decline in eGFR is significantly higher in rivaroxaban compared to warfarin (hazard ratio: 2.09; 95% confidence interval: 1.35 to 3.24; p = 0.001). After multivariate analysis (using age, stage of chronic kidney disease, eGFR, CHAD2VAS and HASBLED score), dabigatran was also shown to significantly increase the incidence of $>$ 30% decline in eGFR. In subgroup analysis, rivaroxaban resulted in higher incidence of $>$ 30% decline in eGFR, in eGFR $<$ 60 ml/min/1.73 m^2 subgroup and higher incidence of doubling of the serum creatinine level in eGFR $>$ 60 ml/min/1.73 m^2 subgroup. There was no occurrence of major bleeding.

Conclusion: NOACs, especially rivaroxaban, may increase adverse renal outcomes in patients with nonvalvular AF.

P0707 UREMIC TOXINS IMPAIR SKELETAL MUSCLE REGENERATION PROCESS INDUCING CELL CYCLE ARREST AND APOPTOSIS IN CULTURED MYOBLASTS

Elena Alcalde-Estévez[1], Ana Asenjo-Bueno[2], Patricia Sosa[1], Patricia Plaza[2], Diego Rodríguez-Puyol[1,3,4], Manuel Rodríguez-Puyol[1,4], Gemma Olmos[1,4], Susana López-Ongil[2,4], Maria Piedad Ruiz[1,4]

[1]Facultad de Medicina, Universidad de Alcalá, Departamento de Biología de Sistemas, Alcalá de Henares, Spain, [2]Hospital Príncipe de Asturias, Fundación para la Investigación Biomédica, Alcalá de Henares, Spain, [3]Hospital Príncipe de Asturias, Servicio de Nefrología, Alcalá de Henares, Spain and [4]Instituto Reina Sofía de Investigación Nefrológica (IRSIN) y Red Renal (REDinREN) del ISCIII, Madrid, Spain

Background and Aims: The loss of muscle mass and function has been related to chronic kidney disease (CKD). About 37% of dialysis patients show symptoms of sarcopenia and this has been related to an increased risk of mortality. Changes in sarcopenic muscle include the loss of its regenerative capacity due to a reduction in the number and function of satellite cells, the muscle stem cells. The concentration of serum uremic toxins (UT) increases in parallel to a decline in the glomerular filtration rate in patients with CKD and this uremia may be involved in the development of sarcopenia. Previous studies showed as serum concentration of UT found in the early stages of CKD inhibits myogenic differentiation of cultured myoblasts. Nevertheless, the effect of those concentrations found in the advanced stages of CKD has not been described. The study aimed to analyse whether UT affect the muscular regeneration process by modifying the proliferation capacity of myoblasts (activated satellite cells).

Method: Cultured mouse myoblasts C_2C_{12} cells were used for all experiments. Cells were grown with 0% or 10% FBS culture media in the presence or absence of indoxyl sulphate and para-cresol at doses of 100μg/ml each one, which are similar to ones found in the advanced stages of CKD. Proliferation was evaluated by scratch wound healing and cell cycle by flow cytometry with propidium iodide and the fluorescent probe CFSE, an intracellular protein binding dye that is divided equally between daughter cells, allowing the discrimination of successive rounds of cell division. Chromosome condensation was assessed by immunofluorescence staining by confocal microscopy. Apoptosis was analysed by annexin V staining.

Results: C_2C_{12} cells treated with UT shown a significant decrease in the proliferation rate. A significant delay in wound closure was observed in cells treated with UT compared to control cells. Myoblasts treated with UT suffered a significant decrease in the proliferation rate since the probe remained higher than in the vehicle-treated cells. Proliferating cells treated with UT suffered a dramatic cell cycle arrest between the phases S and G2/M. Chromosome condensation was also analysed, finding that in the presence of colcemid, vehicle-treated cells condensed their chromosomes, as expected, whereas UT-treated cells did not, suggesting that UT stop the cell cycle at any point before the entry of cells in the mitosis phase. Besides, there was strong phosphorylation of cdc2 in the presence of UT indicating that cdc2 and the complex cdc2-cyclin B were inactive. This result explains why cells did not enter in the mitosis phase under UT exposition. Finally, UT induced the death of proliferating C_2C_{12} cells by apoptosis.

Conclusion: In the advanced stages of CKD, uremic toxins concentration increases, thereby inducing a dramatic arrest in the cell cycle of myoblasts, inactivating the cdc2-cyclin B complex, interrupting their proliferation and leading them towards cell apoptosis. These results point to a role of uremic toxins impairing the skeletal muscle regeneration process, which could be involved in CKD-related sarcopenia and frailty.

P0708

ASSOCIATION OF OBESITY WITH KIDNEY CYST GROWTH IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE; RESULTS FROM KNOW-CKD COHORT DATA

Chang Seong Kim[1], Hong Sang Choi[1], Eun hui Bae[1], Seong Kwon Ma[1], Soo Wan Kim[1]

[1]*Chonnam National University Medical School, Department of Internal Medicine, GWANGJU, Korea, Rep. of South*

Background and Aims: Overweight or obese patients with autosomal dominant polycystic kidney disease (ADPKD) are associated with the decline of glomerular filtration rate. However, little is known about the annual rate of change in total kidney volume (TKV) in patients with ADPKD according to the body mass index (BMI) corrected by TKV and total liver volume (TLV).

Method: We analyzed 364 patients with ADPKD from the KoreaN Cohort Study for Outcomes in Patients with Chronic Kidney Disease. We compared the changes in TKV in less than 1-year, 2-years and 4-year follow-up from patients by dividing baseline body mass index (BMI) by 18.5 to 22.9 (normal), 23 to 24.9 (overweight), and > 25 kg/m^2 (obesity).

Results: During the 4-year follow-up period, TKV tended to increase statistically with increasing BMI ($P = 0.032$). Similarly, higher BMI group showed higher TKV than lower BMI group ($P = 0.016$). Conventional BMI is affected by TKV and TLV in advanced ADPKD patients. Therefore, we reclassified patients by corrected BMI using the adjusted body weight (body weight – TKV – TLV). Although the statistical significances between absolute value of TKV and corrected BMI groups were disappeared during the follow-up, TKV% change/year showed significantly higher in ADPKD patients with obesity among corrected BMI groups (normal; 20.2%, overweight; 17.6% and obesity; 30.6%, P for trend = 0.022)

Conclusion: Even after correcting the TKV and TVL, obese patients showed a high of TKV% change/year compared to non-obese patients with ADPKD.

P0709

RENAL OUTCOMES AND MORTALITY FOLLOWING TRANSCATHETER AORTIC VALVE IMPLANTATION IN CHRONIC KIDNEY DISEASE PATIENTS

Amir Shabaka[1], Rafael Lucena Valverde[1], Andres Escudero[2], Gabriela Tirado-Conte[2], Luis Nombela Franco[2]

[1]Hospital Clinico San Carlos, Nephrology, Madrid, Spain and [2]Hospital Clinico San Carlos, Cardiology, Madrid, Spain

Background and Aims: Transcatheter aortic valve implantation (TAVI) is indicated for the treatment of patients with severe aortic stenosis with a high surgical risk that are rejected for surgical valve placement. The aim of this study is to evaluate the effect of TAVI on long-term kidney function in stage 3-4 chronic kidney disease (CKD) patients.

Method: We performed a single-center retrospective observational study of 529 consecutive patients that underwent TAVI between August 2007 and January 2018. We included patients with stage 3 or 4 CKD, with at least two stable measurements of glomerular filtration rate during the three months before TAVI. We excluded patients that presented with an acute kidney injury during the three months that preceded TAVI.

Results: 165 patients (31.3%) of the patients who underwent TAVI had a stable stage 3 or 4 CKD before implantation. Their mean age was 83.61 ±5.08 years, BMI of 27.79 ± 4.54 kg/m^2, baseline serum creatinine of 1.62 ± 0.49 mg/dl for an eGFR measured by MDRD-4 of 40.19 ± 10.79 ml/min, EuroScore-II of 6 (IQR 4-8). 42 patients (28.6%) had a post-procedural acute kidney injury (AKI), 2 of them required temporary renal replacement therapy and 30 patients (71.4%) recovered to their baseline kidney function. Mean contrast media administered was 162.0 ±77.8 ml. Mean serum creatinine decreased from 1.64 ± 0.51 mg/dl to 1.46 ± 0.52 ml/min after 1 year of follow-up (p=0.032). Only 2.4% of patients showed a >50% increase in serum creatinine after 1 year. Median follow-up was 3.8 years (IQR 2.3-5.7 years) during which time no patient progressed to end-stage kidney disease. 33.3 % of patients died during follow-up, with a one-year survival rate of 87% and two-year survival of 82%. Post-interventional major bleeding (14.6 vs 5.8%, p<0.001) and the need for post-interventional pacemaker implantation (25 vs 13.3%, p<0,001)were the only risk factors associated with the development of AKI. Contrast volume was not associated with the development of AKI. AKI was associated with an increased in-hospital stay (13.2 vs 7.4 days, p<0.001), but was not associated with either a reduced kidney function at end of follow-up or an increased mortality (Log-rank X2=1.72, p=0,578).

Conclusion: Despite the high incidence of post-interventional AKI after TAVI, our study did not show an association between AKI and increased mortality or reduced renal survival. In most cases after AKI patients recovered to their baseline kidney function. There is an improvement in kidney function after one year of treatment of severe aortic stenosis with TAVI in patients with CKD Stage 3-4.

P0710 DUAL GPR40/GPR84 FATTY ACID RECEPTOR DELETION IMPROVES ADENINE-INDUCED RENAL INJURY IN MICE

Véronique Cheff[1], Amelie Blais[1], Chet Holterman[1], Richard Hébert[1,2], Chris Kennedy[1,2], Jean-Francois Thibodeau[1,2,3]

[1]Kidney Research Centre, Ottawa Hospital Research Institute, Ottawa, Canada, [2]Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Canada and [3]Liminal R&D BioSciences Inc., Laval, Canada

Background and Aims: Fatty acid receptors have recently been implicated in the progression of fibrotic disorders. GPR40 deletion predisposes to AKI and CKD-induced fibrosis, while deletion of the pro-inflammatory GPR84 receptor was beneficial in this context. PBI-4050, a novel therapeutic compound with excellent safety and efficacy profiles in both experimental and clinical settings, is a dual GPR40 agonist and GPR84 antagonist. In this study, we sought to determine which of these receptors had a predominant effect in adenine-induced CKD.

Method: Ten-week-old male GPR40/84 double knockout mice (40/84ko) and age/strain matched WT C57BL/6 mice were subjected to a regular or adenine-supplemented diet (0.25%) for 4 weeks (n=10 per group). Plasma samples were collected on a weekly basis for hematocrit assessment. At endpoint, mice were placed in metabolic cages for 24 hours for urine collection. Plasma minerals and electrolytes, urinalysis and a comprehensive blood count were performed at endpoint.

Results: Adenine feeding led to early and sustained weight-loss, which was significantly worse in WT mice compared to 40/84ko mice. At day 14, Hct was significantly decreased in adenine-fed WT mice, while unaffected in the 40/84ko group. Adenine-induced reductions in hemoglobin and red blood cells counts were also greatly improved in 40/84ko mice. Adenine-feeding led to increased circulating neutrophils and decreased lymphocyte in WT mice, which was not seen in 40/84ko mice. Importantly, renal function assessed by plasma creatinine, urea and creatinine-clearance and renal hypertrophy were significantly improved in Ad-fed 40/84ko mice. Moreover, fractional excretion for sodium, potassium and calcium were increased by adenine-feeding in WT, but not in 40/84ko mice.

Conclusion: Overall, the loss of both GPR40 and GPR84 led to major improvements in several key renal functional abnormalities associated with adenine-induced CKD including weight-loss, anemia and renal functional decline. These studies, along with our previous work highlight the potential of targeting fatty-acid GPCR's, notably GPR84, for the treatment of inflammation/fibrosis related kidney diseases.

P0710A DOJUKSAN AMELIORATES OBSTRUCTIVE KIDNEY INJURY IN MICE

Songling Jiang[1], Hunjoo Ha[1]

[1]*Ewha Womans University, Graduate School of Pharmaceutical Sciences, College of Pharmacy, Seoul, Korea, Rep. of South*

Background and Aims:

Sarcopenia and physical inactivity synergistically progress in patients with chronic kidney disease (CKD). Sarcopenia is also strongly associated with the risk of mortality in the end-stage kidney disease. Exercise improves skeletal muscle mass and strength, and PGC-1α is significantly upregulated in muscle after exercise. Since patients with CKD have physical limitation to exercise, the present study aimed to find natural compounds that mimic exercise. Dojuksan, a traditional decoction was confirmed to increase PGC-1α expression in c2c12 muscle cells.

Method:

Unilateral ureteral obstruction (UUO) surgery was performed in 6-week-old male C57BL/6 mice to induce renal tubulointerstitial fibrosis, a key feature of CKD. Either Dojuksan (50, 100, and 200 mg/kg/day) or losartan (1.5 mg/kg/day), a standard clinical treatment for CKD, was administered orally for 7 days, started one day prior to surgery. Phytochemicals of Dojuksan were identified by LC-MS analysis.

Results:

UUO-induced renal inflammation and fibrosis were decreased by Dojuksan as much as losartan. Interestingly, Dojuksan significantly increased PGC-1α level and AKT phosphorylation in skeletal muscle of UUO mice. Losartan did not increase PGC-1α expression and AKT activation under our experimental condition. LC-MS analysis showed that the main compounds of Dojuksan were chlorogenic acid, liquiritigenin, akeboside, and glycyrrhizic acid.

Conclusion:

These data suggest that Dojuksan may inhibit the progression of interstitial fibrosis possibly through mimicking exercise.

P0711 CHRONIC KIDNEY DISEASE STAGES 3-5 PROGRESSION: PATTERNS AND OUTCOMES

Daria Sadovskaya[1], Ara Grigoryan[1], Alexander Zemchenkov[1,2,3], Roman Gerasimchuk[1,2], Natalia Kulaeva[2], Irina Konakova[1], Aleksander Rumyantsev[4]

[1]City Mariinsky hospital, dialysis department, Saint Petersburg, Russia, [2]North-Western State Medical University named after I.I.Mechnikov, department of internal diseases, clinical pharmacology and nephrology, Saint Petersburg, Russia, [3]Pavlov First Saint Petersburg State Medical University, department of nephrology and dialysis, Saint Petersburg, and [4]Saint Petersburg State University, department of faculty therapy, Saint Petersburg, Russia

Background and Aims: We evaluated the natural history of chronic kidney disease with regard to progression to renal replacement therapy or death in a prospective cohort of patient. Few studies are published concerning patterns of kidney function decline before initiation of dialysis while decreasing glomerular filtration rate (GFR) trajectories can influence the outcomes of the following treatment.

Method: The analysis of Saint-Petersburg City nephrology center data among 5935 patients with GFR below 60 ml/min/1.73㎡ with five and more follow-up visits. The outcomes data were collected from clinical and administrative databases.

Results: The most common causes of end stage renal failure were chronic glomerulonephritis (19%, decreasing over time 2009-2019), diabetes (16.9 %, stable), and hypertension (13.8 %, increasing). In 18.9% cases diagnosis was not established. 49% of patients show the rate in range 0-5 ml/min/1.73㎡ per year; 33% had the rate more than 5 ml/min/1.73㎡ per year; 17% of pts revealed slow but stable improvement of kidney function. Overall mean of the GFR change rates were -3.86±0.21 and -3.19±0.23 ml/min/1.73㎡ per year for men and women; being significantly different for CKD stages: -1.23 (-1.93 ÷ - 0.61); -2.69 (-3.17 ÷ - 2.14); -4.91 (-5.55 ÷ - 4.47) and -6.42 (-7.52 ÷ -5.63) for CKD 3A, 3B, 4 and 5. CKD progression rates differed between patients with various diagnoses and were associated with phosphate, calcium, anemia and iron deficiency, serum albumin and proteinuria levels. In women, total cholesterol levels out of normal range were linked with higher progression rates. In the multiple regression male gender was linked with higher GRF slope by 1.01 ml/min/1.73㎡ per year. The reduced baseline GFR by 10 ml/min/1.73㎡ per year; the reduced albumin - by 2 g/l, Hb - by 5 g/l, elevated phosphate - by 0.1 mmol/l, uric acid - by 0.2 mmol/l and proteinuria by 0.33 g/d were associated with similar increase of GFR slope (by about 10%). We found three different trajectories for GFR slope during three-year period before dialysis initiation: slow progression (-2.53, 95%CI -5.02÷-0.69 mL/min/1.73㎡ per year) from CKD3B-CKD4 – 74% of patients, faster progression (-7.96, 95%CI -11.32÷-5.89) from CKD3 – 21% of patients, initially no progression (+0.24, 95%CI -1.54÷-2.05) with following acceleration of GFR slope (-19.2, 95%CI -29.7÷-10.8) from CKD3 – 5% of patients.

Dialysis was started at eGFR 7±3 ml/min/1.73㎡ in "slow" group (31% - urgent start), 6±4 ml/min/1.73㎡ in "fast" group (58% - urgent start) and 5±4 ml/min/1.73㎡ in "accelerated" group (61% - urgent start).The rate of renal replacement therapy initiation over the 5-year observation period was 0.9%, 2.1%, 12.9% and 46.3%, respectively, for CKD stages 2, 3, 4, 5 while the mortality rate was 20.1%, 30.2%, 51.9 and 41.3% mainly for cardiovascular reasons. Thus, death was far more common than dialysis at all stages but CKD5, where it was comparable.

Conclusion: The identifying of the modifiable factors linked to CKD progression gives the opportunity to improve comprehensive renoprotective therapy. The efforts to decrease mortality in CKD3-4 cohort should be focused on prevention and treatment of coronary artery disease, congestive heart failure, diabetes mellitus, phosphatemia and anemia.

P0712 TRANSGELIN AS A POTENTIAL MARKER OF RENAL IMPAIRMENT IN MULTIPLE MYELOMA PATIENTS

Karolina Woziwodzka[1], Jolanta Malyszko[2], Małgorzata Banaszkiewicz[1], Ewa Koc- Żorawska[3], Paulina Dumnicka[4], Artur Jurczyszyn[5], Krzysztof Batko[1], Aleksandra Maleszka[6], Marcin Krzanowski[1], P. Miarka[1], Marcin Zorawski[7], Jacek Małyszko[8], Ryszard Drozdz[4], Marek Jan Kuznieswki[1], Katarzyna Krzanowska[1]

[1]Jagiellonian University Collegium Medicum, Department of Nephrology and Dialysis Unit, Kraków, Poland, [2]Medical University of Warsaw, Department of Nephrology and Dialysis Unit, Warszawa, Poland, [3]Medical University of Bialystok, Second Department of Nephrology and Hypertension with Dialysis Unit, Białystok, Poland, [4]Jagiellonian University Collegium Medicum, Department of Medical Diagnostics, Kraków, Poland, [5]Jagiellonian University Collegium Medicum, Department of Hematology, Kraków, Poland, [6]University Hospital, Department of Medical Diagnostics, Kraków, Poland, [7]Medical University of Bialystok, Department of Clinical Medicine, Białystok, Poland and [8]Medical University of Bialystok, Department of Nephrology and Dialysis Unit, Białystok, Poland

Background and Aims:

Transgelin (SM22) is a cytoskeletal actin-binding protein involved in differentiation of smooth muscle cells, osteoblasts and adipocytes. It is present in fibroblasts, some epithelium, immune cells and acts as a tumor suppressor. It was found ~~as~~ a marker of interstitial fibrosis and glomerulosclerosis. Transgelin upregulation depends on the etiology of the disease in various cells (glomerular parietal or visceral, or tubular interstitial cells). Elevated SM22 expression was detected in glomerular and in tubulointerstitial injury. Among patients with multiple myeloma (MM) up to 50% suffer from renal insufficiency (RI) in early stages. Free light chains (FLCs), potential nephrotoxic substances, where lambda light chains are more commonly associated with renal damage, appear to have a prognostic value in MM and indicate the stages of MM.

The aim of the study was to analyse the utility of transgelin in case of renal impairment in MM patients and investigate its relationship with acclaimed parameters of renal failure and markers of MM stages.

Method:

The analysis included 126 patients (73 women and 53 men) in mean age 66 $\pm$ 10 years. Symptomatic MM was diagnosed in 119 patients, including 84 (67%) with ISS stage 1, 20 (16%) with stage 2 and 15 (12%) with stage 3; 7 (6%) patients had smoldering MM. Mean baseline eGFR (CKD-EPI$_{Cr}$) was 74 $\pm$ 24 ml/min/1.73 m^2 and 31 (25%) patients had eGFR $<$60 ml/min/1.73 m^2. The examined parameters included creatinine, urea, NGAL urine, serum and urine cystatin C, periostin, FLC kappa and lambda in serum and urine. The association between transgelin, markers of renal failure, MM were determined by the Pearson's test and multivariate stepwise regression analysis. The p-value $<$0.05 was considered statistically significant.

Results: Median serum transgelin in the whole studied group was 84.1 (IQR: 65.4; 116.4) ng/ml. Transgelin concentrations were higher in men (median 96.2 versus 78.8 ng/ml; p=0.022) and in patients with smoldering MM (median 149.2 versus 82.4 ng/ml; p=0.003). Transgelin did not differ according to ISS stage (p=0.3) or disease state (regression, stable disease or progression) (p=0.3). Significant correlations were detected between transgelin and serum creatinine (R=0.29; p=0.001), eGFR (CKD-EPI$_{Cr}$) (R=-0.25; p=0.007), uric acid (R=0.19; p=0.036), alanine (R=0.18; p=0.048) and aspartate (R=0.26; p=0.003) aminotransferases, ferritin (R=-0.22; p=0.049), hepcidin (R=-0.25; p=0.033), and urine cystatin C (R=0.19; p=0.042). Moreover, after exclusion of patients with smoldering MM, transgelin significantly correlated with serum FLC lambda (R=0.18; p=0.047) and serum periostin (R=-0.22; p=0.013). After median follow-up of 21 (IQR: 15; 24) months, eGFR decreased in 47 (37%) of patients and increased in 71 (56%) patients (no follow-up data were available in 8, i.e. 6% of patients). Patients in whom eGFR decreased had higher transgelin (median 106.6 versus 83.9 ng/ml), although the difference was marginally significant (p=0.05). However, baseline transgelin positively correlated with serum creatinine after follow-up (R=0.37; p$<$0.001) and negatively correlated with eGFR after follow-up (R=-0.33; p$<$0.001). Moreover, higher baseline serum transgelin (beta=-0.11 $\pm$ 0.05; p=0.032) significantly predicted lower eGFR values after the follow-up, independently of baseline eGFR and the duration of follow-up.

Conclusion:

Transgelin may be useful in investigating renal damage because of its proven role in regulation of fibrosis, especially in kidney. As a biomarker it may indicate diagnosis and etiology of MM-related chronic kidney disease, which can lead to ~~beginning of~~ early therapeutic interventions and improved overall survival and quality of life in patients with MM. Moreover, elevated transgelin at the beginning of the disease may induce future development of chronic kidney disease.

P0713 DIFFERENTIAL PREDICTION OF DECLINE IN GFR IN PROTEINURIC VS NON-PROTEINURIC DIABETIC PATIENTS

Hiroshi Tanaka[1]

[1]*Mihara Red Cross Hospital, Internal Medicine/Nephrology, Mihara, Hiroshima, Japan*

Background and Aims: Diabetes mellitus (DM) is known to cause a progressive loss in renal function in at leaset 2 types of clinical presentation: classical diabetic nephropathy with overt proteinuria and non-proteinuric kidney diseases. The mechanisms of the progression should be multifactorial and are considered different at least in some ways in each patient. Now it is important to predict whether each diabetic patient has progressive renal disease or not, hopefully before overt proteinuria appears.

Method: A hospital-wide study with all the laboratory data for a period of 4 years and 2 months was conducted. A total of 2,804 non-dialysis patients with an age 18 or more in whom the eGFR slope was calculated over 731 days or more with HbA1c measured at least twice were retrieved. Medians were used for each laboratory datum, including dipstick proteinuria and haematuria (both changed to numeric variables, e.g. 1+ into 1.0), blood cell count, serum chemistry, and HbA1c. Medication class counts were defined as a total number of groups (DPP4, SGLT2, SU, ..) where insulin was classified into 3 groups (rapid, mixed, and basal); the required prescription period was 3 months or more for each class. Statistical analysis was performed with R 3.6.0 on Ubuntu. For prediction, missing values were imputed by an R package {mice}.

Results: A total of 2,804 patients (M:F = 1375:1429, age 66.9+-13.6 (18–101, median 68) years) were analyzed whose median HbA1c was 6.14+-0.79 (3.6-11.6, median 5.95)%.

This population was further divided into a proteinuric group (the median of dipstick proteinuria of 1+ or more, n=296) and a non-proteinuric group (the median of dipstick proteinuria of +- or less, n=2508). In the multivariate analysis, the proteinuric DM patients had the eGFR slope associated with initial eGFR, proteinuria, uric acid, and the number of classes of the anti-diabetic medications; higher uric acid and less number of DM medication were significantly associated with faster decline in eGFR. The non-proteinuric DM patients had eGFR slope associated with age, initial GFR, uric acid, chloride, and haemoglobin, but not with proteinuria; the patients with higher uric acid with lower haemoglobin had significantly faster decline in eGFR (-1.86 vs -1.34, P = 0.013). Prediction of faster eGFR decline was analyzed with machine learning technologies, ie, {ranger} and {randomForest}, where precision was 68.9%/67.9% (proteinuric group, ranger/randomForest) vs 76.8%/75.9% (non-proteinuric group, ranger/randomForest).

Conclusion: Propensity to lose kidney function is different in each diabetic patient, which should to be ideally predicted in individual basis.

P0714

RELATIONSHIP BETWEEN BIOLOGICAL AGE ESTIMATED BY SKIN AUTOFLUORESCENCE, CHRONOLOGICAL AGE, AND MORTALITY IN CHRONIC KIDNEY DISEASE

Hokuto Morohoshi[1,2], Ken Iseri[1,3], Lu Dai[1], Thomas Ebert[1], Anna Witasp[1], Bengt Lindholm[1], Olof Heimbürger[1], Franz Peter Barany[1], Louise Nordfors[1], Karolina Kublickiene[1], Abdul Rashid Tony Qureshi[1], Paul Shiels[4], Peter Stenvinkel[1]

[1]Karolinska Institutet, Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden, [2]Showa University, Clinical Research Institute for Clinical Pharmacology & Therapeutics, Tokyo, Japan, [3]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Tokyo, Japan and [4]Institute of Cancer Sciences, University of Glasgow, Wolfson Wohl Cancer Research Center, Glasgow, United Kingdom

Background and Aims: While chronological age associates with increased risk of death, there is a quest for markers of biological age in chronic kidney disease (CKD) that better reflect accumulation of tissue and cellular damage, which could contribute to shorter life span. Skin autofluorescence (SAF) is a biomarker for accumulation of advanced glycation end products in skin that associate with chronological age and with factors that may increase mortality risk. However, the predictive capacity of SAF for mortality has not been fully elucidated in CKD. We have investigated the relationship between biological age calculated by SAF, chronological age and all-cause mortality in patients with CKD stage 5.

Method: In a cohort of 199 CKD5 patients (non-dialysis CKD5, n=100, hemodialysis, n=27 and peritoneal dialysis, n=72; median age 66 years, 34% females, 21% diabetes (DM), 20% cardiovascular disease (CVD), and 34% malnourished), we calculated biological age by a formula based on SAF measurements using the AGE Reader. Framingham risk score, coronary artery calcium score, the heart rate-corrected augmentation index, body composition, nutritional status, handgrip strength, and various biochemical markers (hemoglobin, albumin, creatinine, intact-parathyroid hormone, triglyceride, cholesterol, HDL-cholesterol, high-sensitivity C-reactive protein (hsCRP), and interleukin (IL)-6) were recorded at baseline. During median follow-up of 38 months, 34 patients died, and 51 patients underwent renal transplantation. We analyzed spline curves showing sub-distribution hazard risk (sHR) for all-cause mortality with biological age calculated by SAF and chronological age by the Fine and Gray competing risk analysis.

Results: There was a significant association between biological age calculated by SAF and chronological age (rho=0.48; $p<0.001$). IL-6 and hsCRP were positively associated both with biological age according to SAF measurement (IL-6: rho=0.34, $p<0.001$; n=155 and hsCRP: rho=0.31, $p<0.001$; n=199) and chronological age (IL-6: rho=0.47, $p<0.001$; n=155 and hsCRP: rho=0.40, $p<0.001$; n=199). The multivariate spline curve showing sHR for all-cause mortality associated positively with chronological age (sHR: 1.04, p=0.035) and biological age calculated by SAF (sHR: 1.01, p=0.048) when adjusted for sex, DM, CVD, nutritional status, 1-standard deviation increase of hsCRP, and CKD5 groups.

Conclusion: All-cause mortality risk increased linearly with higher chronological age and SAF-estimated biological age - and with similar magnitude of sHR for the two - suggesting that prediction of mortality risk based on SAF is not superior compared to chronological age in CKD. We conclude that biological age calculated by SAF and chronological age are equally robust predictors of clinical outcomes in CKD; however, both indices are influenced by the inflammatory status.

P0715

SUPERB MICROVASCULAR IMAGING: AN INNOVATIVE ULTRASOUND TECHNIQUE FOR EARLY DETECTION OF KIDNEY DYSFUNCTION AND RENAL FIBROSIS

Munai Abu-rahme[1], Suheil Artul[2], Safa Kinaneh[1], Zaid Abassi[3], Zaher Armaly[1]

[1]Nazareth Hospital EMMS, Nephrology, Nazareth, Israel, [2]Nazareth Hospital EMMS, Radiology, Nazareth, Israel and [3]Technion - Israel Institute of Technology, Faculty of Medicine-Physiology, Haifa, Israel

Background and Aims: Superb microvascular imaging (SMI) is an innovative ultrasound image processing technique that shows greater details and better visualization of small branching vessels by using a unique algorithm that offer high frame rates, less clutter, and fewer tissue motion artefact that were not previously possible without the use of contrast agent. We assume that SMI provides superb information regarding the severity of chronic kidney disease (CKD) and associated the fibrotic changes. Therefore, the present study was designed to examine whether SMI can detect early renal fibrosis as compared with the reference standard renal biopsy.

Method: The SMI was performed in patients (n=47) with CKD stage 2-4, where some of them underwent biopsy proven chronic renal dysfunction and fibrosis as part of the diagnosis and therapeutic judgment as needed. In addition, biochemical tests were performed in order to obtain the serum parameters of kidney function (BUN, Serum Creatinine), a urine collection test for the assessment of proteinuria, and estimation of GFR by MDRD formula in patients with CKD of various severity and healthy controls (n=17). In addition, all patients underwent SMI US imaging, where vascularity is expressed as SMI index (low index reflects low vascularity/fibrosis and vice versa).

Results: As expected, SMI vascular index was significantly lower in CKD patients as compared with healthy control (72.2±3.1 Vs 49.1±2.6 %, $P<0.001$). Interestingly, strong correlation between the SMI index and eGFR was found among the CKD patients ($r=0.595$, $P<0.001$). Similarly, a keen correlation was found between the SCr and SMI index of the diseased subjects. Among those who underwent renal biopsy, SMI index corresponds with the histological alterations as well as CKD staging.

Conclusion: This study demonstrates that in patients with CKD of various stages, SMI imaging may be utilized as a simple and practical method for evaluation of the chronic renal morphological changes and for the differentiation between CKD grades.

P0716 **RAAS INHIBITION MODULATES KYNURENINE LEVELS IN A CKD POPULATION WITH AND WITHOUT TYPE 2 DIABETES MELLITUS**

Valeria Cernaro[1], Saverio Loddo[2], Vincenzo Macaione[2], Valentina Teresa Ferlazzo[2], Rosalia Maria Cigala[3], Francesco Crea[3], Concetta De Stefano[3], Antonina Rita Rosalia Genovese[1], Guido Gembillo[1], Davide Bolignano[4], Domenico Santoro[1], Roberto Vita[5], Michele Buemi[1], Salvatore Benvenga[5,6,7]

[1]University of Messina, Unit of Nephrology and Dialysis, Department of Clinical and Experimental Medicine, Messina, Italy, [2]University of Messina, Department of Clinical and Experimental Medicine, Messina, Italy, [3]University of Messina, Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, Messina, Italy, [4]Magna Graecia University of Catanzaro, Department of Medical and Surgical Sciences, Catanzaro, Italy, [5]University of Messina, Endocrinology, Department of Clinical and Experimental Medicine, Messina, Italy, [6]University of Messina, Master Program on Childhood, Adolescent and Women's Endocrine Health, Messina, Italy and [7]University Hospital, Policlinico Universitario G. Martino, Interdepartmental Program of Molecular & Clinical Endocrinology, and Women's Endocrine Health, Messina, Italy

Background and Aims: Kynurenine pathway of tryptophan metabolism is involved in the pathophysiology of chronic kidney disease (CKD) and diabetes mellitus (DM), mainly through the inflammation-induced activity of indoleamine 2,3-dioxygenase (IDO). Renin-angiotensin-aldosterone system inhibitors (RAASis) [angiotensin converting enzyme inhibitors (ACEis) and angiotensin II receptor antagonists (ARBs)] are recommended in these conditions to decrease proteinuria, slow CKD progression and reduce cardiovascular risk. The interactions between RAAS and the kynurenine pathway and the potential effects of RAASis have been reported in few experimental models but whether these drugs influence kynurenine levels in humans is unknown. We performed a single-centre cross-sectional observational study to evaluate tryptophan and kynurenine serum levels and IDO activity in CKD patients with and without type 2 DM, their correlations with markers of renal dysfunction, and their relationship with RAAS-inhibiting therapy.

Method: We enrolled 72 consecutive adult patients with CKD, of which 38 had DM, who were admitted to the Unit of Nephrology and Dialysis of our Hospital. Of them, 55 were receiving RAASis whereas 17 were not. Tryptophan was assessed by HPLC (high-performance liquid chromatography) analysis with an UltiMate^{TM} 3000 chromatograph (Thermo Fisher Scientific, 168 Third Avenue Waltham, MA, USA); kynurenine was measured using an enzyme-linked immunosorbent assay (ELISA) kit (Catalogue n. K 7728; Immundiagnostik AG, Bensheim, Germany); IDO activity was calculated with the formula (kynurenine/tryptophan) x 100.

Results: Patients receiving RAASis and patients not under therapy only differed for frequency of arterial hypertension (100% vs 76.47%; P=0.002) and kynurenine levels, the latter being significantly lower in the treated group compared to the untreated one (1.56 ± 0.79 vs 2.16 ± 1.51 μmol/l; P=0.0378). Kynurenine did not correlate with estimated glomerular filtration rate (eGFR), proteinuria or albuminuria in the whole study cohort. Conversely, in patients not receiving RAASis it was inversely related to eGFR (r=-0.4862; P=0.0478) and directly related to proteinuria (ρ=0.493; P=0.0444) and albuminuria (ρ=0.542; P=0.0247); moreover, it varied across classes of albuminuria, being lower in patients with normoalbuminuria (0.98 ± 0.55 μmol/l) and higher in those with micro- (2.63 ± 1.53 μmol/l) and macroalbuminuria (3.09 ± 1.61 μmol/l) at the ANOVA test (F=4.008; P=0.042). In the same group, the relationship between IDO activity and eGFR was significant (ρ=-0.554; P=0.0210) and IDO activity differed across classes of albuminuria (F=3.702; P=0.05). Moreover, IDO activity was higher in patients with history of cardiovascular disease compared to those with no such history [10.22 (8.39 to 22.92) vs 7.57 (4.76 to 8.09) %; P=0.0343] whereas tryptophan had an opposite behaviour (17.00 ± 2.06 vs 22.00 ± 3.78 μmol/l; P=0.0036).

Conclusion: We observed lower kynurenine levels in CKD patients treated with RAASis compared to untreated patients, independently of the presence of DM, and a

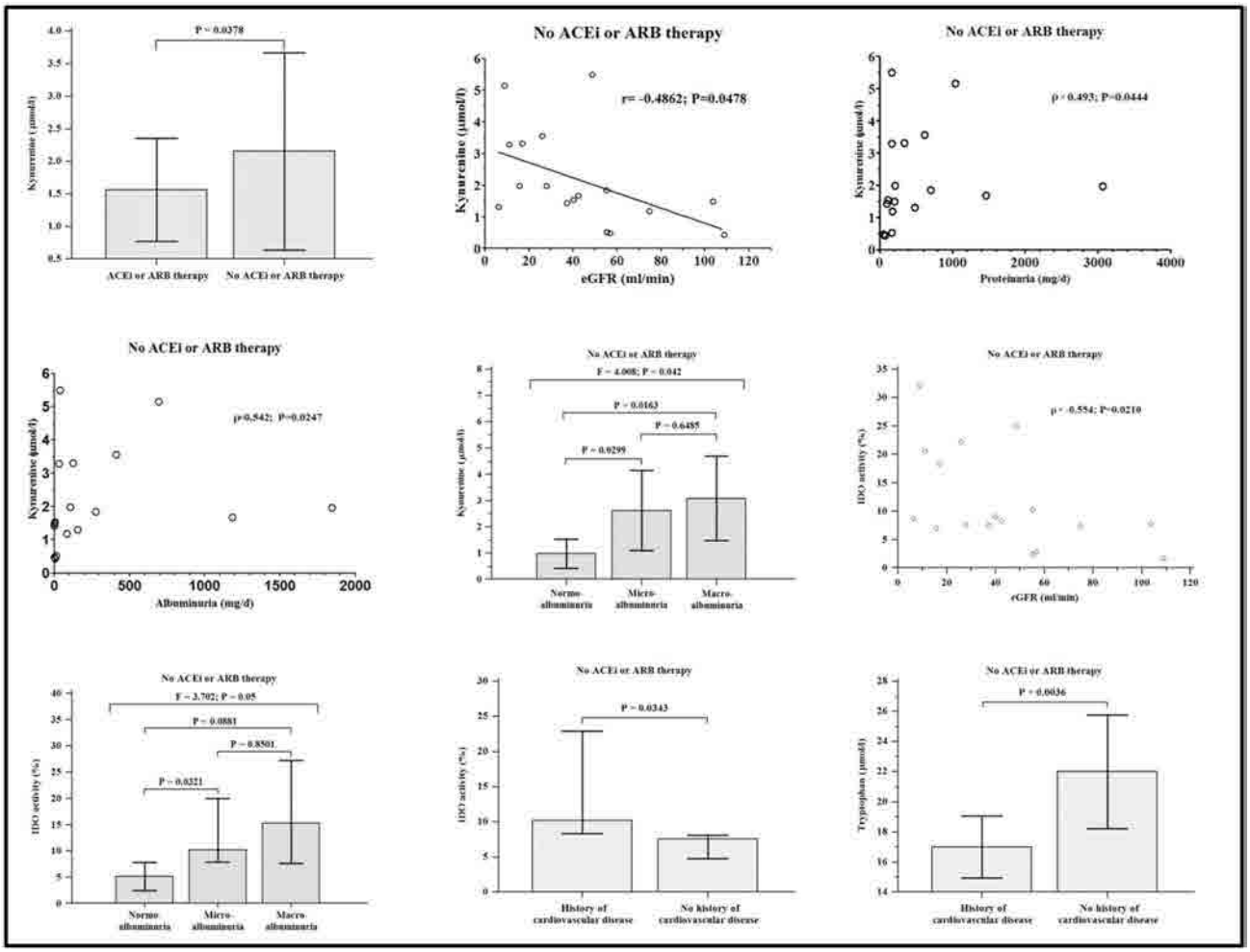


Figure:

significant association between kynurenine and markers of renal damage only in the group not receiving RAASis. We could hypothesize that kynurenine may play a role in the pathophysiology of renal damage, as already suggested, and that drugs interfering with RAAS activation may act also by reducing kynurenine levels, in addition to their already known effects at the renal level. Indeed, kynurenine synthesis results to be higher in states of inflammation and RAAS has pro-inflammatory and pro-fibrotic actions; accordingly, RAASis could reduce the enzymatic activity responsible for kynurenine increase and this could be one of the mechanisms mediating the beneficial effects of RAAS inhibition on CKD progression. This may be relevant because kynurenine has shown pro-thrombotic effects and is emerging as a potential new biomarker of CKD.

P0717 EPIGENETIC REGULATION OF CHRONIC KIDNEY DISEASE ACCELERATED-ATHEROSCLEROSIS

Nuria Doladé[1], Sandra Rayego-Mateos[1], Alicia García-Carrasco[1], Aurora Pérez-Gomez[1], Maria Crespo-Masip[1], Maryse Guerin[2], Pierre-Louis Tharaux[3], José M. Valdivielso[1]

[1]Institut de Recerca Biomédica de Lleida (IRBLleida), Medicina, Lérida, Spain, [2] INSERM UMR_S 1166 – ICAN, Faculté de Médecine Pitié-Salpêtrière, Paris, France and [3]Paris Cardiovascular Research Centre, (PARCC) Institut National de la Santé et de la Recherche Médicale (INSERM), Paris, France

Background and Aims: Atherosclerosis and its related clinical complications are the leading causes of death in western countries. Multiple processes are involved in atherosclerosis like endothelial dysfunction, inflammation, vascular proliferation, neovascularization, oxidative stress, apoptosis, extracellular matrix degradation and thrombosis. Moreover atherosclerosis could be accelerated in some diseases like chronic kidney disease (CKD). In this regard, miRNAs have been elucidated as important factors in the regulation of different cellular and molecular processes involved in atherosclerosis development. Our aim is to identify specific miRNAs that could be involved in chronic kidney disease (CKD) accelerated-atherosclerosis.

Method: A CKD accelerated-atherosclerosis mouse model was developed by subtotal nephrectomy (5/6 nephrectomy) in APOE-/- mice fed on a high fat diet (HFD) during 10 weeks and compared to mice with normal renal function. Urine and blood samples were collected every week. Western-blot, RT-PCR, immunohistochemistry and confocal microscopy analysis were performed. In previous studies mir23a-3p and miR652-3p have been suggested as possible regulators of the atherosclerotic process. Therefore the expression levels of these miRNAs and its possible target genes (FER and BTLA) were analyzed in mice total blood.

Results: APOE-/-+ERC+HFD mouse showed a progressive decrease in renal function and an increase of renal damage markers such as KIM-1. These animals showed structural glomerular damage characterized by de-cellularization, mesangial cell expansion and podocyte (WT1+,podocalixin+), endothelial (CD31+) and mesangial (GATA3+) loss. Lipid profile modifications were also observed in APOE-/-+ERC+HFD mice with an increase in plasma total cholesterol levels. Moreover atherosclerotic plaque size was also increased in APOE-/-+ERC+HFD animals in comparison with atherosclerotic plaque size of APOE-/-+HFD mice. CKD mice showed lower fibrosis (sirius red staining) and higher inflammatory markers in its atherosclerotic plaques. The presence of macrophages (CD68+) and T lymphocytes (CD3+) was increased in APOE-/-+ERC+HFD group in contrast with APOE-/-+HFD animals. Moreover, in samples from the aortic arch of APOE-/-+ERC+HFD mice, ICAM1 protein levels were increased. Finally we found decreased levels of mir23a-3p and mir652-3p gene in total blood samples of APOE-/-+ ERC+ HFD mice. On the other hand, in aortic arc and descendent aorta tissues, mir23a-3p and mir652-3p expression levels were similar between groups. The expression levels of mRNAs of potential targets of this miRNAs (FER and BTLA) were increased in total blood and aortic arch samples. In addition, we observed that BTLA and FER expression were localized in vascular smooth muscle cells and endothelial cells respectively.

Conclusion: Levels of mir23a-3p, mir652-3p and its related mRNA (FER and BTLA) are altered in CKD and may be a potential therapeutic target for CKD-accelerated atherosclerosis treatment.

P0718 HEALTH CARE COSTS IN CHRONIC KIDNEY DISEASE: A LONGITUDINAL STUDY FROM THE PIRP COHORT

Paola Rucci[1], Dino Gibertoni[1], Claudio Voci[2], Maria Pia Fantini[1], Marcora Mandreoli[3], Antonio Santoro[4]

[1]Alma Mater Studiorum - Università di Bologna, Department of Biomedical and Neuromotor Sciences, Bologna, Italy, [2]Bologna University Hospital Authority St. Orsola-Malpighi Polyclinic, Bologna, Italy, [3]Ospedale S.Maria della Scaletta, Nephrology and Dialysis Unit, Imola, Italy and [4]Alma Mater Studiorum - Università di Bologna, Specialty School in Nephrology, Bologna, Italy

Background and Aims:

Health care costs in patients with chronic kidney disease (CKD) vary widely according to patients' severity. In patients followed up in a community-based project, it is of interest to determine cost variations over time, as a result of treatment and CKD progression. The aim of the study was to estimate the costs incurred by the health care system for CKD patients in an Italian region.

Method:

Patients recruited in the Emilia-Romagna (Italy) PIRP project in the years 2007-2014 with CKD stage 3a to 5 were included in the study. Patients were stratified at baseline into 7 groups at different risk of progression according to the CT-PIRP classification (Rucci et al., *A clinical stratification tool for chronic kidney disease progression rate based on classification tree analysis*, NDT 2014). To calculate the annual medical costs, we multiplied the number of services used by the respective unit cost. Per capita costs were obtained dividing overall costs by person-years. We used DRG tariffs as a proxy of costs for hospital admissions, the regional nomenclator for outpatient visits and lab tests, and cost unit for prescribed drugs. Mixed effects generalized linear models were used to estimate the annual direct costs of CT-PIRP groups, adjusted for calendar year of entry in PIRP and local health authority of residence.

Results:

The study cohort includes 7737 CKD patients, aged 73.2±11.6 years, 64.5% males, mostly in CKD stage 4 (3136, 40.5%) and 3b (2799, 36.2%); 697 patients (9.0%) entered the study at stage 5. The CT-PIRP classification and frequency distribution is shown in Tab.1. After 4 years, 5017 (64.8%) were still alive, 1743 (22.5%) died, 546 (7.2%) were on ESKD and 422 (5.5%) were lost. The overall direct costs of patients while still enrolled in the PIRP project decreased from 36.89 million € in the first year to 32.22 in the fourth year, while the per capita annual median costs were stable around 2200 €. The cost breakdown showed a decrease of hospitalization and drugs costs and an increase in specialty visits costs (Fig.1).

The model-estimated average annual costs were significantly higher for proteinuric, low GFR patients of CT-PIRP groups 2 and 3 (7239 € and 8825 € respectively), while non-diabetic, younger patients of group 5 determined a significantly lower burden (3350 €).

P0719

SRC KINASES AGGRAVATE DIABETIC KIDNEY INJURY THROUGH ACTIVATION OF ENDOPLASMIC RETICULUM STRESS

Debra Dorotea[1], Hunjoo Ha[1]

[1]*Ewha Womans University, Graduate School of Pharmaceutical Sciences, College of Pharmacy, Seoul, Korea, Rep. of South*

Background and Aims: Diabetic kidney disease (DKD) is the major cause of end-stage kidney disease which is characterized by prominent kidney fibrosis. Src family kinases (SFKs), a family of proto-oncogenes, has been acknowledged to mediate the development of kidney fibrosis. While, several studies in liver and skeletal muscle suggested the role of Src kinases in activating endoplasmic reticulum (ER) stress. The present study aimed to investigate the mechanism of Src kinases-ER stress in mediating the progression of DKD.

Method: Type 1 diabetes was induced by a single 60 mg/kg i.p injection of streptozotocin (STZ) in 7-week-old male, Sprague-Dawley rats. Diabetic rats received 8-week-treatment of either KF-1607 (30 mg/kg/day), a pharmacological inhibitor of SFKs, or losartan (1 mg/kg/day), a standard treatment for patients with DKD.

Results: Among SFKs, Fyn and Lyn kinases were particularly increased in the diabetic kidney. Inhibition of Src kinases by KF-1607 improved kidney function and inhibited tubular injury, presented by decreased serum creatinine, albuminuria, and urinary KIM-1 excretion. Pathological changes in the kidney, such as enhanced glomerular volume, tuft area, and fractional mesangial area, were ameliorated in KF-treated rats. Highly-accumulated collagen network as well as increased TGF-β and α-SMA mRNA levels in the diabetic kidney were also significantly reduced in response to KF treatment. Furthermore, it consistently attenuated kidney inflammation and oxidative stress. The renoprotective effects of KF were interestingly similar to those of losartan. We showed increases in protein levels of phosphorylated IRE-1α, ATF6, GRP78 as well as CHOP indicating an exacerbated ER stress in the diabetic kidney. These ER stress markers were significantly decreased in KF treated mice.

Conclusion: Altogether, Src kinases through activation of ER stress aggravates kidney injury in STZ-induced diabetic rats.

P0720

CARVEDILOL AND NON-DIHYDROPYRIDINE CALCIUM CHANNELS BLOCKERS DELAY THE PROGRESSION OF CHRONIC KIDNEY DISEASE BEYOND ACE-INHIBITION IN KWAZULU-NATAL (SOUTH AFRICA)

Verushka Reddy[1,2], Alain Assounga[1,2]

[1]*Inkosi Albert Luthuli Central Hospital, Dept of Nephrology, Durban, South Africa and* [2]*University of KwaZulu-Natal, Dept of Nephrology, Durban, South Africa*

Background and Aims:

Chronic kidney disease (CKD) is on the rise worldwide. It is associated with increased morbidity and mortality and places a huge burden on cost constrained health systems in developing countries such as South Africa. ACE inhibition is well established as major factor of reduction of the decline of renal function. The aim of this study to evaluate carvedilol, non-dihydropyridine calcium channel blockers (NDCCB) as potential renal protection factor beside ACE inhibition.

Method:

This is a retrospective cohort study using the medical records of 300 patients attending the outpatient renal clinic department at Inkosi Albert Luthuli Central Hospital for the period January 2007 – December 2009. The average patient age was 43 years. The patients were followed up for 24 months following their first clinic visit. Socio-demographic (age sex, residence) and clinical characteristics including eGFR, blood pressure, BMI (body mass index), proteinuria, haemoglobin, cholesterolemia, were recorded. Treatments received including ACE inhibitors, carvedilol, non-dihydropyridine calcium channel blockers (NDCCB), Beta blockers were also recorded. Patients were divided into 2 outcome categories, according to changes in eGFR (estimated glomerular filtration rate): patients with eGFR decline of 1ml/min/year or less and those with accelerated eGFR decline (>1ml/min/year). Data analysis using SPSS version 23 (IBM) comprised of descriptive tests and logistic regression analysis (expressed as OR (odd ratio) and confidence interval) for the study of the association of above characteristics with patients' outcome.

Results:

ACE inhibition was used by 92% of patients. The use of carvedilol and NDCCB was associated with a reduction of the decline of eGFR with OR: 0.144[0.207-0.953] p=0.037 and OR: 0.543[0.329-0.884], p=0.016 respectively. No significant association was found between eGFR change and daily proteinuria or cholesterolemia. The aetiology of the chronic kidney disease did not affect rate of progression of eGFR. In addition, the rate of progression was not dependent on eGFR.

Conclusion:

These results suggest that beyond ACE inhibition, the control of BMI, and use of carvedilol and NDCCB further delay the progression of chronic kidney disease in KwaZulu-Natal.

P0721 **PPAR-GAMMA ACTIVATION INHIBITS TGF-BETA INDUCED RENAL COMPLEMENT AND GALECTIN-3 EXPRESSION IN VIVO AND IN VITRO**

Helga Popovics[1], Krisztina Mikone[1], Miklos Mozes[1,2], JiYeon Kwon[1], Georg Hansmann[3], Gabor Kokeny[1,2]

[1]Semmelweis University, Dept of Translational Medicine, Budapest, Hungary, [2]Semmelweis University, International Nephrology Research and Training Center, Budapest, Hungary and [3]Hannover Medical School, Department of Pediatric Cardiology and Critical Care, Hannover, Germany

Background and Aims: Reduced peroxisome proliferator-activated receptor-γ (PPARγ) activity has been observed in chronic kidney disease and fibrosis. We have recently shown that the PPARγ agonist pioglitazone dampens TGF-β induced renal pro-fibrotic transcription factors in vivo. Several studies have shown that renal complement expression is associated with fibrosis, yet the role of galectin-3 (Lgals3) remains controversial. However, the effect of PPARγ agonists on renal complement (C3, C4b) and Lgals3 expression has not been studied. We investigated how pioglitazone treatment affects TGF-β–driven renal inflammatory molecule expression in transgenic mice and in primary tubular epithelial cell (PTEC) culture.

Method: Ten weeks-old male C57Bl6 control (CTL) and TGF-β transgenic mice (with elevated circulating TGF-β1 level) were divided in two sets. The first set of mice received regular chow (CTL and TGFβ, n=4/group). The second set of mice were treated orally with pioglitazone (20mg/kg/day) for 5 weeks (CTL+Pio and TGFβ+Pio, n=5/group), when the kidneys were analyzed for mRNA and protein expression. PTEC were isolated from 4-weels old CTL mouse kidneys using graded sieving and characterized by immunoblot. Isolated cells were maintained in DMEM/F12 medium supplemented with 2% FBS and insulin/transferrin/selenium, and cells of passage 4-6 were used in triplicate for the experiments. Cells were treated for 24h with 10 ng/ml TGF-β and/or 5 μM pioglitazone, then mRNA expression levels were assessed. Statistical significance was verified using Mann-Whitney test.

Results: TGFβ kidneys depicted 13-fold and 4-fold overexpression of C3 and C4b mRNA ($p<0.05$), respectively, accompanied by a 1.7-fold Lgals3 expression ($p<0.05$). Oral treatment with the PPARγ agonist pioglitazone inhibited the TGF-β1 induced overexpression of C3, C4b, Lgals3, as well as IL-6 and CCL2 (MCP-1) mRNA ($p<0.01$). This was accompanied by reduced alfa-SMA (Actca2) and fibronectin mRNA expression. Renal Lgals3 showed significant correlation with alfa-SMA expression ($p<0.01$, see Figure). PTEC treated with TGF-β also depicted increased C3aR, alfa-SMA and collagen-1 mRNA expression by 1.7-fold, 2-fold and 2.1-fold, respectively ($p<0.01$), that were reduced to control levels by pioglitazone treatment ($p<0.05$).

Conclusion: Our data indicate that PPARγ activation exert strong anti-inflammatory effects in the renal tubular epithelial cells, implicating its possible therapeutic benefit by attenuating renal EMT and fibrosis in CKD patients.

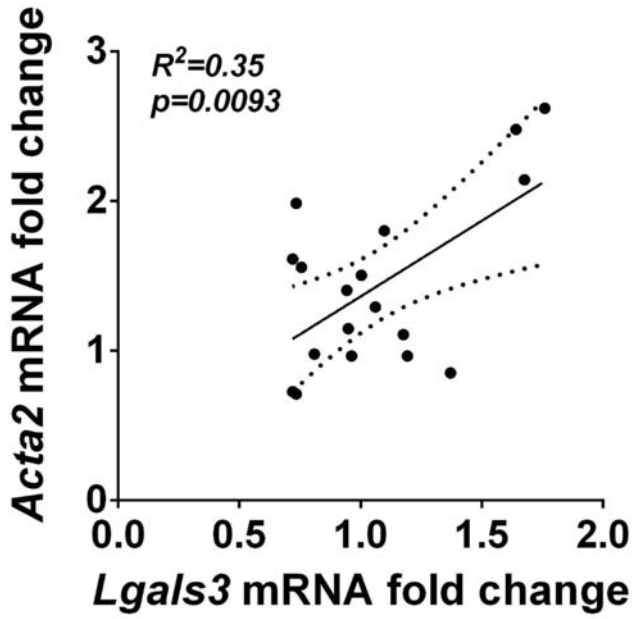


Figure:

P0722 **VITAMIN D-DEFICIENT RATS RECOVER RENAL ALTERATIONS AFTER VITAMIN D REPLACEMENT FOLLOWING ISCHEMIA-REPERFUSION INJURY**

Antonio Carlos Seguro[1], Michele S. Santos[1], Desiree Rita Denelle Bernardo[1], Daniele Canale[1], Maria Heloisa Massola Shimizu[1], Rildo Aparecido Volpini[1], Ana Carolina De Braganca[1]

[1]*Faculty of Medicine - University of Sao Paulo, Nephrology, São Paulo, Brazil*

Background and Aims: Several studies have been linking vitamin D deficiency (VDD) as a non-traditional risk factor to acute kidney injury (AKI). It has been shown that VDD associated with AKI potentiates the injury and may accelerate the progression of kidney disease. Conversely, some lines of evidence have been describing that vitamin D sufficiency can be considered as a renal protective factor. Thus, we aimed to verify the effect of vitamin D replacement (R) on the renal disease progression post ischemia-reperfusion injury (IRI) in vitamin D deficient rats.

Method: We performed bilateral 45 min IRI on day 30 in all animal groups. Male Wistar rats were randomized into three groups: **1- IRI** (fed a standard diet for 120 days); **2- VDD+IRI** (fed a vitamin D-free diet for 120 days); and **3- VDD+IRI+R** (fed a vitamin D-free diet for 30 days and just after IRI, on day 31, we reintroduced the standard diet for more 90 days). We evaluated inulin clearance (Cin); mean arterial pressure (MAP); renal blood flow (RBF); plasma levels of Vitamin D_2+D_3 [25(OH)D] and Parathormone (PTH) by ELISA. In addition, we performed histomorphometrical studies for CD3+ cells, fibronectin and vimentin as well as the fractional interstitial area (FIA). Moreover, we run qPCR studies and immunoblotted for vitamin D receptor (VDR) and Klotho. All the results are described in table 1.

Table 1

Parameters	IRI	VDD+IRI	VDD+IRI+R
Cin (mL/min/ 100g BW)	0.47±0.02	0.46±0.03	0.57±0.02 [c,f]
RBF (mL/min)	7.90±0.43	6.08±0.03 [c]	8.80±0.49 [e]
MAP (mmHg)	124.9±2.5	142.0±3.7 [a]	122.0±2.5 [d]
25(OH)D (ng/mL)	42.62±2.28	undetectable	42.89±2.58
PTH (pg/mL)	806.5±89.2	1,378±215.4 [c]	778.4±135.4 [f]
FIA (%)	15.98±1.32	22.69±1.39 [a]	12.00±0.65 [c,d]
Fibronectin (%)	5.43±0.84	10.88±1.29 [a]	5.27±0.42 [d]
Vimentin (%)	2.75±0.39	5.95±0.52 [a]	2.57±0.20 [d]
CD3+ cells (%)	0.38±0.07	1.39±0.23 [a]	0.29±0.04 [d]
VDR (%)	100.8±3.9	58.9±3.6 [a]	148.3±5.5 [a,d]
VDR (**ΔΔ**Ct)	0.86±0.06	0.54±0.05 [c]	0.82±0.08 [f]
Klotho (%)	99.6±3.9	80.4±5.4 [c]	108.8±7.9 [f]
klotho (**ΔΔ**Ct)	1.21±0.12	0.60±0.06 [a]	0.85±0.02 [b,f]

Data are expressed as mean±SEM. BW: body weight.
a $p<0.001$,
b $p<0.01$,
[c] $p<0.05$ vs IRI;
d $p<0.001$,
e $p<0.01$,
f $p<0.05$ vs VDD+IRI.

Results: Vitamin D replacement restored the plasma levels of 25(OH)D and PTH in VDD+IRI+R group. Also, VDD+IRI+R presented an improvement of renal function and hemodynamic parameters. In addition, we observed more evident alterations in tubulointerstitial compartment, featuring interstitial expansion (renal fibrosis and inflammatory cell infiltrates) and fibronectin and vimentin expression in VDD+IRI rats. These alterations were recovered by vitamin D replacement. Concerning VDR and Klotho data, our results revealed a decreased expression of these targets in VDD+IRI group. On the other hand, vitamin D replacement retrieved the expression of VDR and Klotho.

Conclusion: Our study suggests that vitamin D replacement improved the recovery of renal function, hemodynamics, inflammatory and morphological alterations. In addition, vitamin D replacement was able to reestablish the expression of VDR and Klotho in IRI-AKI associated with vitamin D deficiency. Thus, it is recommendable that vitamin D levels should be observed as well as its reposition should be taken into account in renal patients.

P0723

CHRONIC KIDNEY DISEASE AS AND INDICATION FOR MINIMIZATION OF IMMUNOSUPPRESSION IN LIVER TRANSPLANT RECIPIENTS

Krzysztof Mucha[1], Emilia Knioła[1], Bartosz Foroncewicz[1], Barbara Moszczuk[1], Krzysztof Zieniewicz[2], Michaå, Pac[1], Leszek Pączek[1]

[1]Medical University of Warsaw, Department of Immunology, Transplantology and Internal Diseases, Warsaw, Poland and [2]Medical University of Warsaw, Department of General, Transplant and Liver Surgery, Warsaw, Poland

Background and Aims: Liver transplantation (LT) requires patients to take immunosuppression (IS). Long term IS leads to hypertension and chronic kidney disease (CKD). Calcineurin inhibitors (CNi) are known to have nephrotoxic effects. Thus, liver transplant recipients (LTRs) that are taking either long-term or high cumulative doses of CNi are at a significantly higher risk of developing CKD. This study aimed to find predictive factors for development of CKD post-LT. Furthermore, it introduced IS minimization protocol in LTRs with clinical or laboratory indications with the aim to prevent the CKD progression and decrease the burden of other comorbidities.

Method: 212 out of all 870 LTRs from our center were screened for eligibility and 93 were recruited in 2018 for IS minimization after obtaining informed consent. They were deemed eligible if the primary cause of LT was a non-autoimmune disease and the graft function was stable. At the time of screening, patients were on IS either triple-, dual- or monotherapy (Table 1). The IS were reduced in 3 months intervals and was minimized until monotherapy with subtherapeutic serum levels (tacrolimus <5mg/ml or cyclosporine <50mg/ml).

Results: The indications for IS minimization were hypertension (73.87%), CKD (35.87%), cardiovascular diseases (32%), diabetes mellitus (23.91%) or malignancies (6.52%). It was found that LTRs with CKD were older (61.8 CKD vs. 49.6 non-CKD) and predominantly male (84.85% male; 15.15% female) when compared to non-CKD patients (33.9% male; 66.1% female). Another risk factor for post-LT CKD development was higher BMI (27.57 vs. 25.35). Time from transplantation of LTR with CKD was 129.12 months while for non-CKD was 150.19 months, suggesting that longer time since transplantation is not a predictive factor for development of CKD after LT. LTRs with CKD concomitantly had hypertension (84.85% vs. 67.80%) and DM (48.48% vs. 27.12%) more often than non-CKD LTRs. It was found that CKD-LTRs at the beginning of the IS minimization were more commonly taking IS polytherapies (triple 6.06% and dual 45.45% vs. triple 0% and dual 33.9%) than monotherapy (48.48% vs. 67.80%). In the first 12 months of the study, 22 out of the 33 patients with CKD safely reached monotherapy, 11 of those reached subtherapeutic levels of CNi (50,0%). Moreover, when kidney function was compared before and after IS reduction any progression of CKD was observed. Liver function tests were elevated in 4 patients with CKD, but return to the previous dose of IS resulted in normalization of liver function.

Conclusion: Minimization of IS should be considered in patients after LT who suffer from IS related comorbidities, particulary CKD. Its incidence post-LT was found to be associated with male gender, BMI and IS polytherapy. Our protocol of IS minimization seems to be safe in respect to graft rejection.

Table 1. Comparison of CKD and non-CKD LTRs.

			CKD		NON-CKD	
			n=33	%	n=59	%
		Age	61.8		49.6	
	Gender	Female	5	15.15	39	66.10
		Male	28	84.85	20	33.90
	Months from Tx		129.12		150.19	
Concomitant	BMI at baseline		27.57		25.35	
diseases		BMI after 12 mo.	27.90		25.84	
		Hypertension	28	84.85	40	67.80
	Diabetes Mellitus		16	48.48	16	27.12
GFR	At baseline		51.16		92.95	
	After 12 month		50.21		90.37	
IS at Baseline	Monotherapy		16	48,48	39	66,10
		Dualtherapy	15	45.45	20	33.90
	Tripletherapy		2	6.06	0	0
IS After	Monotherapy		22	66.67	49	83.05
12 month		Dualtherapy	9	27.27	10	16.95
	Tripletherapy		2	6.06	0	0.00
Number of LTRs taking CNi	At baseline		29	87.88	54	91.53
	After 12 mo.		28	84.85	55	93.22

P0724

ASSOCIATIONS OF URINARY POLYMERIC IMMUNOGLOBULIN RECEPTOR PEPTIDES IN THE CONTEXT OF CARDIO-RENAL SYNDROM

Tianlin He[1,2], Justyna Siwy[1], Jochen Metzger[1], William Mullen[3], Harald Mischak[1,3], Joost Schanstra[4,5], Petra Zürbig[1], Vera Jankowski[2]

[1]mosaiques diagnostics GmbH, Hannover, Germany, [2]Institute for Molecular Cardiovascular Research (IMCAR), University Hospital RWTH Aachen, Aachen, Germany, [3]Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, United Kingdom, [4]INSERM U1048, Institute of Cardiovascular and Metabolic Diseases, Toulouse, France and [5]Université Toulouse III Paul-Sabatier, Toulouse, France

Background and Aims: The polymeric immunoglobulin receptor (pIgR) which transports immunoglobulins from the basolateral to the apical surface of epithelial cells was recently shown to be associated with kidney dysfunction. The immune defense is initiated at the apical surface where the N-terminal domain of pIgR, termed secretory component (SC), is proteolytically cleaved and released either unbound (free SC) or bound to immunoglobulins. The aim of our study was to show the association of pIgR peptides with the cardio-renal syndrome in a large cohort and to get information on how the SC will be released.

Method: We investigated urinary peptides of 2707 individuals available in the Human Urine Proteome Database using capillary electrophoresis coupled to mass spectrometry.

Results: The mean abundance of 23 different pIgR peptides correlates negatively with the estimated glomerular filtration rate (eGFR, $r=-0.314$, $p<0.0001$). Furthermore, pIgR peptides are significantly increased in coronary artery disease after adjustment for eGFR. We further predicted the proteases involved in urinary peptide generation using the Proteasix tool. Peptide cleavage site analysis suggests that several, and not one, proteases are involved in the generation of the SC.

Conclusion: In this large cohort, we could demonstrate that pIgR is associated with the cardio-renal syndrome and provide more detailed insights on how pIgR can be potentially cleaved to release the SC.

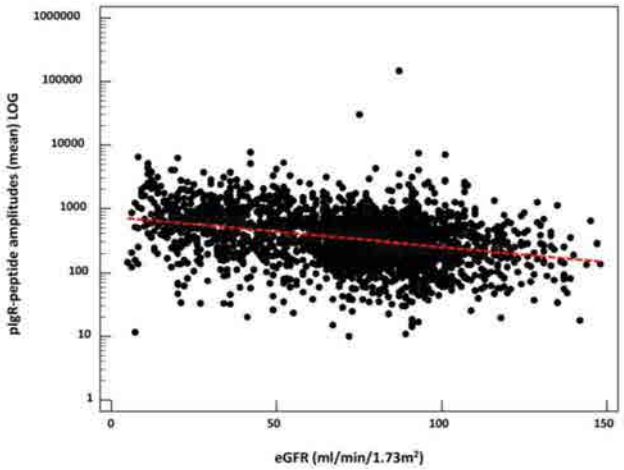


Figure: Scatter diagram of the correlation between mean amplitudes of the pIgR peptides and estimated glomerular filtration rate (eGFR).

P0725 **INDICATORS OF AGING KIDNEY, MEDIATORS OF EXTRACELLULAR MATRIX REMODELING**

Dae Cha[1], Jee Young Han[2], Jeong Hoon Park[1], Young Sun Kang[1], Jung Yeon Ghee[1], Ji Ae Yoo[1], Jin Joo Cha[1]

[1]Korea University Ansan Hospital, Internal Medicine, Ansan, Korea, Rep. of South and [2]Inha University, Pathology

Background and Aims: The main characteristics of aging kidney are age dependent glomerulosclerosis, tubular atrophy and interstitial fibrosis, therefore aging is now considered as an independent risk of chronic kidney disease. Extracellular matrix accumulation (ECM) is an early indicator of aging. Therefore in order to search for early indicator of aging kidney, we examined the expressions of regulators of ECM in the kidney in biologically aging and disease aging mice.

Method: C57BL/6 mice were studied at 2, 6, 12, 24 months of age, and leptin-deficient db/db mice were studied at 3, 6, 9 months of age. Gene and protein expressions of the kidney were examined as well as kidney injury markers in blood and urine.

Results: As expected, the biologically aging B6 mice exhibited progressive microalbuminuria during the lifespan. Systemically, the aging mice showed decreased levels of adiponectin, insulin and cholesterols. In the kidney tissue, proinflammatory and profibrotic gene expressions, in association with its regulators were significantly increased in age-dependent manners. At 24months, MCP-1, PAI-1, Collagen IV, MMP7, MMP9, angiotensin II, FGF23 and β-catenin gene expressions were significantly increased, whereas MMP2 and Snail, a direct activator of MMP-2 were significantly decreased. Protein expressions showed similar patterns. In high glucose condition, several markers showed diverse features in aging mice. As compared to db/m control, gene expressions of proinflammatory, profibrotic molecule as well as its regulators were all significantly increased in diabetic condition. Angiotensin II, FGF23, MCP-1, MMP7 and MMP9, TIMP-1 were significantly upregulated in diabetic kidney according to ages and interestingly Klotho was significantly downregulated in aged diabetic kidney. Snail and MMP2 showed no significant differences.

Conclusion: MMPs are involved in the crosstalk of the cells and surrounding extracellular matrix and can be considered as the marker of aging kidney. The regulators of ECM matrix seems to be different according to its' pathological conditions. Human clinical data is needed to render the clinical significance.

P0726

ENDOTHELIAL DYSFUNCTION ASSOCIATED TO ATHEROSCLEROSIS OF KNOCKOUT APOE MICE COULD BE MEDIATED BY VASCULAR FIBROSIS.

Ana Asenjo-Bueno[1], Elena Alcalde-Estevez[2], Patricia Sosa[2], Patricia Plaza[1], Lucia Serrano-Garcia[1], Mariam El Assar de la Fuente[3], Manuel Rodriguez-Puyol[2,4], Gemma Olmos[2,4], Maria Piedad Ruiz[2,4], Susana López-Ongil[1,4]

[1]Hospital Universitario Príncipe de Asturias, Fundacion para la Investigacion Biomedica, 5ºD, Alcala de Henares, Spain, [2]Universidad de Alcala, Facultad de Medicina, Biología de Sistemas, Alcala de Henares, Spain, [3]Hospital universitario de Getafe, Unidad de Investigación, Getafe, Spain and [4]Instituto Reina Sofía de Investigación Nefrológica (IRSIN) y Red Renal (REDinREN) del ISCIII, Madrid, Spain

Background and Aims: Patients with chronic kidney disease (CKD) present a high rate of cardiovascular mortality mainly associated with endothelial dysfunction, which causes more cardiovascular events in presence of atherosclerosis. Atherosclerosis is characterized by a significant increase of low density lipoproteins (LDL), reactive oxygen species (ROS) and inflammation. ROS can oxidize LDL generating oxidized-LDL (oxLDL) that promotes the development of cardiovascular pathologies. The aim of this study was to evaluate whether oxLDL induce endothelial dysfunction analysing the involvement of vascular fibrosis.

Method: The model used for *in vivo* studies was the Knockout apolipoprotein E (KO-apoE) mice, which resemble human atherosclerosis and shown high levels of cholesterol (LDL) that can be oxidized to oxLDL. In mice, blood pressure was registered before sacrificed them. After that, we measured different parameters as serum cholesterol levels, vascular function by vascular reactivity in mesenteric arteries and vascular fibrosis in aorta by Sirius Red staining and by the protein expression of fibronectin and collagen-I by immunohistochemistry. In order to investigate the mechanism of action of oxLDL, *in vitro* studios were performed on human smooth muscle cells (SMC) incubated with oxLDL at different times. Fibrosis was evaluated by the expression of TGF- β and extracellular matrix proteins such as fibronectin and collagen-I by Western blot and by immunofluorescence. ROS production was also measured by fluorescence confocal microscopy, using the CellROX Deep Red probe.

Results: KO-apoE mice shown higher levels of serum cholesterol and blood pressure than WT animals. Moreover, KO-apoE mice showed endothelial dysfunction since their arteries were less relaxed and more contracted. In addition, these mice presented thickening of vascular wall (SMC layer), more fibrosis showing intense Sirius Red staining and less expression of elastin, all compatible with their vascular dysfunction compared to WT mice. Furthermore, aortas from KO-apoE mice showed a slight increase in fibronectin and collagen-I expression assessed by immunohistochemistry. In vivo studies were confirmed in vitro after treating SMC with oxLDL. oxLDL induced fibrosis in SMC by increasing TGF-β, fibronectin and collagen-I protein expressions evaluated by Western blot and immunofluorescence assays. Treatment with oxLDL also increased ROS production, which seem to be responsible of oxLDL-induced fibrosis in human SMC, as it was blocked in the presence of the antioxidant N-Acetyl-cysteine.

Conclusion: In summary, these results point to endothelial dysfunction associated to atherosclerosis (oxLDL) could be mediated by an increase in the development of vascular fibrosis where ROS could play an important role. Therefore, the endothelial dysfunction typical of CKD patients could impair with more vascular fibrosis when atherosclerosis is also present.

P0727

P-CRESYL SULFATE AND INDOXYL SULFATE: A POSSIBLE ROLE AS BIOMARKERS IN THE PREDICTION OF RENAL FUNCTION AND CKD PROGRESSION

Valentina Corradi[1,2], Francesca Martino[1,2], Llaria Godi[2], Cecilia Mattarollo[2,3], Elena Barzon[3], Massimo De Cal[1,2], Carlotta Caprara[2], Davide Giavarina[3], Claudio Ronco[1,2,4]

[1]ULSS 8 BERICA - San Bortolo Hospital, Department of Nephrology, Vicenza, Italy, [2]IRRIV, Vicenza, Italy, [3] ULSS 8 Berica - San Bortolo Hospital, Department of Laboratory Medicine, Vicenza, Italy and [4]Universiy of Padova, Department of Medicine (DIMED), Padova, Italy

Background and Aims: Uremic toxins are markedly accumulated in chronic kidney disease (CKD) patients. Among these two protein-bound compounds, indoxyl sulfate (IXS) and p-cresyl sulfate (PCS) derived from gut bacterial transformation, play an important role. Recent evidences demonstrate their toxic effects in vitro and may contribute in vivo to CKD progression and mortality in uremic patients. For this reason, bacterial metabolism and its metabolites are therapeutic targets in CKD. While, several studies have evaluated possible associations between these two compounds and renal function decline in CKD, while no study has evaluated them according to the stage of progression (CKD stage). In this study, PCS and IXS are considered to highlight the possible role as biomarkers in the prediction of renal function and CKD progression (GFR stage 1-5).

Method: In our observational, prospective study we evaluated total (t) and free (f) PCS and IXS plasmatic fractions using Ultra High Performance Liquid Chromatography Infinity 1260 (Agilent technologies) coupled to an API 3200^{TM} triple quadrupole mass spectrometry (ABSciex). Data were shown as mean ± SD or median (25th-75th). Statistical analysis was done by SPSS version 24.0

Results: We evaluated 80 CKD patients: 54.68 ± 12.88 yrs, 39 F and 41 M. The median creatinine was 1.58 (0.90-3.32) mg/dL, median urea 58.50 (42.0-121.25) mg/dL and eGFR (CKD-EPI) 42 (17.25-85.75) mL/min/1.73 m^2. On the table 1, it was summarized the levels of PCS and IXS in all patients and classified by GFR (G) stages. We found the statistically significant increase of total and free fractions of PCS ($p<0.001$) and IXS ($p<0.001$) with the progression of CKD by G stage and inverse strong correlation between eGFR (CKD-EPI) and PCSt (*Spearman's Rho* (r)=-0.70, $p<0.001$), PCSf (r=-0.75, $p<0.001$), IXSt (r=-0.76, $p<0.001$), IXSf (r=-0.82, $p<0.001$).

Moreover, the increase of PCS and IXS predicts the eGFR decline significantly, according to the linear regression model using eGFR as dependent variable: PCSt (R-squared (R^2)= 0.34, $p<0.001$). PCSf (R^2=0.21, $p<0.001$). IXSt (R^2=0.27, $p<0.001$). IXSf (R^2=0.19, $p<0.001$). By multivariate analysis, the total compounds of both toxins remain predictive of eGFR: PCSt (β=-0.72, p=0.003; 95%CI:-2.43;-0.54) and IXSt (β=-0.70, p=0.011; 95%CI:-5.15;-0.70).

Conclusion: In conclusion, in our study we show the strong correlations between and PCS and IXS and eGFR and we found the significantly increase of PCS and IXS (total and free) with the progression of CKD in all G stage (1-5). We highlight the use of mass spectrometry in the evaluation of renal function especially in the earliest stages of CKD with the possibility of measuring minimum concentrations of PCSf and IXSf.

Assuming the predictive value of PCS and IXS towards the reduction of eGFR, we could hypothesize the identification of cut-offs based on confidence intervals, for the prediction and progression of renal function impairment.

	PCSt (mg/L)	PCSf (mg/L)	IXSt (mg/L)	IXSf (mg/L)
ALL pts	6.42 (3.15–19.81)	0.02 (0.00–0.33)	2.27 (1.17 – 6.78)	0.04 (0.01–0.15)
G1 (20pts)	2.7 (0.78–5.94)	0.00 (0.00–0.00)	1.15 (0.41–1.99)	0.01 (0.00–0.01)
G2(20pts)	4.26 (2.94–7.84)	0.00 (0.00–0.00)	1.33 (0.85– 1.73)	0.01 (0.00–0.00)
G3(20pts)	4.86 (3.17–9.41)	0.01 (0.0–0.14)	1.46 (1.07 – 2.29)	0.04 (0.01–0.05)
G4(20pts)	14.74(8.82–23.72)	0.22 (0.06–0.36)	4.92 (2.98–6.84)	0.09 (0.06–0.15)
G5(20pts)	29.74 (20.23–58.34)	0.73 (0.29–1.34)	11.76 (8.12–19.91)	0.38 (0.23–0.53)

P0728 **ASSOCIATIONS BETWEEN LUNG WATER NON-TRADITIONAL PARAMETERS AND FUNCTIONAL TEST IN CKD G4-5 WITH PRESERVED EJECTION FRACTION**

Anna Szymczak[1], Kusztal Mariusz[1], Letachowicz Krzysztof[1], Tomasz Gołębiowski[1], Anna Goździk[2], Krajewska Magdalena[1]

[1]University Teaching Hospital in Wroclaw, Department and Clinic of Nephrology and Transplantation Medicine, Wrocław, Poland and [2]University Teaching Hospital in Wroclaw, Department and Clinic of Heart Surgery, Wrocław, Poland

Background and Aims Patients with chronic kidney disease (CKD) are characterized by higher cardiovascular risk resulting amongst others from fluid expansion. Lung water measured by ultrasound (US) technique is increasingly recognised as an effective, quick and objective technique of even subclinical congestion/fluid overload. We aim to search correlates between the amount of artifact b-lines in lungs ultrasound (US-B lines; a metric of lung water), intra- and extracellular water (ICW, ECW), arterial stiffness by pulse wave velocity, result of functional six minute walk tests (6MWT) and global longitudinal strain score (GLS) assessed during heart ultrasound in patients with preserved ejection fraction.

Method: ICW/ ECW was assessed by bioimpedance (BIA 101 Akern), pulse wave velocity (PWV) by oscillometric method (mobilograph, IEM Germany). GLS was calculated using 2-dimensional speckle tracking. Traditional biochemical cardiac and renal markers and inflammatory markers were also assessed.

Results: The study included 51 consecutive patients (34 male) with CKD stage 4 and 5 (median eGFR MDRD4 11 ml/min IQR 9; 17) with oligosymptomatic congestion. The median (IQR) EF was 60 (60; 65)%, GLS was -18,7 (-21; -14)%, US-B lines was 10,5 (6; 17). Factors that were associated with US-B lines include BNP (r 0,5), ECW (r 0,4), distance in 6MWT (r –0,48) and hemoglobin (r -0,37).

In comparison between groups (below vs above median) with more lung water (>11 US-B lines) and less lung water amount (<11) assessed after 5 min in a supine position we found markedly higher concentration of BNP and more extracellular water (ECW) in the first mentioned group (table). Patients with more B-lines have had lower hemoglobin level and shorter distance walked in 6MWT.

Conclusion: Lung water assessed by US is an quick and objective measure of congestion in advanced CKD with normal EF showing correlation with BNP concentration, distance walked in 6MWT and with extracellular water in bioimpedance. Its application into daily practice can be recommended.

	<11 US-B lines N=26		>11 US-B lines N=25		
parameter	median	IQR	median	IQR	p-value
Age	57	47; 64	56	42; 66	>0,05
BNP	96,6	62; 261	599	90; 1053	0,05
TnT	9,15	5; 24,5	14,4	8,9; 34	>0,05
HGB	11	10; 12,6	9,6	9,2; 11	0,04
eGFR	12,5	9; 17	10	8; 15	>0,05
albumin	3,9	3,7; 4,3	3,85	3,3; 4,25	>0,05
CRP	3,3	1,8; 5	4,4	1; 7,1	>0,05
PCT	0,14	0,09; 0,2	0,12	0,01; 0,23	>0,05
US-B lines	6	4; 9	18,5	14,5; 27	<0,01
echo EF	65	60; 65	65	60; 65	>0,05
GLS	-17,5	-20; -13,3	-18,4	-21,75; -15	>0,05
LVM index	0,5	0,6	150	114; 165	>0,05
PWV (m/s)	7,8	7; 9,1	8,6	7; 10,2	>0,05
ECW (L)	19,6	16,6; 22,8	23	19,4; 26,4	0,02
6MWT (m)	400	360; 480	360	260; 400	0,05
RR2sys	155	130; 168	157	146; 170	>0,05
RR2dia	80	80; 94	88,5	80; 97	>0,05
pulse2	98	78; 112	85	73; 102	>0,05

P0729 **AKARDI: A NEW PREDICTIVE MODEL FOR RENAL DECAY AFTER NEPHRECTOMY**

FEDERICO DI MARCO[1], Umberto Capitanio[1], Arianna Bettiga[1], Riccardo Vago[1], Alessandra Cinque[1], Alessandro Larcher[1], Giacomo Dell'Antonio[2], Alberto Briganti[1], Andrea Salonia[1], Antonello Pani[3], Francesco Montorsi[1], Francesco Trevisani[1]

[1]IRCCS San Raffaele Scientific Institute, Urological Research Institute, Milan, Italy, [2]IRCCS San Raffaele Scientific Institute, Unit of Pathology, Milan, Italy and [3]Azienda Ospedaliera G. Brotzu, Struttura Complessa di Nefrologia e Dialisi, Italy

Background and Aims:

Radical Nephrectomy is usually associated to the risk of future development of a mild to severe chronic kidney disease stage especially for those patients who already present early stages of CKD (e.g CKD class II and IIIa). Any insight on this topic could influence the clinical decision about the surgery. But how can we know for sure the magnitude of the renal function's decay? In this preliminary work, our aim was to identify a new model able to predict at time surgery the renal function's variation at 1 year from the operation

Method:

We collected prospectively clinical data of a group of consecutive 114 patients who underwent radical nephrectomy (RN) for the presence of a benign or malignant renal mass. We estimated Glomerular Filtration Rate (eGFR) with MDRD formula. We considered the following clinical varibles: AKI onset (according to RIFLE criteria), age, gender, presence of blood hypertension, diabetes type II and BMI. Moreover, to investigate a possible correlation between renal basal histology and renal functional decay, renal biopsies were performed on each on the healthy part of the removed kidney > 3cm far from tumor. A pathological evaluation using a chronicity score (Remuzzi Score) was subsequently carried out evaluating damage on four parameters: (a) glomerular global sclerosis, (b) tubular atrophy, (c) interstitial fibrosis and (d) arterial narrowing. Statistical analysis were performed using generalized linear model (GLM), Kruskal-Wallis test and chi-square test. Multivariate analysis were applied using stepwise regressions method in order to select the best fitting model. Statistically significant correlations were considered for p-value<0.05.

Results:

At t0, 21% of the patients had an eGFR>90ml/min/1.73m^2, 45% between 60 and 90, 23% between 30 and 45, and 11% under 45. Median observed decay after 12 months was 32.8% (IQR= 17.9%:41.9%).Taking in account the eGFR decay's percentage there was a strong correlation with AKI onset (decay increased by 22.4%, CI= 14%:30.8%, p<0.0001), with Diabetes (decay increased by 13%, CI= 2%: 24.5%, p=0.02) and with the CKD stages at t0 (p=0.0007). Considering the histology, a significative negative correlation was found with the presence of arterial narrowing (-14%, CI=-23%:-6%, p<0.01) even though the whole chronicity score did not correlate (p=0.5). No significative correlations were found between the decay of eGFR and other variables such as age, gender or comorbidities. The multivariate analysis by stepwise regression, including all the significative variables from the univariate analysis, proposed as best model to predict the decay the use of AKI onset (14%, CI=6%:22%, p=0.001), arterial narrowing (-13%, CI=-22%:-5%, p=0.001) and diabetes (p=0.14) as variables.

Conclusion:

A precise and reliable prediction of renal function decrease after RN represents a cornerstone for urologist and nephrologist in order to create a personalized medical approach and management.In our cohort of study, CKD stage I and II patients displayed a huge decrease of eGFR in respect to CKD stages III-IV over time. One possible biological explanation can be that the healthy kidney of the patients affected by moderate and severe CKD starts working with a compensatory mechanism before the entire removal of the kidney with cancer so that the surgical acute nephron loss does not represent a shock in comparison to healthy patients with an eGFR >90 ml/min. Our preliminary study identified a new clinical and pathological panel of variables able to predict at time zero the magnitude of eGFR decay after 1 year from surgical operation. Further studies are needed in order to validate and improve this model.

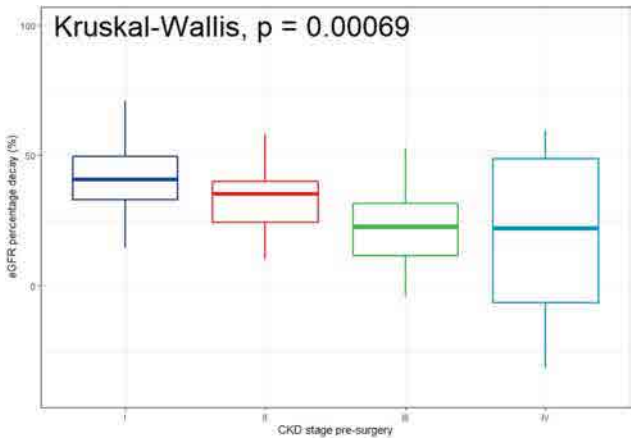


Figure:

P0730

ALTERATION OF BRAIN CONNECTIVITY IN NEUROLOGICALLY ASYMPTOMATIC PATIENTS WITH CHRONIC KIDNEY DISEASE

Yang Wook Kim[1], YOO JIN Lee[1], Bong Soo Park[1], Sihyung Park[1], Chang min Heo[1], Yoojin Lee[1]

[1]*Inje University Haeundae Paik Hospital, Department of Internal Medicine, Busan,*

Background and Aims: Our previous study demonstrated that patients in End stage renal disease had decreased structural and functional brain connectivity, and there was significant association between brain connectivity and cognitive function. The aim of this study was to evaluate the alterations of structural and functional connectivity using graph theoretical analysis in the neurologically asymptomatic patients with relatively early stage chronic kidney disease (CKD).

Method: We prospectively enrolled neurologically asymptomatic 20 patients with CKD stage 3 and 20 healthy controls, and all of the subjects underwent diffusion tensor imaging (DTI) and resting state functional MRI (rs-fMRI). Using data from the structural and functional connectivity matrix based on DTI and rs-fMRI, we calculated network measures, including global efficiency, local efficiency, mean clustering coefficient, characteristic path length, and small-worldness index, and investigated the differences between the patients with CKD and healthy controls.

Results: The patients with CKD had altered global structural connectivity and preserved functional connectivity compared to healthy controls. The all of the measures of global structural connectivity were significantly different between the patients with CKD and healthy controls. However, all of the measures of global functional connectivity in the CKD patients were not different from those in healthy participants. In the CKD patients, the functional betweenness centrality of the right insular cortex, right occipital pole, and right thalamus was significantly different from that in healthy subjects. The structural betweenness centrality of the left calcarine, right posterior cingulum was significantly different from that in healthy subjects.

Conclusion: There were significant alterations of global structural connectivity between patients with CKD and control. However, functional connectivity of brain network was preserved in contrast to ESRD patients.

P0731 LOW BIRTH WEIGHT IS ASSOCIATED WITH LOWER MEASURED GLOMERULAR FILTRATION RATE IN ADULT AGE

Bjørn Steinar Lillås[1,2], Camilla Tā̧ndel[2,3], Bjørn Egil Vikse[1,2]

[1]Haugesund Hospital, Medicine, Haugesund, Norway, [2]University of Bergen, Clinical Medicine, Bergen, Norway and [3]Haukeland University Hospital, Pediatrics, Bergen, Norway

Background and Aims: Low birth weight (LBW) has been shown to increase the risk of severe kidney disease. Studies have also shown that LBW is associated with lower estimated glomerular filtration rate (eGFR) or creatinine clearance in young adults. In the present study we investigated whether LBW associate with measured glomerular filtration rate (mGFR) in 40-50 year old adults.

Method: Retrospective longitudinal cohort study using the Medical Birth Registry of Norway to invite 200 individuals with LBW (birth weight $\leq$ 2300 gram) and 200 individuals with normal birth weight (NBW, 3500 – 4000 grams). All participants were aged 41 – 52 at time of examination. GFR was measured using plasma clearance of iohexol. Birth weight and gestational age were reported from the Medical Birth Registry. Main outcome was difference in measured GFR.

Results: We included 105 individuals – 57 LBW and 48 NBW – 55% females. Mean GFR was 94.8 $\pm$ 14.2 ml/min/1.73m^2 in the LBW group and 100.2 $\pm$ 12.5 ml/min/1.73m^2 in the NBW group (p=0.043). In females the mean GFR was 90.4 $\pm$ 12.2 ml/min/1.73m^2 in the LBW group and 100.5 $\pm$ 14.0 ml/min/1.73m^2 in the NBW group (p=0.005). In males the mean GFR was 101.4 $\pm$ 14.5 and 100 $\pm$ 11.2 ml/min/1.73m^2 in the LBW and NBW groups respectively (p=0.7). In a multi-regression model adjusting for age, maternal age and maternal civil status, we found an increase in mGFR of 4.5 ml/min/1.73m^2 for an increase of 1 kg in birth weight (p= 0.02) for women. For men there was a non-significant decrease of 1.2 ml/min/1.73m^2 for an increase of 1 kg in birth weight (p=0.6).

Conclusion: Women aged 41-52 years with low birth weight had significantly lower measured GFR as compared with participants with normal birth weight, there was no difference for men.

P0732 **DOES KIDNEY FUNCTION INFLUENCE PLASMA ADIPONECTIN CONCENTRATION IN ELDERLY CAUCASIANS?**

Marcin Adamczak[1], Sylwia Dudzicz[2], Jerzy Chudek[3], Jan Zejda[2], Tomasz Zdrojewski[4], Andrzej Jan Wiecek[1]

[1]Medical University of Silesia in Katowice, Department of Nephrology, Transplantation and Internal Medicine, Katowice, Poland, [2]Medical University of Silesia in Katowice, Department of Epidemiology, Katowice, Poland, [3]Medical University of Silesia in Katowice, Department of Internal Diseases and Oncological Chemotherapy, Katowice, Poland and [4]Medical University of Gdansk, Department of Hypertension and Diabetology, Gdansk, Poland

Background and Aims: Adiponectin is a hormone produced almost exclusively by the adipose tissue with vaso-protective activity and mostly metabolized in the kidneys. Glomerular filtration rate (GFR) is declining with age in elderly subjects and therefore it is expected to be followed by accumulation of adiponectin in the circulation. The aim of this study was to assess the plasma concentration of adiponectin in relation to GFR in the older population-based on the PolSenior study cohort.

Method: The PolSenior study was a multicenter cross-sectional study which assessed the health status of older adults in Poland. In 3913 subjects aged 65 years or above (2041 male and 1872 female, BMI 28.1±5.1 kg/m^2, mean age 79±9 years) plasma adiponectin concentration (ELISA; B-Bridge International) was measured. GFR was estimated using a short MDRD formula. All results are presented as means with standard deviations.

Results: In studied subjects eGFR was 76 ml/min/1.73 m^2. eGFR below 60 ml/min/1.73 m^2 was observed in 842 (22%) subjects. Plasma concentration of adiponectin was 11.9±6.4 μg/ml. In subjects with eGFR $<$ 60 ml/min/1.73 m^2 significantly higher plasma adiponectin concentrations were observed compared to subjects with eGFR $\geq$ 60 ml/min/1.73 m^2 (12.5±6.7 vs. 11.8±6.3 respectively, p=0.01). Plasma adiponectin concentration depends strongly on BMI (R= -0.28; p$<$0.001) and marginally on the kidney function (R=-0.05; p=0.005). Multivariate regression analysis including plasma adiponectin concentration, BMI, eGFR, occurrence of diabetes mellitus and hypertension, showed that BMI and prevalence of diabetes (b=-0.24, p$<$0.001, b=-0.11, p$<$0.0001, respectively) but not eGFR explain variability of plasma adiponectin concentration.

Conclusion: Plasma adiponectin concentration is only slightly affected by kidney function in elderly Caucasians from the PolSenior study.

P0733 PULSE MASS PRESSURE PRODUCT AND GLOMERULAR HEMODYNAMIC FUNCTION IN HEALTHY ADULTS.

Rina Oba[1], Go Kanzaki[1], Kotaro Haruhara[1], Takaya Sasaki[1], Yusuke Okabayashi[1], Izumi Yamamoto[1], Nobuo Tsuboi[1], Takashi Yokoo[1]

[1]*The Jikei University School of Medicine, Division of Nephrology and Hypertension, Department of Internal Medicine, Tokyo, Japan*

Background and Aims:

Recent studies have conflicting findings on the association between obesity and the risk of chronic kidney disease (CKD). BMI by itself is an imperfect marker of metabolically unhealthy obesity. The Pulse Mass Index (PMI) and the Pulse Mass Pressure Product (PMPP) show strong correlation with the risk of cardiovascular disease and may reflect an individual's metabolic energy state. However, it is still unknown whether the PMI and PMPP can be helpful to evaluate glomerular hyperfiltration or hypertrophy, which may exacerbate the progression of CKD. In this study, we measured mean glomerular volume (GV) and single nephron glomerular filtration rate (SNGFR) by estimating the number of nephrons from living kidney donors and we evaluated the effects of PMI and PMPP on glomerular hemodynamic function.

Method:

We identified 43 living kidney donors at the Jikei University School of Medicine Hospital from 2007 to 2017 who underwent an enhanced CT scan and a kidney biopsy at donation. The GV was determined by Weibel-Gomez methods and the SNGFR was calculated as eGFR divided by the total number of non-sclerosed glomeruli. The PMI is equal to BMI by resting heart rate (RHR) divided by 1730 and The PMPP is equal to BMI by RHR by systolic blood pressure.

Results:

Of 43 subjects, 34.9% were males and with a mean age of 56.1 ± 9.9 years old. Mean Arterial Pressure (MAP) was 86.3±9.9 mmHg, eGFR was 77.4±12.4 ml/min/1.73m2, and urinalysis was normal. The estimated total nephron numbers were 743,204±242,020 /kidney, and SNGFR was 61.7±20.5 nl/min/1.73m2. The GV was strongly associated with both of PMI and PMPP (P=0.0291 and 0.0326, respectively). Interestingly, SNGFR was only associated with PMPP (P=0.0443) but whereas not associated with either age, BMI, or MAP.

Conclusion:

In healthy adults, we observed a strong positive correlation between PMPP and both GV and SNGFR. This study indicates that PMPP is a more suitable physical measurement for glomerular hyperfiltration or hypertrophy, and a possible maker of the relative risk of CKD at the long term.

P0734

THE DELETION OF AKT1 PROMOTES THE RENAL FIBROSIS IN THE MURINE MODEL OF UNILATERAL URETERAL OBSTRUCTION

Il Young Kim[1], Byung Min Ye[1], Min Jeong Kim[1], Dong Won Lee[1], Soo Bong Lee[1], Sang Heon Song[2], Eun Young Seong[2]

[1]Pusan National University Yangsan Hospital, Yangsan, Korea, Rep. of South and [2]Pusan National University Hospital, Korea, Rep. of South

Background and Aims: Previous studies have found the increased Akt activity in experimental renal fibrosis. We investigated the role of Akt1, one of the three Akt isoforms, in renal fibrosis using the murine model of unilateral ureteral obstruction (UUO).

Method: In vivo, we subjected the wild type and $Akt1^{-/-}$ mice to UUO. In vitro, gene silencing of Akt1 was achieved using the short hairpin RNA delivered by the lentiviral vector in immortalized human proximal tubular cells (HK2 cells) and rat kidney fibroblasts (NRK-49F cells).

Results: In immunohistochemical stain, the expression of Akt1 was significantly higher in obstructed kidneys of wild type mice compared with control sham kidneys and increased gradually as UUO progressed. The fibronectin, type I collagen, and heat shock protein 47 (HSP47) were markedly more expressed in obstructed kidneys of $Akt1^{-/-}$ mice than in those of the wild type mice. Transforming growth factor β1 (TGFβ1) was highly induced within 1 day of UUO in obstructed kidneys of $Akt1^{-/-}$ mice and the expression of TGFβ1 was significantly higher in the $Akt1^{-/-}$ mice than in the wild type mice as UUO progressed. Western blot showed that silencing of Akt1 increased the expression of TGFβ1, which was enhanced by angiotensin II stimulation in HK2 cells, but not in NRK-49F cells. Immunohistochemical stain demonstrated that the expression of cleaved caspase-3 in renal tubules was significantly higher in the $Akt1^{-/-}$ mice than in the wild type mice. Western blot showed that silencing of Akt1 increased the expression of cleaved caspase-3 in HK2 cells, but not in NRK-49F cells.

Conclusion: Our findings suggest that the deletion of Akt1 might contribute to tubulointerstitial fibrosis and tubular apoptosis via TGFβ1 induction. We also showed that TGFβ1 upregulation by genetic deletion of Akt1 is associated with activation of STAT3 independently of the TGFβ1/Smad signaling pathway.

P0735

ELAVATED INTRACELLULAR COPPER CONTRIBUTES A UNIQUE ROLE TO KIDNEY FIBROSIS BY LYSYL OXIDASE MEDIATED MATRIX CROSSLINGKING

Yangyang Niu[1], Chen Yu[2]

[1]Shanghai Tongji Hospital, Tongji University School of Medicine, Department of Nephrology, Shanghai, P.R. China and [2]Shanghai Tongji Hospital, Tongji University School of Medicine, Department of Nephrology, Shanghai, P.R. China

Background and Aims: Copper is an essential trace element required for many biological processes. Some studies have demonstrated that copper accumulating was related to liver fibrosis and lung fibrosis, but the underlying mechanism is not very clear. Copper is the essential unit of lysyl oxidase (LOXs), which are the key enzymes of crosslinking of extracellular matrix.

Method: Sprague-Dawley rats were divided into the sham group, unilateral ureteral obstruction (UUO) operated group and UUO treated with copper chelating agents tetrathiomolybdate (TM). Rat kidney fibroblast cells (NRK-49F) were used in vitro. The concentration of copper, the LOXs activity and the degree of cross-linking of extracellular collagen were detected in vivo and vitro.

Results: (1) The copper concentration in serum, urine and kidney of rats increased significantly at 7 days after UUO surgery; After treatment of TGF-β1, the intracellular copper concentration was increased significantly in cells; The concentration of copper in patients' serum is on the rise with the progression of chronic kidney disease (CKD). (2) The expression of CTR1 was upregulated in the kidneys of UUO rats; The level of CTR1 was increased significantly by TGF-β1 in vitro; (3) Blockage of Smad2/3 suppresses TGF-β1-induced expression of CTR1; (4) Downregulation of CTR1 significantly inhibited the intracellular copper concentration; (5) The activity of LOXs was increased significantly after TGF-β1 treatment; (6) Downregulation of CTR1 significantly inhibited the activity of LOXs and the cross-linking of extracellular collagen induced by TGF-β1 in vitro; (7) The concentration of copper, the degree of collagen cross-linking and the deposition of collagen were decreased in the kidney tissue of UUO rats after treatment with TM. The concentration of intracellular copper, the activity of LOXs and the degree of collagen cross-linking were attenuated with treatment of TM in vitro.

Conclusion: We firstly found that the intracellular copper accumulating was closely to renal fibrosis. The underlying mechanism was related with the increasing expression of CTR1 and activity of LOXs. Treatment with TM ameliorated the renal fibrosis. This study presented a novel treatment target for renal fibrosis.

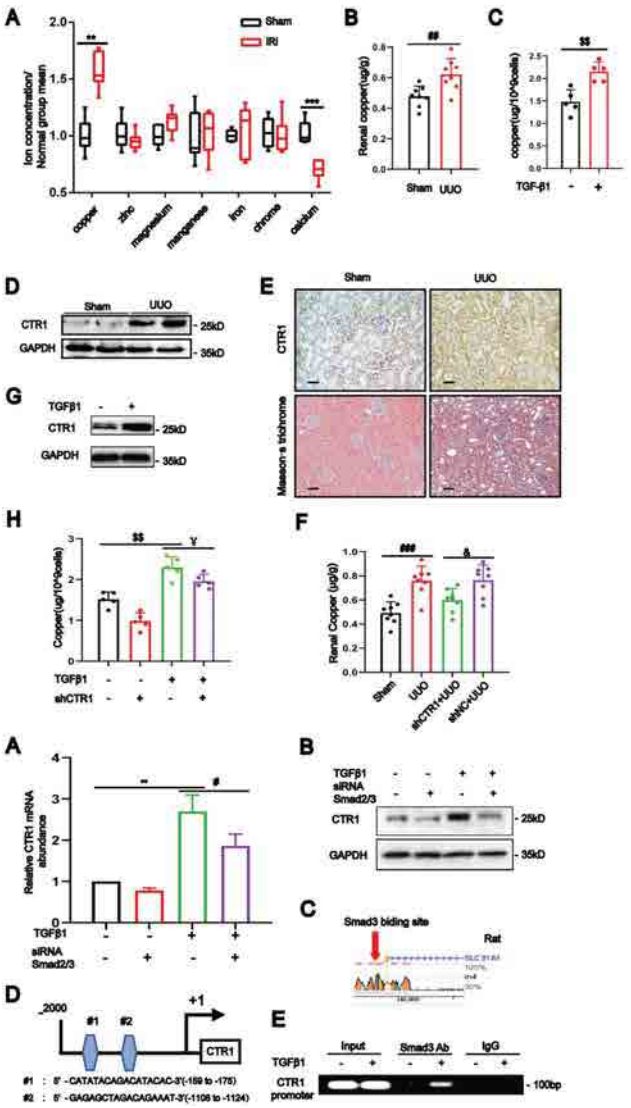


Figure:

P0736 A NOVEL MODEL OF CHRONIC KIDNEY DISEASE AND HEART FAILURE WITH PRESERVED EJECTION FRACTION

Alejandro Chade[1], Maxx Williams[2], Jason Engel[2], Michael Hall[3]

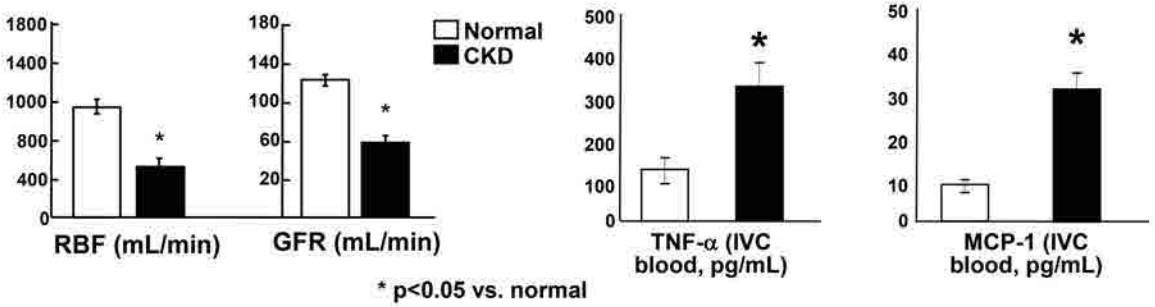
[1]University of Mississippi Medical Center, Physiology and Biophysics; Medicine; Radiology, Jackson, United States of America, [2]University of Mississippi Medical Center, Physiology and Biophysics, Jackson, United States of America and [3]University of Mississippi Medical Center, Physiology and Biophysics; Medicine, Jackson, United States of America

Background and Aims: Patients with chronic kidney disease (CKD) have a significantly higher cardiovascular risk that non-CKD patients, and over 50% of CKD patients die of cardiovascular events. We recently developed a model of CKD that displays major pathological features of clinical CKD: GFR of about 60 ml/min (stage 2-3a), significant renal inflammation, fibrosis, microvascular dysfunction and remodeling, and hypertension. The current study aims to define the cardiac phenotype of this model and, if cardiac abnormalities are present, the potential pathological traits involved.

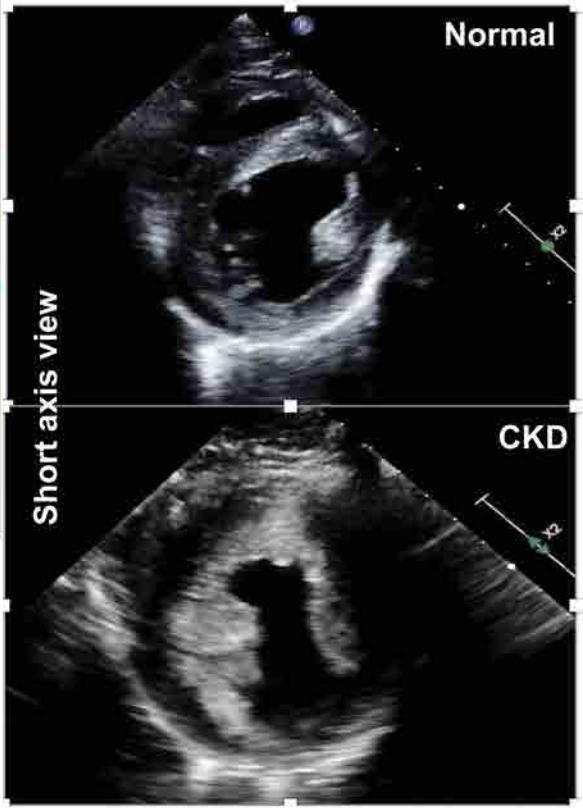
Method: CKD was induced in 6 pigs via bilateral renovascular disease and dyslipidemia and observed for 14 weeks. After 14 weeks, renal hemodynamics (RBF, GFR) were quantified using multi-detector CT and echocardiographic assessment (morphology and function) performed using ultrasound-doppler. Mean arterial pressure (MAP) was continuously measured by telemetry. Blood was collected to measure circulating inflammatory cytokines (TNF-α, MCP-1, IL-6) and biomarkers of heart failure (ANP, BNP, NT-proBNP). Animals were then euthanized and kidneys and hearts collected for *ex vivo* studies. Normal pigs were used as time-matched controls.

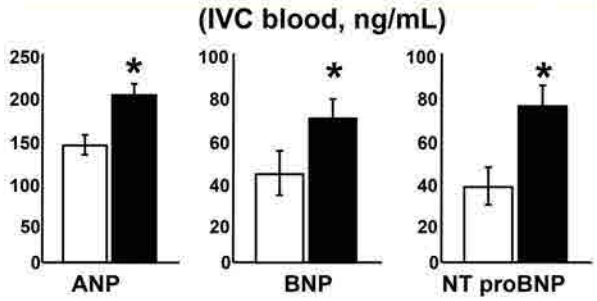
Results: Loss of renal function in CKD was accompanied by left ventricular hypertrophy, left atrial dilatation, diastolic dysfunction (E/A ratio) with preserved ejection fraction (pEF), elevated ANP, BNP, and NT-proBNP, and hypertension (average MAP of 131.2 mm/Hg, $p<0.05$ vs. normal). CKD also increased renal (but not cardiac) mRNA expression of TNF-α, MCP-1, IL-6, accompanied by increased circulating inflammatory cytokines (Figure).

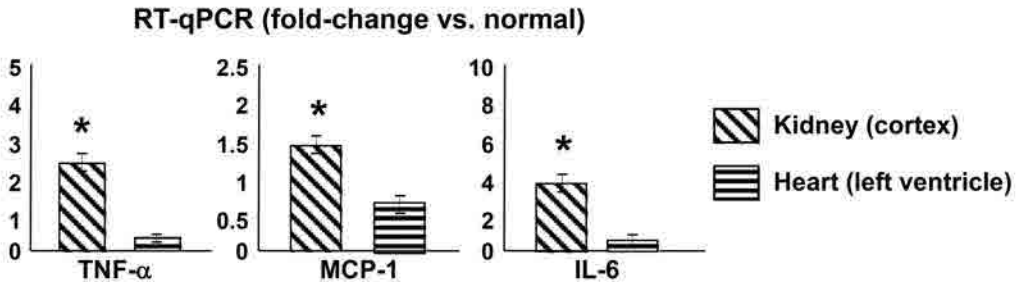
Conclusion: This study shows that CKD in the swine model leads to cardiac hypertrophy and diastolic dysfunction (with pEF) and increased biomarkers of heart failure, meeting the criteria for a potential novel model of heart failure with pEF (HFpEF). Our data also suggest that hypertension and inflammatory mediators (possibly originated in the kidney) target the heart and may contribute to HFpEF pathophysiology. HFpEF is considered the largest unmet need in cardiology with no specific treatments and associates with CKD in about 50% of cases. Thus, our study offers a promising new experimental platform to increase our understanding of CKD-HFpEF and to test new treatments in a translational fashion.



Echocardiographic parameters	Normal	CKD
Morphology		
LV wall thickness (cm)	*0.7*	*1.45*
LV dimension (diastole, cm)	6.8	5.41
LV dimension (systole, cm)	4.03	3.6
Left atrial diameter (cm)	*4.8*	*6.6*
Function		
Ejection fraction (EF, %)	>50%	>50%
E/A	1.42	1
E/e'	6.7	7.7







Figure

P0737 THE ASSOCIATION BETWEEN CYSTATIN C AND ARTERIAL STIFFNESS IN NON-CKD PATIENTS

Nejc Piko[1,2], Tadej Petreski[1], Robert Ekart[2,3], Radovan Hojs[1,3], Sebastjan Bevc[1,3]

[1]Maribor, Nephrology, Maribor, Slovenia, [2]Maribor, Dialysis, Maribor, Slovenia and [3]Maribor, Medical faculty, Maribor, Slovenia

Background and Aims: Serum cystatin C (cysC) is produced by all nucleated cells at a constant rate, is filtered freely by the glomerulus and metabolized after tubular reabsorption. It is influenced less by age, gender and muscle mass compared to serum creatinine. These properties make it an important marker in detecting renal impairment. Arterial stiffness is a hallmark of atherosclerosis and is connected to cardiovascular events and mortality. In patients with chronic kidney disease (CKD), cysC correlates with increased arterial stiffness, but less is known about the association between cysC and arterial stiffness in non-CKD patients.

Method: The study was performed at the University Medical Centre Maribor between October 1st 2018 and January 1st 2020. Basic demographic and laboratory data were recorded. To estimate glomerular filtration rate (eGFR), Chronic Kidney Disease Epidemiology (CKD-EPI) equation was used. Patients with previously diagnosed CKD and/or eGFR $\leq$ 60 ml/min/1.73m^2 at the time of admission, known malignancy, thyroid disease and/or on steroid therapy were not enrolled in the study. Arterial stiffness was measured with applanation tonometry (Sphygmocor®, Australia), carotid-femoral pulse wave velocity (cfPWV) was used as the gold standard of central arterial stiffness and subendocardial viability ratio (SEVR) was used as the marker of myocardial perfusion. SPSS® version 22 was used for statistical analysis.

Results: 111 patients (65.8% male, average age 64.3$\pm$9.4 years) were included in our study. Most common comorbidities were arterial hypertension (n=86, 77.5%), hyperlipidaemia (n=64, 57.7%) and diabetes mellitus (n=22, 19.8%). Mean creatinine value was 77.7$\pm$13.8 µmol/L (range 49-108 µmol/L), mean eGFR was 81.3$\pm$9.4 ml/min/1.73m^2 (range 62-90 ml/min/1.73m^2) and mean value of cysC was 0.94$\pm$0.18 mg/L (range 0.67-1.63 mg/L). Mean SEVR value was 165.7$\pm$36.1% (range 92-299%) and mean cfPWV value was 10.1$\pm$2.4 m/s (range 6.2-16.8 m/s). Significant correlation was found between cysC and SEVR (r=-0.316, p<0.001) and between cysC and cfPWV (r=0.472, p<0.001). Multiple regression analysis of arterial stiffness indices and cysC, age, gender, diabetes mellitus, arterial hypertension, eGFR and hyperlipidemia, showed statistically significant association between cysC and cfPWV (ß=0.220, p=0.038) and cysC and SEVR (ß=-0.278, p=0.017).

Conclusion: Serum cysC is independently associated with increased arterial stiffness, reduced myocardial perfusion and increased cardiovascular risk in non-CKD patients.

P0738 **RELATION BETWEEN BLOOD LEAD AND CADMIUM LEVELS AND CHRONIC KIDNEY DISEASE**

Amira Emam[1], Sameera Hamed[2], Ahmed Elmowafy[3], Mahmoud Awad[2], Sahar Eldakroory[2], Adel Elmansoury[2]

[1]Mansoura Specialized Hospital, Toxicology, Mansoura, Egypt, [2]Faculty of Medicine, Forensic Medicine and Clinical Toxicology, Mansoura, Egypt and [3]Urology & Nephrology center Mansoura university, Nephrology, Mansoura, Egypt

Background and Aims: Chronic kidney disease (CKD) was one of the three reasons of mortality with the furthermost increase from 1990 to 2010 between the top 20 killers. Environmental toxins (Lead Pb and Cadmium Cd) are hidden factors incorporated in the increased prevalence of CKD. The aim of this study is to determine whether there is a relationship between CKD and alteration in blood Pb and Cd levels.

Methods: This is a case-control study which was held in Forensic department, Mansoura University, Egypt. The individuals were divided into 2 groups: Group I: 40 persons with normal kidney function used as a control group, group II: 40 patients suffering from CKD secondary to unknown cause who are attending to follow up at nephrology outpatient clinic, Mansoura insurance hospital. All participants were subjected to full history taking (Personal history about gender, age, residence and occupation (mechanics, plumbers, battery manufacturers, manufacturers and users of paint and electricians), The history of special habits like smoking, seafood, canned food consumption, using colored mugs and living in old houses, History about medical disorders associated with renal failure as diabetes and hypertension), laboratory investigations including serum creatinine, creatinine clearance, serum Pb and serum Cd.

Results: Eighty persons (49 males and 31 females) were included in the study with age range from 15 to 76 years. The majority was above 40 years and was coming from rural areas (62.5% in group I and 60% in group II) with no statistical significance (Figure 1). In group I (45.0%) was smokers and (55.0%) were non smokers while in group II (70.0%) were smokers and (30.0%) were non smokers. The difference was statistically significant (p =0.026). Among group I, (42.5%) out of them were using frequently colored food container ceramics while (65%) among group II were frequently use them and the difference was statistically significant (p =0.048). Other risk factors showed no significance (Figure 2). In **group I** Pb levels range from (9.51µg/100ml) to (42.67µg/100ml) while Cd levels range from (1.59µg/100ml) to (3.87µg/100ml); whereas in **group II** Pb levels range from (19.43µg/100ml) to (82.3µg/100ml) while Cd levels range from (2.04µg/100ml) to (6.12µg/100ml). There is statistically significant difference among both groups as regard blood Pb levels (p <0.001) with higher blood Pb levels in C.K.D patients (mean±SD=52.76±15.65) than healthy controls (mean±SD=18.06±5.61). Also, there is statistically significant difference among both groups as regard blood Cd levels (p <0.001) with higher blood Cd levels in C.K.D patients (mean±SD=4.27±0.87) than healthy controls (mean±SD=2.62±0.62) (Figure 3 & 4). There was negative correlation between blood Pb,Cd levels and patients' creatinine clearance (for Pb;R:-0.755, p=0.001, for Cd;R:-0.712, p=0.001) (Figure 5, 6). There was positive correlation between blood Pb, Cd levels and serum creatinine (for Pb;R: +0.713, p =0.00, for Cd; R: +0.707, p =0.00) (Figure 7, 8).

Conclusion: Pb and Cd toxicity may lead to CKD and these environmental factors may explain the unknown etiology of many renal failure cases. With chronic exposure, blood level >25.8 µg/dl for Pb and >3.46 µg/dl for Cd carry the risk for renal failure incidence.

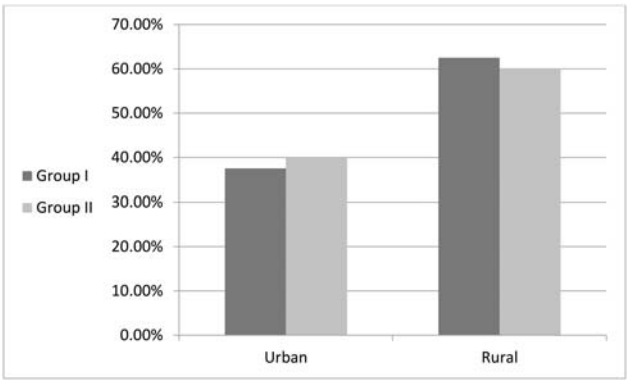


Figure (1): Residence distribution among studied groups

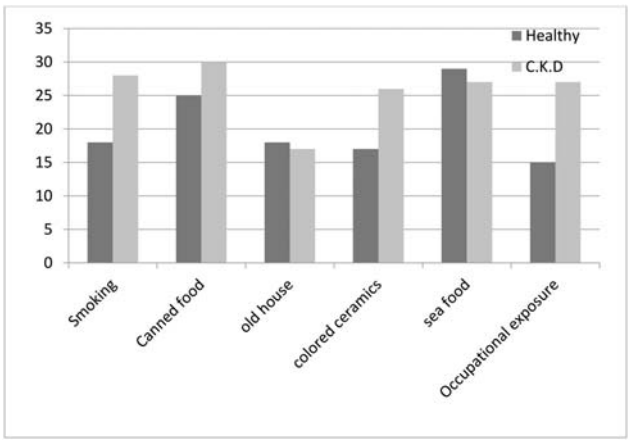


Figure (2): Risk factors for Pb and Cd nephrotoxicity among studied cases

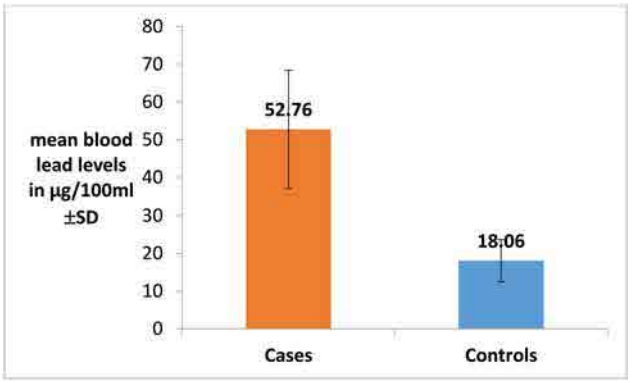


Figure (3): Blood Pb levels within CKDs and control groups

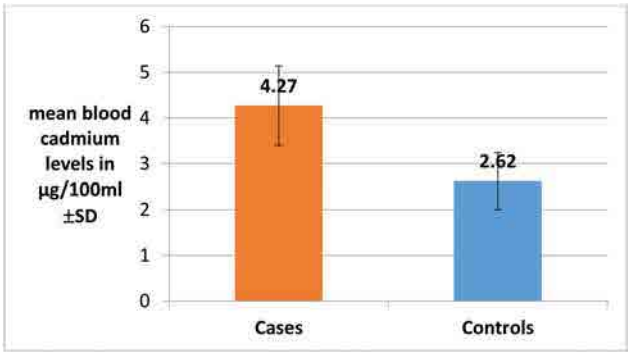


Figure (4): Blood Cd levels within CKDs and control group

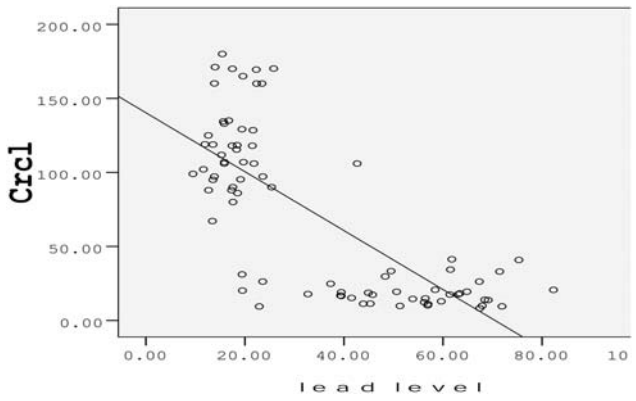


Figure (5): Pearson correlation between Pb levels in the blood and creatinine clearance

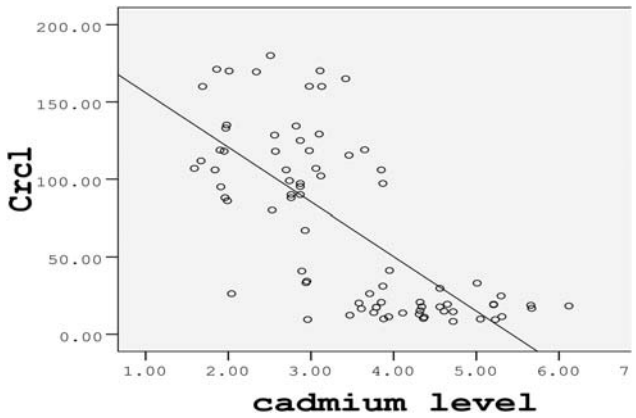


Figure (6): Pearson correlation between Cd levels in the blood and creatinine clearance

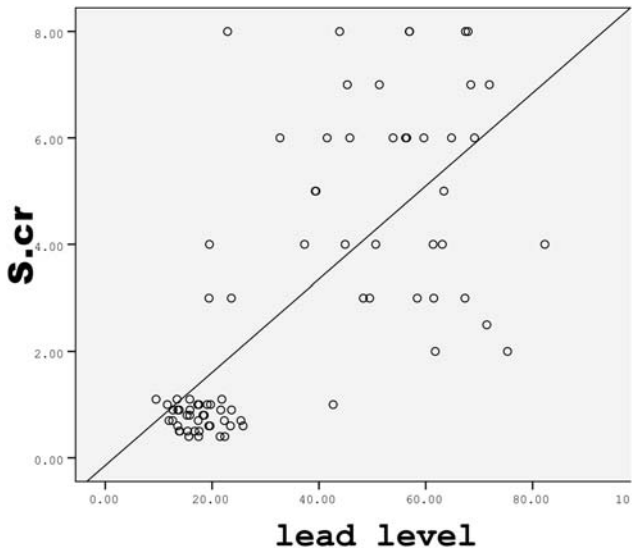


Figure (7): Pearson correlation between Pb levels in the blood and serum creatinine

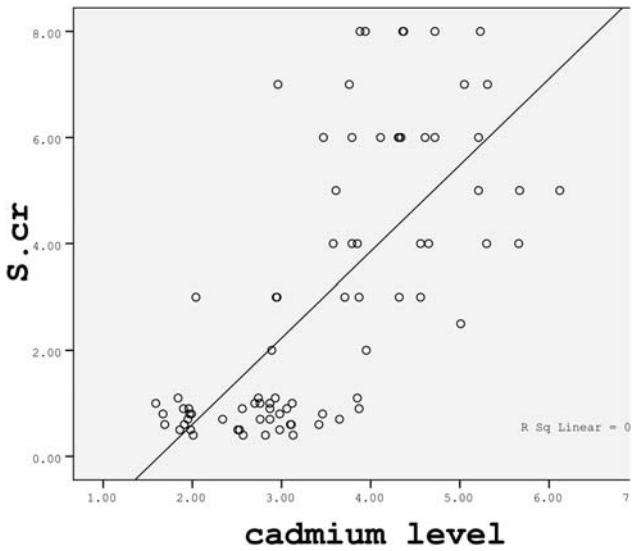


Figure (8): Pearson correlation between Cd levels in the blood and serum creatinine

P0739 **PANEL OF SENSITIVE BIOMARKERS OF THE PRIMARY RESPONSE TO RENAL INJURY FOR AN EARLY DIAGNOSIS OF CHRONIC KIDNEY DISEASE**

Maria João Valente[1], Susana Rocha[2], Irina Lousa[1], Flávio Reis[3], Sara Nunes[3], Sofia D. Viana[3,4], Inês Preguiça[3], Filipe Mira[5], Rui Nogueira[6] , Susana Coimbra[1,7], Cristina Catarino[1], Petronila Rocha-Pereira[1,8], Elsa Bronze-da-Rocha[1], Maria do Sameiro Faria[1,9], Rui Alves[5], Sofia Santos[10], Sofia Correia[10], Idalina Beirão[10,11], Luís Belo[1], Alice Santos-Silva[1]

[1]UCIBIO, REQUIMTE, Laboratory of Biochemistry, Department of Biological Sciences, Porto, Portugal, [2]LAQV, REQUIMTE, Laboratory of Applied Chemistry, Department of Chemical Sciences, Porto, Portugal, [3]Institute of Pharmacology & Experimental Therapeutics, Coimbra Institute for Clinical and Biomedical Research (iCBR), Faculty of Medicine, & CIBB Consortium, University of Coimbra, Coimbra, Portugal, [4]Polytechnic Institute of Coimbra, ESTESC-Coimbra Health School, Pharmacy, Coimbra, Portugal, [5]Department of Nephrology, Coimbra University Hospital, Coimbra, Portugal, [7]CESPU, Institute of Research and Advanced Training in Health Sciences and Technologies (IINFACTS), Gandra PRD, Portugal, [8]Health Science Research Centre, University of Beira Interior, Covilhã, Portugal, [9]Hemodialysis Clinic of Felgueiras, Felgueiras, Portugal, [10]Nephrology and Kidney Transplantation Department, Hospital de Santo António, Centro Hospitalar do Porto, Porto, Portugal and [11]Unit for Multidisciplinary Investigation in Biomedicine (UMIB), Abel Salazar Institute of Biomedical Sciences, University of Porto, Porto, Portugal

Background and Aims:

The identification of early kidney injury biomarkers is of utmost importance, since most widely used markers of kidney function vary only after several biological changes. Biomarkers allowing an earlier diagnosis of chronic kidney disease (CKD) would avoid delays in the treatment of patients. It is unlikely that a single marker is sufficient to detect the onset of CKD considering the multiple pathophysiological changes underlying primary renal response to renal injury. Several markers of inflammation, endothelial (dys)function, glomerular and tubulointerstitial injuries have been proposed and could be used combined as a panel of markers with different specificities, allowing an early detection of renal injury.

Our aim was to study a panel of biomarkers proposed as early markers of renal injury, with different specificities, to evaluate and compare their sensitivities at different CKD stages.

Method:

In this preliminary study, we enrolled 22 healthy individuals and 27 CKD patients separated into 3 groups, according to the CKD stage: 9 in stages 1 and 2; 9 in stage 3, and 9 in stages 4 and 5. None of the patients presented inflammatory, infectious or neoplastic diseases. Diagnosis and CKD stage assignment were performed according to KDIGO guidelines. We evaluated circulating levels of cystatin C (CystC), creatinine (Cr), beta trace protein (BTP) as markers of renal function; tissue inhibitor metalloproteinase 1 (TIMP-1), neutrophil gelatinase-associated lipocalin (NGAL) and transforming growth factor-β (TGF-β) as markers of interstitial tubulointerstitial injury; asymmetric dimethylarginine (ADMA) and tissue plasminogen activator (t-PA), as markers of endothelial (dys)function; pentraxin 3 (PTX3), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), as markers of inflammation; and, pro B-type natriuretic peptides (proBNP), as a marker of cardiac (dys)function.

Results:

In early stages of CKD (1 and 2), we found significant changes in markers of renal function (BTP, but not Cr and CystC), of tubular interstitial injury (TIMP-1 and TGF-β), of inflammation (TNF-α), of endothelial (ADMA) and cardiac (proBNP) dysfunction (*vs.* controls). In stage 3, we found significant changes (*vs.* stages 1-2) in markers of renal function (Cr and CystC), inflammation (TNF-α, IL-6), endothelial dysfunction (t-PA) and tubulointerstitial injury (TIMP-1); in stages 4-5 (*vs.* stage 3), we found significant changes only in the classic marker, Cr, and a trend towards increased CystC. Moreover, we found that at stages 1-2 all patients showed higher levels of BTP and proBNP when compared to the median value in the control group; TIMP-1 and ADMA were increased in 7/9 patients; TNF-α was increased in 7/9 patients; and 7/9 patients had lower values of TGF-β compared to the median value of controls. For the classical markers, Cr and CystC, we found that 5/9 and 4/9 patients, respectively, had lower values than the median value of controls; however, only 2/9 patients showed abnormal creatinine values (*vs.* reference values).

Conclusion:

Our data suggest that a panel including classic (Cr and CystC) and more sensitive blood markers of the primary response to renal injury (BTP, TIMP-1 or TGF-β, ADMA, TNF-α and proBNP) would allow an earlier diagnosis of CKD, avoiding a delay in diagnosis and management of CKD patients.

P0740 HYPERKALEMIA, CKD AND RAAS INHIBITION: A TRIAD WITH A FINE BALANCE TO PREVENT MORTALITY

Luis Falcao[1], Adriana Paixão Fernandes[1], Sara Fernandes[1], Beatriz Donato[1], Mário Raimundo[1], Catarina Teixeira[1], Ana Cortesão Costa[1], Sónia Silva[1], Ana Macedo[1], Edgar Almeida[1]

[1]*Hospital Beatriz Angelo, Nephrology, Loures, Portugal*

Background and Aims: Hyperkalemia (HK) is a common and dangerous complication of CKD because of impaired kidneýs ability for potassium elimination. On the other hand, HK is a common complication of extremely beneficial therapeutic agents acting on the renin–angiotensin–aldosterone system (RAAS). Its initiation at early CKD stages is even more benefic but HK could lead to stop it. We wonder if there is a possible relation between HK, therapeutic changes in RAAS inhibition (not initiating or stopping it) and mortality. Our goal was to investigate incidence, prevalence and clinical outcomes of at least one episode of HK in a CKD population outpatient setting. Additionally, we investigated the association of HK with changes in RAAS inhibition and mortality risk.

Method: We conducted a patient-level, retrospective, cohort analysis of all adult patients referred to a nephrology clinic over a 6 years period. We included CKD stage 3 patients with at least 24 months of follow up and three or more serum potassium determinations. The prevalence of HK (blood potassium level $\geq$ 5,5mmol/L) at first consultation and incidence during follow up were accessed. Patients were spited in two groups prior to analysis: A) Patients without any HK episode and B) Patients with at least one HK episode. Baseline and follow up covariates included demographics, comorbid conditions, laboratory values, HK-associated drugs [ACEis, ARBs, potassium-sparing diuretics and diuretics]. The impact of HK and therapeutic changes on mortality was evaluated through a logistic regression.

Results: Out of the 3008 patients referred to the nephrology clinic, 575 (19.1%) met the inclusion criteria (mean age: 70.4 years; 63.7% male and 94.0% caucasians). Mean follow-up was 4.1$\pm$1.8 years. Important cardiovascular comorbidities included hypertension (HTN) (90.3%); overweigh (67.4%), DM (49.0%) and Heart Failure (31.4%). CKD stage progression was present in 122 (21.2%). The prevalence of HK at first consultation was 8.7% and follow up incidence 21.7%. From this cohort, 164 (28.5%) had at least on episode of HK (Group B) and 101 (17.6%) died. During the follow up, RAAS inhibition drugs was removed or not started in 200 (34.8%) patients and diuretic was initiated in 165 (28.7%). In univariate analysis, at least one HK episode was associated with Diabetes (65.9 vs 42.3%, $p<0.001$), Heart failure (36.6 vs 28.0%, $p=0.007$), Macroalbuminuria (34.1 vs 21.2%, $p=0.001$), CKD progression (33.5 vs 16.3. $p<0.001$) higher frequency of diuretic initiation (38.4 vs 24.8%, $p<0.001$) and higher mortality (27.6 vs 13.7%, $p<0.001$).

In multivariate logistic regression analysis, the independent predictors of mortality were: At least one HK episode (OR 1.82, 95% CI 1.08-3.04, p=0.02); Heart Failure (OR 1.97, 95% CI 1.16-3.35, p=0.01); Older age (OR per 1 year increase 1.04, 95% CI 1.02-1.07, p=0.001); CKD progression (OR 4.18, 95% CI 2.43-7.19, $p<0.001$). Predictors of lower mortality risk were: Patients who maintained RAAS inhibition during follow up (OR 0.50, 95% CI 0.26-0.96, p=0.03); Patients who started RAAS inhibition during follow up (OR 0.38, 95% CI 0.16-0.88, p=0.02).

Conclusion: Our study confirms that RAAS inhibition had a protector and independent impact in mortality when prescribed in CKD early stages. On the other hand, patients with at least one episode of HK have a higher risk of mortality. All efforts should be made to maintain these therapeutic agents, looking for other ways to control hyperkalemia rather than stop it.

P0741 **CHRONIC KIDNEY DISEASE PROGRESSION IN A LARGE PREVENTION COHORT IN COLOMBIA**

Angela Rivera[1], Angelito Bernardo[2], Jasmin Vesga[3], Izcay Ronderos[4], Mauricio Sanabria[5]

[1]Baxter Healthcare Corporation, RCS Medical & Quality, Deerfield, United States of America, [2]Baxter Healthcare Corporation, REN-Chronic-Medical, Deerfield, United States of America, [3]Renal Therapy Services (RTS) Colombia, Clinical Research, Bogota, Colombia, [4]Renal Therapy Services (RTS) Colombia, Medical, Bogota, Colombia and [5]Baxter Renal Care Services (BRCS) Latin America, Clinical Research, Bogota, Colombia

Background and Aims: Chronic kidney disease (CKD) is a syndrome that today has important implications for the health of populations and the economic sustainability of health systems around the world, therefore strategies to slow disease progression are necessary.

Aims: To estimate the incidence of renal replacement therapy (RRT) in a cohort of patients included in a CKD secondary prevention program and to describe the decrease of the estimated glomerular filtration rate (eGFR).

Method: This is a historical, multicenter, observational cohort study in a prevention program between January 1, 2010, and December 31, 2017, with follow-up until December 31, 2018, at the Renal Care Services (RCS) network. Socio-demographic and clinical characteristics of all patients were summarized descriptively. We estimated the incidence of RRT rate with Kaplan Meier analysis. Progression rate to RRT was analyzed by mixed-effects model adjusted for the eGFR reduction rate at 180 days; the model considered the diagnosis of diabetes.

Results: 7131 patients met the inclusion criteria for data analysis. The mean age was 65 years, 50.5% were female, (**Table 1**). There were 577 events of RRT with a rate of 2.02 events of RRT per 100 patients-year [95% CI,1.86 to 2.19], characteristics at the RRT initiation are presented in **Table 2**. At the beginning of the program the eGFR was 45.3 ml / min / 1.73m^2 in non-diabetics, and 40.9 3 ml / min / 1.73m^2 in diabetics. The CKD progression was - 0.48 ml / min / 1.73m^2 per 180 days in diabetics and - 0.20 ml / min / 1.73m^2 per 180 days in non-diabetics. The final events of the cohort are presented in **Figure 1**; the mortality rate was 0.89 events per 100 patients-year [95% CI, 0,79 to 1,01].

Conclusion: This population of patients in a CKD prevention program presented a low rate of initiation of dialysis therapy and a slight decrease of eGFR; the diabetic status influences the CKD progression.

Table 1. Baseline demographic and clinical characteristics

Characteristics		N=7131	%
Age	[mean; SD] years	64.82	10.9
Sex	Female	3599	50.4
CKD cause	Chronic interstitial tubule nephritis	49	0.7
	Polycystic Kidney	89	1.2
	Glomerulonephritis/ Autoimmune	311	4.3
	Obstructive	411	5.7
	Other	706	9.9
	Unknown	780	10.9
	Diabetes	1712	24.0
	Hypertension	3063	42.9
Hypertension history	Yes	6068	85.1
Diabetes history	Yes	2444	34.3
Ischemic heart disease history	Yes	736	10.3
Cerebrovascular disease history	Yes	142	1.9
Congestive heart failure history	Yes	376	5.2
Obesity	Yes	1395	19.5
Smoking history	Yes	1843	25.8
CKD grade at the program start	3	5675	79.5
	4	1456	20.4
Late entry to the CKD program*	Yes	359	5.0
Uncontrolled blood pressure	Yes	1683	23.6

*Start with less than 20 ml / min / 1.73m2 of eGFR

Table 2. Characteristics at the beginning of dialysis

Characteristics		N=577	
Modality, [n, %]	Hemodialysis	321	55.6
	Peritoneal dialysis	256	44.4
Dialysis access, [n, %]	AVF	53	9.2
	AV Graft	1	0.2
	Vascular catheter	267	46.3
	Peritoneal catheter	256	44.4
Route of dialysis admission, [n, %]	Urgencies/ Hospitalization	212	36.7
	Referred by the CKD program	365	63.3
Albumin; g/dL [mean, SD]		3.6	0.6
Hemoglobin; g/dL [mean, SD]		10.4	1.7
Phosphorus, mg/dL [mean, SD]		4.9	1.4
BUN, mg/dL [mean, SD]		66.7	23.4
PTHi, Pg/mL [mean, SD]		293.3	240.5

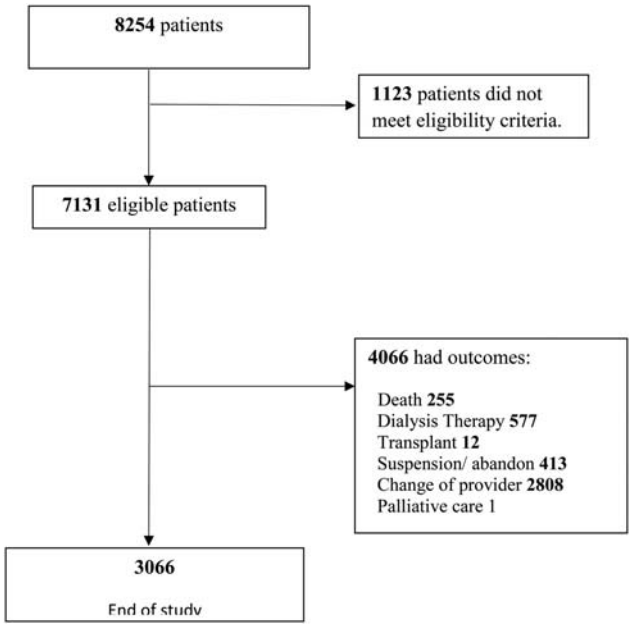


Figure: Figure 1. Study flow chart

P0742

ASSOCIATION BETWEEN EOSINOPHILIA AND RENAL PROGNOSIS IN PATIENTS WITH CHOLESTEROL CRYSTAL EMBOLISM

Yasuhiro Mochida[1], Takayasu Ohtake[1], Marie Morota[1], Kunihiro Ishioka[1], Hidekazu Moriya[1], Sumi Hidaka[1], Shuzo Kobayashi[1]

[1]*Shonan Kamakura General Hospital, Kamakura, Japan*

Background and Aims:

Approximately, 20%-70% of patients with cholesterol crystal embolism (CCE) have eosinophilia. However, it remains unknown how eosinophilia influences on renal prognosis in patients with CCE. In this study, we investigated an association between eosinophil count (Eo) and renal prognosis in CCE patients on steroid therapy.

Method:

The present study is a single-center retrospective cohort study in patients with pathological proven CCE and Chronic kidney disease from April 2007 to May 2018. This study included the patients who are not treated with maintenance dialysis nor steroid, and moreover followed until November 2019. We analyzed the validity of eosinophil counts using receiver operating characteristic (ROC) curve analysis. In the statistical analysis, renal survival was calculated with the Kaplan– Meier method, and comparisons between higher and low Eo groups were made with the log-rank test.

Results:

Thirty-two patients with pathological diagnosed CCE were enrolled and followed-up for 11.0 (4.7-43.6) months. There were significant differences in the white blood cell (p=0.03), hemoglobin (p=0.007), serum creatinine levels (p=0.03), phosphate (p=0.045), Calcium×Phosphate (p=0.03), and Eo (p=0.016) between the renal survival and renal death groups. Using the receiver operating characteristic curve analysis with Youden index, Eo of 810/μL showed the sensitivity and specificity 71% and 88% for detecting renal death, respectively (area under the carve; 0.789). Comparing the outcomes in patients having Eo ≥ and <810/μL by using the log-rank test, there are significantly higher renal death rate in CCE patients with Eo ≥810/μL (p=0.004).

Conclusion:

Higher eosinophilia was a prognostic risk factor for renal death in the patients with CCE.

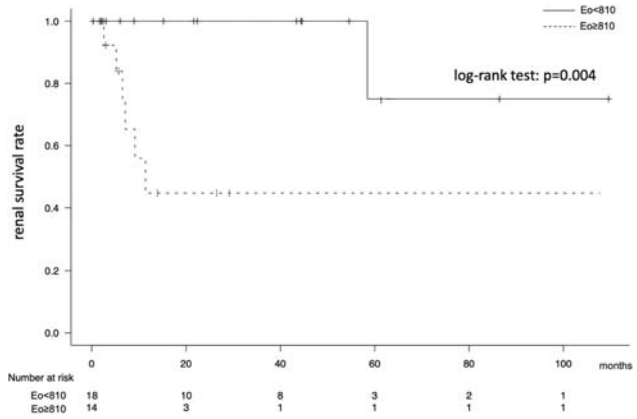


Figure:

P0743 COMPARISON OF PROTEINURIA LEVELS BETWEEN PROFESSIONAL AND RECREATIONAL CROSSFIT ATHLETES

Renan Diniz[1], Elizabeth De Francesco Daher[2], Geraldo Bezerra da Silva Junior[3], Julio Cesar Chaves Nunes Filho[4], Marilia Porto Oliveira Nunes[4]

[1]Hospital Geral Waldemar de Alcantara, Clínica Médica, [2]Unversidade Federal do Ceara, Medicina Clinica, [3]Universidade de Fortaleza, Faculdade de Medicina and [4]Universidade Federal do Ceara, Medicina Clinica

Background and Aims: High intensive sports athletes are under risk of muscular injuries and likely renal damage secondary to it. As CrossFit is becoming more popular in last years, few consistent studies are available evaluating renal damage associated to this sport. The purpose of this study was to compare proteinuria levels between recreational and professional CrossFit athletes who were under training for a local competition.

Method: These athletes were invited to answer a survey. After this step, they were submitted to proteinuria analysis through urine dipstick reading. They also were divided into two groups (professional X recreational athletes) and the results were compared using chi-square test.

Results: A total of 99 athletes have concluded all the steps of the study. Among professional athletes, age average was 34.1 $\pm$3.9 year old, body mass index (BMI) 27.14 $\pm$ 3.14 kg/m^2 while in the recreational group the age average was 28.7 $\pm$ 5.9 and BMI 26.49 $\pm$ 4.56 kg/m^2. Comparing proteinuria analysis, 44.4% of professional group have shown levels between 300 and 1000mg/dL and 14.8% have reached levels above 1000mg/dL, while only 2.8% among recreational ones have reached levels above 300mg/dL ($p=0.001$) with no one in this groups showing levels $>$ 1000mg/dL.

Conclusion: This study has shown high proteinuria levels among professional CrossFit athletes comparing to recreational ones. As the literature is scarce in showing long-term kidney damage among CrossFit athletes, epidemiological studies warn about likely kidney damage related to this practice, a fact that can suggest better medical follow-up for CrossFit athletes.

P0744

CLINICAL IMPACT OF SERUM INDOXYL SULPHATE MEASURED BY NEW ENZYMATIC METHOD IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Yoshinari Yasuda[1], Ryosuke Kikuchi[2], Kazunori Goto[1], Ahmad Baseer Kaihan[1], Sawako Kato[1], Shoichi Maruyama[1]

[1]Nagoya University Graduate School of Medicine, Department of Nephrology/CKD Initiatives, Nagoya, Japan and [2]Nagoya University Hospital, Department of Medical Technique, Nagoya, Japan

Background and Aims: Uremic toxins have been highlighted as serious risk factors for deterioration of renal function and onset/progression of cardiovascular diseases (CVD). Serum level of indoxyl sulphate (IS), a major uremic toxin, was demonstrated its significant association with vascular disease and mortality in a cohort of chronic kidney disease (CKD) patients, however, IS has not been available in clinical setting due to time consuming and expensive measurement cost. Recently epoch-making IS measurement method applicable for general auto analyzer has been developed, which could explore new therapeutic avenue in CKD from the view point of uremic toxin management.

In this study, clinical utility of new enzymatic IS measurement method was analyzed in association with renal function and CVD among CKD patients.

Method: Subjects were consecutive 150 CKD patients in Nagoya University Hospital whose serum samples were collected between 2009 and 2014. Serum IS levels were measured by "NIPRO" reagent and analyzed with eGFR, CVD events and renal outcomes defined by 30% decrease in eGFR.

Results: Characteristics of patients were 69 ± 10 years old, 29% female, eGFR: 44 ± 20 mL/min/1.73m2 (∼G3a: 43%, G3b: 29%, G4: 24%, ï¼5: 4%), proteinuria 2.8 ± 3. 5ï½‡/ï½‡Cr (A1: 29%, A2: 29%, A3: 42%), HTN: 83%, and DM: 39%. Serum IS levels (μmol/L) were 10.5 ± 7.5 (∼G3a: 1.8 ± 0.6, G3b: 2.1 ± 0.6, G4: 15.8 ± 8.1, ï¼5: 22.9 ± 13.5), and strongly correlated with eGFR ($r = 0.518$, $P < 0.001$). Among IS low (<6), middle and high (≥12) tertiles, significantly different factors were age, eGFR, Hb, iPTH and LDL-C. In multiple logistic regression analysis, only eGFR was significant associating factor with IS tertiles. IS levels in 2 patients prescribed AST-120 (Kremezin) were 8.1 and 10.3, which seems to be very low in comparison to their eGFR of 13.8 and 13.7. During observation period of 5.1 ± 1.0 years, 59 renal outcomes and 9 CVD events were observed. Kaplan-Meier survival curve analysis free from renal outcomes revealed better tendency in IS low group ($p = 0.0617$ in log-rank test). According to IS levels adjusted by eGFR, only 1 out of 9 CVD events occurred in low IS/eGFR tertile group.

Conclusion: Serum IS levels could be measured in new enzymatic method. Strong correlation between IS and eGFR was demonstrated, and AST-120 might be effective to improve IS. In renal and CVD outcome analysis, more sample size is needed for further study.

P0745 URINE TIMP-2 AND IGFBP-7- NEW BIOMARKERS OF KIDNEY INJURY IN MULTIPLE MYELOMA PATIENTS

Karolina Woziwodzka[1], Jolanta Malyszko[2], Małgorzata Banaszkiewicz[1], Ewa Koc- Żorawska[3], Paulina Dumnicka[4], Artur Jurczyszyn[5], Krzysztof Batko[1], Paulina Mazur[4], Marcin Krzanowski[1], Marcin Zorawski[6], Jacek Małyszko[7], Ryszard Drozdz[4], Marek Jan Kuznieswki[1], Katarzyna Krzanowska[1]

[1]Jagiellonian University Collegium Medicum, Department of Nephrology and Dialysis Unit, Kraków, Poland, [2]Medical University of Warsaw, Department of Nephrology and Dialysis Unit, Warsaw, Poland, [3]Medical University of Bialystok, Second Department of Nephrology and Hypertension with Dialysis Unit, Białystok, Poland, [4]Jagiellonian University Collegium Medicum, Department of Medical Diagnostics, Kraków, Poland, [5]Jagiellonian University Collegium Medicum, Department of Hematology, Kraków, Poland, [6]Medical University of Bialystok, Department of Clinical Medicine, Białystok, Poland and [7]Medical University of Bialystok, Department of Nephrology and Dialysis Unit, Białystok, Poland

Background and Aims: Urine tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor-binding protein 7 (IGFBP7) seem to be novel kidney injury related biomarkers, especially in tubular cells damage. Free light chains (FLCs) are associated with renal failure in multiple myeloma (MM) and appear to have a prognostic value and indicate stages in MM. The aim of the study was to investigate the correlation between new biomarkers and acclaimed parameters of renal failure and markers of MM stages and prognosis.

Method: The study included 124 patients with MM in the mean age of 66 +/- 10 years, with median time from MM diagnosis of 30 (lower; upper quartile 14; 63) months. There were 7(6%) patients with smoldering MM, 80(65%) with ISS stage 1, 22 (18%)with stage 2 and 15 (12%) with stage 3 MM. Mean eGFR was 71 +/- 25 ml/min/ 1.73 m^2 and 30 (24%) patients had eGFR <60 ml/min/1.73 m^2. The examined parameters included creatinine, urine NGAL, urine and serum cystatin-C, urine and serum FLC kappa and lambda, serum monoclonal protein, IGFBP-7 and TIMP-2 in serum and urine, WBC count, IL-6, NT-proBNP, serum albumin and β2-microglobulin. IGFBP-7 and TIMP-2 in serum were measured in a subgroup of 73 patients, including 26 (36%) with eGFR <60 ml/min/1.73 m^2. The association between between these parameters were determined by multivariate stepwise regression analysis. The p-value <0.05 was considered statistically significant.

Results: Except for urine cystatin C and urine TIMP-2, all the studied markers were higher among patients with eGFR <60 ml/min/1.73m^2: urine NGAL: 23.3 (9.2; 68.4) vs. 7.8 (3.9; 16.8) ng/ml; p<0.001; urine IGFBP-7: ; serum IGFBP-7: 86.2 (29.3; 125.0) vs. 33.7 (13.2; 61.5) ng/ml; p=0.003; and serum TIMP-2: 628 (498; 663) vs. 431 (360; 614) ng/ml; p=0.011, respectively.

Serum and urine IGFBP-7 and urine NGAL were also higher among patients with ISS grade 3 comparing to the rest of the group (p=0.008, p<0.001 and p=0.033, respectively). Patients with smoldering myeloma did not differ from those with symptomatic disease. No differences in studied markers were observed between patients with newly diagnosed MM in comparison to those who had been treated with one or more schemes. Only urinary IGFBP-7 differed between patients who were on treatment at the time of samples' collection (median ng/ml) in comparison to untreated (median ng/ml; p=0.009). No differences in TIMP-2 and IGFBP-7 levels in patients divided according to MM state were observed (remission vs stable vs progressive disease). In whole studied group, urinary markers of tubular injury were interrelated: cystatin C correlated positively with NGAL monomer (R=0.22; p=0.016), IGFBP-7 (R=0.26; p=0.004) and TIMP-2 (R=0.22; p=0.016), NGAL correlated positively with IGFBP-7 (R=0.39; p<0.001) and TIMP-2 (R=0.25; p=0.005), and IGFBP-7 correlated positively with TIMP-2 (R=0.31; p<0.001). In multiple linear regression, the negative correlation between urinary IGFBP-7 and eGFR was independent of other studied urinary markers of tubular injury. However, after adjustment for confounders (age, smoldering versus symptomatic MM, ISS, LDH, remission versus stable or progressive disease, and the concentrations of involved urine light chains), only urinary NGAL was independently associated with eGFR.

Conclusion: Urine TIMP-2 and IGFBP-7 may be useful in investigating tubular renal damage in patients with chronic kidney injury among patients with MM. This can lead to noninvasive biomarker-targeted diagnostic interventions and contribute to early beginning of treatment that may improve life expectancy quality of life in MM.

P0746 SUSTAINABILITY OF AN ELECTRONIC TECHNOLOGY BASED INTERVENTION IN GENERAL PRACTICE TO IMPROVE THE DETECTION AND MANAGEMENT OF THE INTERRELATED CHRONIC VASCULAR DISEASES

Julia Jones[1,2,3], Natalie Lumsden[1,2], Koen Simons[1,2,3], Jo-Anne Manski-Nankervis[3], Valerie Frattaroli[1,2], Maximilian DeCourten[4], Peter Hamblin[1,2,3], Edward Janus[1,2,3], Craig Nelson[1,2,3]

[1]Western Health, St Albans, Australia, [2]Western Health Chronic Disease Alliance, St Albans, Australia, [3]University of Melbourne, Parkville, Australia and [4]Victoria University, Footscray, Australia

Background and Aims:

Chronic kidney disease (CKD), type 2 diabetes (T2DM) and cardiovascular disease are interrelated chronic vascular diseases that cause substantial morbidity and mortality. A recent 15-month randomised stepped wedge trial targeting these conditions using an electronic technology audit tool together with education, monitoring and support to general practices (Chronic Disease IMPACT) showed increased diagnostic testing for CKD and T2DM in those at risk, increased urinary albumin monitoring in people with T2DM and increased coded diagnosis of CKD, no changes for cardiovascular disease and reduced coded eye examinations in patients with T2DM. This study aimed to test if these outcomes would be sustained 12 months after the initial study period (27 months after study commencement).

Method:

15 months after initial trial commencement the 9 practices involved in the original trial received further training on quality improvement and electronic technology tool use as well as a folder containing educational resources. They retained access to the electronic technology tool but received no further education or support for 12 months. Only 8 practices were included (as with the original analysis) due to compromised data quality in one practice resulting from a recent merging of practices with different electronic medical record systems. Active patients (having attended their GP practice $\geq$3 times within 24 months) age $\geq$18 were included. Variables with evidence for effect at 15 months were re-assessed at 27 months to test sustainability of outcomes. As there were no control practices at 27 months, time was considered as a linear predictor instead of a random intercept in the analysis. Net effect is defined as the product of effect over the course of the entire 27 months and change between effect at 15 and 27 months. Raw proportion and net effect odds ratio (OR) with 95% credible interval (CI) generated through stepped wedge analysis are presented below. Analysis was conducted with R version 3.5.1.

Results:

In the 8 included practices, at baseline, prior to intervention, there were 37,946 patients, at 15 months 37,385 and at 27 months 37,813. Testing for kidney disease in those at risk was completed in 19% at baseline, 25% at 15 months and 26% at 27 months with OR 1.4 (CI 1.2-1.6). CKD diagnosis was coded in 4.5% at baseline, 5.8% at 15 months and 6.8% at 27 months with OR 1.9 (CI 1.6-2.2). Testing for diabetes in those at risk was completed in 34% at baseline, 50% at 15 months and 57% at 27 months with OR 1.1 (CI 0.95-1.2). Urine albumin:creatinine ratio testing in people with T2DM was up-to-date in 56% at baseline, 65% at 15 months and 66% at 27 months with OR 1.9 (CI 1.4-2.5). Up-to-date eye checks in people with T2DM were coded in 39% at baseline, 36% at 15 months and 36% at 27 months with OR 0.97 (0.71-1.3). These results are consistent with sustained improvement in diagnostic testing of people at risk of CKD, coded diagnosis of CKD and urinary albumin monitoring in people with T2DM. Evidence for a sustained change in diabetes diagnostic testing in those at risk and coded eye examinations in people with T2DM was inconclusive.

Conclusion:

There was evidence for sustained improvement in three out of four areas that improved with the initial intervention. These results suggest a lasting benefit in outcomes achieved through clinical audit facilitated by the electronic technology-based intervention, with persistent effects 27 months from the start of the intervention with ongoing access to the electronic technology tool. Qualitative research investigating which elements of the intervention led to long-term changes would be beneficial.

P0747

STRESS ERGOMETRY PERFORMANCE AND ABDOMINAL AORTIC CALCIFICATION PREDICT PATIENT OUTCOMES IN CKD STAGE 4-5

Roosa Lankinen[1], Markus Hakamäki[1], Kaj Peter Metsarinne[1], Jussi Pärkkä[2], Tapio Hellman[1], Noora Kartiosuo[3], Olli Raitakari[3], Mikko Järvisalo[4]

[1]Turku University Hospital, Nephrology, Turku, Finland, [2]Turku University Hospital, Clinical Physiology, Turku, Finland, [3]University of Turku, Research Centre of Applied and Preventive Cardiovascular Medicine, Turku, Finland and [4]Turku University Hospital, Intensive Care Unit, Turku, Finland

Background and Aims: Patients with chronic kidney disease (CKD) stage 4-5 have an increased risk of cardiovascular morbidity and mortality.

Method: We recruited 174 consecutive patients with CKD stage 4-5 between 2013 and 2017 into a prospective follow-up study assessing arterial disease, quality of life, mortality and their predictors. Together with baseline medical data, standard maximal bicycle ergometry stress testing, abdominal aortic calcification score (AAC) and echocardiography was collected. Patients were followed up for mean 42 months.

Results: Mean age at recruitment was 61 years, 54 (31%) were women and estimated glomerular filtration rate (eGFR) was 12.9 ml/min. Altogether, 36 (21%) patients died during follow-up with a mean time to death of 835 days. At baseline, all but one patient were hypertensive, 75 patients had diabetes and 21 patients had coronary artery disease. Mean AAC was 6.27±5.68 and work load of the last 4 minutes of maximal stress (WMAX) was 83.7±36.5W, respectively. In the multivariate proportional hazard models pro-BNP [1.98 (95% CI 1.36 – 2.90), p=0.0004], WMAX [HR 0.45 (95% CI 0.27 – 0.77), p=0.0033], AAC [HR 2.51 (95% CI 1.37 – 4.61), p=0.0030], E/e' –ratio [HR 1.66 (95% CI 1.08 – 2.56), p=0.0221] and albumin [HR 0.59 (95% CI 0.39 – 0.90), p=0.0134] were significant predictors for mortality when adjusted with age, sex, diabetes and previous coronary artery disease. Patients who perished, especially those who died in less than 2 years, within follow-up had significantly higher AAC and lower WMAX compared to those surviving to the end of the study (Figure 1).

Conclusion: Maximal stress ergometry test work load and AAC are associated with patient survival in severe CKD.

Figure 1

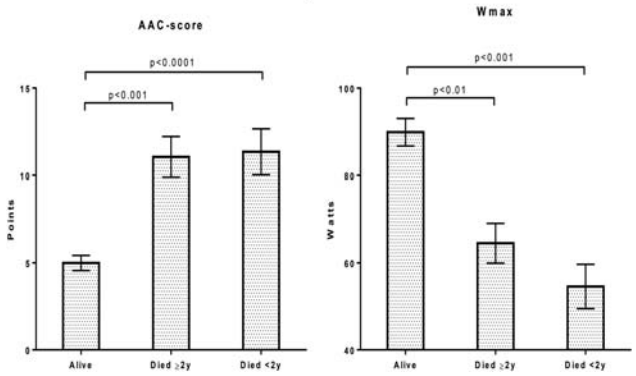


Figure:

P0748

CLINICAL OUTCOMES OF JAPANESE ANTI-MYELOPEROXIDASE ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-RELATED RAPIDLY PROGRESSIVE GLOMERULAR NEPHRITIS

Yoshihiro Nishida[1], Kenji Ito[1], Yuki Yasui[1], Koji Takahashi[1], Tetsuhiko Yasuno[1], Naoko Himuro[1], Katsuhisa Miyake[1], Kosuke Masutani[1]

[1]*Faculty of Medicine, Fukuoka University, Division of Nephrology and Rheumatology, Fukuoka, Japan*

Background and Aims: Anti-myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA)-related nephritis constitutes 60% of rapidly progressive glomerular nephritis (RPGN). In 2014, Japanese Society of Nephrology (JSN) created RPGN clinical guidelines for Japanese MPO-ANCA-related RPGN patients, and proposed the clinical grading system for predicting their prognosis, which took into consideration factors such as age, renal function, lung involvement, and serum CRP (Yoshihiro Arimura et al. Clin Exp Nephrol. 2016). However, evidence regarding clinical outcomes is still limited. In the study reported here, we conducted a single-center retrospective study to evaluate the outcomes of MPO-ANCA-related RPGN patients and to establish an efficacy of RPGN guidelines of JSN.

Method: We retrospectively investigated 54 patients (female, n=32; average age ± 13.0 years) with MPO-ANCA-related nephritis. The patients were admitted to Fukuoka University Hospital between 2009 and 2018. Their clinical grade determined by JSN guideline and method of treatment were retrospectively evaluated for prediction of survival, as well as laboratory data and clinical features.

Results: 12 patients (22.2 %) has deceased during a median observation period of 17.1 months. 7 patients are died of infectious disease (Bacterial pneumonia 4, Sepsis 2, pulmonary aspergillosis 1), and 10 patients died within 1 year. Median estimated glomerular filtration rate (eGFR) was 15.5 mL/min/1.73m2 at admission. 14 patients (25.9%) presented with end-stage renal disease (ESRD) during the observation period, 8 of them were died. The distribution of clinical grade of JSN guideline was grade I for 10, II for 27, III for 10 and IV for 7. (grade IV is the most severe) Patients with high clinical grade showed significantly high mortality (Log Rank test, $p<0.05$; figure 1). Multivariate Cox proportional hazards model analysis revealed that high clinical grade was a significant risk factor for all-cause death (Hazard ratio (HR), 7.09; 95% confidence interval (CI), 2.01-15.69, $p<0.05$) and for infectious disease death (HR, 16.9; 95% CI, 2.56-121.5, $p<0.05$). On the other hands, the preventive administration of Trimethoprim-Sulfamethoxazole (TS) decreased the risk of infectious disease death (figure 2).

Conclusion: The MPO-ANCA-related RPGN clinical grading system created by JSN was a useful tool for prediction of prognosis. Furthermore, TS should be administrated for all immune-suppressive patients to prevent variable infections not only Pneumocystis.

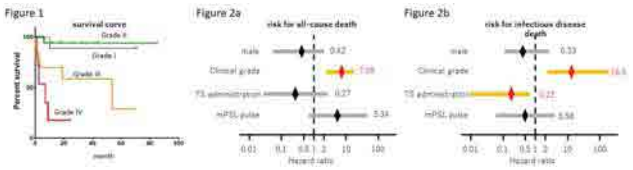


Figure:

P0749 THE ASSOCIATION OF VISCERAL ADIPOSITY INDEX WITH PROGRESSION OF CHRONIC KIDNEY DISEASE

Zelal Adibelli[1], Soycan Mizrak[2], Cevdet Duran[3]

[1]Usak University School of Medicine, Nephrology, Usak, Turkey, [2]Usak University School of Medicine, Endocrinology, Usak, Turkey and [3]Usak University School of Medicine, Biochemistry, Usak, Turkey

Background and Aims:

Obesity is becoming an important health problem as its prevalence is increasing. Obesity is also a factor that causes an increase in chronic kidney disease (CKD) cases by facilitating the development of diabetes and hypertension, which leads to CKD, and by a direct effect on the kidney and endocrine mechanism. Obesity is generally defined by body mass index (BMI), which is not a good indicator for visceral adipose tissue (VAT), as visceral fat has been shown to be more metabolically active. A new method called the visceral adiposity index (VAI) has been developed, which is considered to be an indicator for the metabolic function of VAT. Previous studies have confirmed the association between the VAI and CKD prevalence. In this study, we attempted to investigate the association between estimated glomerular filtration rate (eGFR) decline and visceral adiposity.

Method:

Data were collected from 129 patients aged 18-80 years with stage 2-5 CKD and not on dialysis; these patients were followed up in the Nephrology Department of Usak University Hospital between December 2017 and November 2018.

Results:

Of 129 patients with stage 2-5 CKD enrolled in this study, 64 (40.6%) were females and 66 (59.4%) were males. The mean age was 66.8 (35-80 years). The mean VAI values of patients were 2.86 ± 1.63, and the mean eGFR decline was -12.8 ± 19.0 ml/min/1.73m^2. No correlation was observed between the VAI values and decline in eGFR in 1 year. Patients with DM had statistically significant higher eGFR decline ($p=0.04$) and higher VAI values ($p=0.03$).

Conclusion:

The VAI, which is used to assess the metabolic function of VAT, was not associated with the eGFR decline in 1 year for patients with stage 2-5 CKD.

P0750

ASSOCIATION OF SERUM POTASSIUM LEVELS WITH RAPID KIDNEY FUNCTION DECLINE IN PATIENTS WITH CONGENITAL SINGLE KIDNEY

FLORICA GADALEAN[1], Florina Parv[2], Ligia Petrica[3], SILVIA VELCIOV[3], Cristina Anca Gluhovschi[3], Flaviu Bob[3], MILAS OANA[3], Adelina Mihaescu[3], ALINA GOLEA-SECARA[3], ANCA SIMULESCU[3], Iulia Dana Grosu[3], Lazar Chisavu[3], Madalina Floroiu[4], Adalbert Schiller[3]

[1]University of Medicine and Pharmacy "Victor Babes" Timisoara, Nephrology, Romania, [2]University of Medicine and Pharmacy "Victor Babes" Timisoara, Cardiology, [3]University of Medicine and Pharmacy "Victor Babes" Timisoara, Nephrology and [4]University of Medicine and Pharmacy "Victor Babes" Timisoara

Background and Aims: Hypokalemia is associated with progression of chronic kidney disease (CKD), although the possible underlying mechanisms are not well established. Several observational studies showed that low or even low to normal serum potassium levels predict the decline of kidney function in the general population. However, this hypothesis has not been yet investigated in patients with reduced nephron number as are congenital single kidney (cSK) patients.

Our aim was to prospectively examine the association of plasma potassium with risk of rapid kidney function decline in a cSK patients' cohort.

Method: A cohort of 67 consecutive patients with cSK (mean age = 44.4+/-15.7 years; males 29p (43.28%)), with a mean estimated glomerular filtration rate (eGFR) = 65.2+/-28 ml/min/1.73m2, were enrolled in this longitudinal observational study. We evaluated the associations of plasma potassium levels with longitudinal kidney function decline by estimated glomerular filtration rate (eGFR). The eGFR was assessed with CKD-EPI formula. The rapid kidney function decline was defined as a fall in eGFR of more than 5 ml/min/1.73 m2/year, according to the KDIGO guidelines.

Results: During a mean follow-up time of 20.16+/-9.3 months, 31.34% (21p) of patients presented decline of eGFR, with a fall of mean – 11.6+/-5.43 ml/min/1.73m2/year. In univariable regression analysis, the decline of eGFR was associated with baseline eGFR (R2=0.09, p=0.013), age (R2=0.31, p<0.001), male gender (R2=0.14, p=0.001), arterial hypertension (R2=0.17, p=0.001), diabetes mellitus (R2=0.13, p=0.003), coronary artery disease (R2=0.12, p=0.005), uric acid (R2=0.23, p<0.001), C-reactive protein (R2=0.09, p=0.011), proteinuria/24h (R2=0.14, p=0.002) and serum potassium (R2=0.29, p<0.001). The serum potassium levels were significantly lower in the group with rapid decline of eGFR, with a mean of 3.62+/-0.41 mmol/L vs. 4.51+/-0.74 mmol/L, p<0.001. In multivariable regression analysis, the association between lower serum potassium levels and risk of rapid eGFR decline remained significant (HR=1.65; 95%CI, 1.105-2.49; p=0.015).

Conclusion: These results suggest that lower serum potassium levels may play a role in rapid kidney function decline in the cSK population. Further research is required to assess whether the higher risk of kidney function decline in cSK individuals could be diminished when optimised serum potassium levels strictly.

P0751 **METFORMIN, A CLASSIC TREATMENT FOR TYPE 2 DIABETES WITH POSSIBLE RENOPROTECTIVE EFFECTS**

Adriana Acosta Barrios[1], Marian Goicoechea[1], Eduardo Verde[1], Ángela González-Rojas[1], Andres Delgado[1], Alejandra Muñoz de Morales[1], Javier Carbayo[1], Ursula Verdalles[1], Pérez de José Ana[1], Jose Luno Fernandez[1]

[1]*Hospital General Universitario Gregorio Marañon, Nephrology, Madrid, Spain*

Background and Aims: Metformin is the antidiabetic of choice in patients with type 2 diabetes mellitus. Experimental studies and clinical observations have shown that metformin could have a beneficial effect on the progression of kidney disease through the activation of cAMP due to its anti-inflammatory, antifibrotic, and anti-oxidative action. The objective was to compare the progression of CKD in diabetic patients with or without metformin as antidiabetic in their treatment and the prevalence of cardiovascular events in both groups.

Method: Unicentric retrospective observational analysis. Inclusion criteria: outpatients seen in nephrology consultation during the year of 2012 with diabetes mellitus and stage 3 CKD. Renal, cardiovascular outcomes and mortality were analyzed between patients treated with / without metformin. Median follow-up of 76.5 months (41-84). Renal end-point: estimated glomerular filtration rate drop (MDRD-4) by 50% and / or start of dialysis program. Cardiovascular end-point: ischemic heart disease, stroke, arterial revascularization and / or amputation. Cardiovascular or any cause mortality.

Results: 148 patients (96M, 52W) with a mean age of 75±9 years and an eGFR of 40±9 ml / min / 1.73 m2 were included. In relation to hypoglycemic therapy: 45 received metformin, 61 insulin and 31 DPP4i. 80% received treatment with RAAS blockers. After the follow-up, the progression of the renal disease was greater in patients who did not receive metformin: eGFR fall of -7.0±16 vs -0.15±16 ml / min in those treated with metformin (p = 0.019). 25 patients in the group without metformin suffered a renal event vs. 5 in the metformin group (logRank: 4.186, p = 0.045). In the Cox analysis, metformin treatment decreases the progression of kidney disease in a model adjusted for baseline renal function and treatment with RAASB (HR 0.368, p = 0.043), losing its predictive power in a proteinuria-adjusted model. During the follow-up, 45 patients died (20 metformin, 25 non-metformin) and 45 patients suffered a cardiovascular event (15 metformin, 30 non-metformin), with no differences between the two groups.

Conclusion: Metformin treatment in patients with stage 3 CKD could slow the progression of CKD, this effect should be demonstrated in randomized studies with larger sample size.

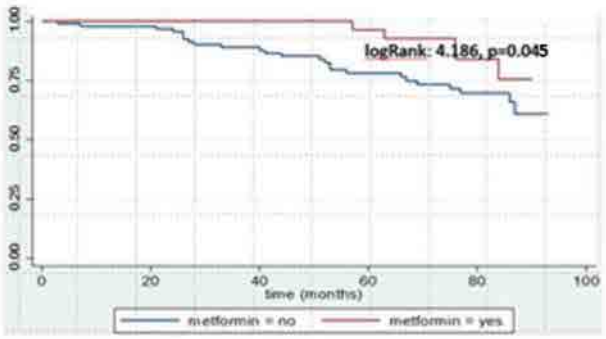


Figure 1. Effect of treatment with Metformin in progression of CKD

Figure:

P0752 THE EXPRESSION AND DIAGNOSTIC VALUE OF URINE ANGIOTENSINOGEN IN CHRONIC KIDNEY DISEASE

Qiuyan Huang[1,2], Junzhe Chen[1,2], Ying Tang[1,2], Yanchun Xu[1,2], Anping Xu[1,2]

[1]Sun Yat-sen Memorial Hospital,Sun Yat-sen University, Department of Nephrology, Guangzhou, P.R. China and [2]Sun Yat-sen Memorial Hospital,Sun Yat-sen University, Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Guangzhou, P.R. China

Background and Aims: This article aims to detect the expression of urine angiotensinogen (uAGT) in patients with chronic kidney disease (CKD) and its correlation with clinical and renal pathology.

Method: Patients who diagnosed with CKD and undergoing renal biopsy for the first visit to Sun Yat-sen Memorial Hospital from March 1st ,2018 to October 1st, 2019 were enrolled. First morning urine samples from CKD patients before renal biopsy and healthy volunteers as controls were collected during the same period. These samples were tested for uAGT by ELISA. Linear regression analysis was used to explore the correlation between uAGT and clinical indicators as well as renal pathology in CKD patients. The receiver operating curve (ROC curve) was used to explore the diagnostic value of uAGT for CKD stage 3 or above and glomerular sclerosis ratio>50%.

Results: A total of 133 CKD patients with 59 (44.4%) in stage 1, 31 (23.3%) in CKD stage 2, 17 (12.8%) in stage 3, 17 (12.8%) in stage 4 and 9 (6.7%) in stage 5 were included in our study. At the same time, 20 healthy volunteers were included as control. uAGT levels of CKD patients were significantly higher than healthy controls(275.0 vs 774.2,P<0.001). Compared with CKD stage 1-2 patients, uAGT levels in patients with stage CKD 3 or above were significantly increased, and the difference was statistically significant (P<0.001) (Table 1). The result of multivariate linear regression analysis showed that uAGT levels in CKD patients were positively correlated with 24h urine protein (beta = 0.193, P = 0.012) and negatively correlated with eGFR (beta = -0.489, P<0.001) (Table 2). We also demonstrated that uAGT was positively correlated with the ratio of glomerular sclerosis(P = 0.003) (Table 3). Our results showed that the area under the curve (AUC)of uAGT for the diagnosis of renal function with CKD stage 3 or above was 0.789 (Figure 1) with the cut-off value was1959.9pg/ml. The sensitivity and specificity were 51.2% and 97.3% respectively, Furthermore, the positive predictive value (PPV) was 88.0% and negative predictive value (NPV) was 82.95%.The AUC of uAGT for the diagnosis of renal pathological glomerular sclerosis ratio>50% was 0.677 (Figure 2).The cut-off value of uAGT was 2131.8pg/ml.The sensitivity and specificity were 50% and 89.5% respectively. Meanwhile, the PPV was 41.67% and the NPV was 92.25%.

Conclusion: uAGT was significantly increased in CKD patients, which is closely related with the urinary protein, eGFR, and renal pathology.The specific cut-off value of uAGT can be used as a predictive indicator of advanced CKD stage and severe glomerular sclerosis.

Table 1. The baseline of uAGT between non-CKD and CKD group

	non-CKD	CKD			
		Total	CKD1-2	CKD3-5	
	(n=20)	(n=133)	(n=90)	(n=43)	*P*
uAGT	275.0 [186.6-362.1]	774.2 [394.0-1517.7]	652.1 [366.8-1040.3]	1981.6 [722.4-4416.0]	<0.001

Table 2. The relationship between uAGT and clinic parameters in CKD patients

Parameters	Linear regression			
	Univariate analysis		Multivariate analysis	
	Beta	*P*	Beta	*P*
Sex（%）	**0.216**	**0.013**		
Age(year)	0.219	0.110		
SBP(mmHg)	**0.194**	**0.025**		
DBP(mmHg)	0.122	0.163		
BMI(Kg/m^2)	-0.029	0.743		
Glu(mmol/L)	**0.184**	**0.034**		
Cr(umol/L)	**0.348**	**<0.001**		
Urea(mmol/L)	0.114	0.190		
UA(umol/L)	0.08	0.363		
Alb(g/L)	-0.127	0.146		
CysC(mmol/L)	**0.307**	**<0.001**		
eGFR(ml/min/1.73m^2)	0.485	<0.001	-0.489	<0.001
Urine protein(g/24h)	0.219	0.012	0.193	0.012

Table 3. The relationship between uAGT and chronic lesion parameters in CKD patients

Parameters	Linear regression	
	Univariateanalysis	
	Beta	*P*
Ratio of glomerular sclerosis	0.257	0.003
Atrophic area of renal tubular epithelium	0.167	0.055

Figures:

P0753

HOW FREQUENTLY PATIENTS WITH RISK FACTORS FOR CHRONIC KIDNEY DISEASE ACHIEVE RECOMMENDATIONS OF FOOD CONSUMPTION FREQUENCY

Elizabeth Corona Rodríguez[1], Roxana Michel Márquez Herrera[1], Laura Cortés Sanabria[1], Gabriela Karen Nuñez Murillo[1], Erika Fabiola Gomez Garcia[1], Enrique Rojas Campos[1], Hector Ramon Martinez Ramirez[1], Jorge López Leal[1], Alfonso Martín Cueto Manzano[1]

[1]*Mexican Institute of Social Security, Biomedical Research Unit 02, Guadalajara, Mexico*

Background and Aims:

Risk factors for chronic kidney disease (CKD) such as type 2 diabetes mellitus (DM2), high blood pressure (HBP) and obesity are strongly related to negative lifestyle and nutritional habits. The aim of this study was to estimate the proportion of patients with and without risk factors for CKD who meet recommendations for food consumption.

Method: Cross-sectional study. A qualitative food frequency questionnaire (FFQ) was applied. Consumption of each food group was classified as adequate or inadequate based on dietary guidelines (DASH and ENSANUT Mexican Guidelines). Sociodemographic, biochemical and clinical variables were measured. DM2, HBP and obesity were defined as risk factors.

Results: 744 adults were evaluated, age 51±16 y, 68% women, 59% without risk factors, 7% DM2, 17% HBP, 8% DM2+HBP, and 18% obesity. Glomerular filtration rate was 99 (89-100) mL/min/1.73m^2. Differences in FFQ between groups were found in relation to consumption of legumes, fast food, sugar, sweets and desserts ($p<0.05$). Figure A shows the frequency of consumption of healthy and B, unhealthy foods.

Conclusion: In general, subjects in this sample had negative dietary habits, with <50% consuming healthy food and >50% consuming unhealthy food. Subjects without risk factors for CKD displayed a similar pattern of food consumption than those with risk factors, with only a significantly lower legumes intake than patients with HBP, and higher intake of sweets and desserts, sugar, and fast food compared to patients with DM2+HBP. It is necessary to implement strategies to prevent the long-term development of CKD in groups with poor adherence to healthy food consumption recommendations.

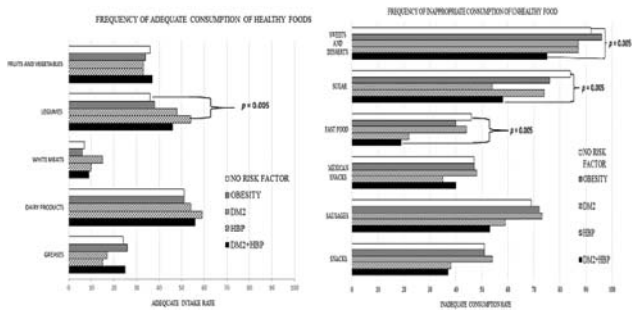


Figure:

P0754

FGF23 AND URINARY PHOSPHATE EXCRETION FOR ESTIMATION OF NEPHRON NUMBER: DIFFERENCES BETWEEN CHRONIC KIDNEY FAILURE AND KIDNEY TRANSPLANTATION

Marzia Pasquali[1], Natalia De Martini[2], Lida Tartaglione[1], Silverio Rotondi[3], Marta Catalfamo[1], Maria Josè Ceravolo[1], Domenico Bagordo[1], Sandro Mazzaferro[1]

[1]Policlinico Umberto I Sapienza University, Nephrology, Rome, Italy, [2]Sapienza Univerity, Nephrology, Rome, Italy and [3]ICOT, Dialysis, Latina, Italy

Background and Aims: Assuming that FGF23 levels correlate with phosphate excretion per nephron, nephron number can be estimated by measuring FGF23 levels and urinary phosphate excretion (FEP). Kuro-O proposed that the ratio of FEP to serum FGF23 levels should correlate with nephron number and is defined as the Nephron Index (NI).

The aim of the study is calculating NI as nephron number estimation in patients affected by various degree of chronic kidney disease, both transplanted and not.

Method: In 147 CRF patients kidney function, mineral metabolism biomarkers and NI were evaluated. Nephron Index was calculated following Kuro-o's equation (kuro-o 2019): $NI = \frac{FEP \cdot P_s \cdot eGFR}{FGF23}$

Observed patients were divided into two groups: patients with CKD (noTX) and transplanted ones (TX).

Results: noTX group was made up of 67 patients (40 males and 27 females) affected by CKD stages from G1 to G5. TX group was composed by 80 patient (49 males and 31 females) with various degree of CKD (G1T-G4T) showing mean graft age of 83,2 ± 54,8 months (range: 10,3-268,0). The two groups differed for age (mean age 59 ± 15,6 years in CKD, 55± 10,3years in TX). Mean eGFR did not differ between TX and noTX but NI was higher in TX since FEP was higher despite lower FGF23 levels in TX. The difference in FGF23 levels does not appear to depend on Klotho and PTH whose serum levels were no different between Tx and noTx. (Table1). As far as correlations are concerned, NI correlated with eGFR, FGF23, PTH and 1,25D in both group, while NI correlated with FEP only in the TX group. It's interesting that no correlation existed between FGF23 and sP, FEP, eGFR and sKlotho in TX differently from noTX (Table2).

Discussion. NI could not be properly defined as nephron number estimation in TX pts. However it may represent higher function of residual nephrons, since higher FEP did not correlate to FGF23 and could be determined by compensatory hyperfiltration (increased single nephron GFR) in transplanted patients.

Conclusion: After kidney transplantation, high NI value could have a functional meaning rather than represent residual number of nephrons.

Table1

	noTX (n.67)	TX (n.80)	Pvalue
Age (years)	59±15	55±10	0,051
eGFR (mL/min/1.73mq)	50,0±25,2	48,4±16,7	Ns
Nephron Index	64,0 ± 57,3	131,0 ± 131,0	<0.001
sCa (mg/dL)	9,44±0,54	10,1±0,8	<0,00001
sP (mg/dL)	3,5±0,6	3,0±0,6	<0,0001
FEP %	21,3 ± 10,2	31,4 ± 15,7	<0,0001
sKlotho (pg/mL)	522±185	477±141	Ns
FGF23 (pg/mL)	74,3±52,4	47,3±28,8	<0,0001
1,25D (pg/mL)	25,1±13,4	42,4±15,5	<0,00001
25D (ng/mL)	23,9±11,1	26,1±11,7	Ns
PTH (pg/mL)	60,0±32,1	59,3±51,5	Ns

Table2

CORRELATION	r	P value	r	P value
NI-age	-0.1433	0.2474	-0.0333	0.7693
NI- eGFR	0.7115	**<0.0001**	0.2894	**0.0092**
NI- Ps	-0.4426	**0.00020**	-0.2110	0.0603
NI- FEP	-0.1234	0.319	0.2980	**0.0074**
NI- FGF23	-0.7713	**<0.0001**	-0.7826	**<0.0001**
NI- klotho	0.3039	**0.0131**	0.0197	0.8634
NI- PTH	-0.4314	**0.00027**	-0.2310	**0.0392**
NI- 25D	-0.0183	0.883	-0.0357	0.7531
NI- 1,25D	0.3258	**0.007**	0.2941	**0.0083**
FGF23- Ps	0.5075	**<0.0001**	0.1660	0.141
FGF23- FEP	0.4878	**<0.0001**	0.1248	0.27
FGF23-eGFR	-0.6972	**<0.0001**	-0.1973	0.079
FGF23- Klotho	-0.2786	**0.02**	-0.0569	0.6181

P0755 **CALCIUM/MAGNESIUM RATIO: NEW PREDICTOR OF INCREASED PULSE PRESSURE IN CHRONIC KIDNEY DISEASE PATIENTS**

Eduarda Carias[1], Filipa Mendes[1], André Fragoso[1], Pedro Leão Neves[1], Ana Silva[1]

[1]*University Hospital Center of Algarve, Faro, Nefrologia, Faro, Portugal*

Background and Aims:

Cardiovascular disease (CVD) is the main cause of death in chronic kidney patient. Increase pulse pressure (PP) is associated with adverse cardiovascular outcomes and is an independent risk factor of progression of chronic kidney disease.

In this study we aim to identify the risk factors associated with increased PP in a population with severely decreased glomerular filtration rate.

Method:

This was a prospective analysis conducted in an outpatient nephropathy clinic between 2005-2018, enrolling 692 patients with stage 4 CKD.

Patients were divided into two groups according to their pulse pressure. Group 1 mean PP< 50 mmHg, Group2 mean PP >50 mmHg.

Based on the calcium/magnesium ratio (rCaMg), the subjects were also divided into 4 risk groups according to the following criteria: <25th percentile (rCaMg < 3.8mg/dl; n=168) – G1; 25-50th percentile (rCaMg: 3.8-4.7; n=171) – G2; 50-75th percentile (rCaMg: 4.7-8.6; n=188) – G3; and >75th percentile (rCaMg: > 8.6; n=165) - G4.

We used descriptive analysis, Student's t test, Univariate logistics regression analysis and CHAID analysis to determine the relationship between variables and PP.

Results:

Total of 682 patients, with mean age 70 (SD 12.5), female 54%.

An independent t-test was conducted to compare groups. There was a significant difference in mean hemoglobin level (p=0.005), calcium (p=0.029), phosphorus (p=0.017), magnesium (p<0.001), Ca/Mg ratio (p<0.001) and eGFR (p=0.034).

Phosphorus OR 1.906 (CI 1.338-2.715) p<0.001, eGFR OR 1.440 (CI 1.023-2.027) p=0.037 were all associated with increased PP. We also compared PP with the subjects of the 4 groups based on calcium/magnesium ratio. Results: G2= OR 7.003 (CI 4.162-11.783) p<0.001; G3= OR 5.136 (CI 3.205-8.230) p<0.001; G4= OR 6.695 (CI 3.999-11.208) p<0.001.

After adjusting for confounding variables only sex OR 0.613 (CI 0.420-0.896) p=0.012 and rCa/Mg groups: G1 OR 7.392 (CI 4.362-12.527) p<0.001, G2 OR 6.436 (CI 3.361-12.323) p<0.001 and G3 OR 8.485 (CI 4.009-17.957) p<0.001, showed significant differences.

CHAID analysis identified rCa/Mg G2, G3, G4 (82.4%) as the more likely significant predictor to PP> 50 mmHg (p<0.001) in association with male gener (86.2%) (p=0.037). The model correctly classified 76.2% of patients and the estimate of the risk misclassification of events was 0.238±0.016.

Conclusion:

These results suggest increased calcium/magnesium rate and male gender were associated with increased pulse pressure in a population with stage 4 CKD.

Further studies are needed to understand this relationship.

P0756

THE RELATIONSHIP BETWEEN ABDOMINAL AORTIC CALCIFICATION AND PROGRESSION OF RENAL INSUFFICIENCY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

SO MI KIM[1], Jong Tae Cho[2], Ji Hyun Jeon[2], Yong-Moon Lee[3], Eun Kyoung Lee[2], Hwa Young Lee[4]

[1]Dankook University Hospital, Division of Nephrology, Department of Internal Medicine , [2]Dankook University Hospital, Division of Nephrology, Department of Internal Medicine , [3]Dankook University Hospital, Department of Pathology and [4]Jeju National University Hospital, Division of Nephrology, Department of Internal Medicine

Background and Aims: Although abdominal aortic calcification (AAC) is known to be associated with cardiovascular mortality in patients with chronic kidney disease (CKD), there are little information about the impact of AAC on progression of CKD. Therefore, we investigated the relationship between the AAC and progression of renal insufficiency in CKD patients with early stage.

Method: A total of 183 patients with CKD, stage 3 was included. The degree of AAC was evaluated by computed tomography and the score was calculated as follows: abdominal calcification index (ACI)= (total score of calcification on all slices)/12 × 1/ (number of slices) × 100%. Based on tertile of ACI, the patients were divided into three groups: low-, intermediate-, and high-groups. The annual decline of glomerular filtration rate (GFR) and time to dialysis were assessed.

Results: The AAC was found (ACI > 0) in 129 patients (70.4%), and the mean ACI was 21.3 %. The average duration of follow-up was 46.9 months. The high ACI group showed higher annual decline in GFR compared to other groups (27.8 vs 14.5 vs 11.3 mL/min, p=0.042). During the follow-up, 68.8% (42/61) of high ACI group received dialysis and the time to dialysis was significantly shorter than other groups (14.8 vs. 25.8 vs.29.1 months, p=0.038)

Conclusion: In this study, we showed the AAC was associated with rapid progression of CKD. Evaluation of the AAC in CKD with early stage provides useful information for predicting the progression of CKD.

P0757 **THO ROLE OF MARKERS TO ASSESS RISK FOR DEVELOPING CARDIORENAL SYNDROME**

Danijela Tasic[1], Sonja Radenkovic[2], Gordana Kocic[3], Mileta Poskurica[4], Dijana Stojanovic[5]

[1]Ubiversity of Nis Faculty of medicine, CC Nis Clinic of nephrology, Nis, Serbia, [2]University of Nis CC Nis faculty of Medicine, Nis, Serbia, [3]Univeristy of Nis Faculty of medicine, Nis, Serbia, [4]University of Kragujevac, CC Clinic of nephrology, Kragujevac, Serbia and [5]University of Nis CC Nis Faculty of Medicine, Nis, Serbia

Background and Aims: Biomarkers are circulating proteins and metabolites, which are released in the body fluids from the damaged organ or tissue is detected specific essays and plays a role in the diagnosis, evaluation and monitoring of patients. Today there is a large number of markers that assess the intensity of pro-inflammatory and oxidative processes in the cardio-renal syndrome, whose determination would have great diagnostic and prognostic significance. The aim of our investigation was to identifying which of the examined parameters stand out as independent risk factors for the development of the cardiorenal syndrome (CRS).

Method: The study included 114 subjects older than 18 years, of both sexes, divided into clinical and control group. The control group was consisted of 35 healthy males and females with similar characteristics as well as clinical groups. The clinical group was consisted of 79 patients: 40 (50.63%) male and 39 (49.37%) female, mean age of 70.72 ± 9.26 years, diagnosed on the basis of the current classification of cardiorenal syndrome. The respondents were familiar with the case studies and signed informative consent. The study was approved by the Ethics Committee and conducted in compliance with the Helsinki Declaration on Medical standards of Good Clinical Practice.

Results: With correlation analysis of examined biomarkers in respondents of the clinical group was established positive correlation between plasma BNP and IL-8 ($r = 0.383$, $p = 0.006$), BNP and cTnhsT ($r = 0.518$, $p = 0.001$) BNP and cystatin C ($r = 0.447$, $p = 0.001$) and BNP and CRP ($r = 0.306$, $p = 0.046$), while a negative correlation was observed between the BNP and the activities of MDA ($r = - 383$, $p = 0.007$). Negative correlations were also between the activity of the MDA and the IL-8 concentration ($r = -0.237$, $p = 0.038$), and MDA cTnhsT ($r = -0.321$, $p = 0.009$) and MDA and cystatin C ($r = -0.315$, $p = 0.005$). XOD activity cost was positively correlated with the XD ($r = 0.942$, $p < 0.001$), and the activity of XO was positively associated with TnI ($r = 0.522$, $p = 0.009$) and negatively correlated with the XD ($r = -0.423$, $p < 0.001$). The concentration of IL-8 was positively associated with cTnhsT concentrations ($r = 0.427$, $p < 0.001$) and with concentrations of CRP ($r = 0.411$, $p = 0.001$), the concentration of PAI-1 with cTnhsT concentration ($r = 0.558$, $p < 0.001$), with TnI concentration cTnhsT ($r = 0.852$, $p < 0.001$), and cTnhsT with cystatin C ($r = 0.338$, $p = 0.006$) and CRP ($r = 0.358$, $p = 0.011$). Cystatin C stood positively related to the concentration of CRP ($r = 0.510$, $p < 0.001$).

Conclusion: Early detection of occurrence of functional and structural damage to the heart and kidneys, highly sensitive and specific markers would enable not only their discovery, but also prevention and treatment.

Table 1. Univariate odds ratio (OR) and 95% confidence interval (CI) for the development of CRS in the clinical group, according to the tested parameters

Parameters	OR	95%CI	P*
Sex (male) ♂	0,129	0,026-0,683	**0,012**
Age (years)	1,826	0,791-4,217	0,158
Hypertension (yes/no)	36,471	4,358-305,214	**0,001**
Type 2 diabetes mellitus (yes/no)	4,038	0,001-15,382	0,998
BNP (pg/ml)	1,244	0,953-1,624	0,109
cTnI (ng/ml)	-		0,828
hsTnT (ng/ml)	8,735	0,001-25,291	0,762
ACR (mg/mmol)	50,124	0,001-∞	0,353
MDRD (ml/min/1,73 m^2)	0,877	0,795-0,967	**0,009**
Cystatin C (mg/l)	49,345	13,026-189,98	**0,010**
AOPP (μM/l)	1,044	1,012-1,076	**0,006**
MDA (μM/l)	1,733	1,223-2,456	**0,002**
XOD (IJ/l)	1,034	1,008-1,060	**0,009**
XO (IJ/l)	0,988	0,958-1,039	0,922
XD (IJ/l)	1,024	1,004-1,044	**0,020**
IL-8 (pg/ml)	1,015	0,992-1,038	0,214
PAI-1 (ng/ml)	0,982	0,905-1,065	0,654
CRP (mg/l)	4,394	1,096-17,620	**0,037**

*p<0.05. Statistically significant differences is given in bold letters.

P0758

THE CORRELATION BETWEEN THE MANAGEMENT OF COMORBIDITIES AND THE PROGRESSION OF THE RENAL DYSFUNCTION OR ADVERSE EVENTS OF CHRONIC KIDNEY DISEASE.

Kuragano Takahiro[1], Aritoshi Kida[1], Mana Yahiro[1], Yoshimasa Nanami[1], Yasuyuki Nagasawa[1], Takeshi Nakanishi[1]

[1]*Hyogo College of Medicine, Division of Kidney and Dialysis, Nishimomiya, Japan*

Background and Aims: Several factors, such as anemia, hypertension, hyperuricemia, metabolic acidosis, and chronic kidney disease (CKD)-mineral and bone disorder (MBD), are associated with the progression of CKD or adverse events in CKD patients. However, the significant factors associated with the progression of CKD or adverse events in patients under the condition of appropriate control according to guidelines have not been clarified.

Method: The study was a 3-year observational study conducted in a single center. In 88 patients with various stages of CKD (not on renal replacement therapy (RRT)) who were treated by nephrologists, blood levels of Hb, ferritin, iron, total iron-binding capacity, and albumin were measured every 3 months, and high-sensitivity C reactive protein (hCRP), β2-microglobulin (MG), HCO3-, and intact-parathyroid hormone (int-PTH), in addition to urinary sodium, potassium, calcium, phosphorus, protein, and β2-MG levels, were measured every 6 months. We also evaluated the doses of iron, erythropoiesis-stimulating agent (ESA), vitamin D, phosphate binder, anti-hypertensive agents, and anti-hyperuricemic agents. All patients were treated according to the clinical practice guidelines for CKD (Japanese Society of Nephrology 2013). A time-dependent Cox hazard model was applied to evaluate the associations between clinical parameters and adverse events (initiation of RRT and hospitalization resulting in cardiovascular disease or infection).

Results: Unexpectedly, under the condition of appropriate control by nephrologists, hypertension, hyperuricemia, metabolic acidosis, iron metabolism, and inflammation were not selected as significant predictors of the progression of renal dysfunction or adverse events. *(Factors associated with the progression of renal dysfunction)* In multiple regression analysis, lower baseline blood levels of Hb (β=0.497, P<0.001) and vitamin D 125 (β=0.258, P=0.006) and higher baseline blood levels of int-PTH (β=-0.334, P=0.001), urinary phosphorus (β=0.328, P=0.001), urinary β2-MG (β=-0.225, P=0.031) and urinary protein (β=0.280, P=0.02) were selected as significant predictors of reduced estimated glomerular filtration rate (eGFR) or 1/creatinine (Cr) at the end of the study. *(Factors associated with the initiation of RRT and adverse events)* In the Cox hazard model, low calcium (HR: 0.37, P=0.026), high phosphate (HR: 5.90, P<0.001), low 1,25-vitamin D (HR: 0.94, P=0.013), high int-PTH (HR: 1.02, P<0.001), use of a phosphate binder (HR: 4.95, P=0.012), and use of vitamin D analogs (HR: 3.75, P=0.014) were selected as risks for adverse events, including the initiation of RRT.

Conclusion: In this study, we found that among several factors, anemia and CKD-MBD-related factors (phosphate, calcium, vitamin D, int-PTH) were selected as significant predictors of the progression of renal dysfunction. Furthermore, although phosphate binders or vitamin D analogs were administered appropriately, CKD-MBD-related factors (phosphate, calcium, vitamin D, and int-PTH) were associated with RRT initiation or adverse events in these patients. From these results, we presumed that early intervention or strict control of CKD-MBD factors might attenuate the risk for adverse events in CKD patients.

P0759 **ORTHOSTATIC SYSTOLIC BLOOD PRESSURE CHANGE AND THE RISK OF CHRONIC KIDNEY DISEASE: A COMMUNITY-BASED PROSPECTIVE STUDY IN KOREA**

Hyang Ki Min[1], Sung Woo Lee[1]

[1]*Nowon Eulji Medical Center, Eulji university, Internal Medicine, Seoul, Korea, Rep. of South*

Background and Aims: There have been no studies which explored the relationship between orthostatic blood pressure (BP) change and incident chronic kidney disease (CKD) in Asian population.

Method: We reviewed the data of 7,461 non-CKD adults aged 40-69 years who participated in Ansung_Ansan Cohort, a prospective community-based cohort study. BP was measured on supine position and 2 minute–upright position, and the difference was defined as orthostatic BP change. Incident CKD was defined as the first event to be estimated glomerular filtration rate < 60 ml/min/1.73 m^2, which was confirmed at least 2 or more times thereafter.

Results: Of 7,461, orthostatic diastolic BP change was not associated with incident CKD in multivariate Cox proportional-hazard regression model. However, per 1 mmHg increase of orthostatic systolic BP was associated with decreased hazard of incident CKD: hazard ratio 0.988 and 95% confidence interval (0.982-0.994, $P < 0.001$). In penalized spline curve analysis, we identified L-shaped relationship between orthostatic systolic BP change and incident CKD, with the threshold of - 2.4 mmHg. In subgroup analysis, the relationship between orthostatic systolic BP change and incident CKD was evident, particularly in participants without central obesity and reduced high density lipoprotein cholesterol and those with increased white blood cells.

Conclusion: Orthostatic SBP change was independently associated with incident CKD development. Future studies need to be followed to confirm the results.

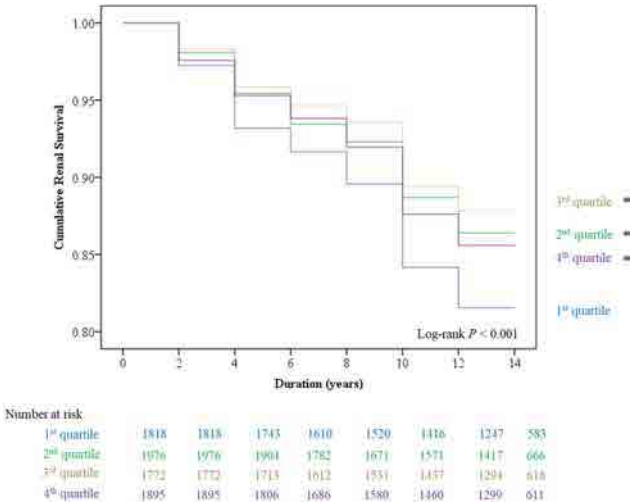


Figure 1. Kaplan-Meier survival curve of orthostatic SBP change quartile group for incident CKD. SBP, systolic blood pressure; CKD, chronic kidney disease. *, †, and ‡ meant $P < 0.01$ when compared to 1-3Q of orthostatic SBP change quartile group, respectively, using log-rank test.

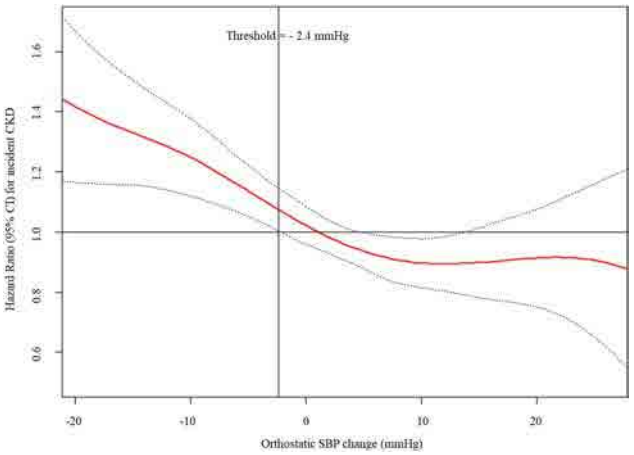


Figure 2. Penalized smoothing splines showing the relationship between orthostatic SBP change and incident CKD. HR, hazard ratio; CI, confidence interval; SBP, systolic blood pressure; CKD, chronic kidney disease. The red solid line indicates the HR and the black dotted lines indicate the 95% CI for the relationship between orthostatic SBP change and incident CKD. HR and 95% CI were calculated using multivariate Cox proportional hazard regression analysis entering into age, sex, the status of alcohol drinking, smoking, and education, elevated blood pressure, elevated fasting glucose, central obesity, elevated triglyceride, reduced high density lipoprotein cholesterol, estimated glomerular filtration rate ≥ 94 ml/min/1.73m^2, C-reactive protein, and white blood cells as covariates

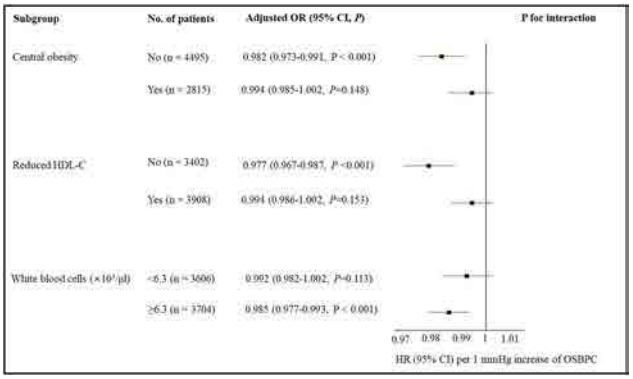


Figure 3. Subgroup analysis for the relationship between OSBPC and incident CKD. OSBPC, orthostatic systolic blood pressure change; CKD, chronic kidney disease; HR, hazard ratio; CI, confidence interval. HR and 95% CI were calculated using Cox proportional hazard regression analysis, entering age, sex, the status of alcohol drinking, smoking, and education, elevated blood pressure, elevated fasting glucose, central obesity, elevated triglyceride, reduced high density lipoprotein cholesterol, estimated glomerular filtration rate ≥ 94 ml/min/1.73m^2, C-reactive protein, and white blood cells as covariates. When covariates were chosen as subgroup, they were excluded from the model.

P0760 THE INFLUENCE OF MICROBIOME COMPOSITION ON THE DEVELOPMENT OF IGA NEPHROPATHY

Farid Nakhoul[1,2], Nakhoul Nakhoul[3], Rula Nakhoul[4], Evgeny Farber[1]

[1]Baruch padeh Poria Medical Center, Nephrology and Hypertension, Lower Galilee, Israel, [2]Baruch padeh Poria Medical Center, Azrieli Faculty of Medicine Ramat Gan University, Nephrology and Hypertension, Lower Galilee, Israel, [3]Baruch padeh Poria Medical Center, Diabetes &Metabolism Lab, Lower galilee, and [4]Baruch padeh Poria Medical Center, Diabetes &Metabolism Lab, Lower Galilee, Israel

Background and Aims: Overall, human microbiota contains 1014 bacterial cells. The human intestine is particularly dense of microbes, 1012 bacteria per g (dry weight), especially at colon level. Under healthy conditions, the human microbiota provides trophic and protective functions. Bacteroidaceae, and Prevotellaceae differed among IgA and Healthy Control subjects (HC). Enterobacteriaceae species were almost the highest in the fecal samples of patients.

Bifidobacterium species decreased in the fecal samples of Patients compared to HC subjects. Increasing evidence indicates that changes in the microbiota composition known as Dysbiosis, can affect human health and disease. Altering the balance of the gut microbiota can also affect kidney physiology and pathology, such as IgAN. we hypothesize that the aberrantly IgA1 that produced in IgAN in response to a mucosal infection may be influenced by the composition of the patient microbiome by inducing excessive abnormal mucosal IgA responses.

Study aim is to explore if IgAN patients have different microbiome composition compared with the healthy control individuals.

Method: Stool sample from 26 IgAN patients & from 26 healthy control individuals subjected to microbiome array and to taxonomic analysis, to characterize their microbiome compositions. Serum Creatinine\ albumin and urine proteinuria levels are used for evaluate the renal function of each IgAN patient. The clinical and laboratory evaluations will be crossed with the taxonomic data using statistical analysis methods.

Results: Based on our preliminary result with 11 IgAN patients and 11 healthy control individuals, there are significant differences in the microbiome composition between the two groups.

IgAN patients have a significant increase in the Bacteroides phylum accompanied with a significant decrease in the amount of both the Actinobacteria and Verrucomicrobia phyla, compared with the healthy individuals.

At the genus level, there is a significant increase in the Prevotella bacteria in the IgAN subjects compared with the healthy individuals.

Conclusion:

1. A strong association between specific bacteria population and IgAN disease, we isolate specific population of bacteria that leads to IgAN or even aggravate its manifestation.

2. It may help to predict the tendency of each individual to develop IgAN and even predict the prognosis of each IgAN patient according to their microbiome.

3. it is rational to alter the intestinal barrier, the content of gut microbiota and its metabolites in the realm of CKD using different strategies such Prebiotics and symbiosis.

4. To develop disease-specific therapies based on microbiome modulations and manipulations such as modifying the gut microbiota through diet, antibiotic therapies, probiotic, bariatric surgery, fecal transplants.

P0761 **STUDY ON THE MECHANISM OF MICROINFLAMMATION WITH UREMIA CAUSED BY LACTOBACILLUS ACTIVATION OF INTESTINAL MACROPHAGES BY MINCLE**

Lingshuang Sun[1]

[1] *First Affiliated Hospital of Medicine School, Xi'an Jiaotong University, Dialysis Department of Nephrology Hospita, xi'an, P.R. China*

Background and Aims: My previous studies have found that Intestinal macrophages in the uremic rats are polarized towards a proinflammatory phenotype and had dysfunction of phagocytosis leading to aggravate microinflammation and assist bacterial translocation in uremia resulting in microinflammation. However, it is still unclear what kind of mechanism of action of intestinal bacteria activates intestinal macrophages and thus participates in the occurrence and development of microinflammation in uremia.

Method: Male Sprague-Dawley rats were randomly divided into two groups: sham, uremia. The macrophage ultrastructure was examined by transmission electron microscopy. Immunochemistry was used to analyze the expression of macrophage-inducible C-type lectin (Mincle). RT-PCR and western blot were employed to assess the mRNA and protein expression of toll-like receptor 4 (TLR4).

Results: Our RCT study found that the number of Lactobacilli in the intestines of patients with end-stage diabetic nephropathy was significantly higher than that in non-diabetic patients(Figure 1). The plasma levels of endotoxin, CRP, IL-6, and TNF-a in the uremia group were greater than those in the sham group ($p>0.05$)(Table 1).Compared with the sham group, the uremic macrophages showed fewer cytoplasmic protrusions and pseudopodia(Figure 2) and the uremia group exhibited macrophages with higher staining intensities for Mincle and higher mRNA and protein expression of TLR4(Figure 3-5).

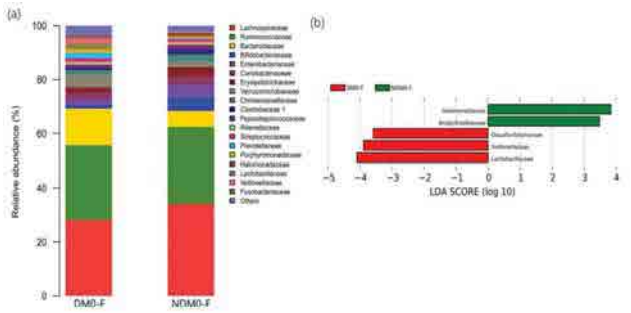


Figure 1.

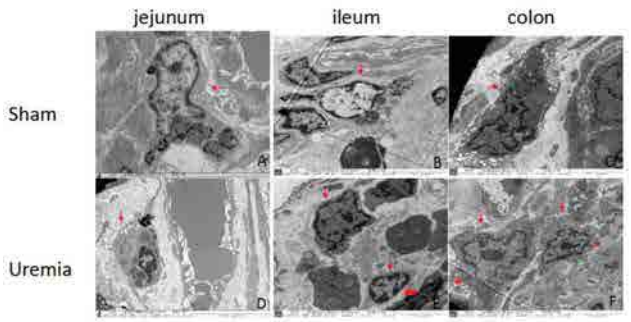


Figure 2. Transmission electron microscopy photomicrographs of intestinal macrophages. (A, D) Jejunum, (B, E) ileum, (C, F) colon, (A–C) sham group, (D–F) uremia group. Thin arrows indicate macrophages (A–F). Long thick arrow indicates a dying macrophage (E). Short thick arrows indicate decreases in macrophage electron density (F). Scale bar = 2 μm.

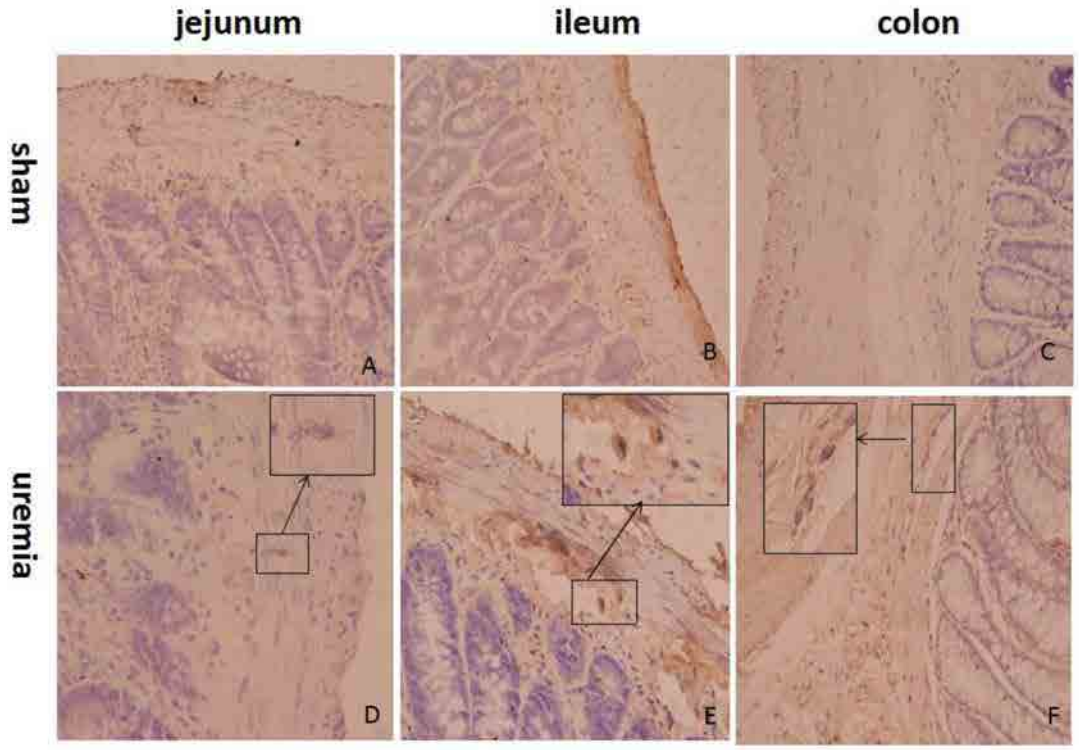


Figure 3. Intestinal Mincle staining immunohistochemistry, coloring cells were seen in the ileum and colon lamina propria in the uremic group.

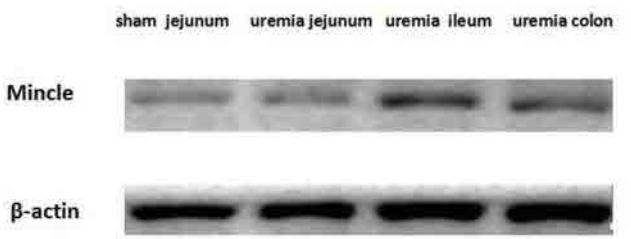


Figure 4. Immunoblot band densities of Mincle.

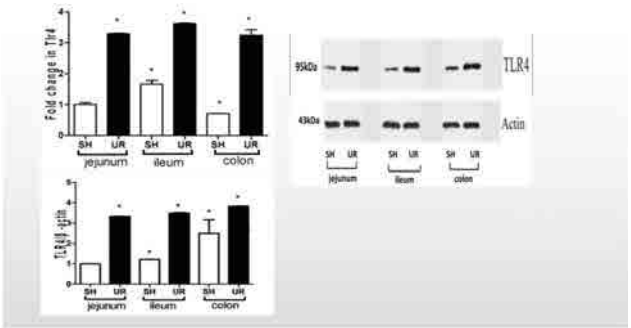


Figure 5. Expression of TLR4. SH, sham group; UR, uremia group. Fold-change in the gene expression levels of TLR4. Immunoblots of TLR4 proteins. Immunoblot band densities. each column represents the mean ± SD of 10 replicates. * indicates $p < 0.05$ compared to the sham group jejunum.

Conclusion: Studies have shown that Lactobacillus planta can directly activate Mincle. The relationship between Mincle and the activation of intestinal macrophages was verified. The solution to this scientific problem will not only clarify the molecular mechanism of intestinal bacteria in controlling the activation of intestinal macrophages, but also link the immune regulation of intestinal macrophages with the micro-inflammation of uremia so as to clarify the micro-inflammation state of uremia.

Table 1. Body weight, hematocrit, and blood chemistry results

Group (n = 10)	Body weight (g)	Creatinine (μmol/L)	Urea (mmol/L)	Endotoxin (Eu/mL)	CRP(mg/mL)	IL-6(pg/mL)	TNF-α (pg/mL)
sham	560.4 ±16.6	31.5 ±6.7	6.05 ±0.85	0.016±0.005	2.48 ±0.28	18.26 ±3.72	20.9 ±0.28
Uremia	516.6 ±14.5*	95.7 ±35.6*	18.10 ±8.50*	0.033 ±0.009*	5.2 ±0.77*	31.07 ±10.06*	30.4 ± 7.73*

Data are presented as the mean ±SD.

***** $p < 0.05$ vs. the sham group

P0762

THE SERUM URIC ACID HAS A INDEPENDENT ASSOCIATION WITH 1-YEAR RENAL OUTCOMES IN CHRONIC KIDNEY DISEASE PATIENT WITH HYPERTENSION

JIWON RYU[1], Chung Sik Lee[2], Sejoong Kim[3], Ran-Hui Cha[4], Hajeong Lee,[5], Jung Pyo Lee[6], Young Rim Song[7], Yon su Kim[5], Sung Gyun Kim[7]

[1]Cheju Halla general hospital, internal medicine, Cheju, Korea, Rep. of South, [2]Cheju Halla general hospital, Internal medicine, Cheju, Korea, Rep. of South, [3]Seoul National University Bundang Hospital, Internal medicine, Seongnam-si, Korea, Rep. of South, [4]National Medical Center, Internal medicine, Seoul, Korea, Rep. of South, [5]Seoul National University College of Medicine, Internal medicine, Seoul, Korea, Rep. of South, [6]Seoul National University Boramae Medical Center, Internal medicine, Seoul, Korea, Rep. of South and [7]Hallym University Sacred heart Hospital, Internal medicine, Anyang-si, Korea, Rep. of South

Background and Aims: Serum uric acid (UA) is associated with renal disease. Hyperuricemia can be a risk of hypertension, intrarenal vascular disease and renal injury. We investigate the serum UA has an association with renal disease progression in patients with chronic kidney disease (CKD) with hypertension.

Method: We recruited 270 CKD patients with hypertension from 4 centers in Korea through the APrODiTe study and followed for 1 year. Serum UA was evaluated as a continuous value and groups divided by quartiles. The renal outcomes were an increase in random urine protein/creatinine ratio (PCR) than baseline value or estimated glomerular filtration rate (eGFR) deterioration which means a decrease in eGFR $\geq$ 5 (ml/min/1.73m^2).

Results: Baseline serum UA was 6.58 $\pm$ 1.73 mg/dl and 6.52 $\pm$ 3.59 mg/dl after 1 year. For proteinuria progression, a 1 mg/dl higher serum UA has independent correlation in multivariate regression (odds ratio (OR): 1.272; 95% confidence interval (CI): 1.031-1.568; P = 0.024). The higher quartile of serum UA showed a correlation with the odd ratio than lower quartile (OR: 2.243; 95% CI: 0.862-5.837; P = 0.098, OR:3.417; 95% CI: 1.275-9.152; P= 0.015, OR: 2.754; 95% CI: 1.013-7.488; P $<$ 0.047). In subgroup analysis, the patients with late CKD stage (3-5) showed serum UA has a positive correlation with proteinuria progression (OR: 1.311; 95% CI: 1.022-1.682; P= 0.033) and the top quartile group was correlated with the increased odds ratio compared to lower quartile (OR: 3.811; 95% CI: 1.153-12.59; P = 0.028). For eGFR deterioration, the higher quartile of UA was positively correlated with the odd ratio in only univariate analysis.

Conclusion: Serum UA level has an independent correlation with proteinuria progression in especially late CKD patient with hypertension. Whereas for eGFR deterioration, serum UA did not show a significant correlation.

P0763

A COMPARATIVE STUDY OF ARTERIAL STIFFNESS AND WAVE REFLECTIONS IN DIABETIC AND NON-DIABETIC PATIENTS WITH CKD

Maria Schoina[1], Charalampos Loutradis[1], Evangelos Memmos[1], Rafael Papadopoulos[1], Eleni Intzevidou[1], Michael Doumas[2], Asterios Karagiannis[2], Aikaterini Papagianni[1], Panteleimon Sarafidis[1]

[1]Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece and [2]Aristotle University of Thessaloniki, Second Propedeutic Department of Internal Medicine, Hippokration Hospital, Thessaloniki, Greece

Background and Aims: Arterial stiffness is associated with increased risk for target-organ damage, cardiovascular events and overall mortality in the general population, patients with diabetes mellitus and patients with chronic kidney disease (CKD) of all stages. This is the first study to evaluate in comparison arterial stiffness and arterial wave reflections in diabetic and non-diabetic patients with CKD.

Method: This study included 48 diabetic and 48 non-diabetic adult patients (>18 years) with CKD (eGFR: <90 και ≥15mL/min/1.73m^2), matched in a 1:1 ratio for age, sex and eGFR within each CKD stage (2, 3a, 3b and 4). All patients underwent carotid-femoral pulse wave velocity (PWV), central blood pressure (BP), and wave reflections measurement with applanation tonometry (Sphygmocor, Atcor Medical, Australia).

Results: Office systolic and diastolic blood pressure was similar between diabetic and non-diabetic subjects with CKD in total and across CKD stages. Office brachial pulse pressure (PP) was significantly lower in non-diabetics (49.00±8.0 vs 52.67±8.7 mmHg, p= 0.034). Office PWV was marginally higher in diabetics compared with non-diabetics (10.89±2.0 vs 10.06±2.2 m/sec, p=0.056). In CKD stages 2 and 4, no significant difference in PWV between the two groups was noted, but PWV was higher for diabetics in CKD stages 3a (11.28±1.4 vs 9.83±1.5 m/sec, p=0.023) and 3b (11.13±1.9 vs 9.46±1.2 m/sec, p=0.016). Heart-rate-adjusted augmentation index [AIx(HR75)] was higher in diabetic compared with non-diabetic subjects only in CKD stage 4 (32.08±4.2 vs 25.92±6.6%, p=0.013).

Conclusion: Diabetic CKD patients present higher arterial stiffness than non-diabetic counterparts. The additional contribution of diabetes towards increased arterial stiffness is more prominent in patients with moderately impaired renal function (CKD stage 3a and 3b), whereas at stage 4, PWV was increased independent of diabetes presence.

P0764 **STUDY OF 15 CASES OF CHOLESTEROL CRYSTAL EMBOLISM WITH LOW-DENSITY LIPOPROTEIN APHERESIS.**

Taisuke Shimizu[1], Tatsuro Sano[1], Kaori Takayanagi[1], Kouki Ogawa[1], Takatsugu Iwashita[1], Tomonari Ogawa[1], Hajime Hasegawa[1]

[1]*Saitama Medical Center, Saitama medical University, Nephrology and Hypertension, Kawagoe, Japan*

Background and Aims: Cholesterol crystal embolism (CCE) causes renal damage, and there is a high risk of end-stage renal disease. Corticosteroids, statins and low-density lipoprotein apheresis (LDL-A) have been used to treat CCE, but the prognosis remains poor and treatment not yet established. This study evaluated the efficacy of LDL-A in patients with CCE.

Method: We performed a retorospective study of 15 Japanese patients in clinical and histological diagnosis of CCE was made April 2015 to December 2017. 10(67%) patients were diagnosed pathologically on skin biopsy and others were diagnosed clinically. All patients had shown CKD with eGFR <60 mL/min/1.73m^2 before being diagnosed with CCE. All patients received LDL-A; of these, 13 (87%) also received corticosteroids. The median estimated GFR diagnosis (at baseline) were 13.4 mL/min/1.73m^2, and were analyzed stratified into High eGFR group(H) and Low eGFR group(L). Differences in eGFR, 1 month, 3 months and 1 year after LDL-A, were compared in these groups.

Results: High eGFR group was significantly higher than Low eGFR group over all observation periods (at 1 month; H:21.3 $\pm$ 8.9 vs L:15.9 $\pm$ 5.6, P=0.023, at 3 months; H:25.9 $\pm$ 10.3 vs L:15.4 $\pm$ 5.4, P=0.035, at 1 year; H:21.7 $\pm$ 8.9 vs L:13.2 $\pm$ 5.7, P=0.01). In high eGFR group, eGFR was no change during the observation period and no decrease significantly. In Low eGFR group, eGFR increased significantly at 1 month and 3 months compared to baseline (10.5 $\pm$ 2.1 at baseline, 15.9 $\pm$ 5.6 at 1month, P=0.007, 15.4 $\pm$ 5.4 at 3month, P=0.01), but was comparable to baseline at 1 year.

Conclusion: In this study, introduction of LDL-A may have the effect of maintaining renal function over the long term at 1year regardless of eGFR at diagnosed as CCE.

P0765 **RHEUMATOID ARTHRITIS AND CHRONIC KIDNEY DISEASE: DOES INFLAMMATION SAY IT ALL?**

Marina Sofia Rodrigues Reis[1], Pedro Salvador[1], Ana Marta Gomes[1], Sara Beça[1], João Carlos Fernandes[1]

[1]*Vila Nova de Gaia, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal*

Background and Aims: Rheumatoid arthritis (RA) increase risk of developing chronic kidney disease (CKD), but it is unknow which risk factors contributes to CKD in this population. This study aims to determine predictors for the development of CKD in RA patients.

Method: A retrospective study was conducted in 106 patients with RA followed at a sub-specialized internal medicine appointment between January 2007 and December 2017. RA was defined according to the American College of Rheumatology criteria and CKD was defined as an estimated glomerular filtration rate less than 60mL/min/ $1.73m^2$ or presence of abnormalities of urinary sediment for 3 months.

Results: The mean age was 61 ± 12.83 years, and 67.9% (n=72) were female. The prevalence of CKD was 20.8% (n=22). Renal disease had multifactorial etiology in 20 patients, and one case of ANCA negative glomerulonephritis and other of diabetic nephropathy. Individuals with RA and CKD were older, presented more cardiovascular disease, diabetes and hypertension. There was no statistically significant association between gender and the presence of CKD (p = 0.131). Age (p = 0.031) and diabetes (p = 0.031) were independent risk factors for development of CKD in RA patients. RA duration in patients with CKD (8, 4-13) was not statistically different from RA duration in non-CKD patients (7.50, 4,75 – 12,25), (p=0.890).

Conclusion: Patients with RA and CKD had higher incidence of cardiovascular events, diabetes and hypertension which are a major cause of mortality and morbidity in this group. The presence of diabetes mellitus that often arise as an adverse effect of drugs used in the treatment of RA, significantly increased the risk of developing CKD. Otherwise, RA duration didn't represent a risk factor for developing CKD. Thus, it is important to control diabetes, particularly glucocorticoid-induced diabetes to prevent development of CKD in AR patients.

	CKD (n=22)	**No CKD (n=84)**	**Univariate analysis** p value	**Multivariate analysis** p value
Age, median (AIQ)	73,50 (64-78)	58 (51,0-65,75)	**<0,05**	**0,031**
Male, n (%)	24 (28,6)	10 (41,5)	ns	Ns
RA Duration, median (IQR)	7,5 (4,75 – 12,25)	8 (4-13)	ns	
Hypertension, n (%)	17 (77.3)	32 (38.1)	**0,046**	Ns
Diabetes Mellitus, n (%)	9 (40.9)	9 (10.7))	**0,046**	**0,031**
Cardiovascular disease, n (%)	12 (54.5)	16 (19.0)	**0,001**	ns
NSAID, n (%)	16 (26.2)	24 (16.4)	ns	

P0766 **ACUTE KIDNEY INJURY INCREASES THE RISK OF PROGRESSION OF RENAL DISEASE AFTER CARDIAC SURGERY : A SINGLE CENTER EXPERIENCE**

Mahesh Kota[1]

[1]*Star Hospitals,Hyderabad, Nephrology, Hyderabad, India*

Background and Aims:

With increasing global burden of cardiovascular diseases and advances in managing them, the number of cardiac surgeries performed in India has been increasing in the last couple of decades.A lot of western data from the last 5 to 10 years say that AKI episodes can cause significant renal damage and progress to chronic kidney disease (CKD) ,however the association between acute kidney injury (AKI) and chronic kidney disease (CKD) remains elusive in cardiac surgery. We investigated the association between postoperative AKI and CKD development, emphasizing the role of AKI in post cardiac surgery patients.

Method:

We observed the incidence of cardiac surgery associated AKI (CSA-AKI), determinants of progressive kidney disease after CSA-AKI and followed the patients with CSA-AKI for three months to find out the incidence of CKD or progressive renal dysfunction.

Results:

150 consecutive post cardiac surgery patients were included in the study. CSA-AKI incidence was 35.4%[Figure 1].Incidence of AKI was significant with prior AKI episodes($P<0.01$) and with pre-existing CKD ($P<0.01$)[Figure 2].Among intraoperative risk factors for CSA-AKI, need for CPB(P-0.01), prolonged pump time(P-0.01), blood transfusion(P-0.04) and ultrafiltration(P-0.01) during surgery were found to be significant[Figure 3,4].Duration of ICU stay ($P<0.01$), hospital stay ($P<0.01$) and death rate (P-0.04) was higher in patients with AKI[Table 1]. Out of 53 patients who developed CSA-AKI, follow up for the progression of renal disease was done for 50 patients, as 3 patients with AKI died during hospital stay. Progressive renal dysfunction (new development of CKD or progressive CKD) after 90 days was seen in 48% of patients with CSA-AKI. All the risk factors for the progression of renal disease after AKI like increased age, low serum albumin, presence of hypertension, diabetes mellitus, protein loss in urine, severe AKI(KDIGO stage>2) and multi factorial AKI was higher in patients who had progressive renal disease after AKI in the study group, however the relation was not statistically significant[Table 2].

Conclusion:

AKI is not uncommon after cardiac surgery, progressive renal dysfunction was seen in 48% of patients after CSA-AKI and progressive renal dysfunction was common in those with increased age, low serum albumin, presence of hypertension, diabetes mellitus, protein loss in urine, severe AKI(KDIGO stage>2) and multi factorial AKI.

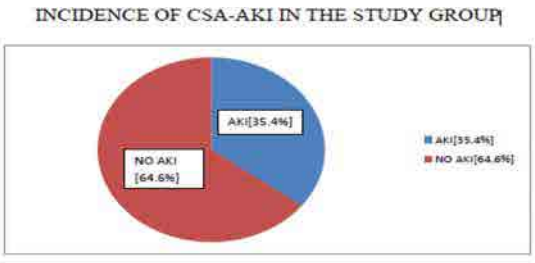
Mean age of patients with AKI in the study group was found to be 61±10 years and for NO AKI group mean age was found to be 58±12 years. This variation was not found to be statistically significant.

Among other pre-operative risk factors, though there was some difference in percentage for many risk factors, but the percentage variation was quite significant for subjects with prior AKI episodes and those with existing CKD. The increased incidence of AKI in patients with prior AKI episodes ($P<0.01$) and in those with pre-existing CKD ($P<0.01$) was found to be statistically significant.

Low socioeconomic status was found to be high in NO AKI group, however this was not found to be statistically significant (P-0.11).

When compared to both the groups, duration of stay in ICU ($P<0.01$), overall duration of hospital stay ($P<0.01$) and death rate (P-0.04) was higher in AKI group and this variation was found to be statistically significant.

All the risk factors for the progression of renal disease after AKI like increased age, low serum albumin, presence of hypertension, diabetes mellitus, protein loss in urine, severe AKI(KDIGO stage>2) and multifactorial AKI was higher in patients who had progressive renal disease after AKI in the study group, however the relation was not statistically significant.



Among 150 subjects in the study group, AKI of KDIGO stage ≥1 was seen in 53(35.4%) patients

Figure 1:

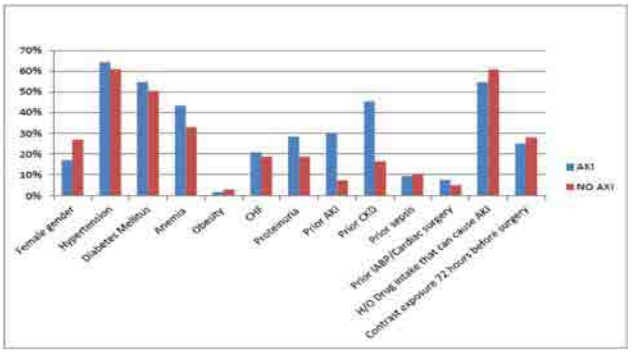


Figure 2:

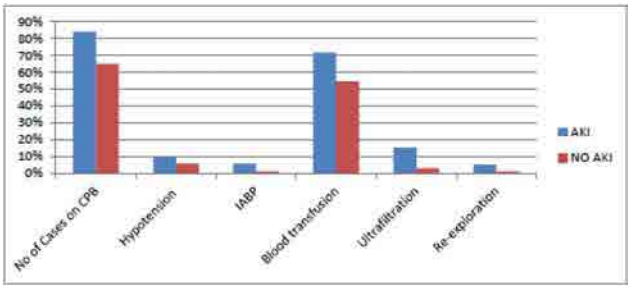


Figure 3:

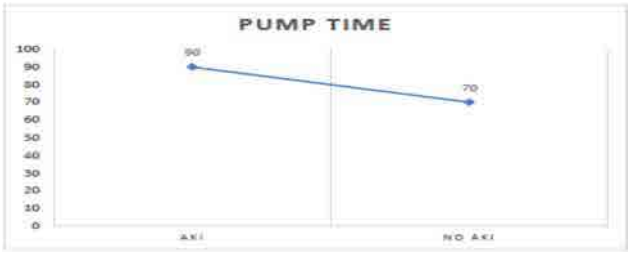


Figure 4:

Nephrology Dialysis Transplantation 35 (Supplement 3): iii1096–iii1176, 2020

CKD. CLINICAL EPIDEMIOLOGY

P0770 IMPAIRED FASTING GLUCOSE AND CHRONIC KIDNEY DISEASE: A MENDELIAN RANDOMIZATION STUDY

Hyunjin Noh[1], Hyoungnae Kim[1], Su Yeon Park[2], Dohui Hwang[1], Kyoungin Choi[1]
[1]Soon Chun Hyang University, Dept of Internal Medicine, Hyonam Kidney Laboratory, Seoul, Korea, Rep. of South and [2]Soon Chun Hyang University, Dept of Biostatistics, Seoul, Korea, Rep. of South

Background and Aims: Diabetes mellitus is a risk factor of chronic kidney disease (CKD); however, the relationship between fasting glucose and CKD remains controversial in non-diabetic population.

Method: This study included 6,354 participants without diabetes and CKD from the KoreanGenome Epidemiology Study. The genetic risk score (GRS9) was calculated using nine genetic variants associated with fasting glucose in previous genome wide association studies. Incident CKD was defined as estimated glomerular filtration rate (eGFR) $<$60 mL/min/1.73 m^2 or proteinuria ($\geq$1+). The causal relationship between fasting glucose and CKD was evaluated using Mendelian randomization (MR) approach.

Results: The GRS9 was strongly associated with fasting glucose (β, 1.01; $P < 0.001$). During a median follow-up of 11.6 years, 531 (8.4%) CKD events occurred. After adjusting for confounding factors, fasting glucose was not associated with incident CKD (odds ratio [OR], 0.991; 95% confidence interval [CI], 0.980–1.003; P =0.139). In the MR analysis, GRS9 was not associated with CKD development (OR per 1 standard deviation increase, 1.179; 95% CI, 0.819–1.696; $P = 0.376$). Further evaluation with various other MR methods using inverse-variance weighted, MR-Egger, and weighted median methods for multiple genetic variants and strict CKD criteria (decrease in the eGFR of $\geq$ 30% to a value of $<$ 60 mL/min/1.73m^2) found no significant relationship between GRS9 and incident CKD.

Conclusion: Impaired fasting glucose was not causally associated with CKD development in nondiabetic population.

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P0771

STOPPING MINERALOCORTICOID RECEPTOR ANTAGONISTS AFTER HYPERKALEMIA AND RISK OF ADVERSE OUTCOMES IN PATIENTS WITH HEART FAILURE

Marco Trevisan[1], Yang Xu[1], Yao Qiao[2,3], Gianluigi Savarese[4], Lars Lund[4], Morgan Grams[3,5], Arvid Sjolander[1], Juan Jesus Carrero[1]

[1]Karolinska Institutet, Medical Epidemiology and Biostatistics, Stockholm, Sweden, [2]Johns Hopkins Bloomberg School of Public Health, Center for Drug Safety and Effectiveness, Baltimore, United States of America, [3]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, United States of America, [4]Karolinska Institutet, Department of Medicine, Stockholm, Sweden and [5]Johns Hopkins Bloomberg School of Medicine, Department of Medicine, Baltimore, United States of America

Background and Aims:

Stopping mineralocorticoid receptor antagonists (MRAs) after an episode of hyperkalemia is common, particularly among patients with chronic kidney disease (CKD). This may involve therapeutic compromises, in that the cessation of MRAs deprives patients of their beneficial cardiovascular effects. The aim of this study is to determine the risks of adverse health outcomes in heart failure patients after an episode of hyperkalemia, comparing users of MRA who stop treatment to those who continue the drugs.

Method:

Observational study from the Stockholm Creatinine Measurements (SCREAM) project. We identified patients with heart failure patients initiating MRAs and surviving a first-detected episode of hyperkalemia (plasma potassium >5.0 mmol/L). We used Cox regression, adjusting for multiple confounders, to estimate hazard ratios (HR) for adverse events following hyperkalemia. The primary outcome was the composite of hospital admission with heart failure, stroke, myocardial infarction or death. The secondary outcome was a new hyperkalemia event. We compared risks between people who stopped MRA treatment and those who continued MRA within 4 months from the hyperkalemia event (landmark analysis at month 4 after event).

Results:

We identified 1,330 patients with heart failure that developed hyperkalemia after initiating MRA therapy. Their median age was 80 years, 46% were women and their median eGFR was 43 ml/min/1.73m^2. Of those, 595 (45%) had discontinued MRA by 4 months after hyperkalemia. Patients who stopped MRA were more likely to have eGFR <60 ml/min/1.73m^2 (81% vs 71%), had a more severe index hyperkalemia (potassium>5.5 mmol/L, 35% vs 21%), and had hyperkalemia occur earlier in the course of MRA therapy (within 3 months from MRA initiation, 66% vs 51%).

During median 1.5 years of follow-up, a total of 846 patients (64%) experienced the primary composite outcome. Compared to patients who discontinued MRA, those who continued had a similar risk of the primary composite outcome (HR 0.95, 95% CI 0.82-1.10). A total of 569 patients (43%) developed a subsequent hyperkalemia event. Compared to patients who discontinued MRA, those who continued with the therapy were at higher risk of another hyperkalemia (HR 1.46, 95% CI 1.21-1.75). Results were consistent across age strata, sex and presence of CKD.

Conclusion:

Continuing treatment with MRA after an episode of hyperkalemia was not associated with different medium-term cardiovascular risk compared to those who stopped the drugs.

P0772

CLINICAL CHARACTERISTICS OF THE UK CHINESE POPULATION WITH KIDNEY FAILURE: A UK RENAL REGISTRY ANALYSIS

Katie Wong[1,2], Fergus Caskey[1,2], Yoav Ben-Shlomo[1], Anna Casula[3], Pippa Bailey[1,2]

[1]University of Bristol, United Kingdom, [2]Southmead Hospital, United Kingdom and [3]United Kingdom Renal Registry, Bristol, United Kingdom

Background and Aims:

Data from the UK Renal Registry (UKRR) has shown that 0.5% of those in the UK with kidney failure are of Chinese ethnicity. The UK Chinese population is growing. Ethnic differences in cause of renal disease and dialysis rates have been described in UK individuals of White, South Asian, and Black ethnicity. However, the clinical demographics of the UK Chinese population with renal disease have not previously been investigated.

The China Kidney Disease Network and the Hong Kong Renal Registry have reported the main cause of chronic kidney disease in their populations is diabetes, but the causes of renal disease in other Chinese diaspora have not been well described.

We investigated the clinical characteristics of the UK Chinese population on renal replacement therapy (RRT) as compared with the UK White RRT population in this UKRR analysis.

Method:

Data on all adult patients >=18 years who started RRT between 1/1/97 and 31/12/16 were extracted from the UKRR. Patients with ethnicity recorded as anything other than "Chinese" or "White" were excluded from analysis. Patients with ethnicity data missing were also excluded.

Socioeconomic status was measured using country-specific Index of Multiple Deprivation (IMD) quintiles derived from patients' postcodes (1= most deprived, 5= least deprived). The Chi-square (*) and Mann-Whitney U (**) tests were used to compare baseline characteristics between Chinese and White ethnic groups.

Results:

The dataset comprised of 92,857 incident RRT patients, of which 0.5% (n=501) were of Chinese ethnicity and 76% (n=70,575) were White. Clinical characteristics of the UK Chinese population as compared to the UK White population are presented in Table 1.

UK Chinese patients were younger at start of RRT than white patients (61.4 years vs 65.6 years, $p<0.001$**). Any difference in the proportion of male patients (60.7% vs 63.0%, $p=0.29$*) or socioeconomic status ($p=0.75$*) between the two groups was consistent with chance.

There were marked differences in the causes of renal disease: UK Chinese patients had more diabetic renal disease (29% versus 20%, $p<0.001$*) and glomerulonephritis that white patients (21% vs 13%, $p<0.001$*) There was modest evidence that more UK Chinese patients started RRT on peritoneal dialysis (PD) compared to the White population (26% vs 23%, $p=0.01$*)

Conclusion:

We found evidence that the UK Chinese RRT population differs from the UK White RRT population. To our knowledge, this is the first study describing renal disease in the UK Chinese population, and one of the first to describe disease in the Chinese diaspora.

Our finding of a greater burden of diabetes in the UK Chinese RRT population compared to the White RRT population may reflect the high prevalence of diabetes in the UK Chinese, as in mainland China and Hong Kong. Further investigation is needed to understand the causes behind the higher burden of glomerulonephritis in the UK Chinese population.

The increased rates of PD in UK Chinese patients may be associated with lower average Body Mass Index (BMI) in the Chinese population. The quantity of missing BMI data in the UKRR dataset prevented investigation of this association. Hong Kong has had a successful "PD first" policy for >30 years. Familiarity with this as a mode of dialysis may have led to higher rates of PD in the UK Chinese population. Studies from Hong Kong have also suggested that lower dialysis volumes are required for Chinese PD patients, and that high transporter status is less common in their population. It would be beneficial to elucidate whether this is also the case in UK Chinese patients.

Table 1: Characteristics of UK Chinese and White RRT populations

	Chinese n=501	White n=70,575	p value
Median age at start of RRT, years (IQR)	61.4 (47.5-71.9)	65.6 (51.8-75.2)	<0.001 **
Sex, n (%)			
Male	304 (61)	44,451 (63)	0.29 *
Female	197 (39)	26,124 (37)	
IMD quintile, n (%)			
1 Most deprived	119 (24)	17,873 (25)	
2	120 (24)	15,383 (22)	0.75 *
3	97 (19)	13,811 (20)	
4	91 (18)	12,423 (18)	
5 Least deprived	74 (15)	11,085 (16)	
Cause of renal failure, n (%)			
Diabetes	143 (29)	14,105 (20)	
Glomerulonephritis	105 (21)	9,217 (13)	
Hypertension	33 (7)	4,208 (6)	
Polycystic kidney disease	27 (5)	5,438 (8)	
Pyelonephritis	15 (3)	5,496 (8)	<0.001*
Renovascular disease	10 (2)	5,122 (7)	
Uncertain	106 (21)	13,055 (18)	
Other	43 (9)	11,694 (17)	
Missing	19 (4)	2,240 (3)	
Treatment at start RRT, n (%)			
Haemodialysis	351 (70)	50,112 (71)	0.01*
Peritoneal dialysis	132 (26)	15,967 (23)	
Transplant	18 (4)	4,496 (6)	

*Chi^2 test; **Mann-Whitney U test
RRT= Renal Replacement Therapy

Figure:

P0773

ESTIMATING THE BURDEN OF CHRONIC KIDNEY DISEASE (CKD) IN THE UK: COMPARISON OF TWO HEALTH ECONOMIC POLICY ANALYSIS METHODS.

Juan Jose Garcia Sanchez[1], Michael Xu[2], Elisabeth Sörstadius[3], Oliver Darlington[4], Phil McEwan[4,5], Simon Lande[2], Jonathan Pearson-Stuttard[6], Laura Webber[2]

[1]AstraZeneca, Global Pricing and Market Access, Cambridge, United Kingdom, [2]Health Lumen, London, United Kingdom, [3]AstraZeneca, Global Pricing and Market Access, Mölndal, Sweden, [4]HEOR Ltd., Cardiff, United Kingdom, [5]Swansea University, School of Human & Health Sciences, Swansea, United Kingdom and [6]Imperial College London, Faculty of Medicine, School of Public Health, London, United Kingdom

Background and Aims: Chronic kidney disease (CKD) represents an important health policy concern due to a growing population and its associated morbidity and mortality. Predicting the future burden of CKD overall and in high-risk populations such as patients with elevated albuminuria, type 2 diabetes (T2D) or heart failure (HF) is important if healthcare services are to be resourced properly. Health economic policy models based on epidemiological and clinical outcomes data provide a useful way by which to make such predictions; different methods of varying complexity have been employed to do this. This study aims to compare two different analytical approaches to estimating the burden of CKD in the UK, and to estimate how this is predicted to change in the future.

Method: Analysis 1 and 2 characterised the prevalent and incident CKD population, disease progression, clinical outcomes, costs and quality of life sourced from published data over a 5-year horizon.

Analysis 1 utilised an open cohort analysis based on a Markov framework, with health states defined by CKD stages. Disease progression was modelled through the application of published estimates of the rate of estimated glomerular filtration rate (eGFR) decline, stratified by the presence of T2D, HF and albuminuria.

Results:

Conclusion:

P0774

KIDNEY FUNCTION, KIDNEY FUNCTION DECLINE AND THE RISK OF ALL CAUSE, VASCULAR AND ALZHEIMER'S DEMENTIA: THE STOCKHOLM CREATININE MEASUREMENTS (SCREAM) PROJECT

Hong Xu[1], Marco Trevisan[2], Marie Evans[3], Bengt Lindholm[3], Juan Jesus Carrero[2]

[1]Karolinska Institutet, Div of Clinical Geriatrics, Dept of Neurobiology, Care Sciences and Society, Stockholm, Sweden, [2]Karolinska Institutet, Dept of Medical Epidemiology and Biostatistics, Stockholm, Sweden and [3]Karolinska Institutet, Renal unit and Baxter Novum, CLINTEC, Stockholm, Sweden

Background and Aims: Community-based reports regarding the association between the estimated glomerular filtration rate (eGFR) and dementia risk are conflicting. In this large Swedish population-based cohort, we explore the links between kidney function, kidney function decline and dementia incidence.

Method: In the Stockholm CREAtinine Measurements (SCREAM) project, we studied the association of baseline eGFR with the risk of incident dementia among 329,822 residents of Stockholm who accessed healthcare, were $\geq$65 years and had no previous history of dementia. We estimated the rate of eGFR decline among the 205,622 residents with repeated eGFR measurements during the first year and investigated its association with dementia risk. The primary outcome was dementia incidence based on ICD-10 codes or use of anti-dementia drugs. Secondary outcomes were incidence of the dementia subtypes Alzheimer's and vascular dementia.

Results: 18,983 cases of dementia (5.8% of participants) were detected throughout 1,185,304 person-years. Dementia incidence rates (IR) were progressively higher with lower eGFR: from 6.56/1000 person-years in persons with eGFR 90-104 ml/min to 30.28/1000 person-years in those with eGFR$<$30 ml/min). Compared with eGFR of 90-104 ml/min, lower eGFR was associated with a higher dementia risk [adjusted hazard ratio (HR), 1.69; 95% confidence interval (CI], 1.52-1.89 in eGFR 30-59 ml/min and HR 2.55, 1.86-3.50 in eGFR$<$30 ml/min). A steeper decline in eGFR within one year was linearly associated with higher dementia risk for declines greater than 2ml/min/1.73 m^2/year. Risk magnitudes were stronger for vascular dementia than for Alzheimer. Sensitivity analyses across predefined strata or after excluding early events yielded similar results. As many as 11% (95% CI 7-14%) of dementia cases were attributed to chronic kidney disease (eGFR$<$60 mL/min/1.73m^2), a proportion higher than that attributed to other dementia risk factors such as cardiovascular disease and diabetes.

Conclusion: In the general population, both low kidney function and faster kidney function decline are associated with increased risk of developing dementia, particularly vascular dementia.

P0775

A RETROSPECTIVE OBSERVATIONAL COHORT STUDY TO ASSESS THE PREVALENCE OF CHRONIC KIDNEY DISEASE AMONG TYPE 2 DIABETES MELLITUS PATIENTS IN ONTARIO, CANADA

Wally Rapattoni[1], David Zante[2], Sha Kang[2], Ali Tehrani[3], Varun Myageri[4], Shane Golden[5], Brad Millson[3], Jennifer B. Rose[1]

[1]Janssen Inc, CVM, Medical Affairs, Toronto, Canada, [2]Janssen Inc, Market Access, Toronto, Canada, [3]IQVIA Solutions Canada Inc, Health Access and Outcomes, Kirkland, Canada, [4]IQVIA Solutions Canada Inc, Health Access and Outcomes, Kirkland, Canada and [5]IQVIA solutions Canada Inc, Statistics, Kirkland, Canada

Background and Aims: The CREDENCE trial with canagliflozin demonstrated definitive evidence of renal benefits to slow the progression of end stage renal disease (ESRD) in type 2 diabetes (T2D) patients with chronic kidney disease (CKD). This real-world study was undertaken to better understand the prevalence of CKD among T2D patients in Ontario using the CREDENCE trial criteria. Ontario is the largest province, accounting for 38.8% of Canada's population in 2019[1]. Patients were identified in the following cohorts: T2D-CKD, T2D-CKD+cardiovascular disease (CVD), T2D-CKD+stroke, and T2D-CKD+CVD or stroke.

Method: This population-based retrospective cohort study was conducted in partnership with IQVIA and the Institute for Clinical Evaluative Sciences (ICES). The ICES data repository contains publicly funded administrative health service records for the Ontario population eligible for universal health coverage since 1986. Patients' eligibility for this study was aligned with enrolment criteria in the CREDENCE trial. Patients were ≥30 years of age at index and were identified as having both T2D and CKD. Diabetes patients were identified using the validated Ontario Diabetes Database (ODD), patients <19 years of age when first diagnosed with diabetes were excluded due to suspected type 1 diabetes (T1D). Additionally, patients with a T1D diagnosis at any time-point were excluded. CKD patients were identified through diagnosis/billing codes or estimated glomerular filtration rate(eGFR)<90 ml/min/1.73ml^2 derived from serum creatinine laboratory values. Diagnosis/billing codes are expected to have poor sensitivity[2,3] when used as the sole method to identify CKD. To account for anticipated missing information in each dataset, the capture-recapture method was used to obtain a more accurate estimate for the total prevalence. Capture-recapture accounts for incomplete ascertainment of administrative datasets by using the overlap between the datasets to derive an estimate of the total population[4,5] (Figure 1). This method was used in Manitoba to estimate the total CKD population, using administrative and laboratory datasets[4]. Therefore, each cohort (T2D-CKD, T2D-CKD+CVD, T2D-CKD+stroke, and T2D-CKD+CVD or stroke) has utilized each of the following four methods to identify CKD patients: diagnosis/billing codes, eGFR, diagnosis/billing codes or eGFR, and capture-recapture method. Yearly point prevalence of CKD among T2D patients is reported for the five fiscal years (FY) between 2011/12 and 2015/16.

Results: The prevalence of T2D patients ≥30 years of age in Ontario has increased from 959,850 in FY2011/12 to 1,169,759 in FY2015/16 (Figure 2). The prevalence of CKD among T2D patients ≥30 years of age in Ontario has increased across all methods from FY2011/12 to FY2015/16: from 21% to 28% based on diagnosis/billing codes, 47% to 63% based on eGFR, 55% to 70% based on diagnosis/billing codes or eGFR, and 76% to 84% based on capture-recapture. Similarly, prevalence of T2D-CKD+CVD, T2D-CKD+stroke, and T2D-CKD+CVD or stroke has increased in most cases (Figure 3).

Conclusion: CKD is a common comorbidity amongst T2D patients ≥30 years of age. The study provides estimates of the prevalence of CKD in four cohorts of T2D patients with defined co-morbidities and shows that the use of diagnosis/billing codes alone may underestimate the prevalence of CKD in T2D patients.

Furthermore, this real-world analysis highlights a significant, increasing prevalence of CKD among T2D patients ≥30 years of age in Ontario with all methods. On-going research aims to assess the burden of illness of patients with both T2D and CKD who are incident to T2D-related outcomes (CKD or CVD related death, kidney transplant, kidney dialysis, doubling of serum creatinine).

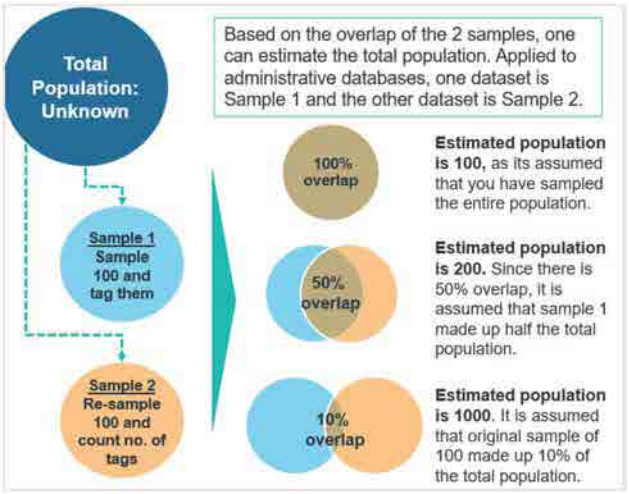


Figure 1: Illustrative example capture-recapture method

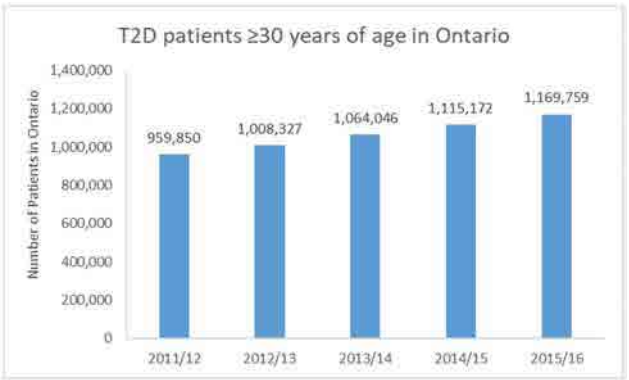


Figure 2: Number of T2D patients ≥30 years of age in Ontario

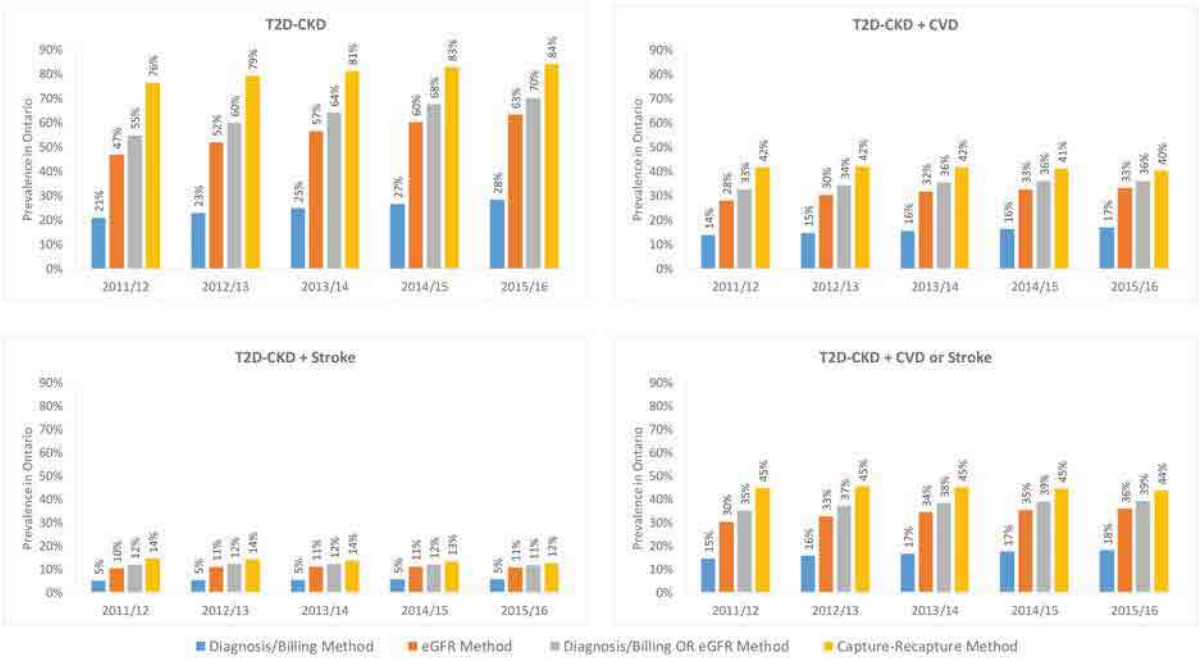


Figure 3: CKD Prevalence among T2D patients ≥30 years of age in Ontario

P0776

THE ADVERSE EFFECT OF CIGARETTE SMOKING ON THE NEW-ONSET OF CKD (CHRONIC KIDNEY DISEASE) IS MORE PREDOMINATE IN YOUNGER PEOPLE IN JAPANESE GENERAL POPULATION: IKI EPIDEMIOLOGICAL STUDY OF ARTEROSCLEROSIS AND CKD (ISSA-CKD) RETROSPECTIVE PHASE

Kenji Ito[1], Toshiki Maeda[2], Kazuhiro Tada[1,2], Koji Takahashi[1], Tetsuhiko Yasuno[1], Hitoshi Nakashima[1], Shigeaki Mukoubara[3], Kosuke Masutani[1], Hisatomi Arima[2]

[1]Faculty of Medicine, Fukuoka University, Division of Nephrology and Rheumatology, Fukuoka, Japan, [2]Faculty of Medicine, Fukuoka University, Department of Preventive Medicine and Public Health, Fukuoka, Japan and [3]Nagasaki Prefecture Iki Hospital, Nagasaki, Japan

Background and Aims: The prevention of chronic kidney disease (CKD) is one of the most important targets all over the world. The harmful effect of smoking was widely reported in patients with CKD, especially in diabetes patients, however, the studies regarding association between smoking and new-onset of CKD in general population has been limited. To clarify this issue, we have collected data from the annual health check-ups on residents in Iki-City (Nagasaki prefecture, Japan), the residents of which show one of the largest morbidity of end-stage kidney disease undergoing dialysis in Japan (3,588 per million), for large-scale cohort study as Iki Epidemiological Study of Atherosclerosis and Chronic Kidney Disease (ISSA-CKD) Project. In the study reported here, we conducted a retrospective cohort study using 8 years of data obtained from the project to identify the effect of smoking on new-onset of CKD.

Method: Iki-City is an island which located in the north of Nagasaki prefecture and has approximately 27,000 residents. From 2008 to 2016, a total of 4,540 adults were enrolled into this study. Information on smoking habits was obtained by a self-reported questionnaire. Current smokers were defined as participants who had smoked continuously for more than 6 months at the baseline examination, regardless of the past history of smoking. New-onset CKD was defined as reduction of eGFR down to less than 60mL/min/1.73m^2 and/or new-onset proteinuria during the follow-up examinations. Effects of smoking on development of CKD were evaluated using a Cox's proportional hazards model, and trend in the effects of smoking on outcomes across subgroups defined by age was tested by adding interaction terms to the statistical models.

Results: The average age of the enrolled residents was 59.6 ± 10.6 years (mean ± SD). During an average follow-up of 4.6 years, CKD was developed in 759 people (36.3 per 1,000 person-years). In the people who developed CKD, proteinuria was developed in 218 people (10.4 per 1,000 person-years) and eGFR decline to less than 60 mL/min/1.73mm^2 was confirmed in 594 people (28.3 per 1,000 person-years) including 53 people who showed both proteinuria and eGFR reduction (2.8 per 1,000 person-years). In terms of proteinuria, current smokers showed a higher incidence of 14.1 per 1,000 person-years than non-smoker whose incidence was 9.17 per 1,000 person-years (p=0.001), and a significantly high HR of 1.39 with a 95% CI of 1.01 to 1.92 in multivariable Cox's proportional-hazards analyses. The incidence of current smokers was almost similar throughout all age, while that of non-smokers increased with their age. (Table 1) The effect of smoking for the incidence of proteinuria was more drastic among younger participants (p=0.015 for trend): younger current smokers (<50 years-old) had a significantly higher HR of 2.55 with a 95% CI of 1.01 to 6.45 (p=0.004) than non-smokers.

Conclusion: Smoking significantly increased the risk for the new-onset of CKD according to the development of proteinuria in general Japanese population, and the association was more predominate in younger people. From the result of our present study, discontinuing smoking as soon as possible is strongly recommended for all cigarette smokers to prevent CKD.

Table 1: Result of Cox's Proportional-Hazards Analysis on the association of current smoking with the new-onset of proteinuria in each generation (Adjusted for sex, obesity, hypertension, diabetes mellitus, hyperuricemia, and dyslipidemia)

smoking status	N of Events / participants (Incidence*)	HR	95% CI	p for trend (linear)
Age <50 years				0.015
non-smoker	8 / 458 (4.2)	Reference		
current smoker	18 / 301 (13.7)	2.55	1.01 - 6.45	
Age 50 - 59 years				
non-smoker	27 / 629 (8.2)	Reference		
current smoker	18 / 274 (13.0)	1.31	0.64 - 2.70	
Age 60 - 69 years				
non-smoker	80 / 1,754 (8.8)	Reference		
current smoker	34 / 454 (15.3)	1.42	0.90 - 2.23	
Age ≥70 years				
non-smoker	30 / 576 (19.7)	Reference		
current smoker	3 / 94 (11.5)	0.64	0.18 - 2.27	

P0777 **REPRODUCTIVE HISTORY AND INCIDENT CKD IN MIDDLE-AGED WOMEN**

Kipyo Kim[1], Gang-Jee Ko[2], Ju-Young Moon[3]

[1]Inha University Hospital, Department of Internal Medicine, Korea, Rep. of South, [2]Korea University, Department of Internal Medicine, Seoul, Korea, Rep. of South and [3]Kyung Hee University, Department of Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Previous epidemiologic data showed female has slower renal function decline compared to male and experimental studies showed the renoprotective effects of estrogen. Nevertheless, clinical studies that supports the beneficial effects of female sex hormone on chronic kidney disease (CKD) progression are limited. Middle age in women is the period of experiencing hormonal alteration. Therefore, we investigated that the associations of reproductive history with incident CKD in middle-aged women.

Method: A total of 4481 women aged $\geq$ 40 years with normal renal function were included in the study from the Korean Genome and Epidemiology Study database. The cohort consisted of community-based general population and were followed up from 2001 to 2016. Primary outcome was the incident occurrence of CKD (eGFR< 60 ml/min/1.73m2 and 25% decline from baseline creatinine). We additionally defined the endogenous estrogen exposure (menopausal age - age at baseline - 0.75 x each childbirth) to examine the effect of estrogen exposure on renal function. Multivariable Cox proportional hazards analysis was performed with time-varying covariates including childbirth, menopausal status, and hormone replacement therapy.

Results: The mean age of participants was 52.3 $\pm$ 8.9 years, and 51.5% (n=2306) of patients have reached menopause at baseline. The mean eGFR was 94.1 $\pm$ 12.7 mL/min/1.73 m2 and 7.0% (n=315) participants experienced childbirth during follow-up period. Age-adjusted Cox model showed that childbirth (HR 1.58, CI 1.24-2.02) and menopause (HR 1.31, CI 1.04-1.63) were significantly associated with high risk of incidental CKD, but not in hormonal therapy. These associations remained after multivariate adjustment (childbirth, HR 1.55, CI 1.21-1.98; menopause, HR 1.26, CI 1.01-1.57). Endogenous estrogen exposure ranged 0 to 14 years, and was categorized into no exposure (51.5%), moderated exposure (1-6 years), and high exposure (>6 years). High exposure group was associated with the lower risk of CKD compared to no exposure group (HR 0.74, CI 0.58-0.94). Restricted cubic spline analysis also showed the inverse relationship between estrogen exposure and the risk of incident CKD.

Conclusion: In middle-aged women, menopause and childbirth were significantly associated with higher risk of incident CKD. These associations could be attributable to the reduction of endogenous estrogen exposure.

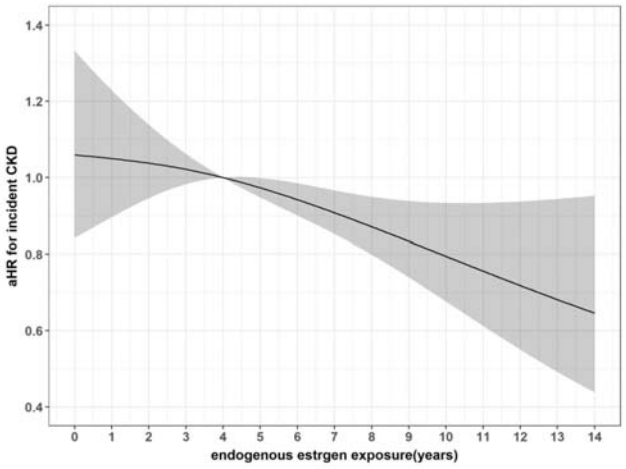


Figure: The association between endogenous estrogen exposure and incident CKD using restricted cubic spline analysis. The model was adjusted with age, eGFR at baseline, body mass index, diabetes, hypertension, smoking status, physical activity, hormone therapy, systolic blood pressure, albumin, and proteinuria.

P0778

INVESTIGATION THE EFFECT OF SERUM URIC ACID ON NEW-ONSET AND PROGRESSION OF CHRONIC KIDNEY DISEASE(CKD) IN JAPANESE GENERAL POPULATION : IKI EPIDEMIOLOGICAL STUDY OF ARTHEROSCLEROSIS AND CHRONIC KIDNEY DISEASE(ISSA-CKD) RETROSPECTIVE PHASE

Kazuhiro Tada[1], Toshiki Maeda[2], Koji Takahashi[1], Kenji Ito[1], Tetsuhiko Yasuno[3], Shigeaki Mukoubara[4], Kosuke Masutani[1], Hisatomi Arima[2], Hitoshi Nakashima[1]

[1] Faculty of Medicine, Fukuoka University, Division of Nephrology and Rheumatology, Department of Internal Medicine, Fukuoka, Japan, [2] Faculty of Medicine, Fukuoka University, Department of Preventive Medicine & Public Health, Fukuoka, Japan, [3]Faculty of Medicine, Fukuoka University, Division of Nephrology and Rheumatology, Department of Internal Medicine, Fukuoka, Japan and [4]Nagasaki Prefecture Iki Hospital, Nagasaki, Japan

Background and Aims: Chronic kidney disease is one of the most urgent public health issue in Japan as well as other countries. Many risk factors for development and progression of CKD have been recognized, such as hypertension, diabetes, obesity. However, it is still unclear whether increase of serum uric acid has negative impact on kidney function. The aim of this study is to investigate how serum uric acid influences the new-onset and progression of CKD in Japanese general population.

Method: The Iki epidemiological Study of atherosclerosis And Chronic Kidney Disease (ISSA-CKD) is a population-based retrospective cohort study using annual health check-up data in the Iki Island (Nagasaki Prefecture, Japan), which has approximately 27,000 residents. A total of 7,645 residents underwent annual health check-ups from fiscal year 2008 to 2016. After excluding residents who visited only 1 health check-up and those with missing information of serum creatinine or serum uric acid, a total of 5507 adults were included in the present analysis. The outcome of the present analysis was new-onset of CKD (reduction in estimated glomerular filtration rate [eGFR] less than 60mL/min/1.73m^2 or development of proteinuria among participants without CKD at baseline) and CKD progression (worsening of the stages of eGFR or proteinuria according to the KDIGO guideline among participants with CKD at baseline).

Results: During a mean follow-up of 4.6 years, 757 (16.7%) new-onset CKD and 193 (19.7%) progression of CKD were observed. Serum uric acid had significant relationship with new-onset CKD even after adjustment for sex, age, obese, hypertension, dyslipidemia, and diabetes mellitus: hazard ratio 1.14 per 1 mg/dL increase, 95% confidence interval 1.07-1.21, P<0.001). On the other hand, serum uric acid did not have significant relationship with CKD progression: hazard ratio 1.08 per 1 mg/dL increase, 95% confidence interval 0.96-1.21, P=0.190). Similar results were observed for hyperuricemia defined as serum uric acid level ≥7mg/dl.

Conclusion: The findings of the present analysis show that serum uric acid was significantly associated with increased risks of new onset of CKD, but was not associated with progression of CKD in Japanese general population.

Table1.i nfluence of serum uric acid/hyperuricemia on all of CKD

	N/Person-yr	Incident ratio	Crude HR	95%CI		p	Adjusted HR	95%CI		p
(All)										
UA(continuous)			1.13	1.08	1.18	<0.001	1.11	1.05	1.17	<0.001
Non hyperuricemia	844/22955	36.8	1.00	(Reference)			1.00	(Reference)		
Hyperuricemia	106/2274	46.6	1.35	1.11	1.66	0.003	1.30	1.05	1.62	0.017

Table2.i nfluence of serum uric acid/hyperuricemia on new-onset/progression of CKD

	N/Person-yr	Incident ratio	Crude HR	95%CI		p	Adjusted HR	95%CI		p	p for int
(New-onset CKD)											
UA(continuous)			1.13	1.07	1.19	<0.001	1.14	1.07	1.21	<0.001	0.1037
Non hyperuricemia	691/19481	35.5	1.00	(Reference)			1.00	(Reference)			0.0224
Hyperuricemia	66/1450	45.5	1.38	1.07	1.78	0.012	1.58	1.21	2.07	0.001	
(Progression of CKD)											
UA(continuous)			1.09	0.99	1.20	0.087	1.08	0.96	1.21	0.190	0.1037
Non hyperuricemia	153/3474	44.0	1.00	(Reference)			1.00	(Reference)			0.0224
Hyperuricemia	40/825	48.5	1.13	0.80	1.60	0.499	1.08	0.73	1.59	0.694	

P0779

THE POPULATION ATTRIBUTABLE FRACTION OF HYPERURICEMIA FOR ALL-CAUSE AND CARDIOVASCULAR MORTALITY: A NATIONWIDE COMMUNITY-BASED STUDY

Tomomi Tanaka[1], Tomomi Tanaka[2], Masahiro Miyata[1], Kazunobu Ichikawa[1], Tsuneo Konta[3], Shouichi Fujimoto[2], Kunitoshi Iseki[2], Toshiki Moriyama[2], Kunihiro Yamagata[2], Kazuhiko Tsuruya[2], Ichiei Narita[2], Masahide Kondo[2], Shibagaki Yugo[2], Masato Kasahara[2], Koichi Asahi[2], Tsuyoshi Watanabe[2]

[1]Yamagata University, Department of Cardiology, Pulmonology, and Nephrology, Yamagata, Japan, [2]Steering Committee of Research on Design of the Comprehensive Health Care System for Chronic Kidney Disease (CKD) Based on the Individual Risk Assessment by Specific Health Checkup, Japan and [3]Yamagata University, Department of Public Health and Hygiene, Yamagata, Japan

Background and Aims: Hyperuricemia is often observed in subjects with chronic kidney disease and is associated with all-cause and cardiovascular mortality. In this study, we evaluated the effect size of hyperuricemia for all-cause and cardiovascular mortality in a community-based population, using the index of population attributable fraction (PAF).

Method: This large-scale cohort study used the nationwide database of 500,511 health check-up participants (215,728 men, 284,783 women, average age 62 years) and calculated the PAF of hyperuricemia (serum uric acid >7 mg/dL) for all-cause and cardiovascular deaths during the 7-year follow-up period.

Results: The frequency of hyperuricemia at baseline was 9.7% in total subjects (men: 22.0%; women: 2.6%). During the follow-up period, 5,578 deaths (1.1%) were noted (men: 3,749 [1.7%], women: 1,829 [0.6%]), including 1,104 cardiovascular deaths (0.2%) (men: 762 [0.4%], women: 342 [0.1%]). In the Cox proportional hazard analysis adjusted for confounding factors including age, gender, body mass index, smoking, alcohol consumption, hypertension, diabetes, dyslipidemia and eGFR, hyperuricemia was an independent risk factor for all-cause and cardiovascular mortality, (adjusted hazard ratios [95% confidence interval]; 1.39 [1.27-1.53] for all-cause mortality, and 1.76 [1.47-2.11] for cardiovascular mortality). The adjusted PAF of hyperuricemia for all-cause and cardiovascular deaths were 3.1% and 4.7% (approximately 1 in 32 all-cause deaths, and 1 in 21 cardiovascular deaths), respectively. In subgroup analyses, the association between hyperuricemia and death was stronger in men and smokers. The adjusted PAF for all-cause and cardiovascular deaths was 5.5% and 8.6% (approximately 1 in 18 all-cause deaths, 1 in 12 cardiovascular deaths) in men, and 6.2% and 8.2% (approximately 1 in 16 all-cause deaths, 1 in 12 cardiovascular deaths) in smokers, respectively.

Conclusion: This study showed that a substantial number of all-cause and cardiovascular deaths, was statistically attributed to hyperuricemia in the community-based population, especially men and smokers.

P0780

TRENDS IN EMERGENCY DEPARTMENT USE IN PATIENTS DIAGNOSED WITH HYPERKALAEMIA: AN ANALYSIS OF A U.S. NATIONAL EMERGENCY DEPARTMENT DATABASE

Zubaid Rafique[1], Saurabh Aggarwal[2], Ozlem Topaloglu[2], Georgiana Cornea[3], Ansgar Conrad[4], Frank Peacock[1]

[1]Baylor College of Medicine, Ben Taub General Hospital, Houston, United States of America, [2]NOVEL Health Strategies, Bethesda, United States of America, [3]Vifor Fresenius Medical Care Renal Pharma Lth, a Vifor Pharma Group Company, St. Gallen, Switzerland and [4]Relypsa, Inc., a Vifor Pharma Group Company, Redwood City, United States of America

Background and Aims: Hyperkalaemia (HK) refers to increased serum potassium concentration, with possible severe effects on health outcomes and resource utilisation. HK is prevalent in patients suffering from heart failure, chronic kidney disease (CKD) and diabetes mellitus and its risk is increased by medications, e.g. inhibitors of the renin-angiotensin-aldosterone system (RAAS). The objective of this study was to examine trends in emergency department (ED) use in patients diagnosed with HK.

Method: The latest available 2016 Nationwide Emergency Department Sample (NEDS) data set from the Healthcare Cost and Utilization Project was analysed to estimate the burden of ED visits in patients with HK. Patients with an ICD-10 diagnosis code E87.5 (Hyperkalaemia) or E87.8 (Other disorders of electrolyte and fluid balance, not elsewhere classified; included due to the incidence of miscoding HK) were included. The rate of comorbidities (diabetes, CKD, heart failure and hypertension) were assessed using previously validated ICD-10 codes.

Results: In 2016, there were an estimated 1,322,071 ED visits with a diagnosis of HK, out of which 6.7% were recorded as the primary diagnosis. The vast majority of these ED visits resulted in same hospital admission (1,075,492 hospital stays). The rate of ED visits and hospital admission were 409.1 and 332.8 per 100,000 persons respectively. The mean (SE) age was 61.8 (0.21) years and 52% were male. Patients had high rate of comorbidities: diabetes 43.1%, hypertension 62.0%, CKD 44.4%, heart failure 23.1%, non-dialysis CKD 12.1% and CKD requiring dialysis 12.1%. In patients with primary diagnosis of HK, the mean (SD) hospital length of stay was 3.3 (4.2) days and total mean (SD) hospital charges were $34,923 ($100,435).

Conclusion: Patients with HK represent an expensive health care burden, as well as suffering with high rates of comorbidities and ED visits. There is an urgent need for new treatment options in the acute setting to improve outcomes for patients with HK.

P0781 ESTIMATION OF NEPHRON NUMBER IN CKD PATIENTS

Takehiko Kawaguchi[1], Takashi Nakazato[2], Kensei Yahata[3], Hiroshi Kitamura[4], Toshiyuki Imasawa[1]

[1]National Organization Chibahigashi National Hospital, Department of Nephrology, [2]National Organization Chiba Medical Center, Department of Cardiovascular Disease, Chiba, Japan, [3]National Organization Kyoto Medical Center, Department of Nephrology, Kyoto, Japan and [4]National Organization Chibahigashi National Hospital, Department of Pathology, Chiba, Japan

Background and Aims: The nephron number is thought to be associated with clinical outcomes of chronic kidney disease (CKD). If the nephron number can be estimated in a clinical setting, it could become a strong tool to predict the outcomes. This preliminary study estimated nephron number in CKD patients, and examined the relationship between the nephron number and patient characteristics.

Method: Data from a multicenter study of the National Hospital Organization of Japan were analyzed, including 565 CKD patients aged over 14 years who underwent a kidney biopsy. The nephron number was estimated by the glomerular density in biopsy specimens and the renal cortex volume. The renal cortex volume was calculated by the previously established equation using ultrasound measurement of the kidney. Linear regression models were used to investigate the associations of the nephron number separately with age, sex, and estimated glomerular filtration rate (eGFR).

Results: A total of 50% of the patients were women, and the mean (±SD) age of the patients was 51±19 years. The mean eGFR was 63±32 ml/min/1.73m^2, and the mean estimated number of non-sclerotic nephrons was 660,000±320,000 per kidney. A larger number of estimated nephron number was associated with younger age, male sex, and higher eGFR.

Conclusion: To the best of our knowledge, this was the first study to estimate the renal cortex volume and nephron number of CKD patients in the general clinical setting. The results from this study should provide powerful tools for nephrologists in routine clinical practice. Further investigations will be needed to verify the associations between the nephron number and clinical outcomes of CKD patients.

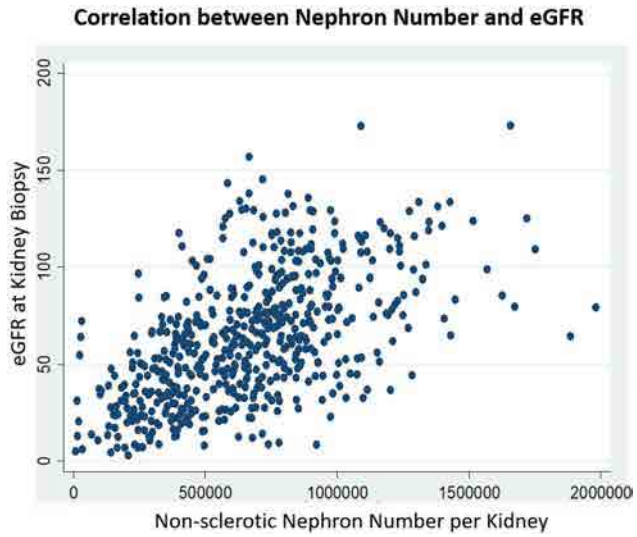


Figure:

P0782

PROGNOSTIC IMPACT OF NECK CIRCUMFERENCE ON CARDIVASCULAR OUTCOMES AND MORTALITY IN PATIENTS WITH MODERATE CHRONIC KIDNEY DISEASE: AN ANALYSIS FROM THE GERMAN CHRONIC KIDNEY DISEASE (GCKD) STUDY

Vladimir Cejka[1], Stefan Störk[1,2], Jennifer Nadal[3], Ulla T. Schultheiß[4,5], Anna Köttgen[5], Claudia Sommerer[6], Thomas Sitter[7], Heike Meiselbach[8], Martin Busch[9], Markus Schneider[8], Turgay Saritas[10], Fruzsina Kinga Kotsis[4,5], Christoph Wanner[11], Kai-Uwe Eckardt[8,12], Vera Krane[1,11]

[1]Comprehensive Heart Failure Center, University of Würzburg, Würzburg, Germany, [2]University Hospital of Würzburg, Department of Medicine I, Division of Cardiology, Würzburg, Germany, [3]Institute for Medical Biometry, Informatics and Epidemiology, University Hospital Bonn, Bonn, Germany, [4]Faculty of Medicine and Medical Center - University of Freiburg, Department of Medicine IV – Nephrology and Primary Care, Freiburg, Germany, [5]Institute of Genetic Epidemiology, Faculty of Medicine and Medical Center, University of Freiburg, Freiburg, Germany, [6]University Hospital Heidelberg, Division of Nephrology, Heidelberg, Germany, [7]Ludwig-Maximilians-University Hospital, Munich, Department of Medicine, Munich, Germany, [8]University of Erlangen-Nürnberg, Department of Nephrology and Hypertension, Erlangen, Germany, [9]Jena University Hospital, Department of Internal Medicine III, Jena, Germany, [10]University Hospital RWTH Aachen, Division of Nephrology and Clinical Immunology, Aachen, Germany, [11]University Hospital Würzburg, Department of Internal Medicine I, Division of Nephrology, Würzburg, Germany and [12]Charité Universitätsmedizin Berlin, Department of Nephrology and Medical Intensive Care Medicine, Berlin, Germany

Background and Aims: Neck circumference (NC) is an approximator of upper body subcutaneous fat tissue and a marker of obesity. It has been shown to be associated with cardiovascular risk factors and incident chronic kidney disease (CKD). In CKD patients, the impact on cardiovascular events and all cause death has not been fully elucidated yet. The prognostic impact on these outcomes in a representative cohort of adult patients with moderate CKD of Caucasian origin was investigated here.

Method: We used data from the GCKD study, a German multi-centric prospective observational cohort study of 5217 adults with moderate chronic kidney disease, defined as eGFR 30–60 mL/min/1.73 m2 or eGFR >60 mL/min/1.73 m2 and significant proteinuria (albuminuria >300 mg/g creatinine or proteinuria >500 mg/g creatinine). Exclusion criteria were active malignancy, heart failure NYHA class IV, organ transplantation, and non-Caucasian origin. NC was measured repeatedly (annually, except at first year of follow-up) during the study, therefore, the mean value was analyzed. We report data from the 4-year follow-up visit regarding 1) a combined endpoint of non-fatal myocardial infarction, non-fatal stroke, cardiovascular death, and peripheral artery disease event (amputation or revascularization) and 2) all-cause death as another endpoint. Cox proportional hazard regression was used to calculate hazard ratios (HR) with 95% CIs. In univariate analysis, ordinal regression with quintiles of NC was applied.

Results: NC was accrued in 4453 participants and analyzed. NC overall was 40±5 cm (43±4 cm in men and 37±4 cm in women, p<0.001), mean age 60±12 years, 41% were female, 96% had hypertension, 35% were diabetic, 58% had ever smoked, eGFR was 50±18 ml/min/1.73 ṁ (CKD-EPI), BMI 28±6 kg/ṁ, LDL-cholesterol 119±43 mg/dl. Higher quintiles of NC were associated increased risk of the cardiovascular outcome in univariate analysis: highest (44 cm) vs. lowest (36.5 cm), HR 2.34 (1.63–3.36; p<0.001). In multivariable analysis adjusted for age, sex, and BMI, this effect was reduced but still apparent: HR 1.04 (1.01–1.08, p=0.025). Age (HR per year 1.05, 1.04–1.07, p<0.001), and female sex (HR 0.69, 0.50–0.95, p=0.023), showed also significant effects, whereas BMI did not (p=0.831). The effect of higher quintiles of NC on the risk of all-cause death in univariate analysis was even stronger: highest vs. lowest, HR 3.2 (1.72–5.81, p=0.006). However, after adjustment this effect was abolished: HR 0.99 (0.95–1.04; p=0.85). Only age (HR 1.07, 1.04–1.09, p<0.001), and female sex (HR 0.45, 0.27-0.74, p=0.002), remained significant predictors of all-cause death in this model.

Conclusion: In patients with chronic kidney disease, we found higher NC to be associated with increased cardiovascular event risk, but not all-cause death, after adjustment for age, sex and BMI. The risk of cardiovascular outcomes and overall mortality was consistently lower in women. Our analysis supports evidence, that upper body subcutaneous adipose tissue might be an independent contributor to cardiovascular event risk.

P0783 PREVALENCE AND PROGNOSIS OF HYPERKALAEMIA IN PEOPLE HOSPITALISED WITH AND WITHOUT AKI

Andrew McLean[1], Corri Black[1], Angharad Marks[2], Simon Sawhney[1]

[1]University of Aberdeen and [2]University of Swansea

Background and Aims: Hyperkalemia is a clinical emergency associated with kidney diseases and hospital mortality. It may be apparent on initial hospital presentation, or develop during the course of admission, and can occur in the context of AKI. The prevalence of hyperkalemia across these different presentations and contexts is not well described. No work has previously described whether the prognosis of hyperkalemia varies depending on timing of presentation, or on AKI status defined by KDIGO creatinine change biochemical criteria.

Method: We constructed a cohort of all adult residents in Grampian (North Scotland) admitted to hospital in 2012 (n=28462). We used a validated and replicated KDIGO based definition of AKI to identify AKI using serial serum creatinine values. We determined the presence of hyperkalemia (serum potassium >= 6 mEq/L) both on first blood test on presentation to hospital, and also during the course of hospital admission. We explored the outcome of 30 day mortality within subgroups of AKI status and timing of hyperkalemia. Covariates of interest included age, CKD, medications prescribed in the preceding 90 days and comorbidities (ICD-10 hospital episode codes). The relationship between hyperkalemia and 30 day mortality was determined using multivariable logistic regression.

Results: Of 28462 hospital admissions, 247 (0.9%) presented with hyperkalemia, whereas 560 (2.0%) had hyperkalemia during the course of hospital admission. Hyperkalemia was common in the presence of AKI (4.2% at hospital presentation, 9.3% during hospital admission and rising to 24.5% during AKI stage 3). Hyperkalemia was uncommon in the absence of AKI (0.3% and 0.7% respectively) (OR AKI vs no AKI 13.9, 11.6-16.6). Other factors associated with hyperkalemia were male gender (OR 1.5, 1.3-1.8), age >70 years (OR 2.4, 2.0-2.9), CKD based on eGFR or proteinuria (5.5, 4.6-6.5), diabetes (OR 3.4, 2.8-4.0), heart failure (OR 3.0, 2.4-3.7), RAAS blockers (OR 2.4, 2.0-2.9), trimethoprim containing antibiotics (OR 2.2, 1.7-2.8)), non-RAAS antihypertensives (OR 1.7, 1.4-2.0), but not NSAIDs (OR 0.9, 0.7-1.1). Hyperkalemia mortality (AKI vs no AKI) was 31% vs 29% when presenting at admission, or 34.3% vs 27.8% when occurring during hospital admission. Although absolute risks were similar irrespective of AKI, the excess relative mortality risk associated with hyperkalemia was lower for those with AKI (OR 2.7, 2.1-3.4) than those without AKI (OR 9.5, 6.8-13.2), which may be explained by a higher mortality for those with AKI even without hyperkalemia.

Conclusion: Hyperkalemia is associated with a high mortality even in the absence of AKI and irrespective of the timing of presentation. Management protocols should draw attention to this poor prognosis across all clinical contexts. As hyperkalemia usually occurs within the context of AKI, it should prompt clinicians to consider ongoing close observation for emerging AKI even when AKI is not yet evident on blood tests.

P0784

RAPID WEIGHT CHANGE OVER TIME IS A RISK FACTOR FOR ADVERSE OUTCOMES IN PREDIALYSIS CHRONIC KIDNEY DISEASE: RESULTS FORM KNOW-CKD STUDY

Hyunjin Ryu[1], Yeji Hong[2], Eunjeong Kang[1], Minjung Kang[1], Jayoun Kim[3], Yun Kyu Oh[4,5], Soo Jin Yang[6], Curie Ahn[1,5], Kook-Hwan Oh[1,5]

[1]Seoul National University Hospital, Internal Medicine, Seoul, Korea, Rep. of South, [2]Biomedical Research Institute, Seoul National University Hospital, Seoul, Korea, Rep. of South, [3]Medical Research Collaborating Center, Seoul National University Hospital, Seoul, Korea, Rep. of South, [4]SMG-SNU Boramae Medical Center, Internal Medicine, Seoul, Korea, Rep. of South, [5]Seoul National University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of South and [6]Seoul Women's University, Food and Nutrition, Seoul, Korea, Rep. of South

Background and Aims: Both obesity and underweight are related to the adverse outcomes in the chronic kidney disease (CKD). However, the effects of longitudinal weight changes on predialysis CKD population has not been studies so far. In this study, we analysed the effects of longitudinal body weight changes on the adverse outcomes in the predialysis CKD population, using the multicentre prospective cohort study in Korean pre-dialysis CKD cohort, so called KNOW-CKD.

Method: In this longitudinal analysis, total 2,022 patients were included. Longitudinal weight changes of study population were calculated into the percent change per year using regression analysis and classified into five groups: group 1; $\leq$ -5%/year (74 subjects), group 2; -5< to $\leq$-2.5 %/year (122 subjects), group 3; -2.5< to <2.5%/year (1642 subjects), group 4; 2.5$\leq$ <5 %/year (123 subjects), and group 5; $\geq$ 5 %/year (61 subjects). The risk of end-stage renal disease (ESRD) development and composite outcome of cardiovascular disease (CVD) and all-cause death were compared according to the longitudinal weight changes.

Results: During the median 4.4 years of follow-up, total 414 and 188 events of ESRD and composite outcome of CVD and death occurred. When cause-specific regression analysis was conducted before and after adjusting age, sex, body mass index, mean blood pressure, estimated glomerular filtration rate, urine albumin-to-creatinine ratio, diabetics, cardiovascular disease, and modified Charlson Comorbidity Index score, all groups showed significant increased HR compared to group 3 for the ESRD. There was U-shape correlation between the degree of longitudinal body weight changes and the renal outcome (HR 3.89, 2.00, 1.89 and 3.34, P <0.001, <0.001, =0.001 and <0.001 for group 1, 2, 4 and 5, respectively). Also similar U-shape relationship was seen with composite outcome, (HR 3.14, 2.05, 1.65 and 2.68, P <0.001, 0.007, 0.123 and 0.007 for group 1, 2, 4 and 5, respectively) when compared to the reference group 3 When spline curve was drawn between the longitudinal body weight changes and adjusted HR for ESRD and composite of CVD and death, clear U-shape relationship was observed (Figure). The U-shape correlation was highlighted in the subgroup of estimated glomerular filtration rate <45 mL/min/1.73m2.

Conclusion: Both rapid weight reduction and gain are independent risk factor for the ESRD development and composite outcome of CVD and death in predialysis CKD patients, especially in advanced CKD stages. Therefore, monitoring bodyweight changes are important and more studies are needed to give safe guideline to the predialysis CKD for maintaining optimal nutritional status.

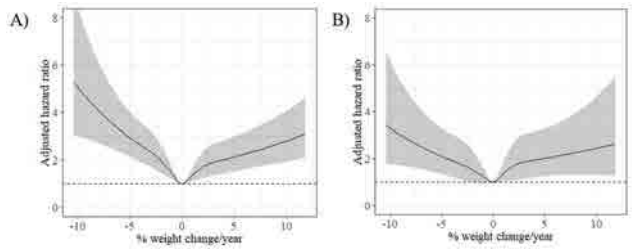


Figure. The U-shaped relationship between the longitudinal body weight changes and the outcomes

P0785 POSITIVE CORRELATION OF SERUM RESISTIN LEVEL WITH PERIPHERAL ARTERY OCCLUSIVE DISEASE IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGE 3 TO 5

Chi-Chong Tang[1], Jia-Sian Hou[1], Bang-Gee Hsu[1,2]

[1]Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Division of Nephrology, Hualien, Taiwan, R.O.C. and [2]Tzu Chi University, School of Medicine, Hualien, Taiwan, R.O.C.

Background and Aims: Resistin named for its ability to resist insulin action has an important link between obesity, insulin resistance and diabetes. Moreover, additional reports suggest that resistin has a pathogenic role in the development and progression of atherosclerosis and coronary artery disease. Chronic kidney disease (CKD) accelerates atherosclerosis via augmentation of inflammation and perturbation of lipid metabolism. Peripheral arterial occlusive disease (PAOD) is associated with an increased risk of death in CKD patients. The aim of this study was to evaluate the relationship between serum resistin level and PAOD by ankle-brachial index (ABI) in CKD patients.

Method: Fasting blood samples and baseline characteristics were obtained from 240 patients with CKD (stage 3-5). ABI values were measured using the automated oscillometric method (VaSera VS-1000). ABI values that were < 0.9 were included in the low ABI group. Concentrations of human serum resistin were determined using a commercially available enzyme immunoassay kit.

Results: Among the 240 CKD patients, 30 of them (12.5%) were in the low ABI group. Compared with patients in the control group, the patients in the low ABI group had higher prevalence of diabetes ($p = 0.033$), hypertension ($p = 0.023$), current smoking ($p = 0.013$), older age ($p < 0.001$), higher systolic blood pressure ($p = 0.013$), glucose ($p = 0.022$) level and resistin ($p < 0.001$) levels. In addition, the multivariable logistic regression analysis showed that serum resistin levels (Odds ratio [OR]: 1.140, 95% confidence interval [CI]: 1.054-1.234, $p = 0.001$) and age (OR: 1.102, 95% CI: 1.051-1.156, $p < 0.001$) were the independently associated with PAOD in CKD patients. The area under the receiver-operating characteristic (ROC) curve predicting PAOD by serum resistin level in CKD patients was 0.699 (95% CI: 0.636-0.756, $p = 0.0001$).

Conclusion: In this study, serum resistin level was found to be associated with PAOD in non-dialysis CKD stage 3-5 patients.

P0786

CLINICAL SIGNIFICANCE AND RELATED FACTORS OF GFR SLOPE IN A LARGE MULTICENTER OBSERVATIONAL STUDY IN JAPAN

Yuji Kamijo[1,2], Koji Hashimoto[1,2], Yosuke Yamada[1,2], Makoto Harada[1,2], Masatsugu Aida[2,3], Shitotomo Yamauchi[2,3]

[1]Shinshu University School of Medicine, Department of Nephrology, Matsumoto, Japan, [2]Nagano Kidney Evaluation Association, Matsumoto, Japan and [3]Ethic Co., Lth., Chiyoda-ku, Japan

Background and Aims: Recently, glomerular filtration rate (GFR) slope has attracted attention as an important surrogate marker for the prognosis of chronic kidney disease (CKD), with a reduction in slope of eGFR decline by 0.75 mL/min/1.73 m2 per year reportedly having clinical significance. As few large clinical studies on Japanese CKD patients exist, this investigation addresses the clinical significance of GFR slope and its related factors.

Method: To evaluate the clinical impact of GFR slope, we conducted a prognostic investigation of CKD patients in Japan by means of a large, multicenter, retrospective, observational study. Patients with CKD who were seen at among 15 general hospitals between January and March 2014 were surveyed using medical records. The selection criteria were age $\geq$20 years, estimated GFR (eGFR) $<$60 mL/min/1.73 m2, and receiving medical treatment for CKD. Baseline patient characteristics, eGFR changes, and hard endpoints (death or end-stage kidney disease requiring renal replacement therapy) during observation were analysed. We calculated GFR slope using GFR data of 2 years following the observation start point by 2 calculation methods, the linear mixed model and least squares linear regression, and examined the relationship of GFR slope with the hazard ratio of the composite hard endpoints. The factors related to GFR slope were also assessed by multiple regression analysis.

Results: Among a total of 11233 collected patients, we analyzed the data of 7490 CKD G3 and G4 patients whose GFR data during 2 years could be obtained (60% male, mean age: 71 years, CKD G3a: 55%, G3b: 30%, G4: 15%, mean eGFR: 44.1 mL/min/1.73 m2, urine protein positive: 51%, diabetes mellitus: 49%, use of RAS inhibitors: 57%). The mean observation period was 1040 days. Hard endpoints after the GFR slope measurement period occurred in 301 subjects. The GFR slope of the cohort was -0.948 mL/min/1.73 m2 per year (95% confidence interval [CI] -1.016, -0.880) in the linear mixed model and -0.982 mL/min/1.73 m2 per year (95% CI -1.075, -0.889) according to least squares linear regression. Both calculated GFR slopes were significantly related to the hazard ratio of the composite hard endpoints. Hazard ratio decreased by 0.85 (linear mixed model) and 0.9 (least squares linear regression) times in case of a reduction in slope of eGFR decline by 0.75 mL/min/1.73 m2 per year. Multiple regression analysis revealed strongly significant associations for GFR slope with urine protein and CKD stage and undetectable relationships for GFR slope with diabetes and age.

Conclusion: This study demonstrated the clinical significance of GFR slope as a surrogate marker for renal prognosis in Japanese CKD patients. In order to reduce slope of eGFR decline, active intervention for proteinuria before the progression to an advanced CKD stage appears to be effective.

P0787 THE IMPORTANCE AND BENEFITS OF THE REGISTRY OF PREDIALYSIS PATIENTS - ROMANIAN EXPERIENCE

Ileana PERIDE[1,2], Andrei NICULAE[1,2], Ionel Alexandru CHECHERITA[1,2]

[1]"Carol Davila" University of Medicine and Pharmacy Bucharest, Department of Nephrology, Bucharest, Romania and [2]"St. John" Emergency Clinical Hospital, Departement of Nephrology and Dialysis, Bucharest, Romania

Background and Aims: Registries provide an organized and standardized method to systematically collect observational data about specific groups of patients managed in routine clinical practice for a predetermined objective. Data collected by patient registries may help researchers develop hypotheses about disease mechanisms or treatment approaches and inform health care policy thereby potentially improving quality. It is known that chronic kidney disease (CKD) represents the 6th cause of mortality worldwide and it has an increased prevalence. Therefore, the aim of our Registry is to collect epidemiological and medical data regarding the CKD patients from our country in order to drive improvements in health care quality.

Method: Starting from January 2019, all Romanian nephrologist have been collecting demographic and medical data CKD-related from patients diagnosed with CKD stages 1-5. These data are introduced in a special designed software program – ReNal – that is easy to be accessed. The demographic and medical information include: ID, gender, age, region, body mass index, CKD etiology, comorbidities, chronic treatment, CKD stage, laboratory test, such as serum creatinine, urea, uric acid, calcium, phosphates, iPTH, albuminuria, proteinuria, glomerular filtration rate, hemoglobin etc. (results collected from each medical assessment).

Results: During almost 1-year, over 10000 patients with CKD stages 1-5 were introduced in our Registry, with mean age of 69.2 $\pm$ 3.5, 51.22% female patients, 48.78% male patients. From our preliminary results, hypertension and diabetes mellitus represent the main cause of CKD in Romania, according with the international data. In addition, CKD stages 3b and 4 were highly represented. These are part of the preliminary results, future data will be available.

Conclusion: Analyzing the assessed data from our Registry, in future several key points could be achieved: the importance of a correct financial appraisal sustained by health system, adequate and active assessment of CKD patients including the complications, highlighting the disease progression rate depending on the recommended treatment, designing an efficient prevention program.

P0788

HEALTHCARE RESOURCE UTILIZATION AND COSTS IN A DAPA-CKD-LIKE POPULATION USING A CONTEMPORARY US HEALTHCARE COHORT.

Tope Olufade[1], Lois Lamerato[2], Juan Jose Garcia Sanchez[3], Like Jiang[1], Joanna Huang[1], Stephen Nolan[3]

[1]AstraZeneca, Wilmington, United States of America, [2]Henry Ford Health System, Detroit, United States of America and [3]AstraZeneca, Cambridge, United Kingdom

Background and Aims: Recent studies have shown an association between Sodium Glucose Co-Transporter 2 inhibitor (SGLT-2i) class of drugs and lower healthcare costs compared with other glucose lowering therapy, in type 2 diabetes (T2D) patients mainly as a result of reduced rates of cardiovascular and other T2D-associated outcomes. The DAPA-CKD Trial (A study to evaluate the effect of dapagliflozin on renal outcomes and CV mortality in patients with CKD) is the first SGLT-2i renal outcomes trial to test the efficacy and safety of an SGLT-2i, dapagliflozin, in patients with CKD with and without T2D. The objective of this study is to assess the healthcare resource utilization and cost in a "DAPA-CKD-like population" (eGFR 25-75ml/min/1.73m2 and UACR 200-5000mg/g) using a contemporary US healthcare system.

Method: Data from the Henry Ford Health System (HFHS) were used to identify persons with CKD stages 2 through 4 between 2006 and 2016 (based on eGFR labs) and patients were followed through 2018. Persons with no confirmatory eGFR > 90 days from index date, death within 30 days, history of renal transplant, and evidence of renal replacement therapy, or progression to CKD stage 5 during the baseline period (6 months pre or post index date) were excluded.

Inpatient admissions, inpatient days, emergency department encounters, and ambulatory care encounters with primary care, specialty care and overall were assessed. Cumulative utilization was evaluated for all patients and evaluation based on the follow-up time. Patients were censored on date of death, last contact with the Health System or at December 31st, 2018. The utilization rates are the total observed utilization divided by follow-up time and reported as an annual rate. Billing records for all care with HFHS were used to estimate costs.

Results: 6,557 patients (mean age 62.9 years, 46.2% male) met the eligibility criteria and are included in the study cohort. The population was stratified by UACR (0-<30, 30–199, 200–5,000mg/g). The DAPA-CKD-like population (200-5000mg/g) was associated with significantly higher annualized per-patient healthcare costs, $39,222/yr (UACR 200-5000mg/g) vs. $19,547/yr (UACR <30mg/g). This increased healthcare utilization was predominantly driven by increased acute care, including hospital admissions, inpatient days and emergency department visits. Persons in the highest UACR category were almost three times more likely to have a hospital admission compared to the lowest UACR (rates 0.55/year vs. 0.20/year, respectively; see Figure below). Persons in the lowest UACR category had more primary care visits per year compared with those with highest UACR (5.81 vs 5.21). In contrast, the highest number of outpatient specialist visits per year was reported for the DAPA-CKD-like population (7.55 vs. 6.74).

Conclusion: This analysis of a contemporary US healthcare system demonstrated that there exists a high disease burden in the DAPA-CKD-like population as seen by the substantial increase in healthcare resource utilization and costs compared to other cohorts of patients with a lower UACR. These results highlight the need for innovative therapies to improve patient outcomes in this population.

	UACR 0-<30mg/g N= 4331	UACR 30–199mg/g N = 1354	UACR 200-5,000mg/g N= 873	p - value
Acute care				
Hospital admissions (rate/year)	0.20	0.36	0.55	< 0.0001
Inpatient days (length of stay)	1.00	2.25	3.27	< 0.0001
Emergency department visits (rate/year)	0.30	0.40	0.60	< 0.0001
Ambulatory care				
Outpatient primary care visits (rate/year)	5.81	5.93	5.21	< 0.01
Outpatient specialist visits (rate/year)	6.74	7.02	7.55	< 0.05
Total outpatient visits (rate/year)	12.55	12.95	12.77	NS
Costs of care				
Annualized charges ($)	$19,547	$28,338	$39,222	< 0.0001

Figure: Summary of healthcare resource utilization and costs by UACR category

P0789

SERUM URIC ACID IS ASSOCIATED WITH CHRONIC KIDNEY DISEASE PROGRESSION AND MORTALITY: INSIGHTS FROM THE CKD-REIN COHORT

Mathilde Prezelin-Reydit[1,2], Christian Combe[3], Jerome Harambat[4,5], Ziad Massy[6], Marie Metzger[7], Céline Lange[7], Oriane Lambert[7], Benedicte Stengel[7], Karen Leffondré[2]

[1]Aurad Aquitaine, Gradignan, France, [2]INSERM U1219-Bordeaux Population Health, Biostatistic team, Bordeaux, France, [3]Hospital Center University De Bordeaux, Nephrology, Transplantation, Dialysis, Bordeaux, France, [4]Hospital Center University De Bordeaux, Pediatry and Nephrology, Bordeaux, France, [5]INSERM U1219-Bordeaux Population Health, LEHA team, Bordeaux, France, [6]Ambroise Paré Hospital (AP-HP), Boulogne-Billancourt, France and [7]CESP, University of Paris-Saclay, Inserm UMRS 1018, Villejuif, France

Background and Aims: The association between hyperuricemia and CKD progression is not well established in Europe and, to our knowledge, has not yet been investigated using longitudinal measurements.

Method: We used data from CKD-REIN, a prospective cohort study conducted in 40 representative French nephrology clinics, which included 3033 patients with CKD stages 3 to 5 between 2013 and 2016. Patients who had no serum uric acid or no creatinine measure at within 6 months of their inclusion date in the CKD-REIN study were excluded. All uric acid measures were taken into account, from inclusion to the occurrence of renal replacement therapy (RRT), death, or end of follow-up, whichever came first. We used a shared random-effect model for the joint analysis of individual trajectories of uric acid and the hazard of the composite outcome (RRT or death before RRT) and each specific event separately. Hazard ratio were adjusted (aHR) for age, sex, primary kidney disease, metabolic syndrome, cardiovascular disease, proteinuria ($<$ 30, 30-300, $>$ 300 mg/day), and the CKD-EPI estimated glomerular filtration rate (eGFR) at baseline. In a sensitivity analysis, we further adjusted for individual eGFR trajectory.

Results: A total of 2781 patients (65.5% men, median age 69 years) were included. At baseline, the median eGFR was 31.8 mL/min/1.73m2 and the median uric acid value was 425 µmol/L. During a median follow-up of 3.2 years, 434 patients received RRT and 264 died before RRT. At any time of follow-up, an increase of 100 µmol/l of the current value of uric acid was associated with a 16% increased hazard of RRT or death before RRT (aHR 1.16, 95% CI 1.07-1.26). The estimated effect of uric acid was similar with RRT (aHR 1.18, 95% CI 1.04-1.34) and death before RRT (aHR 1.16, 95% CI 1.05-1.28). When further adjusted for eGFR trajectory, the estimated effect of uric acid on the composite outcome was much weaker (aHR 1.06, 95% CI 0.98-1.16).

Conclusion: A higher current level of uric acid is associated with a strong increase in the hazard of RRT or death before RRT in European patients with CKD stage 3 to 5. However, the association is much weaker after adjustment for eGFR trajectory. Further analyses are necessary to better understand the dynamic of the association between uric acid and GFR.

P0790

RISK OF CARDIOVASCULAR DISEASE AND CHRONIC KIDNEY DISEASE ACCORDING TO BLOOD PRESSURE CATEGORIES IN DIABETIC PATIENTS : A POPULATION-BASED STUDY

Jun Young Lee[1], Seung Ok Choi[1], You Jin Kim[1], Hanwul Shin[1], Miryung Kim[1], Jae Won Yang[1], Jae Seok Kim[1], Byoung Geun Han[1]

[1]Yonsei University Wonju Severance Christian Hospital, Nephrology, Wonju, Korea, Rep. of South

Background and Aims: American College of Cardiology/American Heart Association (ACC/AHA) guidelines and cardiovascular disease (CVD) and chronic kidney disease (CKD) in diabetes patients remain unclear. We aimed to examine the effects of BP categories defined by the 2017 ACC/AHA guidelines in diabetes patients on the risk of CVD and CKD.

Method: In this population-based cohort study we analyzed data from the National Health Information Database in Korea during 2009-2017. The BP categories were defined as per the 2017 ACC/AHA guidelines: level 1 (systolic <120 mmHg and diastolic <80 mmHg), level 2 (systolic 120-129 mmHg and diastolic <80 mmHg), level 3 (systolic 130-139 mmHg or diastolic 80-89 mmHg), and level 4 (systolic ≥140 mmHg or diastolic ≥90 mmHg). We obtained the risk of CVD, CKD, cerebrovascular disease and CVD mortality.

Results: Overall, 490,352 diabetes patients (men 313,752 [64·0%], women 176,599 [36·0%]) were included in the analysis. Over a mean follow-up of 5 years, 6,508 CVD events occurred. Compared to people with BP levels 1, the adjusted hazard ratios (HRs) for CVD in people with BP levels 2, 3, and 4 were 1·07 (95% confidence interval [CI], 0·98-1·16), 1·12 (95% CI, 1·04-1·20) and 1·17 (95% CI, 1·08-1·26), respectively.

There were also increased risks of CKD [1·18 (95% CI, 1·12-1·24) and 1·22 (95% CI, 1·15-1·29)], cerebrovascular disease [1·21 (95% CI, 1·14-1·29) and 1·52 (95% CI, 1·42-1·63)], and CVD mortality [1·31 (95% CI, 1·09-1·56) and 1·91 (95% CI, 1·58-2·32)] among subjects with BP levels 3 and 4 compared with those with BP level 1. Moreover, among people not taking antihypertensive medications, there were higher risks of CVD, CKD, cerebrovascular disease, and CVD mortality in those with BP levels 3 and 4 than in those with BP level 1. The risks of CVD, CKD, cerebrovascular disease, and CVD mortality significantly increased in patients with a systolic BP of 130 mmHg and diastolic BP of 80 mmHg. These findings provide evidence supporting the 2017 ACC/AHA guidelines for BP targets in diabetes patients.

Conclusion: The risks of CVD, CKD, cerebrovascular disease, and CVD mortality significantly increased in patients with a systolic BP of 130 mmHg and diastolic BP of 80 mmHg. These findings provide evidence supporting the 2017 ACC/AHA guidelines for BP targets in diabetes patients.

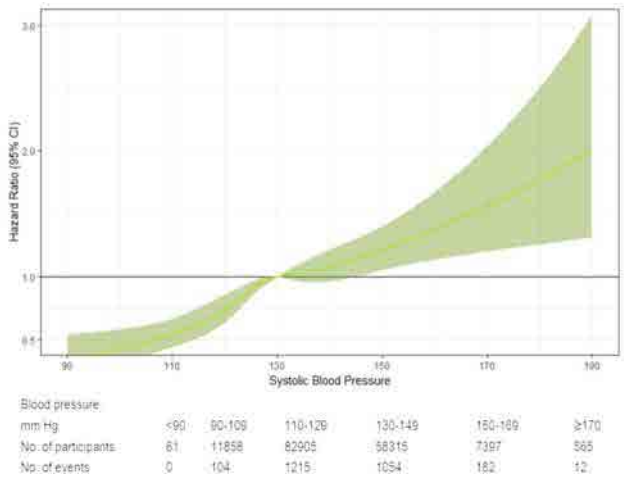


Figure: Risk of CKD according to blood pressure in male and female patients

P0791

MATRIX GLA PROTEIN AND PREMATURE VASCULAR CALCIFICATION IN PATIENTS WITH END-STAGE RENAL DISEASE

Lu Dai[1], Abdul Rashid Tony Qureshi[2], Jonaz Ripsweden[2,3], Torkel.B Brismar[2,3], Magnus Söderberg[4], Franz Peter Barany[1], Leon Schurgers[5], Bengt Lindholm[1], Peter Stenvinkel[1]

[1]Karolinska Institutet, Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden, [2]Karolinska Institutet, Division of Medical Imaging and Technology, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden, [3]Karolinska Institutet, Department of Radiology, Karolinska University Hospital, Stockholm, Sweden, [4] AstraZeneca R&D, Pathology, Clinical Pharmacology and Safety Sciences, Gothenburg, Sweden and [5]Maastricht University, Department of Biochemistry, Cardiovascular Research School Maastricht, Maastricht, Netherlands

Background and Aims: Vitamin K is a potential protective factor against premature vascular aging and vascular calcification (VC). Whether vitamin K supplement could halt VC progression in patients with end-stage renal disease (ESRD) is not clear, partially due to the heterogeneity of measurements of VC in different vascular sites. Here we investigated the associations between non-phosphorylated, uncarboxylated matrix-Gla protein (dp-ucMGP), a circulating marker of vitamin K insufficiency, and premature vascular aging phenotypes evaluated by coronary artery calcium (CAC) scoring, aortic valve calcium (AVC) scoring, and histology scoring of presence of media calcification in vascular biopsies in patients with ESRD.

Method: In this observational cohort study, 223 ESRD patients (median age 54 years, 68% males) comprising non-dialysis patients (n=109), prevalent peritoneal dialysis (PD, n=80, median dialysis vintage 11.6 months) and prevalent hemodialysis patients (HD, n=34, median dialysis vintage 12.0 months) underwent baseline measurements of plasma dp-ucMGP and scoring of CAC and AVC by computed tomography scan. Framingham risk score (FRS), inflammation and other relevant clinical and biochemical data were determined at baseline. In a sub-group of patients (n=94), scoring of media calcification by histology in epigastric artery biopsies was also performed.

Results: Plasma dp-ucMGP levels (median 1568 pmol/L) significantly correlated with age (rho=0.38), presence of cardiovascular disease (CVD, rho=0.16), triglycerides (rho=0.19), FRS (rho=0.33), high-sensitivity C-reactive protein (hsCRP; rho=0.35), CAC score (rho=0.30) and AVC score (rho=0.24) but did not differ with regards to treatment modality (i.e. non-dialysis, PD and HD). In multivariate regression analyses, with adjustment for presence of CVD, FRS, hsCRP and triglycerides, increased dp-ucMGP levels were independently associated with increased CAC score (**coefficients** 0.12, p=0.04), but not with AVC score nor presence of media calcification in epigastric arteries.

Conclusion: Our data suggest that vitamin K insufficiency as indicated by increased dp-ucMGP levels associates with premature vascular calcification evaluated by CAC but not with AVC or media calcification assessed by histology. This discrepancy warrants further studies to explore the pathophysiological background between vitamin K metabolism and susceptibility of calcification in different vascular sites as well as the pattern of VC (i.e. intima and media calcification) within sites.

P0792

FAT ATTENUATION INDEX OF CORONARY ARTERY IN COMPUTED TOMOGRAPHY ANGIOGRAPHY PREDICTS LONG-TERM OUTCOME IN CHRONIC KIDNEY DISEASE

Nam-Jun Cho[1], Soon hyo Kwon[2], Bo Da Nam[3], Kyoungin Choi[2]

[1]Soonchunhyang University Cheonan Hospital, Internal Medicine, Cheonan, Korea, Rep. of South, [2]Soonchunhyang University Seoul Hospital, Internal Medicine, Seoul, Korea, Rep. of South and [3]Soonchunhyang University Seoul Hospital, Radiology, Seoul, Korea, Rep. of South

Background and Aims: Perivascular fat attenuation index (FAI) of coronary artery represents the degree of coronary inflammation. High coronary artery FAI in computed tomography angiography (CTA) is associated with increased all-cause and cardiac mortality in general population. However, the ability of the perivascular FAI using coronary CTA to predict long term outcome in chronic kidney disease (CKD) patients is unknown.

Method: This is a single center retrospective study. We analyzed coronary FAIs on CTA for CKD including patients with end stage renal disease (ESRD). The patients with percutaneous coronary intervention or coronary artery bypass graft were excluded. Mapping and analysis of perivascular FAI were performed around proximal three major coronary arteries. We assessed the prognostic value of FAI of CTA for long-term mortality (data from the Korean National Statistical Office) with Cox regression models, adjusted for age, sex, dialysis vintage, and clinical parameters.

Results: Between January 2012 and June 2018, 268 CKD patients were included. Mean age of this cohort was 64.5 ± 12.0 years, and 132 (49.3%) participants were men. 109 (44.7%) participants has diabetic kidney disease, and 179 (66.4%) participants were on hemodialysis. Median follow-up after coronary CTA was 29.2 (15.1 – 46.3) months. During follow-up, there were 43 (20.6%) deaths. The optimum cut-off value of FAI around the left anterior descending artery (LAD) was ascertained as -65.5 Hounsfield unit. The high perivascular FAI around the LAD was significantly associated with higher adjusted risk of all-cause mortality (hazard ratio, 2.15; 95% CI, 1.07–4.32). In ESRD subgroup, the high perivascular FAI group also has higher adjusted risk of all-cause mortality compared to low perivascular FAI group (hazard ratio, 2.43; 95% CI, 1.16–5.09).

Conclusion: The perivascular FAI around LAD predicts the long-term mortality in patients with CKD. This could provide the chance of early primary intervention in CKD patients.

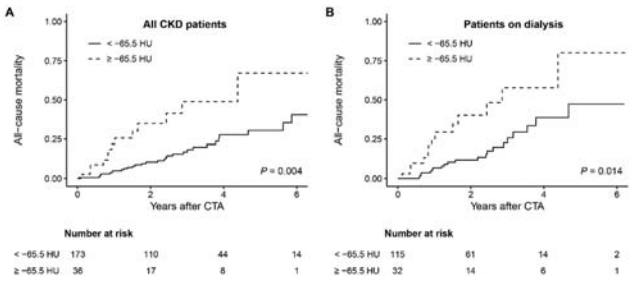


Figure:

P0793 **THE PERFORMANCE OF THE RENAL FUNCTION IN THE STAGE CKD 5: A DESTINY ALREADY WRITTEN?**

Daniela Cecilia Cannarile[1], Matteo De Liberali[1], Rossella Gaggi[1], Giulia Schiavone[1], Dino Gibertoni[2], Elena Mancini[1]

[1]Policlinico Sant'Orsola-Malpighi, Nephrology, Dialysis and Hypertension, Bologna, Italy and [2]Alma Mater Studiorum - Università di Bologna, Department of Biochemical and Neuromotor Sciences, Bologna, Italy

Background and Aims: There is a large amount of data on the factors and progression of Chronic Kidney Disease (CKD), especially in the early stages. Stages 4 and 5, on the contrary, have always been considered hard to modify in their speed and evolution. Recent observational studies have however shown that, even in these stages, the progression is often non-linear, heterogeneous and with frequent changes of trajectory. We retrospectively evaluated our CKD stage 5 patients (pts) from 1/1/2016 to 12/31/2018, with a view to analyzing their functional evolution.

Method: We included only patients with longer than 6 months follow-up (Table 1) and at least 4 clinical-laboratory controls that included measured Creatinine Clearance (ClCr) and estimated GFR with CKD-EPI (eGFR). For each patient we analyzed: comparability between eGFR and ClCr, progression rate (Table 2); correlation between ClCr, GFR and some clinical-laboratory parameters (diabetes, blood pressure control, use of ACEi / ARB, ischemic myocardiopathy, peripheral obliterant arteriopathy (POA), proteinuria, Hb, uric acid, PTH, phosphorus).

Statistics: Linear correlation test for continuous variable analysis, chi-square test for group comparison.

Results: Average slope of eGFR: -2.98 $\pm$ 3.73 ml / min / year, of ClCr: -3.73 $\pm$ 5.8 ml / min / year. The slope of the progression rate by eGFR followed a Gaussian distribution (R 16.9%; L 55.9%; S 18.6%; M 8.4%) with a trend not statistically different from the progression assessed with ClCr (R 32.2%, L 45.7%, S 11.8%, M 10.1%) (Figure 1).

Measured CrCl and eGFR proved well correlated ($r=0.565$, $p<0.001$), especially for GFR values <12ml / min.

No correlation was found between eGFR and diabetes, ischemic myocardiopathy, Hb, uric acid, PTH, phosphorus, ACEi / ARB therapy, whereas a significant correlation emerged between the rate of progression and the presence of POA (70% of rapid progression POA, $p = 0.035$) and pressure control (80% of rapid progression patients do not have adequate pressure control, $p = 0.031$).

Conclusion: This analysis confirms what is transpiring from the literature: even in stage CKD5 careful monitoring and precise therapeutic strategies can still modify and slow down functional progression. Less than one third of the patients have a GFR loss> 5 ml / min / year, and this rapid progression seems to correlate with the presence of AOCP and poor blood pressure control. For the remaining 70% of the patients, however, a slow evolution or even the possibility of stabilization or functional improvement is expected. These data on the slope of the renal function progression in CKD5, despite the limits of the sample size, encourage us not to consider CKD stage 5 as an inexorable short journey towards artificial replacement therapy.

Table 1 – Patients included

Patients	59 (45 M/14 F)
Mean age	68.4 years (range 35-90)
Mean follow-up time	20.5 months
Average number of checks/pt	12

Table 2 - GFR progression criteria

Fast	GFR loss > 5 ml/min/year
Slow	GFR loss: 1-5 ml/min/year
Stability	GFR $\pm$ 1 ml/min/year
Improvement	GFR gain > 1 ml/min/year

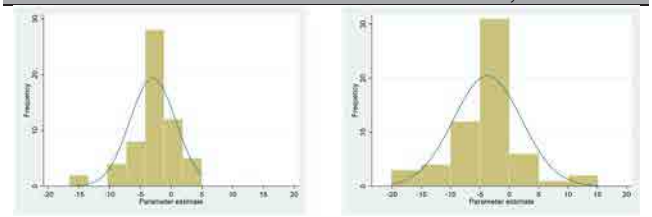


Figure 1 – Slope of eGFR *(-2.98 ml/min/year;SD+3.73;left)* **and creatinine clearance** *(-3.7 ml/min/year; SD+5.8; right).*

P0794

A REAL-WORLD OBSERVATIONAL STUDY OF ETELCALCETIDE USE IN HEMODIALYSIS PATIENTS WITH SECONDARY HYPERPARATHYROIDISM IN EUROPE

Karly Louie[1], Dorothea Papadopoulou[2], Maxime Hoffmann[3], Joaquin Manrique Escola[4], Matthias Kohnle[5], Daniel Cejka[6], Giorgina Piccoli[7,8], Marianne Rix[9], Johannes Boots[10], Andreja Marn Pernat[11], Vicente Torregrosa[12], Kate Tsirtsonis[1], Bruno Fouqueray[13], Jürgen Floege[14]

[1]Amgen Lth, Uxbridge, United Kingdom, [2]Papageorgiou Hospital, Department of Nephrology, Thessaloniki, Greece, [3]Private Hospital La Louviere – Ramsay healthcare, Department of Nephrology and Dialysis, Lille, France, [4]Complejo Hospitalario de Navarra, Nephrology Service, Pamplona, Spain, [5]Nephrologisches Zentrum Mettmann, Mettmann, Germany, [6]Ordensklinikum Linz- Elisabethinen, Department of Medicine III, Nephrology, Transpantation medicine, Rheumatology, Geriatrics, Linz, Austria, [7]Centre Hospitalier Le Mans, Le Mans, France, [8]University of Torino, Torino, Italy, [9]University Hospital Copenhagen Rigshospitalet, Department of Nephrology, Copenhagen, Denmark, [10]Maasstad Hospital, Department of Internal Medicine and Nephrology, Rotterdam, Netherlands, [11]University Medical Center, Ljublijana, Slovenia, [12]University of Barcelona, Nephrology and Renal Transplant Department, Hospital Clinic, Barcelona, Spain, [13]Amgen GmbH, Rotkreuz, Switzerland and [14]RWTH University of Aachen, Division of Nephrology, Aachen, Germany

Background and Aims: Intravenous etelcalcetide was approved in Europe in 2016 for treatment of secondary hyperparathyroidism (SHPT) in adult patients on hemodialysis (HD). Data on real-world use of etelcalcetide are needed to inform clinicians on routine clinical practice with this newly approved therapy.

Method: A multi-country observational medical chart review study was performed to describe clinical management of patients treated with etelcalcetide. Sites with at least 6 months of use of etelcalcetide were eligible for study participation. Chronic HD patients who had at least one record of etelcalcetide prescription were recruited. Abstracted data included demographics, clinical history, laboratory parameters and etelcalcetide use over time. Interim data are being reported.

Results: Medical charts for 238 HD patients who started etelcalcetide between December 24, 2016 and June 7, 2019 were reviewed. Data were obtained from 47 sites from 9 countries (Austria, Denmark, France, Germany, Greece, Netherlands, Russia, Slovenia, and Spain). Forty eight percent of patients (113/238) switched from cinacalcet to etelcalcetide ($\leq$90 days from last cinacalcet prescription), whereas the remaining 125 patients were calcimimetic naive. Median (interquartile range, IQR) age was 62.5 (52-74) and dialysis vintage was 4.7 years (2.4-8.7). Twenty four percent of patients were diabetic and 17% of patients had a history of at least one cardiovascular event (heart failure, myocardial infarction, peripheral vascular disease, or stroke). Parathyroidectomy had been performed in 6% (13/238) of patients and 11% (26/238) had received a kidney transplant. Two-thirds of patients (63%) had a starting etelcalcetide dose of 5 mg and the median weekly dose was 7.5 mg (range: 2.5-15 mg). **Table 1** summarizes the median and IQR for parathyroid hormone (PTH), calcium (Ca) and phosphate (P) levels at baseline, 3, 6 and 12 months following etelcalcetide initiation. At baseline, 85% (201/237) had normal Ca ($\geq$2.1 mmol/L). Among patients who had a normal Ca at baseline, the cumulative incidence of hypocalcemia ($<$2.1 mmol) at 3, 6, 9 and 12 months was, 31%, 45%, 57% and 63%, respectively. Median time to first hypocalcemia event (Kaplan-Meier estimation) was 6.9 months (95% CI: 5.4, 8.9). Etelcalcetide persistence at 3, 6, 9 and 12 months was 96%, 94%, 91% and 87%, respectively. Of the 40 patients who discontinued etelcalcetide by 12 months, 10 patients discontinued for side effects (hypocalcemia=6, nausea=3, and vomiting=1), 5 for parathyroidectomy, 9 for low PTH, 1 for high PTH, and 15 for other reasons. More than half of the patients achieved a $>$30% reduction in PTH from baseline at 6-months (55.9%) and 73.5% at 12 months; and it was 63.2% and 80% for patients who were calcimimetic naive and 47.8% and 66.4% for patients who switched from cinacalcet to etelcalcetide, respectively.

Conclusion: To date, this is the largest study on real-world etelcalcetide use in Europe. Etelcalcetide switchers had higher PTH levels than calcimimetic naive patients at initiation. Persistence of etelcalcetide remained high at 12 months. As expected, we observed a substantial reduction in PTH, Ca, and P, and this was greater among patients who were calcimimetic naive than switchers (-43% vs. -32% at 12 months) for PTH. No new safety signals were observed.

Table 1. PTH, Ca, and P laboratory values at time of etelcalcetide initiation (baseline) and up to 12 months

Median (IQR)	Overall (N=238)				Calcimimetic Naive (n=125)				Swi (N	
	Baseline	*3 mos*	*6 mos*	*12 mos*	*Baseline*	*3 mos*	*6 mos*	*12 mos*	*Baseline*	*3 mos*
PTH (pg/mL)	**595** (433-873)	**488** (367-769)	**382** (217-711)	**333** (234-569)	**586** (479-847)	**492** (371-751)	**376** (170-588)	**298** (216-395)	**608** (395-991)	**484** (348-823
Ca (mmol/L)	**2.3** (2.18-2.43)	**2.18** (2.05-2.30)	**2.15** (2.06-2.29)	**2.16** (2.03-2.28)	**2.33** (2.21-2.46)	**2.18** (2.05-2.30)	**2.15** (2.05-2.29)	**2.17** (2.05-2.28)	**2.26** (2.11-2.37)	**2.18** (2.10-2.3
P (mmol/L)	**1.76** (1.53-2.13)	**1.65** (1.39-1.97)	**1.62** (1.29-1.97)	**1.71** (1.36-2.08)	**1.78** (1.56-2.13)	**1.68** (1.44-1.97)	**1.62** (1.29-1.87)	**1.63** (1.29-2.07)	**1.74** (1.50-2.13)	**1.58** (1.27-1.9

Figure:

P0795

OUTCOME COMPARISON STUDY ACCORDING TO THE CAUSE OF CHRONIC KIDNEY DISEASE: RESULTS FROM KNOW-CKD STUDY

Hyunjin Ryu[1], Yeji Hong[2], Jayoun Kim[3], Curie Ahn[1,4], Yun Kyu Oh[4,5], Kook-Hwan Oh[3,4]

[1]Seoul National University Hospital, Internal Medicien, Seoul, Korea, Rep. of South, [2]Seoul Nation University Hospital, Biomedical Research Institute, Seoul, Korea, Rep. of South, [3]Seoul Naional University Hospital, Medical Research Collaborating Center, Seoul, Korea, Rep. of South, [4]Seoul Nation university College of Medicine, Internal Medicien, Seoul, Korea, Rep. of South and [5]SMG-SNU Boramae Medical Center, Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: The cause of chronic kidney disease (CKD) is one of important factors for predicting the outcome. However, relative risks for the adverse outcomes according to the specific causes of CKD is unknown.

Method: Using the longitudinal data of prospective cohort of Korean predialysis CKD, KNOW-CKD cohort, the relative risk of end-stage renal disease (ESRD), composite of ESRD development or creatinine doubling, and composite of cardiovascular disease (CVD) and all-cause mortality according to the cause of CKD were compared. The patients were subgrouped in to four categories at the study entry according to the cause of CKD: glomerulonephritis (GN), diabetic nephropathy (DN), hypertensive nephropathy (HTN), and polycystic kidney disease (PKD). Since the baseline characteristics differed according to the causes of CKD, the inverse probability of treatment weighting (IPTW) methods was used to exclude the effects of other variables on the outcomes. The estimated glomerular filtration rate (eGFR) slope during follow-up was calculated for each cause of CKD using linear mixed model

Results: During the median follow-up of 4.1 years (interquartile range 1.12-7.12 years) total 441 (21.5%) of ESRD, 556 (27.1%) of composite of ESRD or creatinine doubling and 190 (9.3%) composite of CVD and all cause death occurred. In the IPTW adjusted cohorts, DN and PKD showed significantly increased hazard ratios of 1.85 and 5.57 for ESRD development and 1.74 and 4.57 for composite of ESRD developement or creatinine doubling, respectively, compared to GN in the fully adjusted model. Regarding compsite of CVD and all-cause death, also DN and PKD showed significantly increased hazard ratios of 1.93 and 2.16 compared to GN. The adjusted eGFR slope for DN, HTN and PKD was -2.32, -0.90, and -2.41 mL/min/1.73m^2 per year, respectively, and all differ statistically significantly compared to GN (eGFR slope of -1.49 mL/min/1.73m^2 per year). During the follow-up, GN and DN showed linear declining pattern however, HTN and PKD showed convex linear pattern.

Conclusion: The DN and PKD showed relatively higher risks for renal progression and composite of CVD and death compared to GN.

P0796 **THE PREVALENCE AND INCIDENCE OF COGNITIVE IMPAIRMENT IN A COHORT OF CHRONIC KIDNEY DISEASE PATIENTS WITH CONCOMITANT DIABETES ATTENDING A SPECIALIST NEPHROLOGY CLINIC.**

Mick Kumwenda[1], Peter Hobson[2]

[1]Glan Clwyd Hospital, Department of Nephrology, Bodelwyddan, United Kingdom and [2]Glan Clwyd Hospital, Academic Unit, Bodelwyddan, United Kingdom

Background and Aims: Chronic kidney disease (CKD) is a global healthcare problem associated with several comorbid conditions including, cardiovascular disease, and diabetes, all of which are strong risk factors for the development of significant cognitive impairment. We recently reported the baseline outcomes of our older adult cohort with mild to moderate CKD (stages 3-4) and diabetes, where 48% were found to have a cognitive impairment ranging from mild to severe symptoms. [1] This study reports the outcomes at 36-months post baseline of the prevalence and incidence of cognitive impairment in this cohort the patients who at baseline were considered to have normal cognitive function.

Method: Cognitive function was assessed in patients over aged 55 years, with an estimated glomerular filtration rate < 45ml/min/1.73m 2, attending a renal and diabetes outpatient clinic, at baseline and at 36-months. The diagnosis of cognitive impairment was based upon patient and informant interview, case note review, neuropsychological assessment and application of Diagnostic and Statistical Manual of Mental disorders version 5 (DSM-5) and Petersen's criteria for mild cognitive impairment (MCI). The incidence of cognitive impairment was calculated by dividing the number of new cases during study follow-up, by the person-time at risk throughout the observation period. Since it is not possible to precisely determine when a person actually develops cognitive impairment between baseline and follow-up, the midpoint of time between having normal cognition and becoming a case is assumed.

Results: Ninety-two patients without cognitive impairment at baseline, were included in this investigation (mean age of 75.8 $\pm$ 9.1; 49 males: 43 female). Upon neuropsychological assessment and the application of DSM-5 criteria at follow-up, it was revealed that 25/92 (27%) of the cohort had developed a cognitive impairment ranging from MCI (n=19), to major symptoms (n = 6). The crude prevalence for MCI was 20.6%, and for dementia it was 6.5%. The total person years in the study were 237.38 years, with an overall incidence rate of 10.53 (95% Confidence interval 6.82-15.55) per 100 person-years.

Conclusion: This longitudinal cohort investigation reports the prevalence and incidence of new cases of cognitive impairment ranging from MCI to dementia in CKD. The crude prevalence in the current investigation for the development of cognitive impairment was 27%. The overall incidence rate for new cases of NCD was just over 10%. In other words, for every 100 patients in our current investigation we would estimate that around 10 will develop some a cognitive impairment ranging from MCI to dementia per year. Our findings from this and our previous investigation suggest that a significant number of CKD patients are at risk for the development of significant neurodegenerative conditions and in view of this cognitive function should be screened and monitored routinely in clinical practice. This will assist with appropriate health service planning, service development, clinical interventions and the assessment of the effectiveness of new and existing treatments services.

P0797 **VERY LOW PROTEIN DIET (VLPD) WITH KETOANALOGUE SUPPLEMENTS AS CONSERVATIVE MANAGEMENT OF UREMIA IN ELDERLY PATIENTS: A SINGLE-CENTER EXPERIENCE**

Battista Fabio Viola[1], Alessandra Pola[1], Roberto Zubani[1], Bernardo Lucca[1], Francesco Scolari[1]

[1]*ASST Spedali Civili di Brescia, U.O. Nefrologia, Brescia, Italy*

Background and Aims: EDTA published data gathered between 2012 and 2016 showed greatly reduced survival in elderly prevalent dialysis patients as compared to similar aged individuals in the general population: a 70 year-old dialysis patient had a life expectancy of 5 years (instead of 16), an 80 year-old patient could expect to survive 3 years (instead of 9). This was due to the multiple comorbidities often present in elderly patients with advanced Chronic Kidney Disease (CKD). This burden of disease is further increased by dialysis itself, in particular by hemodynamic instability during treatment and by vascular access problems which often determine the need for central venous catheter insertion and for hospitalization. In 2007 the DODE study (a randomized, controlled, multicentric study in which our center took part) validated a conservative treatment of uremia based upon a Very Low Protein Diet supplemented with ketoanalogues (sVLPD): survival in patients on conservative management was similar to that of patients on chronic dialysis; also, no negative effect on nutritional status was observed. Our aim was to analyse clinical and epidemiologic data and outcomes of patients treated at our center with a sVLPD.

Method: We analized 222 selected from a group of approximately 300 patients with stage 5 CKD managed conservatively with a sVLPD (0.3 g/kg/day proteins). The inclusion criterion was active follow-up for at least six months; patients unable to maintain fluid and electrolyte balance with medical therapy were excluded. Except for one patient, all subjects were aged 75 years and older. Clinical and epidemiologic data were recorded at the beginning, during and at the end of follow-up.

Results: Mean age at the beginning of observation was 80 ± 7 years (51-96); 48% of patients were male (107), 52% were female (115). Median initial Renal Residual Function (RRF, ml/min) was 6,3 ± 2,1 ml/min, at the end of follow-up it was 5,3 ± 2,9 ml/min. The most common significant comorbidities were hypertension (84,5%), heart (61,4%) and vascular disease (48,6%); these and other significant comorbidities are illustrated in Fig. 1. Conservative management allowed to delay the initiation of dialysis by an average of one year; 24% of patients continued on the sVLPD for two year and some patients reached a duration of treatment of 7 years. Median duration of sVLPD is shown in Fig. 2. At the end of follow-up 40% of patients had begun chronic hemodialysis and 9% peritoneal dialysis, 8% were still on conservative management, 27% were deceased (Fig. 3).

Conclusion: The supplemented Very Low Protein Diet is an effective treatment which can delay the beginning of chronic dialysis in elderly stage 5 CKD patients with multiple comorbidities. It is a safe treatment and does not increase morbility and mortality. Current epidemiologic data (incident patients in dialysis: 170 pmp/year, 50% aged over 70 years old) support the use of this conservative strategy which can represent a valid alternative to dialysis in selected patients.

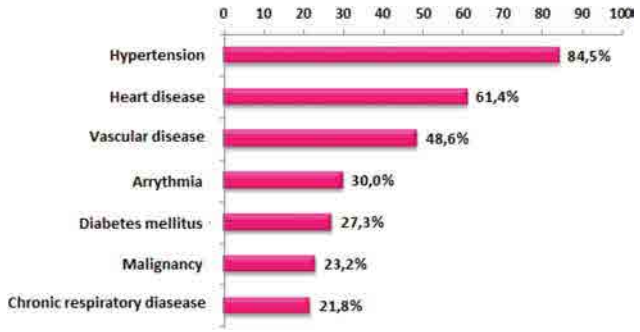


Fig. 1. Patient comorbidities at the beginning of observation.

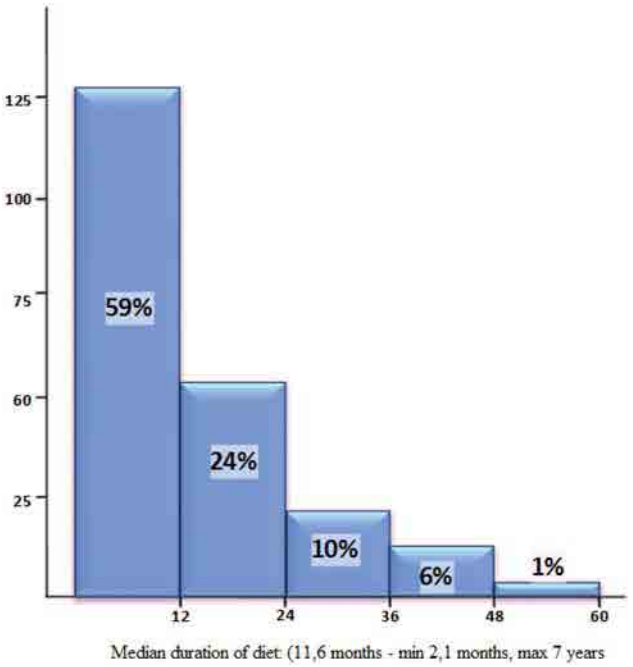


Fig. 2. Median duration of sVLPD.

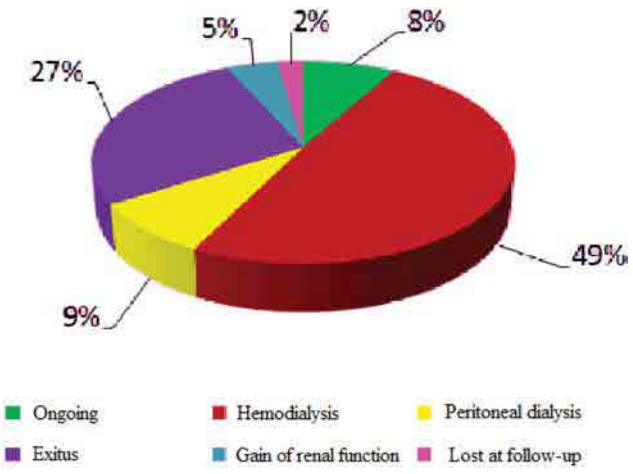


Fig. 3. Status of patients at the end of follow-up.

P0798

ASSOCIATION BETWEEN RENAL DYSFUNCTION AND GENERAL COGNITIVE FUNCTION IN COMMUNITY DWELLING OLDER ADULTS: KOREAN FRAILTY AND AGING COHORT STUDY

Jiyoon Kong[1], Jin Sug Kim[1], Min Hye Kang[1], Shin Yeong Kang[1], Ri Ra[1], Chang Won Won[2], Hyeon Seok Hwang[1], Kyung Hwan Jeong[1]

[1]Kyung Hee University, Internal Medicine, division of Nephrology, Seoul, Korea, Rep. of South and [2]Kyung Hee University, Family Medicine, Seoul, Korea, Rep. of South

Background and Aims: Cognitive impairment is common in older adults. Similarly, the prevalence of renal dysfunction is also increased in the elderly. We conducted this study to clarify the relationship between the renal function and cognitive impairment in community dwelling older adults in Korea.

Method: A cross-sectional analysis was performed on the data of the Korean Frailty and Aging Cohort Study (KFACS), a nationwide cohort study that began in 2016. Of the 3014 participants assessed in the first and second year, 2847 participants (1333 men, 1514 women) who completed baseline assessments were enrolled. The estimated glomerular filtration rate (eGFR, mL/min/1.73m^2) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Renal function of the participants was classified into four groups by eGFR quartile. General cognitive function was accessed with mini-mental state exam in the Korean version (MMSE-KC). Participants who had MMSE-KC score less than 1.5 standard deviation by age, gender, and education level were regarded as the cognitive impairment. Multivariate logistic regression model was used to examine the relationship between renal function and cognitive impairment. In addition, we investigated to find the point of eGFR interval at which the odds ratio begins to increase.

Results: The mean eGFR in quartile 1 was 91.7 $\pm$ 3.22 ml/min/1.73m^2, and 84.9 $\pm$ 1.81 in quartile 2, 76.1 $\pm$ 3.66 in quartile 3, and 57.2 $\pm$ 10.75 in quartile 4. In baseline characteristics, participants with lower eGFR had lower MMSE-KC scores. And the prevalence of cognitive impairment was 10.8% in quartile 1, 15.9% in quartile 2, 15.2% in quartile 3, 14.9% in quartile 4. After multivariate adjustment, the odds ratio (OR) of cognitive impairment in quartile 2 [adjusted OR: 1.569, 95% confidence intervals (CI): 1.141 - 2.158, p = 0.006] compared with quartile 1. And the odd ratios of cognitive impairment were 1.539 (95% CI: 1.113 - 2.127, p = 0.009) in quartile 3, 1.475 (95% CI: 1.062 - 2.049, p = 0.020) in quartile 4 compared with quartile 1, respectively. Among the participants with eGFR above 60 ml/min/1.73m^2, the renal function was grouped by 5 ml/min/1.73m^2 interval. The risk of cognitive impairment started to increase from eGFR between 80 and 85 ml/min/1.73m^2 (adjusted OR: 1.667, 95% CI: 1.128 - 2.463, p = 0.010).

Conclusion: Renal dysfunction was associated with lower global cognitive function in older adults. And the risk of cognitive impairment increased from quartile 2, especially, eGFR between 80 and 85 ml/min/1.73m^2 in this population. These results suggest that mild decline of kidney function is also a risk factor of cognitive decline in the elderly.

P0799

EPIDEMIOLOGY AND TREATMENT PATTERN OF HYPERKALAEMIA AMONG OUTPATIENTS IN CHINA: A DESCRIPTIVE STUDY USING AN ADMINISTRATIVE DATABASE IN CHINA

Jiaming Bian[1], Li Zuo[2], Houyu Zhao[3], Xu Han[1]

[1]Chinese People's Liberation Army General Hospital, Department of Pharmacology, Beijing, P.R. China, [2]Peking University People's Hospital, Department of Nephrology, Beijing, P.R. China and [3]Peking University, Department of Epidemiology and Biostatistics, School of Public Health, Beijing, P.R. China

Background and Aims: At present, the clinical burden and treatment pattern of hyperkalaemia among outpatients in China is not well characterized. The aim of this study was to evaluate the disease distribution and treatment pattern of hyperkalaemia among outpatients in China.

Method: Data were derived from Beijing Data Center for Rational Use of Drugs, which contains primary records of 157 hospitals, covering 30 provinces in China. Patients who accessed outpatients (aged >=≥18 years old) with record(s) of serum potassium (S-K) between 2015.1.1- 2017.12.31 were included. The laboratory test, diagnoses, and treatments were analyzed. Hyperkalaemia defined as S-K > 5.0 mmol/L. A hyperkalaemia episode was defined as one or more consecutive S-K > 5.0mmol/L measurement(s) within 7 days. If there was a return to S-K <5.0mmol/L within 7 days, the subsequent measurement(s) will be recognized as another hyperkalaemia episode. The proportion of hyperkalaemia was defined as the proportion of patients who experienced at least one hyperkalaemia episode. The main outcomes, including the proportion of hyperkalaemia patients, the diagnosis rate, the treatment rate and the S-K retesting rate were analyzed. The geographic and seasonal distribution of the proportion was examined. The diagnosis rate was defined as the proportion of hyperkalaemia episodes that have diagnoses records of hyperkalaemia within the episode. Treatment rate was defined as the proportion of hyperkalaemia episodes that have records of any hyperkalaemia treatment including diuretics, glucose injection + insulin, calcium injection, sodium bicarbonate, potassium binder, transfer to emergency room or dialysis. Retesting rate was defined as the proportion of hyperkalaemia records that have potassium test record(s) within one day, two days or seven days.

Results: A total of 2,997,634 patients with at least one S-K record each were analysed. 115,826 patient (3.86%) experienced hyperkalaemia (S-K >5.0mmol/L), in which 28,254 patients (0.94%), experienced S-K ≥5.5mmol/L. In patients with chronic kidney disease, heart failure, hypertension, and diabetes mellitus, the proportions of patients who experienced hyperkalaemia were 22.89%, 12.54%, 7.11% and 6.51%, respectively. Composition proportion of who experienced S-K ≥ 5.5mmol/L, in the patients with CKD and HF, defined as the proportion of patients experienced S-K≥ 5.5mmol/L in all hyperkalaemia patients, were 39.27% and 32.16% respectively, higher than the general population (16.3%). Geographic analysis showed that provinces with higher proportions of hyperkalaemia were Jiangsu (9.22%), Hebei (8.31%), Tianjin (6.74%), Hunan (6.27%) and Liaoning (5.56%). In addition, the seasonal proportion varied as winter (4.18%), autumn (3.93%), spring (3.83%) and summer (3.57%). In patients with hyperkalaemia, the overall hyperkalaemia diagnosed rate within the episode was 2.53%. Diagnosed rates increased by the severity of hyperkalaemia, patients with S-K ≥7.0 mmol/L showed the highest diagnosed rate of 9.63%. The overall hyperkalaemia treated rate was 8.69%. The treated rate of patients with S-K 5.0 to 5.5mmol/L was much lower than that of patients with S-K 5.5 -6.0mmol/L (6.6% vs. 12.01%). The overall retesting rate within 7 days was 11.41%. Patients with S-K 5.0-5.5 mmol/L were retested less frequently (8.51%) than those with S-K ≥5.5 mmol/L (15.56-21.76%).

Conclusion: The proportions of hyperkalaemia in patients with chronic kidney disease, heart failure, hypertension and diabetes were higher than the proportion in overall outpatients. The severity of hyperkalaemia increased in patients with chronic kidney disease and heart failure. The diagnosed rate, treated rate and resting rate of hyperkalaemia in outpatients were low, showing a slight raise with increased severity.

Table 1. The proportion of patients who experienced at least one hyperkalaemia in outpatients from 2015-2017

	All years	2015	2016	2017
Numbers of patients who have S-K measurements records	2997634	1071033	974634	951967
Numbers of patients who experienced hyperkalaemia	115826	38844	38109	38873
The proportion of patients who experienced hyperkalaemia in outpatients, % *	3.86	3.63	3.91	4.08

* The proportion of patients who experienced hyperkalaemia = Numbers of patients who experienced hyperkalaemia/Numbers of patients who have S-K measurements records

Table 2. The proportion of patients who experienced at least one hyperkalaemia in patients with CKD, HF, hypertension, and diabetes mellitus in outpatients

	Chronic kidney disease	Heart failure	Diabetes	Hypertension	Patients without CKD, HF, diabetes or hypertension
Numbers of patients who have S-K measurements records	127230	6820	142109	252162	2469333
Numbers of patients who experienced hyperkalaemia	29123	855	10108	16427	59309
The proportion of patients who experienced hyperkalaemia, % *	22.89	12.54	7.11	6.51	2.41

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[GRAPHICS]

P0800 **PROFILING HYPOKALAEMIC AND HYPERKALAEMIC STATES IN THE IRISH HEALTH SYSTEM: TESTING RATES, INCIDENCE AND DETERMINANTS**

Leonard Browne[1,2], Stack Austin[1,2,3]

[1]University of Limerick, Graduate Entry Medical School, Limerick, Ireland, [2]University of Limerick, Health Research Institute, Limerick, Ireland and [3]University Hospital Limerick, Department of Renal Medicine, Limerick, Ireland

Background and Aims: Hypo- and hyperkalaemia are potentially life-threatening electrolyte abnormalities often associated with severe adverse clinical outcomes. Real-world incidence and determinants of hypo- and hyperkalaemia in clinical settings are poorly characterised. We studied incidence and determinants of these abnormalities in the Irish healthcare system

Method: Data from the Irish National Kidney Disease Surveillance and Quality Assurance Programme were used to construct a retrospective observational study. We identified all adult individuals (age > 18 years) who accessed health care from 2006 and 2010 in a regional health system (n = 205,334). Cumulative incidence of hypokalaemia (K+ < 3.5 mmol/L), hyperkalaemia (K+> 5 mmol/L), and moderate/severe hyperkalaemia (K+> 5.5 mmol/L) was estimated over a 3-year period. Kidney function was assessed by estimated glomerular filtration rate (eGFR). Multinomial logistic regression explored associations of baseline patient characteristics with dyskalaemia states.

Results: Of 205,334 participants, 85.2% had 1–2 potassium tests, 5.8% had 2–3 tests, 2.7% had 3-4 tests and the remaining 6.4% had > 4 potassium tests/year. Hypokalaemia occurred in 17,145 (8.35%) individuals, of these 43.8% had recurrent hypokalaemia (>1 event). Hyperkalaemia occurred in 44,283 (21.6%) individuals, with 29.7% recurrence. Moderate/severe hyperkalaemia occurred in 9,672 (4.71%) with 18.0% recurrence. The frequency of potassium testing was an important determinant of dyskalaemia risk. In adjusted analyses, advancing age profile, women, inpatients, outpatients and emergency department patients (vs general practice), and frequency of tests had significantly higher risks of hypokalaemia. Additionally, advancing age, men, poorer kidney function, and frequency of potassium testing, and general practice were associated with significantly higher risk of hyperkalaemia.

Conclusion: Both hypo- and hyperkalaemic states are common in the Irish healthcare system with high rates of recurrence. Surveillance strategies should be put in place to allow timely detection and treatment of potassium disturbances in these high-risk groups.

Table 1. 0: Risk factors for Incident hyperkalaemia and hypokalaemia in the Health System

	Odds Ratio (95% CI)		
	K < 3.5 mmol/L	**K > 5.0 & K<= 5.5 mmol/L**	**K > 5.5 mmol**
Age Group			
18-44	ref	ref	ref
45-64	**1.36 (1.29-1.43)**	**1.72 (1.67-1.77)**	**1.77 (1.65-1.89)**
65-74	**2.31 (2.16-2.47)**	**2.13 (2.04-2.22)**	**2.13 (1.95-2.34)**
>75	**2.72 (2.53-2.92)**	**1.78 (1.69-1.88)**	**1.85 (1.67-2.05)**
Sex			
Male	ref	ref	ref
Female	**1.43 (1.38-1.49)**	**0.83 (0.81-0.85)**	**0.82 (0.78-0.87)**
eGFR Category			
G1	ref	ref	ref
G2	0.96 (0.91-1.01)	**1.26 (1.22-1.29)**	**1.33 (1.24-1.42)**
G3	**1.08 (1.00-1.16)**	**1.85 (1.77-1.94)**	**2.25 (2.04-2.47)**
G4	0.93 (0.80-1.10)	**4.11 (3.64-4.63)**	**6.92 (5.81-8.24)**
G5	**3.00 (2.17-4.15)**	**7.91 (5.86-10.68)**	**28.11 (20.32-38.88)**
Frequency of K+ measurements:			
1 to 2	ref	ref	ref
2 to 3	**3.88 (3.65-4.12)**	**2.17 (2.07-2.28)**	**2.27 (2.07-2.50)**
3 to 4	**6.30 (5.84-6.79)**	**2.86 (2.67-3.06)**	**2.77 (2.42-3.18)**
> 4	**16.49 (15.6-17.43)**	**5.22 (4.95-5.51)**	**6.81 (6.24-7.44)**
Location of supervision:			
General Practice	ref	ref	ref
Emergency Department	**2.86 (2.72-3.01)**	**0.42 (0.4-0.44)**	**0.39 (0.35-0.43)**
In-patient	**2.03 (1.93-2.15)**	**0.5 (0.47-0.52)**	**0.53 (0.49-0.59)**
Out-patient	**1.66 (1.57-1.76)**	**0.64 (0.61-0.66)**	**0.69 (0.63-0.75)**

Multivariable odds ratios adjusted for age group, sex, eGFR stage, frequency of tests and location of medical supervision.

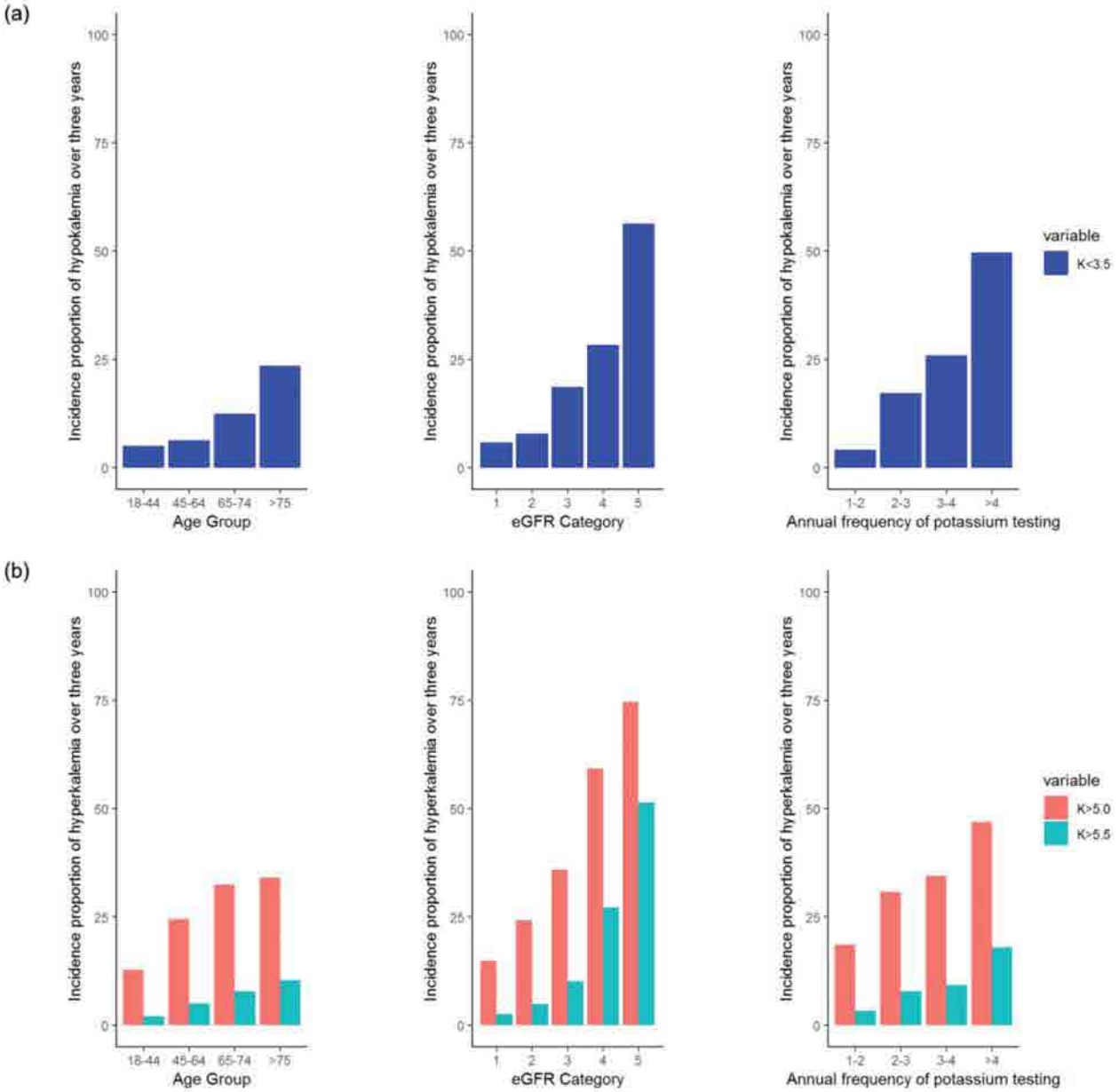


Figure 1: Incidence proportion of hypokalaemia (a) and hyperkalaemia (b) over three years by age group, eGFR category and annual potassium testing frequency

P0801 EGFR LEVEL BEFORE HOSPITALIZATION INFLUENCES OUTCOMES AFTER DISCHARGE REGARDLESS OF ADMISSION DIAGNOSIS

Fiammetta Ravaglia[1], Francesco Profili[2], Giuseppe Spatoliatore[1], Paolo Francesconi[2], Alberto Rosati[1]

[1]AUSL Toscana Centro, Nephrology, Florence, Italy and [2]Regional Agency for Health, Florence, Italy

Background and Aims: The risk of hospitalization and death is known to be greater among patients with chronic kidney disease. Less known are the risks after hospital discharge.

Our aim is to evaluate the prognosis after hospital discharge according to the presence and the degree o CKD before the hospitalization.

Method: Target population: Tuscany population (patients on RRT excluded) aged 50+ years, discharged from medical setting in 2017, ordinary regimen (excluding long-term stay/ rehabilitation, trauma and hospitalizations of a special nature), without hospitalization episodes in the 28 days before, with at least one creatinine determination in an outpatient setting in 2017, prior to admission. Data were extracted from hospital discharge sheets.

Exposure measurement: CKD stage, based on glomerular filtration rate estimated by CKD-EPI equation. Laboratory tests were linked with hospital data with a unique anonymous identifier.

Outcome one month and one year after discharge were:

- hospitalization (medical area, ordinary regime, excluding long-term stay / rehabilitation and special hospitalizations). For all causes and by diagnosis-related group.

- Institutionalization or activation of home care, calculated only one year after discharge.

- all-cause mortality.

Statistical analysis: incidence rates (IR) and ratio of incidence rates (IRR), with 95% confidence intervals, were calculated for institutionalization / home care, hospitalization and death (rough and adjusted for covariates at discharge index: comorbidity, age, gender, discharge department, diagnosis-related group of discharge, days of hospitalization) with Poisson regression model.

Results: 33,253 discharges met the eligibility criteria in 2017 (28,706 subjects). The discharges of patients with a eGFR $>$ 60 were 18,194 (54.8%), with eGFR $<$30 were 4,268 (12.8%). The risk of hospitalization or death increases with decreasing eGFR, both at one month and at one year. One-month death IRR for a GFR $<$30 vs GFR$>$ 60 was 1.59 (CI95%: 1.39-1.83), the hospitalization IRR was 1.61 (CI95%: 1.46-1, 77). One-year death IRR was 1.46 (CI95%: 1.35-1.58), the hospitalization IRR was 1.35 (CI95%: 1.21-1.50). One-year institutionalization IRR was 1.35 (CI95%: 1.21-1.50) As expected, the main causes of hospitalization were cardiovascular, genitourinary or gastrointestinal diseases.

Conclusion: The lower the renal function before the hospital admission, the greater the chances of hospitalization or death, in the short term and at one year, regardless of admission diagnosis. The risk of losing autonomy also increases. For this reason, the patient discharged with known kidney disease can benefit from protected discharge paths and dedicated post-hospital follow-up.

P0802

RELATIONSHIP BETWEEN RENAL INSUFFICIENCY AND AIRFLOW LIMITATION AND THEIR IMPACT ON MORTALITY IN A COMMUNITY-BASED POPULATION: THE YAMAGATA (TAKAHATA) STUDY

Masahiro Miyata[1], Tomomi Tanaka[1], Natsuko Suzuki[1], Kosuke Kudo[1], Kazunobu Ichikawa[1], Sumito Inoue[1], Masafumi Watanabe[1], Takamasa Kayama[2], Tsuneo Konta[3]

[1]Yamagata University, Department of Cardiology, Pulmonology, and Nephrology, Yamagata, Japan, [2]Yamagata University, Institute for Promotion of Medical Science Research, Yamagata, Japan and [3]Yamagata University, Department of Public Health and Hygiene, Yamagata, Japan

Background and Aims: Chronic kidney disease and chronic obstructive pulmonary disease (COPD) are known risk factors for mortality. In this study, we investigated the association between renal deficiency and airflow limitation that characterizes COPD, and its effect on 10-year mortality in a community-based population.

Method: The study subjects were 1,233 health check-up participants (mean age 64 years; 46.7% men). We defined renal insufficiency as GFR <60 mL/min/1.73m^2 estimated using serum creatinine (Cr) or cystatin C (CysC), and airflow limitation (AFL) as forced expiratory volume in 1 second to forced vital capacity ratio $<70\%$ on spirometry.

Results: The prevalence of Cr-based and CysC-based renal insufficiency, and AFL in total subjects was 6.6%, 14.8%, and 11.2%, respectively. Compared with subjects without AFL, those with AFL showed a significantly higher prevalence of CysC-based renal insufficiency (24.6% vs. 13.5%, $P<0.01$), but not of Cr-based renal insufficiency (8.0% vs. 6.4%, $P=0.77$). The prevalence of CysC-based renal insufficiency was increased, along with the progression of AFL severity (P for trend <0.01). During the follow-up period, there were 154 (12.5%) deaths. Cox proportional hazard analysis adjusted for confounders showed that the hazard ratio (95% confidence interval) for all-cause mortality was 1.76 (1.12-2.71) in subjects with CysC-based renal insufficiency alone, 1.13 (0.62-1.94) in those with AFL alone, and 2.30 (1.20-4.18) in those with both CysC-based renal insufficiency and AFL, with subjects without both CysC-based renal insufficiency and AFL as the reference. In contrast, the adjusted hazard ratios for all-cause mortality did not reach statistical significance in subjects with both Cr-based renal insufficiency and AFL, with subjects without both Cr-based renal insufficiency and AFL as the reference.

Conclusion: This study showed that CysC-based renal insufficiency and AFL are strongly associated and that their overlap is a significant risk for mortality in community-based populations.

P0803

SYNERGISTIC INTERACTION OF ACUTE HYPERGLYCEMIC STRESS AND NON-ALCOHOLIC FATTY LIVER DISEASE ON THE DEVELOPMENT OF ALBUMINURIA IN GENERAL POPULATION

Chang Hwa Lee[1], Mi-yeon Yu[1], Jong Wook Choi[2], Joo-Hark Yi[1], Sang-Woong Han[1], Joon-Sung Park[1]

[1]Hanyang University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of South and [2]Konkuk University School of Medicine, Research Institute of Medical Science, Chungcheongbuk-do, Korea, Rep. of South

Background and Aims: Both increased glycemic exposure and non-alcoholic fatty liver disease (NFALD) are independent risks of vascular endothelial dysfunction. To find interactive effects of acute hyperglycemia and hepatic necro-inflammation on initiation of albuminuria, we conducted this nation-wide, population-based interaction analysis using acute-to-chronic glycemic ratio (ACGR) as a candidate indicator of acute increased glycemic exposure and ZJU index as an indicator of NFALD.

Method: Eligible as cases were all native Koreans aged 20 years or older without significant medical illness. A total of 9494 participants were divided into quintiles according to their ACGR results and stratified by sex.

Results: Participants in the highest ACGR quintile were more obese and they were more likely to have elevated BP and increased glycemic exposure as compared with other quintiles. Restricted cubic regression analyses revealed that there was non-linear relationship of ACGR and ZJU index with albuminuria. Multiple logistic regression, adjusted for various conventional risk factor of kidney disease**, demonstrated that both ACGR (adjusted OR = 5.388, 95% *CI* = 1.119-25.95) and ZJU index (adjusted OR = 1.057, 95% *CI* = 1.002-1.114) were independent predictor of albuminuria. Interestingly, our interaction analysis revealed that ACGR had bigger effect on the *risk of* albuminuria in participant with elevated ZJU index than those without (adjusted RERI = 2.296, 95% *CI* = 2.277-2.313; adjusted AP = 0.643, 95% *CI* = 0.472-0.814; adjusted SI = 8.135, 95% *CI* = 7.267-9.003).**

Conclusion: Our findings suggest that the interaction of acute hyperglycemia and abnormal hepatic fat metabolism may exert synergistic biologic effect on the development of albuminuria.

P0804

TRENDS IN BODY MASS INDEX IN PATIENTS WITH INCIDENT CHRONIC AND END STAGE KIDNEY DISEASE FROM 2004 - 2019

Diana Gamio-Izasmendi[1], Keith Gillis[1], Patrick Mark[2], Siobhan McManus[1], Jamie Traynor[1]

[1]*Queen Elizabeth University Hospital, Renal Unit, Glasgow, United Kingdom and* [2]*Institute of Cardiovascular & Medical Sciences, Glasgow, United Kingdom*

Background and Aims: Obesity is increasingly prevalent in the general population. Body mass index (BMI) has a U-shaped relationship with mortality in chronic kidney disease (CKD), but also has implications for service delivery. We analysed the BMI trends in incident patients referred to CKD clinic (CKD), starting haemodialysis (HD), peritoneal dialysis (PD) and receiving a kidney transplant (Tx). Our aim was to establish the trend in BMI across these specified patient groups over the last 15 years.

Method: A single centre retrospective analysis was carried out including adults referred to secondary care nephrology services between 2004 and 2019. Patients were categorised into CKD, HD, PD, or Tx. Those reaching ESKD were grouped according to first method of renal replacement therapy (RRT). Patients with acute kidney injury and with missing BMI data were excluded. As per the World Health Organisation's definition, BMI was categorised into classes I, II and III (>30, 35, and 40kg/m^2 respectively).

Results: Of 10,057 patients, 6,936 patients were included. Of these, 59.96% (n=4,249) were CKD, 7.39% (n=524) were Tx, 4.85% (n=344) were PD, and 27.43% (n=1,944) were HD. BMI was 27.3±7.2kg/m^2 in 2004 and 27.8±7.72kg/m^2 in 2019 with no significant change in BMI as a whole throughout that time period (p=0.07). In subgroup analysis, there was no change in BMI in the CKD (p=0.52) or PD (0.76) groups. However, there was a significant increase in BMI seen in both the HD ($p<0.001$) and Tx (p=0.006) groups. An increase in the proportion of patients with class III obesity was also observed in the HD group (p=0.009) but not the CKD, Tx or PD groups.

Conclusion: In contrast to the general population, the prevalence of obesity has not changed in incident patients with kidney disease over the last 15 years. In subgroup analysis however, there is a trend towards rising BMI in the incident haemodialysis patient group. Limitations of the study include retrospective design, lack of ethnicity data, and inclusion of only a single measure of adiposity.

Although the relationship between BMI and mortality in patients receiving maintenance haemodialysis is non-linear, the increase in the very obese in this patient group will have significant implications for healthcare providers.

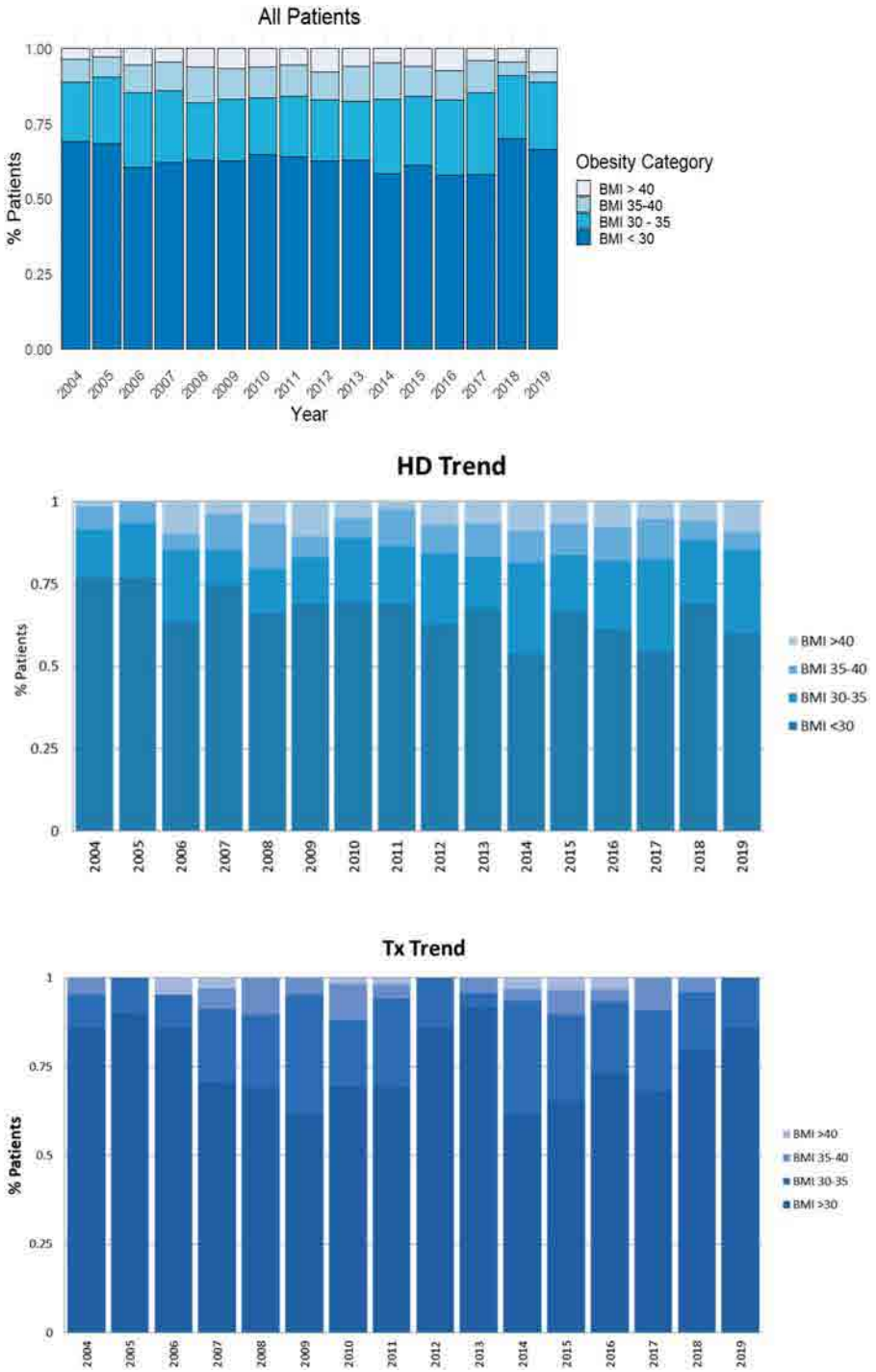

All Patients
% Patients
Year
Obesity Category
BMI > 40
BMI 35-40
BMI 30 - 35
BMI < 30
HD Trend
% Patients
BMI >40
BMI 35-40
BMI 30-35
BMI <30
Tx Trend
% Patients
BMI >40
BMI 35-40
BMI 30-35
BMI >30

Figure:

P0805 SURPRISE QUESTION IN ADVANCED CHRONIC KIDNEY DISEASE

Sara Cardoso Fernandes[1], Nuno Moreira Fonseca[1], Rita Magriço[1], Isabel Mesquita[2], Vasco Fernandes[1], Ana Carina Ferreira[1], Fernando Nolasco[1]

[1]Centro Hospitalar Universitário Lisboa Central, Nephrology, Lisboa, Portugal and [2]Hospital Professor Doutor Fernando Fonseca, Nephrology, Amadora, Portugal

Background and Aims: Nowadays, patients with end-stage chronic renal disease (ESRD) are initiating dialysis at more advanced ages and having multiple comorbidities. Since the initiation of dialysis in the elderly may not result in increased survival or quality of life, it would be useful to define prognostic criteria for those patients. We aim to evaluate the utility of the surprise question ("Would I be surprised if this patient died in the next 12 months?") as a predictor of survival in elderly patients in advanced stages of chronic kidney disease (CKD).

Method: Retrospective cohort study of patients elder than 70 years with CKD stages 4 to 5 according to the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) who attended the CKD information consultation between March 2017 and November 2018. The answer to the surprise question was registered during that office visit. Demographic, clinical and laboratory data (including serum albumin) were analyzed and Charlson Comorbidity Index (CCI) was calculated. Continuous variables are presented as means (±SD) or medians (IQ range), according to normality, and categorical variables as frequencies. Comparisons between groups were made using Student's T-test and Pearson Chi-squared test. Survival analysis was conducted using Kaplan-Meier test and Cox proportional hazard model. STATA software was used and a $p<0.05$ was considered significant.

Results: Of the 60 patients selected, 22 (36.7%) were female, 59 (98%) were white and the median age was 78.6±6.3 years. Half of these patients had diabetes mellitus with end-organ damage and 57% suffered from congestive heart failure. The response to the surprise question was "yes" in 31 (51.7%) patients and "no" in 29 (48.3%) patients. We did not find clinical or demographic differences among these groups. The patients were followed for 26 (20-31) months, during which 19 deaths occurred, 4 (21%) in the SQ-yes group and 15 (79%) in the SQ-no group. The response to the surprise question was associated with patients' survival (KM – p=0.0009), with a positive and negative predictive values of 79% and 66%, respectively. The multivariate analysis (age, sex, race, serum albumin and CCI) showed that the answer to the SQ is an independent predictor of mortality (HR 0.27 [IC 0.08-0.86]).

Conclusion: The SQ seems to be a good predictor of survival in elderly patients in advanced stages of CKD and can be used to assess their prognosis in order to help deciding whether the patient is a good candidate to initiate dialysis or not.

P0806

RESIDUAL RENAL FUNCTION IS COMPLEMENTARY TO GERIATRIC ASSESSMENT SCORE IN ASSESSING CLINICAL RISK OF ELDERLY PATIENTS

Alberto Castagna[1], Davide Bolignano[2], Irma Figlia[2], Rosa Paola Cerra[3], Carmen Ruberto[1], Giovanni Ruotolo[3], Giuseppe Coppolino[2]

[1]Azienda Sanitaria Provinciale Catanzaro, Center for Cognitive Disorders and Dementia, Catanzaro, Italy, [2]Magna Græcia University, Health Sciences, Catanzaro, Italy and [3]Hospital Pugliese Ciaccio, Geriatric Unit, Catanzaro, Italy

Background and Aims: Renal function impairment is highly pervasive in the elderly and triggers increased morbidity and mortality. Comprehensive geriatric assessment (CGA) is a validated multidisciplinary instrument to assess medical, psychosocial and functional limitations of old patients with diagnostic and risk-stratification purposes.

In a focused cohort of frail individuals, we aimed at evaluating possible relationships between single CGA items and renal function.

Method: 254 consecutive elderly subjects (mean age 79.9±6.6 years, female 65.8%) from the geriatric division of a large Italian community hospital were studied. We collected clinical data including CGA and renal function (CKD-EPI formula). CGA single items included the Cumulative Illness Rating Scale (CIRS), the Exton Smith Scale (ESS), the Mini Nutritional Assessment Short Form (MNA-SF), the Katz's Activities of Daily Living (ADL), the Lawton's Instrumental Activities of Daily Living (IADL), the Short Portable Mental Status Questionnaire (SPMSQ) and the amount of drugs administered (AD).

Results: Mean eGFR was 66.37±30.94 mL/min/1.73 m2. Overall, the reported CIRS, ESS, MNA, ADL and AD scores were low (7.6±3.3) while IADL and SPMQ were on a mild range, denoting a potential alarm signal for poor prognosis and the risk for adverse outcomes.

At univariate analyses, eGFR was significantly associated with CIRS (R=-0.389, $p<0.0001$), ESS (R=0.355, $p<0.0001$), MNA (R=0.394, $p<0.0001$), ADL (R=0.394, $p<0.0001$), AD (R=-0.374, $p<0.0001$. while a weak, although significant correlation was found with IADL (R=0.131, p=0.038) and SPMSQ (R=-0.141, p=0.038). In a fully adjusted multivariate analyses only SPMSQ (ß=-0.174, p=0.04), ADL (ß=0.182, p=0.012), IADL (ß =0.209, p=0.003) and AD (ß=-0.354, $p<0.0001$) remained significant predictors of residual renal function.

Conclusion: In elderly frail subjects, residual renal function may influence daily life and cognitive activities, the perceived quality of living and the entity of drug assumption. Inclusion of renal function within a comprehensive geriatric assessment could help improving risk stratification in the elderly

P0807

THE IMPACT OF GLOMERULAR FILTRATION RATE IN HEART FAILURE PATIENTS WITH CARDIAC IMPLANTABLE DEVICES - MYTH OR FACT?

Natacha Rodrigues[1], Afonso N Ferreira[2], Pedro António[2], Mafalda Carrington[3], João De Sousa[2], José António Lopes[1], José Guerra[1], Fausto J Pinto[2], Pedro Marques[2]

[1]Centro Hospitalar Universitário Lisboa Norte, Faculdade de Medicina de Lisboa, Nephrology and Renal Transplantation, Lisboa, Portugal, [2]Centro Hospitalar Universitário Lisboa Norte, Faculdade de Medicina Universidade de Lisboa, Departamento de Coração e Vasos, Centro Cardiovascular da Universidade de Lisboa, Lisboa, Portugal and [3]Hospital Espirito Santo, Évora, Cardiology, Évora, Portugal

Background and Aims: Heart Failure (HF) and chronic kidney disease (CKD) are both epidemic, frequently simultaneous and sharing well knowned risk factors. Implantable devices can improve quality of life and reduce mortality in a selected population. Data derived from meta-analyses show both survival benefit in CKD patients receiving devices and increased risk of death in device patients with CKD. Little is Known about the impact of glomerular filtration rate (GFR) across the different stages of CKD in the vital prognoses of HF patients submitted to cardiac resynchronization therapy (CRT) or implantable cardiac defibrillator (ICD) implants.

To evaluate the impact of CKD in all-cause mortality in HF patients who implanted a CRT or ICD.

Method: Prospective single-center study of patients who implanted CRT or ICD between 2015 and 2019. Clinical characteristics were evaluated at baseline and mortality was assessed using the national registry. CKD was evaluated according to the GFR by CKD-EPI equation according to the KDIGO guidelines. We performed univariate and multivariate analysis to compare clinical characteristics of patients who died and who survived using the Cox regression and Kaplan-Meier methods. For the predictor GFR levels, and according to the KDIGO classification, we assessed the best cut-off value for mortality using the area under the ROC curve (AUC) method.

Results: From 2015-2019, 974 devices were implanted, 414 ICDs and 560 CRTs (23.3% female, 67.6±12.1, follow-up duration 26.4±16.5 months). A total of 161 patients (16.5%) died during follow-up. GFR at the time of device implant was significantly lower in patients who died compared to those who survived (49.7 vs 67.3ml/min/1.73m^2, p<0.001). When evaluating predictors for all-cause mortality by multivariate analysis, GFR at the time of device implant was an independent predictor of mortality, even when adjusted for age, gender, arterial hypertension and diabetes (HR 1.12; 95% CI 1.04-1.16, p<0.001). The best GFR cut-off value to predict mortality with a 69% sensitivity and 65% specificity was 75ml/min/1.73m^2 (AUC 0.70). Patients with a GFR < 75ml/min/1.73m^2 at the time of implant have a 2.5-fold higher risk of death (HR 2.5; 95% CI 1.6-3.9, p<0.001). Risk of death significantly increases along GFR decline, almost doubling each stage, with 2.7 for stage 3a (p=0.2), 5.5 for stage 3b, 9.5 for stage 4 and 14.7-fold higher risk of death for stage 5 (p<0.001).

Conclusion: In our cohort of HF patients who underwent CRT or ICD implant, glomerular filtration rate was an independent predictor for all-cause mortality. Additionally, GFR<75ml/min/1.73m^2 at the time of device implant increased by 2.5-fold the risk of death, the risk doubles for each CKD stage increase, reaching a dramatic 14.7- fold higher risk of death for stage 5 patients.

CKD should not postpone device implant, as its deterioration significantly increases the risk of death.

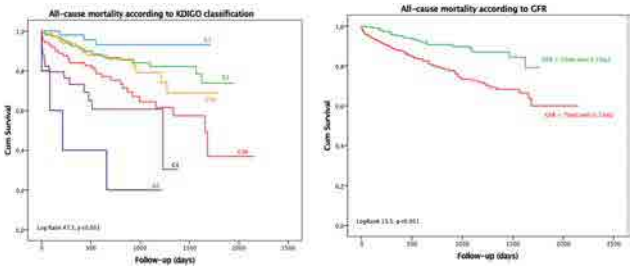


Figure:

P0808

DEFINING CRITERIA FOR CKD STAGE 3 PATIENTS NEPHROLOGY REFERRAL: AN ANALYSIS FOCUSED ON CKD PROGRESSION AND MORTALITY RISK

Luis Falcao[1], Sara Fernandes[1], Adriana Paixão Fernandes[1], Beatriz Donato[1], Mário Raimundo[1], Catarina Teixeira[1], Ana Cortesão Costa[1], Sónia Silva[1], Ana Macedo[2], Edgar Almeida[1]

[1]Hospital Beatriz Angelo, Nephrology, Loures, Portugal and [2]Keypoint, Lisbon, Portugal

Background and Aims: The high prevalence of CKD and its increasing awareness by primary care clinicians is posing a huge burden over health care systems, especially over Nephrology departments. While the referral of CKD stage 4 and 5 to a nephrology clinic is undisputable, the need for stage 3 patients referral is still subject to debate. Our objective was to investigate baseline characteristics of CKD stage 3 patients associated with subsequent CKD progression, in order to help determine which patients should be referred at this stage. Additionally, we investigated the association of CKD stage 3 progression with morbidity and overall mortality.

Method: We conducted a patient-level, retrospective, cohort analysis of all patients referred to a nephrology clinic over a 6 years period. We included CKD stage 3 patients with at least 36 months of follow-up or 24 to 36 months of follow up with more than 3 serum creatinine determinations. CKD progression was defined by one of the following: 1) an eGFR (CKD-EPI) decline superior to 5mL/min/year; 2) Serum creatinine duplication; 3) The need for chronic RRT. Baseline covariates included demographics, comorbid conditions and laboratory values. Univariate and multivariate analysis were employed to determine independent predictors of CKD progression and mortality.

Results: Out of the 3008 patients referred to the nephrology clinic, 1288 (42.8%) were CKD stage 3 patients and from these, 594 (19.8%) met the inclusion criteria (median age: 71.9 years; 63.8% male). Median follow-up was 4.9 years (IQR 2.2). 133 (22.4%) met the criteria for CKD progression and 110 (18.6%) died. In univariate analysis, CKD progression was associated with higher proteinuria (405.7 vs 65.5mg/gr, $p<0.001$), Diabetes (60.9 vs 45.3%, $p=0.002$), Congestive heart failure (CHF) (40.6 vs 28.7%, $p=0.009$), Anemia (OMS definition) (68.0 vs 44.7%, $p<0.001$), higher diuretic use (48.9 vs 34.1%, $p=0.002$) and higher mortality (40.9 vs 12.2%, $p<0.001$)

In multivariate logistic regression analysis, albuminuria over 300 mg/gr [Odds ratio (OR) 3.57, 95% CI 2.20 - 5.80, $p<0.001$] and Anemia (OR 1.97, 95% CI 1.20 – 3.22, $p=0.007$) were associated with CKD progression. The possible association with other variables was not confirmed.

The independent predictors of mortality were: CKD progression (OR 4.49, 95% CI 2.69-7.50, $p=<0.001$), Older age (OR per 1 year increase 1.03, 95% CI 1.01-1.05, $p=0.003$), presence of CHF (OR 1.75, 95% CI 1.03-2.98, $p=<0.037$), presence of Hyperkalemia at first consultation (OR 2.12, 95% CI 1.00 – 4.52, $p=0.049$) and Anemia (OR 1.93, 95% CI 1.03 - 3.62, $p=0.025$). Higher body mass index was associated with a lower risk of mortality (OR 0.58, 95% CI 0.35 – 0.95, $p=0.033$)

Conclusion: Our study suggests that patients with macroalbuminuria and anemia at first consultation are at increased risk for rapid CKD stage 3 progression. In this group, patients with CHF, anemia and hyperkalemia (even at first consultation) have a higher risk of mortality.

This study may be useful and help us in guiding which CKD stage 3 patients should be referred to a nephrology clinic.

P0809 LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PATIENTS WITH DIABETIC CHRONIC KIDNEY DISEASE

Byoung Geun Han[1], Jae Won Yang[1], Ji Hye Huh[2]

[1]Yonsei University Wonju College of Medicine, Nephrology, Wonju, Korea, Rep. of South and [2]Yonsei University Wonju College of Medicine, Endocrinology, Wonju, Korea, Rep. of South

Background and Aims: Left ventricle diastolic dysfunction (LVDD) is common cardiac changes in diabetic patients without renal insufficiency. LVDD is also frequently occurs in chronic kidney disease (CKD). Diabetic patients with CKD are at increased risk of developing cardiovascular diseases. Therefore, early detection and prevention of risk factors are critical. The aim of this study was to evaluate the impact of type 2 diabetes on left ventricular (LV) diastolic function among CKD stage 3 and 5 patients, and whether markers of fluid balance can predict LVDD.

Method: A total of 409 patients (age and sex matched non-diabetic CKD stage 3 [nDMCKD3], n = 106; diabetic CKD stage 3 [DMCKD3], n = 106; non-diabetic CKD stage 5 [nDMCKD5], n = 73; diabetic CKD stage 5 [DMCKD5], n = 124) were analyzed. The stage 3 CKD patients were retrospectively reviewed, and stage 5 CKD patients were prospectively analyzed. All cohort patients with stage 5 CKD were hospitalized to plan their first dialysis treatment. The following exclusion criteria were applied: ejection fraction less than 45%, history of coronary artery disease and/or intervention treatment, history of angina or myocardial infarction, abnormalities of cardiac rhythm, moderate or severe valvular heart diseases, systemic immunologic diseases, liver cirrhosis, malignancy, infection, and previous renal transplantation. Coronary artery disease having regional wall motion abnormalities on echocardiographic examination was also ruled out. Clinical and echocardiographic parameters were compared among groups. Echocardiography, bioimpedance spectroscopy, and serum NT-proBNP were analyzed in patients with stage 5 CKD. The LVDD was defined as E/é ratio greater than 15. Extracellular water/total body water (ECW/TBW) and NT-proBNP were used as markers of fluid balance.

Results: Patients with E/é ratio $>$ 15 presented with more advanced stages of CKD. Prevalence of LVDD in patients with diabetes was higher compared to those without diabetes. Patients in DMCKD5 group demonstrated higher E/é ratios compared to those with nDMCKD5, DMCKD3, and nDMCKD3 (16.63$\pm$5.04 vs. 14.12$\pm$4.60 vs. 14.69$\pm$4.65 vs. 13.07$\pm$3.76, $p < 0.001$). The E/é ratio in patients with DMCKD5 were significantly higher than those with DMCKD3 (16.63$\pm$5.04 vs. 14.69$\pm$4.65, $p = 0.003$). In contrast, the E/é ratio was not significantly different between nDMCKD3 and nDMCKD5 patients (13.07$\pm$3.76 vs. 14.12$\pm$4.60, $p = 0.099$). The ECW/TBW in patients with DMCKD5 were significantly higher than nDMCKD5 patients (0.51$\pm$0.04 vs. 0.48$\pm$0.05, $p <$0.001). In a multiple regression analysis, the presence of diabetes, serum albumin level, NT-proBNP, and ECW/TBW were significantly associated with LVDD in CKD5 patients.

Conclusion: Our results suggest that an echocardiographic examination and assessment of volume status should routinely be performed in patients with type 2 DMCKD. Early detection of LVDD before clinical symptoms are apparent is important, regardless of the stage of DMCKD. Fluid overload could be one of the aggravating factors of LVDD in DMCKD patients. Early evaluation of volume status and control of fluid overload should be considered important therapeutic approaches for LVDD in DMCKD patients, especially for those in advanced stages.

P0810

DOSAGE REDUCTION OF LOW MOLECULAR WEIGHT HEPARIN IN PATIENTS WITH RENAL DYSFUNCTION: EFFECTS ON ANTI-XA LEVELS AND CLINICAL OUTCOMES

Paul Hornung[1], Meriem Khairoun[1], Friedo W. Dekker[2], Karin A.H. Kaasjager[3], Albert Huisman[4], Lily Jakulj[5], Willem Jan Bos[6,7], Frits Rosendaal[2], Marianne Verhaar[1], Gurbey Ocak[1,2,6]

[1]University Medical Center Utrecht, Department of Nephrology and Hypertension, Utrecht, Netherlands, [2]Leiden University Medical Center, Department of Clinical Epidemiology, Leiden, Netherlands, [3]University Medical Center Utrecht, Department of Internal Medicine, Utrecht, Netherlands, [4]University Medical Center Utrecht, Department of Clinical Chemistry and Haematology, Utrecht, Netherlands, [5]Amsterdam University Medical Center, Dianet Dialysis Center and Department of Nephrology, Amsterdam, Netherlands, [6]Sint Antonius Hospital, Department of Internal Medicine, Nieuwegein, Netherlands and [7]Leiden University Medical Center, Department of Internal Medicine, Leiden, Netherlands

Background and Aims: To prevent bio-accumulation of low molecular weight heparins (LMWHs) in patients with an impaired kidney function, guidelines recommend dosage reduction and anti-Xa monitoring. The aim of this study was to investigate the effect of pre-emptive dosage reduction of LMWH on anti-Xa levels. Furthermore, we investigated the association between anti-Xa levels and bleeding, thrombotic events and mortality.

Method: In this single center study, we followed 499 patients with an estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73m2 in whom anti-Xa levels were measured. We observed how many patients had anti-Xa levels that fell within the target range (between 1.0 U/ml and 2.0 U/ml with once daily LMWH and between 0.6 U/ml and 1.0 U/ml with twice daily LMWH), with a standard protocol of a pre-emptive dosage reduction of LMWH (25% reduction in patients with an eGFR between 30 and 60 ml/min/1.73m2 and a reduction of 50% in in patients with an eGFR below the 30 ml/min/1.73m2).

Furthermore, Cox proportional hazard analyses were used to estimate hazard ratios with 95% confidence intervals (CIs) to investigate the association between anti-Xa levels and major bleeding, thrombotic events (ischemic stroke or venous thrombosis) and mortality within three months of follow-up. Hazard ratios were adjusted for age, sex, body mass index, type of LMWH, once or twice daily dosing, antiplatelet drug use, indication for anticoagulation, comorbidities, hemoglobin concentration and eGFR.

Results: In a cohort of 499 patients (445 dalteparin and 54 nadroparin users), the median anti-Xa level was 0.44 U/ml (IQR 0.21-0.75) for the total group (n=499). A pre-emptive dosage reduction of LMWH led to adequate levels of anti-Xa in only 19% of the patients (12% for the dalteparin users and 50% for nadroparin users).

Of the 499 patients, 104 patients had a major bleeding, 27 had a thrombotic event and 146 died within three months. We did not find an association between anti-Xa levels and bleeding or mortality (Table 1). An anti-Xa level below the target range was associated with a non-significant increased risk estimate for thrombosis (HR 2.5, 95% CI 0.7-8.8) after adjustment (Table 1).

Table 1. Anti-Xa levels and bleeding, thrombosis and mortality

	BLEEDING		THROMBOSIS		MORTALITY	
Anti-Xa levels	**Adjusted HR (95% CI)**		**Adjusted HR (95% CI)**		**Adjusted HR (95% CI)**	
Below range	1.0	(0.6-1.8)	2.5	(0.7-8.8)	1.2	(0.8-1.9)
Witdin range	1	ref	1	ref	1	ref
Above range	1.4	(0.6-3.4)	Not applicable		1.0	(0.4-2.4)

Conclusion: Pre-emptive dosage reduction of LMWH leads to low anti-Xa levels in a large proportion of patients and may lead to an undertreatment of patients with an impaired kidney function.

P0811 **CONFUSION BETWEEN ETIOLOGY AND PREDICTION IN CLINICAL OBSERVATIONAL STUDIES; HOW OFTEN DOES IT ARISE AND HOW CAN WE AVOID IT? A SCOPING REVIEW.**

Chava Ramspek[1], Friedo W. Dekker[1], Merel Van Diepen[1]
[1]Leiden University Medical Center, Clinical Epidemiology, Leiden, Netherlands

Background and Aims: In etiological research the aim is to uncover the causal effect of a specific exposure on an outcome. The aim in prediction research is to predict an outcome with the best accuracy, irrespective of possible causality. Although in observational research both types of studies use similar statistical methods (generally multivariable modelling), the interpretation differs. For example, when researching the causal effect of BMI on kidney failure, it is important to correct for confounders such as age (i.e. factors that causally affect both BMI and kidney failure). Judgement of confounders must be made on pre-existing knowledge. If we select confounders based on the data, we might also correct for hypertension and atherosclerosis (as they are associated with BMI and kidney failure). As this correction is in the causal pathway we would erroneously conclude that BMI does not affect the risk of kidney failure. Vice versa, a mortality prediction model for dialysis patients may include antihypertensive medication use as a predictor. It would be wrong to conclude that patients should discontinue this medication to improve prognosis; the medication use is a marker for a certain health status and we cannot interpret it in a causal manner. Similar to these examples, we've found that characteristics from etiology and prediction are often confused, leaving us with studies that may be misinterpreted. The aim of the current study is to quantify the amount of confusion between etiology and prediction in clinical observational studies and identify common mistakes that lead to this confusion.

Method: Studies published in January 2018 in the top journals of four distinct medical fields: General & Internal medicine, Surgery, Cardiology and Nephrology were screened for inclusion. Original research studies on observational cohorts of humans were included. A list of key study characteristics of etiological and prediction research was developed by CLR and MvD in an iterative fashion. From these characteristics signaling questions for confusion were developed to score included studies.

Results: The developed key study characteristics of etiology and prediction are shown in the table. In total, 286 studies were screened of which 123 were included. Overall, 27% (n=33) of included articles contained some form of confusion between etiology and prediction. In the figure the journal impact factor is mapped against proportion of confusion per included journal. We can see a trend that as impact factors increase the amount of confusion decreases. In etiological studies, the most frequent (n=15) form of confusion was adjustment for variables based on predictive performance in the data, instead of known causal structure. **T**he majority selected 'confounders' purely based on p-values and therefore potentially adjusted for intermediate variables, resulting in incorrect effect estimates. Another mistake in etiological studies (n=5) was the reporting of predictive performance measures such as the C-statistic for an etiological model. In prediction studies the most confusion occurred in the discussion (n=14). Seven studies interpreted predictors causally, for example by concluding that these predictors should be modified in order to improve patient outcomes. As the effect estimates of these studies do not account for confounding, this interpretation is invalid. Lastly, seven studies mention residual confounding as a limitation, which is only a problem in etiological research.

Conclusion: Confusion between etiology and prediction is a wide-spread methodological flaw in medical observational studies, particularly those published in lower impact clinical journals. As confusion may lead to erroneous conclusions, the distinction between causal and predictive research deserves more attention in medical research and scientific education.

	ETIOLOGY	PREDICTION
Introduction	Objective is to find a causal association between exposure(s) and outcome(s)	Objective is to predict or improve prediction of an outcome
Methods	Controls for confounding, using knowledge of causal structure	Includes variables based on their ability to predict the outcome and usability in practice
Results	Relative or absolute risk given the exposure, minimizing bias	Performance measures of the multivariable model
Discussion	Causal interpretation and/or recognition of residual or unmeasured confounding as limitation	Multivariable model proposed for use in risk stratification or prediction of prognosis/diagnosis on an individual level

Figure:

P0812 LONG-TERM EFFECTS OF AIR POLLUTANTS ON MORTALITY RISK IN PATIENTS WITH END-STAGE RENAL DISEASE

Jae Yoon Park[1], Jiyun Jung[2], Sung Woo Lee[3], Ho Kim[2], Jung Pyo Lee[4]

[1]Dongguk University Ilsan Hospital, Goyang-si, Korea, Rep. of South, [2]Seoul National University, School of Public Health, [3]Nowon Eulji Medical Center, Department of Internal Medicine and [4]Seoul National University, Department of Internal Medicine

Background and Aims: Long-term exposure to air pollutants significantly increases the morbidity and mortality associated with various diseases. However, little is known about the relationship between air pollutants and end-stage renal disease (ESRD)-related mortality.

Method: A total of 5041 patients who started dialysis between 2008 and 2015 were prospectively enrolled in the Clinical Research Center for End-Stage Renal Disease (CRC-ESRD) cohort study. We assigned a daily mean concentration of air pollutants (PM_{10}, NO_2, and SO_2) to each participant. Time-varying Cox models were used to investigate the relationship between air pollutants and mortality in ESRD patients.

Results: During the follow-up period (mean 4.18 years), 1475 deaths occurred among 5041 participants. We found a significant long-term relationship between mortality risk and PM_{10} (HR 1.33, CI 1.13–1.58), NO_2 (HR 1.46, CI 1.10–1.95), and SO_2 (HR 1.07, CI 1.03–1.11). Elderly patients and patients who lived in metropolitan areas had an increased risk associated with PM_{10}. Elderly patients also had increased risks associated NO_2 and SO_2.

Conclusion: Long-term exposure to air pollutants had negative effects on mortality in ESRD patients. These effects were prominent in elderly patients who lived in metropolitan areas, suggesting that ambient air pollution, in addition to traditional risk factors, is important for the survival of these patients.

P0813

FRAILTY MODIFIES THE ASSOCIATION BETWEEN OPIOID USE AND MORTALITY IN CHRONIC KIDNEY DISEASE PATIENTS: A POPULATION-BASED COHORT STUDY

CHIA-TER CHAO[1]

[1]*National Taiwan University Hospital Beihu branch, Nephrology division, Department of Internal Medicine, Taipei, Taiwan, R.O.C.*

Background and Aims: The prevalence of chronic pain in patients with chronic kidney disease (CKD) is high and is associated with higher frailty risk, but satisfactory pain control frequently fails to be achieved. Opioid remains instrumental regarding optimal pain management, but its influence on outcomes can be of concern in CKD patients. We examined whether opioid use affected patient outcome and whether such relationship was modified by frailty.

Method: From the longitudinal cohort of diabetic patients (n = 840,000), a well-maintained population-based cohort, we identified those with CKD who were opioid user (at least 7 days within any month; n = 26,029), followed by propensity score-matched to opioid never-users from the same cohort in a 1:1 ratio, based on demographic features, comorbidities, and other medications. We analysed the associations between opioid use and survival in these patients according to their baseline frailty status, defined by the modified FRAIL (Fatigue, Resistance, Ambulation, Illness, and Loss of weight) scale.

Results: Among the enrolled CKD participants (mean age 62.9 ± 13.5 years, 48.2% female), 20.3% did not have any FRAIL item satisfied, while 57.2%, 20.6%, and 1.9% had 1, 2, and at least 3 positive FRAIL items at baseline, respectively. After a median of 4.2 years, 16.4% participants died. Univariate analysis showed that opioid users had an elevated risk of morality compared to non-users (hazard ratio [HR] 1.124, 95% confidence interval [CI] 1.08 – 1.17) (**Figure**). Cox proportional hazard regression showed that opioid users exhibited an 18.3% higher risk of mortality compared to non-users (HR 1.183, 95% CI 1.13-1.24) among patients with CKD; furthermore, the mortality risk associated with opioid use was observed in CKD participants without frailty only (HR 1.18, 95% CI 1.13-1.24) but not in those with frailty (HR 1.08, 95% CI 0.83 – 1.4).

Conclusion: Opioid use might lead to a higher risk of mortality among CKD patients, but this relationship was observed among those without frailty only. Interestingly, frail CKD patients who were opioid users were not at an elevated risk of mortality compared to non-users.

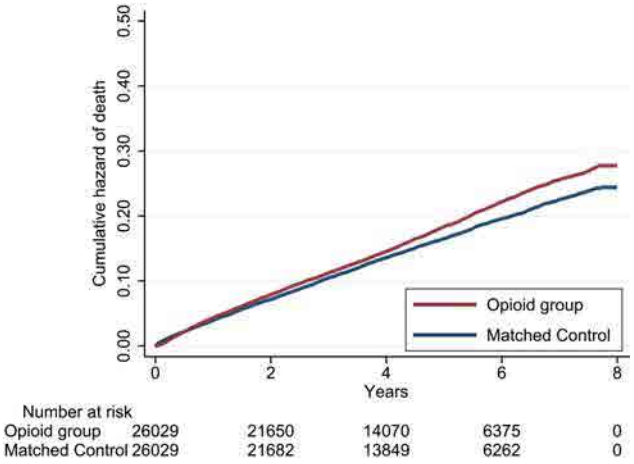


Figure:

P0814 NEW STRATEGIES TO DECREASE THE ANNUAL RATE OF DIALYSIS INITIATIONS AT A HOSPITAL IN CENTRAL TOKYO

Kyohei Ogawa[1], Akira Fukui[1], Yukio Maruyama[1], Masaomi Nangaku[2], Naoki Kashihara[3], Takashi Yokoo[1]

[1]The Jikei University School of Medicine, Division of nephrology and hypertension, Tokyo, Japan, [2]The university of tokyo school of medicine, Nephrology, Tokyo, Japan and [3]Kawasaki Medical School, Nephrology, Kurashiki, Japan

Background and Aims: The Japanese Government and the Japanese Society of Nephrology (JSN) have enacted measures against chronic kidney disease (CKD) since 2008. Since then, the number of age-adjusted dialysis initiations has decreased. However, the absolute number has not decreased due to aging of the population. In response, the Japanese Government launched new CKD measures in 2018, with a focus on earlier intervention by nephrologists, utilizing referral criteria from family doctors to nephrologists. The primary goal of the new measures is to decrease the annual number of dialysis initiations nationwide by 10% by 2028. The Japan Kidney Association (JKA), also established in 2018, has appointed representatives in each prefecture to work on CKD measures according to the local requirements in cooperation with the Government, family doctors, and organizations. The large number of family doctors and medical examinations facilities that refer to the hospital in central Tokyo lead to difficulty determining the referral criteria that is used. Therefore, the aim of this study is to formulate new CKD measures in our hospital as one of the JKA representatives of Tokyo.

Method: A retrospective survey of medical history was conducted for 104 patients who initiated hemodialysis or peritoneal dialysis at our hospital in 2018. These patients represent approximately 3% of the total number of dialysis initiations in Tokyo, with 33 patients originating from outside Tokyo prefecture. Of the 104 patients, 80 were male with an average age 65.9 years. The primary disease of patients was comprised of 30 with diabetic nephropathy, 25 with renal sclerosis, 16 with chronic glomerulonephritis, 4 with polycystic kidney disease, and 29 from other or unknown diseases.

Results: Of the 86 patients whose information was confirmed, 45 patients were referred to nephrologists from 15 departments in our hospital, including 12 from diabetic departments, 7 from urology departments, 4 from cardiovascular departments, 3 from the emergency department, oncology department, and neurology department, and 11 from various other departments. The remaining 41 patients were from outside our hospital (30 from family doctors and 11 from medical examination facilities). Of the 57 patients whose eGFR was confirmed at referral, 21 were referred with eGFR$<$15, 27 at 15$\leqq$eGFR$<$30, and only 9 were referred at eGFR$\geqq$30. Criteria of eGFR$<$45 or proteinuria$\geqq$1+ or 0.5g/gCr is recommended in the 2018 Evidence-based Clinical Practice Guideline for CKD by the JSN.

Conclusion: According to the medical history of 104 patients who initiated dialysis at our hospital in 2018, the timing of referral to nephrologists was often later than recommended. Patients were referred to nephrologists from at least 15 departments in our hospital. Therefore, it is important for the referral criteria to be widely disseminated not only among family doctors but also among hospital departments and medical examination facilities. Specifically, in-hospital referrals are considered to be less burdensome for patients than out-of-hospital referrals and are therefore expected to be first-targets for new strategies. In addition, in recent years, the frequency of measurement of sCr and eGFR has increased in medical examinations, where the dissemination of referral criteria becomes even more important. Furthermore, the JSN and the JKA have committed to develop medical staff, including nurses/public health nurses, registered dietitians, and pharmacists, to be certified kidney disease educators who have basic knowledge of CKD. Since these occupations can intervene before referral to nephrologists, they are expected to have a significant effect on CKD measures.

P0815 ASSOCIATIONS BETWEEN ALCOHOL CONSUMPTION AND CHRONIC KIDNEY DISEASE: A POPULATION-BASED SURVEY

Hon-Yen Wu[1,2,3], Wan-Chuan Tsai[1,2], Le-Yin Hsu[2], Yu-Sen Peng[1,3]

[1]Far Eastern Memorial Hospital, Department of Internal Medicine, New Taipei City, Taiwan, R.O.C., [2]National Taiwan University College of Public Health, Institute of Epidemiology and Preventive Medicine, Taipei City, Taiwan, R.O.C. and [3]National Taiwan University Hospital and College of Medicine, Department of Internal Medicine, Taipei City, Taiwan, R.O.C.

Background and Aims: Observational studies suggest an association between moderate alcohol consumption and cardioprotective effects. However, the role of alcohol consumption on chronic kidney disease (CKD) remains inconclusive, and little is known about whether age influences the effects alcohol consumtion. This study aimed to evaluate the associations between alcohol consumption and chronic kidney disease in a population-based survey.

Method: We used data from the Taiwanese Survey on Prevalences of Hypertension, Hyperglycemia, and Hyperlipidemia. This is a population-based survey which applied a multistage, stratified, and random sampling from population throughout Taiwan in 2007. The survey assessed the prevalence, awareness, and treatment of metabolic syndrome by body measurements, structured questionnaires, and examinations of blood and urine. We obtained data of adult participants, including demographic characteristics, anthropometric measurements, lifestyle habits, and results of blood and urine exams. According to the frequency of alcohol consumption, we categorized participants into frequent drinkers (at least 1 time per week), occasional drinkers (less than 1 time per week), and nondrinkers. The study outcome was CKD, which was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 or a dipstick proteinuria $\geq 1+$. The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. We used univariate and multivariate logistic regression analyses to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for study outcome comparing different levels of alcohol consumption. To evaluate the influence of age, we stratified participants into younger (age < 45 years) and older (age ≥ 45 years) subgroups.

Results: The mean age of the participants were 48 years, with a female prevalence of 53% and CKD prevalence of 12%. There were 2,197 older participants and 1,770 younger participants. There were 548 frequent drinkers, 915 occasional drinkers, and 2,504 nondrinkers. Compared with nondrinkers, occasional drinkers (OR 0.59, 95% CI 0.43-0.81) and frequent drinkers (OR 0.61, 95% CI 0.44-0.87) showed a lower hazard risk of CKD (Table). Among those with an age ≥ 45 years, occasional drinkers (OR 0.56, 95% CI 0.30-0.81) showed a lower risk of CKD but frequent drinkers (OR 0.70, 95% CI 0.49-1.01) showed a borderline lower risk of of CKD compared with nondrinkers (Table). Among those with an age < 45 years, only frequent drinkers (OR 0.36, 95% CI 0.13-1.00) showed a lower risk of CKD compared with nondrinkers (Table).

Conclusion: Our study showed that alcohol consumption was associated with a lower risk of CKD, and this effect seemed to be more prominent among frequent drinkers and those with an age ≥ 45 years. Whether alcohol consumption provides renoprotective effects, as well as the influence of age, requires longitudinal studies.

Table. Logistic regression analyses for chronic kidney disease among participants with different levels of alcohol consumption

	All participants			Age ≥ 45 years			Age < 45 years		
Frequency of alcohol consumption	Number at risk	OR	95% CI	Number at risk	OR	95% CI	Number at risk	OR	95% CI
Nondrinkers	2054			1449			1055		
Occasional drinkers	915	0.59	0.43 – 0.81 *	426	0.56	0.30 – 0.81 *	489	0.63	0.31 – 1.28
Frequent drinkers	548	0.61	0.44 – 0.87 *	322	0.70	0.49 – 1.01	226	0.36	0.13 – 1.00 *

Abbreviations: OR, odds ratio; CI, confidence interval.
*$P \leq 0.05$.
Model adjusted for age, sex, body mass index, education level, stroke, cardiovascular disease, hypertension, gout, hemoglobin, glycated hemoglobin, aspartate aminotransferase, and C-reactive protein.

Figure:

P0816

CLINICAL CHARACTERISTICS AND EGFR AND UACR DISTRIBUTION ACCORDING TO THE 2012 KDIGO CKD CLASSIFICATION: A REPORT FROM THE US DISCOVER CKD COHORT

Juan Jose Garcia Sanchez[1], Juan Jesus Carrero[2], Supriya Kumar[3], Roberto Pecoits-Filho[4,5], Glen James[1], Hiddo Lambers Heerspink[6], Stephen Nolan[1], Carolyn Lam[7,8], Tony Chen[3], Eiichiro Kanda[9], Naoki Kashihara[9], Mikhail Kosiborod[10], Mitja Lainscak[11], Carol Pollock[12], David Wheeler[13]

[1]AstraZeneca, United Kingdom, [2]Karolinska Institutet, Department of Medical Epidemiology, Sweden, [3]AstraZeneca, United States of America, [4]School of Medicine , Pontifical Catholic University of Parana, Brazil, [5]Arbor Research Collaborative for Health, United States of America, [6]University of Groningen, Department of Clinical Pharmacy and Pharmacology, Netherlands, [7]National Heart Centre, Department of Cardiology, Singapore, [8]Duke NUS, Medical School, United States of America, [9]Kawasaki Medical School, Japan, [10]University of Missouri-Kansas City, Saint Luke's Mid America Heart Institute, United States of America, [11]General Hospital Murska Sobota, Division of cardiology, Slovenia, [12]University of Sydney, Kolling Institute, Australia and [13]University College London, Department of Renal Medicine, United Kingdom

Background and Aims: In 2012, the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommended categorising and prognosticating chronic kidney disease (CKD) based on estimated glomerular filtration rate (eGFR) and urine albumin to creatinine ratio (UACR). Contemporary studies describing the prevalence and characteristics of patients with CKD categorised according KDIGO 2012 and how studies of new pharmacotherapies relate to these categories are scarce. One such new therapy class of key interest are the sodium glucose co-transporter 2 inhibitors (SGLT-2i), shown to delay the progression to renal failure and prevent cardiovascular/renal death in patients with CKD. We aimed to describe patient characteristics and the prevalence of CKD according to the 2012 KDIGO categories in a large real-world US cohort of patients with CKD (part A). We also describe a subset of the population according to the DAPA-CKD trial inclusion criteria (eGFR [25-75ml/min/1.73m^2] and UACR [200-5000mg/g]) (part B).

Method: DISCOVER-CKD is an international observational study in patients with CKD. The DISCOVER-CKD retrospective US cohort of patients was extracted using real-world data from the integrated Limited Claims and Electronic Health Record data (IBM Health, Armonk, NY) and HealthVerity. Patients were aged ≥18 years, with ≥1 UACR measure. For part A, required first diagnostic code of CKD (Stages 3A, 3B, 4, 5, or ESRD) or two eGFR of <75 mL/min/1.73 m^2 recorded at least 90 days apart and for part B, two measures of eGFR 25-75 mL/min/1.73 m^2 recorded at least 90 days apart between 1st January 2008 and September 2018. Index date was diagnostic code or 2nd eGFR. The first UACR, recorded +/-12 months of index, was used to categorise patients. Descriptive analyses were used to summarise prevalence and patient characteristics.

Results: Of the overall study cohort (N=4330, 49.1% women, mean age 65.3±10.64 years), by KDIGO categories (part A): 85.7% (n=3601) had normal to mildly increased albuminuria, 11.0% (n=463) had moderately increased albuminuria and 3.3% (n=137) had severely increased albuminuria (Figure 1). 4.6% (n=193) fulfilled DAPA-CKD trial inclusion criteria (part B). In both populations, the most common comorbidities were hypertension (HTN, 73.0% for both) and type 2 diabetes (T2D, 57.6% and 56.2%, respectively). Anti-hypertensive drugs were frequently used (76.4% and 76.9%, respectively).

Conclusion: This study, utilising real-world data, adds to the scarcity of knowledge reporting the characteristics of patients with CKD in different eGFR and UACR strata according to the KDIGO 2012 definitions. We observed a trend in higher UACR in the group of patients with lower eGFR and report a high prevalence of T2D and HTN in the study population, demonstrating the high co-morbidity burden in patients, for whom new therapies may be beneficial.

KDIGO 2012 eGFR & UACR Categories

eGFR (mL/min/1.73m2)	UACR (mg/g) 0-29	30-299	≥300
60-75	2253 (62.6%)	161 (34.8%)	34 (24.8%)
45-59	1002 (27.8%)	244 (52.7%)	63 (46.0%)
30-44	194 (5.4%)	45 (9.7%)	28 (20.4%)
15-29	27 (0.7%)	12 (2.6%)	10 (7.3%)
0-14	125 (3.5%)	1 (0.2%)	2 (1.3%)
Total	3601 (85.7%)	463 (11.0%)	137 (3.3%)

DAPA-CKD Trial eGFR & UACR Categories

eGFR (mL/min/1.73m2)	UACR (mg/g) 200-5000
60-75	48 (24.9%)
45-59	91 (47.2%)
30-44	39 (20.1%)
25-29	15 (7.8%)
Total	193 (100%)

Figure 1: Prevalence of CKD from a retrospective US cohort of patients, included in DISCOVER-CKD, according to the 2012 KDIGO (left figure) and DAPA-CKD trial categories (right figure).

P0817

SMOKING WAS ASSOCIATED WITH LOWER SERUM LEVEL OF SOLUBLE ALPHA KLOTHO IN PATIENTS WITH NON-DIALYSIS CHRONIC KIDNEY DISEASE:RESULTS FROM THE KOREAN COHORT STUDY FOR OUTCOMES IN PATIENTS WITH CHRONIC KIDNEY DISEASE (KNOW-CKD)

DONG-WAN CHAE[1], Yong Jin Yi[1], Jong Chul Cheong[1]

[1]*Seoul National University Bundang Hospital, Internal Medicine, Gyeonggi-do, Korea, Rep. of South*

Background and Aims: Soluble αklotho (sklotho) in systemic circulation, which is mainly derived from renal tubule, has been reported to play important roles in mineral bone disorders, cardiovascular complications and renal progression in CKD. Although decreased renal parenchymal mass is thought to be a main cause of decreased serum level of sklotho in CKD, various factors causing renal tubular injury such as hypoxia, oxidative stress, proinflammatory cytokines and uremic toxins are also known to decrease the renal tubular expression of αklotho. Because smoking contributes to hypoxia and oxidative damage, we hypothesized that smoking might be related to decreased sklotho in patients with non-dialysis CKD.

Method: To test this hypothesis, we analysed data of 2,101 subjects with non-dialysis CKD from a currently on-going Korean multi-centers prospective cohort study of CKD (KNOW-CKD, NCT01630486 at www.clinicaltrials.gov) in whom serum klotho was measured using an enzyme-linked immunosorbent assay kit (Immuno-Biological Laboratories Co, Gunma, Japan). The intra-assay and inter-assay coefficients of variations were 0.57-1.78% and 3.01-6.12% respectively.

Results: Mean age was 53.6±12.2 years and 1282 (61.0%) were men. The number of current, former and never smokers were 338 (16.1%), 642 (30.6%), and 1118 (53.2%) respectively. The median pack-year was 20.0 (interquartile range: 10.0-35.0). Mean eGFR by CKD-EPICr equation was 53.0±30.7 ml/min/1.73m2 and mean UACR was 903.9±1423.8 mg/g. Median serum sklotho was 536.0 (IQR: 419.5 – 667.0) pg/ml. In multivariable linear regression with backward stepwise adjustment by all significant factors for sklotho in univariate linear regression, smoking pack-year was independent variable for sklotho. (β= -0.786, p=0.032 95% CI for β: -1.504 to -0.069). Age and serum uric acid were also negatively associated with sklotho, while eGFR, serum alkaline phosphatase, and serum hemoglobin were positively associated with sklotho in the same analysis. Median sklotho of never, former, and current smokers were 551.0 (IQR:430 – 689.3) pg/ml, 509.5 (IQR: 407.8 – 645.3) pg/ml, and 521. (IQR: 397.8 – 645.0) pg/ml respectively. Linear mixed model adjusted by sex, age, eGFR, hemoglobin, alkaline phosphatase, and uric acid demonstrated that sklotho in never smokers was significantly higher than former (p=0.004) and current smokers (p=0.001). But there was no difference in sklotho between former and current smokers.

Conclusion: Smoking was associated with lower serum sklotho in non-dialysis CKD. But no difference in sklotho between former and current smoker casted doubt on causal relationship between smoking and serum sklotho

P0818

IMPROVING MORTALITY TRENDS FOR PATIENTS WITH CHRONIC KIDNEY DISEASE IN THE IRISH HEALTH SYSTEM: THE IRISH KIDNEY DISEASE SURVEILLANCE SYSTEM (IKDSS)

Matthew Laird[1], Raihan Alheyali[1], Leonard Browne[1,2], Liam Plant[3,4], Cathal Walsh[2,5], Stack Austin[1,2,6]

[1]University of Limerick, Graduate Entry Medical School, Limerick, Ireland, [2]University of Limerick, Health Research Institute, Limerick, Ireland, [3]University College Cork, College of Medicine and Health, Cork, Ireland, [4]Cork university Hospital, Department of Renal Medicine, Cork, Ireland, [5]University of Limerick, Department of Mathematics and Statistics, Limerick, Ireland and [6]University Hopsital Limerick, Department of Nephrology, Limerick, Ireland

Background and Aims: It is unclear whether targeted efforts for the treatment of chronic kidney disease (CKD) has led to a sustained reduction in mortality rates. We examined annual trends in mortality for patients with and without CKD in the Irish health system.

Method: We utilised data from the Irish Kidney Disease Surveillance System (IKDSS) to explore 1-year mortality rates among patients with and without CKD in the health system. The principal data sources included; regional laboratory information systems; dialysis registers; and mortality data files from the national Central Statistics Office (CSO). We created multi-annual cohorts of patients, age > 18 years with one or more serum creatinine values who received healthcare within the Irish health system from 2008 to 2012. Serum creatinine values (first test in fiscal year) were used to calculate glomerular filtration rate (eGFR) and CKD was defined as GFR < 60ml/min/1.73m. Mortality data were available from the national mortality files with vital status up to December 31st 2013. Age standardised death rates were determined for the Irish population (IRE) and the European Standard Population (ESP) (standardised to the age distribution of a standard European population in 2012. Comparisons were conducted using segmented linear regression.

Results: We included 351,223 adult individuals between 2008 and 2012. Age standardised mortality rates (EU) were more than 2-fold higher for patients with CKD than without, *P<0.001*. From 2008-2012, age-standardised mortality rates decreased significantly in patients with CKD from a peak of 47.7 to 31 per 1000 person-years, P for trend=p=0.012, and from a peak of 17.8 to 15.5 per 1000 person-years in patients without CKD, *P*=0.006. Mortality rates for men were significantly higher than for women in patients with and without CKD, but the pattern of improvement was similar for both sexes. These patterns were replicated when comparisons were made using Irish standard age distribution.

Conclusion: Mortality rates among CKD patients have declined in the Irish population from 2008 to 2012 in both men and women. The processes and interventions that have led to these reductions need further exploration.

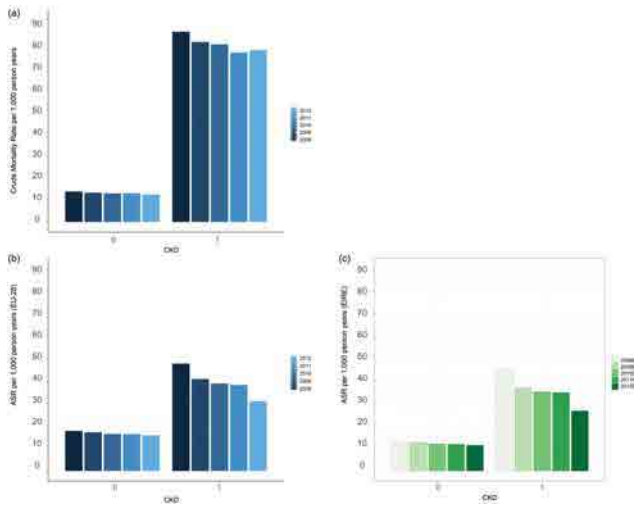


Figure:

Figure 1. (a) Crude and age standardised mortality rates (b-c) of those with and without CKD in the Irish Health System between 2008-2012 .

P0819 **THE EFFECT OF SMOKING UPON CKD IN A JAPANESE NATIONWIDE 6-YEARS FOLLOW UP SERVEY**

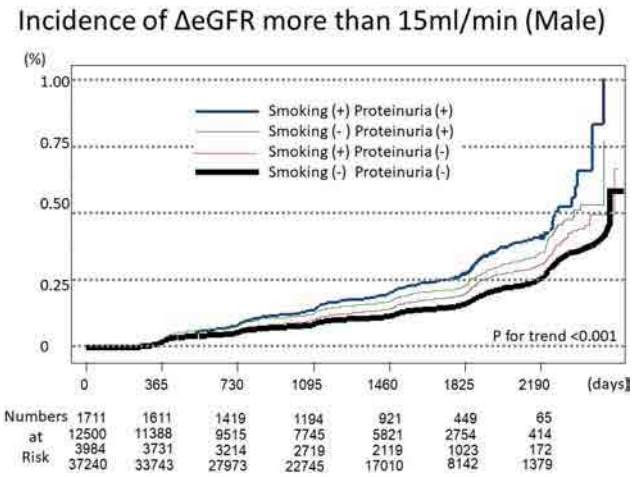
Yasuyuki Nagasawa[1], Ayako Matsumoto[1], Ryohei Yamamoto[2], Maki Shinzawa[2], Yoshitaka Isaka[2], Yoshimasa Nanami[1], Yukiko Hasuike[1], Kuragano Takahiro[1], Kunitoshi Iseki[3], Kunihiro Yamagata[3], Kazuhiko Tsuruya[3], Hideaki Yoshida[3], Shouichi Fujimoto[3], Koichi Asahi[3], Tsuyoshi Watanabe[3], Toshiki Moriyama[2,3]

[1]Hyogo College of Medicine, Devision of Kidney and Dialysis, Nishinomiya, Japan, [2]Osaka University, Department of nephrology, suita, Japan and [3] Steering Committee for the "Research on the Positioning of Chronic Kidney Disease (CKD) in Specific Health Check and Guidance in Japan",, Tokyo, Japan

Background and Aims: Cigarette Smoking is one of important risks for cardiovascular diseases, and also smoking had been reported to have harmful effect upon Choric kidney Diseases. Our group had reported that smoking canceled the beneficial effect caused by alcohol drinking using Japanese Nationwide Survey cross-sectional data (Matsumoto-A et al Hypertension Res, 2017). In this cohort study, we aimed to reveal the effect of smoking upon incidence of proteinuria and decline of kidney function using longitudinal large cohort of general population in Japan.

Method: The present nationwide longitudial survey included members of the general Japanese population who underwent the Specific Health Check and Guidance in Japan between April 2008 and March 2014. 149,260 who were not lack of essential data without chronic kidney diseases and whose kidney function was 60≦eGFR<120mL/min/1.73m^2 were enrolled in this analysis. Demographic, physical, and laboratory data included age, sex, body mass index (BMI; weight [kg]/height^2 [m^2]), mean arterial pressure (MAP, diastolic blood pressure + [systolic blood pressure - diastolic blood pressure]/3), serum concentration of creatinine (enzymatic method), and levels of hemoglobin A1c, triglycerides, high-density lipoprotein (HDL) cholesterol, uric acid, and urinary protein as detected by a dipstick test. Proteinuria was defined as 1+ or more of urinary protein. We made statistical analysis using Kaplan-Meier analysis, Log-rank test, Cox proportional hazard method using STAT ver15. As outcomes, incidence of proteinuria (more than (1+) by dip stick, decline of eGFR more than 15 mL/min/1.73m^2 from baseline kidney function were used.

Results: Smoker had significantly higher incidence rate of proteinuria than non-smoker ($p<0.001$). Smoker also had significantly higher incidence decline of kidney function more than 15ml/min than non-smoker ($p<0.001$). Smoking was significantly risk both for proteinuria (Hazard Rate 1.24(95%CI 1.15-1.34, $p<0.001$)) and for decline of kidney function HR 1.24(95%CI 1.16-1.31, $p<0.001$) in multivariate analyses. After stratification of four groups using smoking status and incidence of proteinuria during study periods. Smoker with incident proteinuria had significantly higher rate of decline of kidney function than non-smoker without incident proteinuria both in male (figure 1) and in female (Figure 2)



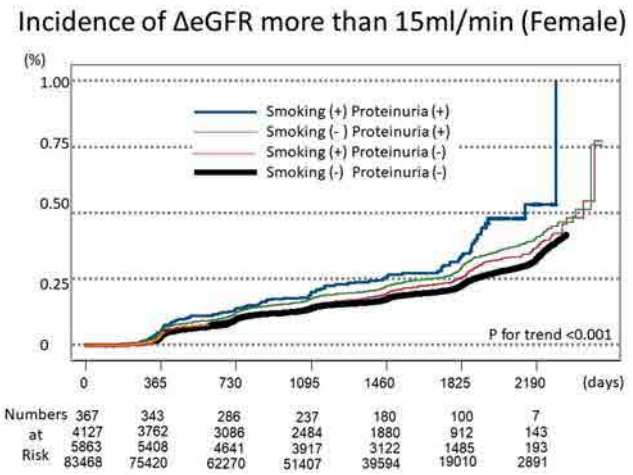


Figure 2 Conclusion: Smoking was risk for proteinuria and decline of kidney function. Moreover, smoker with incident proteinuria had worst kidney prognosis.

Figure 1 :

P0820

EMERGENCY DEPARTMENT UTILIZATION BY PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE AND DIALYSIS: A POPULATION BASED STUDY

Ruchi Chhibba[1,2], Silvia Leon-Mantilla[2,3], Thomas Ferguson[2], Paul Komenda[2,4], Navdeep Tangri[2,4], Claudio Rigatto[2,4]

[1]University of Manitoba, Emergency Medicine, Winnipeg, Canada, [2]Seven Oaks General Hospital, Chronic Disease Innovation Centre, Winnipeg, Canada, [3]University of Manitoba, Community Health Sciences, Winnipeg, Canada and [4]University of Manitoba, Internal Medicine, Winnipeg, Canada

Background and Aims: Chronic Kidney Disease (CKD) is a potent risk factor for kidney failure, cardiovascular events and all cause hospitalizations. In addition to higher outpatient resource use, patients with CKD may present more frequently to the emergency department (ED) and may be more likely to be admitted for hospitalization. In Manitoba, we previously demonstrated an 8-fold increase in the frequency of ED presentations by patients on dialysis as compared to a non-dialysis population. Comparable data on ED visits remain sparse for patients with CKD G3-G5, not on dialysis. Here, we aim to describe the frequency of ED visits and highlight differences in reasons for visit in patients with CKD stages G3-G5 and Those on dialysis when compared to a non-renal population.

Method: We performed a retrospective cohort study using administrative health data from the Winnipeg Regional Health Authority, Canada. We included all adults ($\geq$ 18 years) with CKD stages G3-G5 and patients undergoing dialysis between January 1st, 2010 and December 31, 2014. Secular trends in the in the rates of ED visits were calculated for those with CKD, those on dialysis and in the non-renal population.

Results: Over the study period, patients undergoing dialysis had the highest incidence of ED visits, followed by patients with CKD and those with normal kidney function (150 vs 106 vs 34 per 100 persons per year respectively). These rates were stable over the period studied. Among the non-renal population, the most common reasons for an ED visit were musculoskeletal complaints (25.6%), followed by gastrointestinal (11.04%) and cardiovascular complaints (10.26%). In the CKD and dialysis cohort, ED visits were more commonly secondary to cardiovascular complaints (21.54% and 18.99% respectively), followed by respiratory and gastrointestinal complaints. Admission to hospital was higher in CKD and dialysis populations than in the non-renal population (29.56%, 26.07% vs 10.61%, respectively).

Conclusion: Patients with CKD present frequently to the ED, and are often admitted after presentation. Cardiovascular and respiratory complaints are more common in the CKD population.

P0821 **OBESITY, FAT TISSUE, CELL MEMBRANE INTEGRITY PARAMETERS AND ARTERIAL STIFFNESS IN RENAL TRANSPLANT RECIPIENTS**

Zbigniew Heleniak[1], Sarah Illersperger[2], Susanne Brakemeier[2], Alicja Debska-Slizien[1], Klemens Budde[2], Fabian Halleck[2]

[1]Medical University of Gdansk, Nephrology, Transplantology and Internal Medicine, Gdańsk, Poland and [2]Universitätsmedizin Berlin, Medizinische Klinik mit Schwerpunkt Nephrologie und Internistische Intensivmedizin Charité -, Berlin, Germany

Background and Aims: Arterial stiffness, altered body composition (increased body fat mass and decreased soft lean mass) and cell membrane integrity (Phase Angle) are acknowledged risk factors for adverse outcomes after kidney transplantation related to cardiovascular diseases. Phase angle is a linear method of measuring the relationship between electric resistance and reactance. Taking the arc tangent value of the ratio of reactance versus electric resistance provides us with the phase angle value. Lower phase angles appear to be consistent with low reactance and equals either cell death or a break-down in the selective permeability of the cell membrane. The aim of the study was the assessment of the relationship between arterial stiffness and fat tissue parameters, cell membrane integrity marker in renal transplants recipients (RTRs).

Method: 344 stable RTRs with the mean age 52.7 years, (62.5% M) transplanted between 1994 and 2018 were randomly enrolled to the study. The following parameters of arterial stiffness were measured: brachial-ankle and carotid-femoral pulse wave velocities (baPWV left and right, cfPWV). The obesity and fat tissue (body mass index (BMI), waist to hip ratio (WHR), body fat mass (BFM), fat free mass (FFM), percent fat of the body (PBF), trunk segmental fat analysis (TSFA) and visceral fat area (VFA)) parameters and cell membrane integrity phase angle (PhA) were assessed with InBody 170.

Results: The median time of dialysis and after kidney transplantation was 58.5 and 78 months respectively. The obesity according to BMI, WHR and VFA was diagnosed in 49.7%, 45% and 44.5% of patients, respectively. The median value of BFM, FFM, VFA, TSFA, PhA and the mean value of PBF were 19.3kg, 55kg, 93.2cm^2, 24.9 kg, 4.9 and 27.3%, respectively. We found significant positive correlations between WHR, VFA and baPWV right, baPWV left and cfPWV. PhA correlated with arterial stiffness in univariate (r=-0.34) and multivariate analysis (R=-0.23), negatively ($p<0.05$).

Conclusion:

1. Obesity, visceral fat tissue, cell membrane integrity marker influence on arterial stiffness.

2. The analysis of magnitude of obesity, body fat tissue and cell membrane integrity parameters can be used as an additional cardiovascular risk factor in RTRs.

3. The cell membrane integrity impairment correlated with arterial stiffness.

Table 1. General characteristics of study population.

	Total study population
RTRs n (%)	344
Sex M n(%)	215 (62.5)
Age (years) Mean value+SD	52.7 + 13.9
BMI (kg/m2) Mean value+SD	25.6 + 4.8
Weight (kg) Median (IQR)	75.5 (63.7-86.2)
BFM (kg) **Median (IQR)**	26.7 (20.7; 34)
FFM (kg) **Median (IQR)**	55 (44.9; 63.6)
FFMI (kg/m^2) **Median (IQR)**	18.4 (16.4; 20.1)
VFA (cm^2) **Median (IQR)**	93.2 (65.7; 133.9)
PBF (%)**Mean value±SD**	27.3±9.5
TSFA (kg) **Median (IQR)**	24.9 (19.9; 28.3)
PhA **Median (IQR)**	4.9 (4,2; 5.5)
BFM (kg) **Median (IQR)**	26.7 (20.7; 34)
Serum creatinine level (mg/dl)Median (IQR)	**1.47(1.19-1.92)**
eGFR CKD-EPI (ml/min/1.73m2)Mean value+SD	50.4 + 19.8
Hemoglobin g/dl Mean value+SD	12.7 + 1.7
Albumin g/l Mean value+SD	43.46 + 3.28
Cyclosporine n (%	73 (21.2)
Tacrolimus n (%)	213 (61.9)
Steroids n(%)	176 (51.2)
MMF n (%)	150 (43.6)
MPS n(%)	172 (50)
AZA n (%)	5 (1.5)
mTOR n (%)	10 (2.9)
Belatacept n(%)	41 (11.9)

Figure:

P0822

ESTIMATED GFR DECLINE OF PKD PATIENTS IN CKD G3B-5 WAS AS FAST AS THAT OF DKD PATIENTS: A RESULT FROM A JAPANESE COHORT STUDY FOR PATIENTS WITH ADVANCED CKD, THE REACH-J STUDY

Junichi Hoshino[1], Chie Saito[2], Ryoya Tsunoda[2], Kei Nagai[2], Hirayasu Kai[2], Reiko Okubo[3], Masahide Kondo[3], Hirokazu Okada[4], Ichiei Narita[5], Takashi Wada[6], Naoki Kashihara[7], Bruce Robinson[8], Kunihiro Yamagata[2]

[1]Toranomon Hospital, Nephrology Center, Tokyo, Japan, [2]University of Tsukuba, Department of Nephrology, Ibaraki, Japan, [3]University of Tsukuba, Department of Health Care Policy and Health Economics, Faculty of Medicine, Ibaraki, Japan, [4]Saitama Medical University, Department of Nephrology, Saitama, Japan, [5]Niigata University, Division of Clinical Nephrology and Rheumatology, Niigata, Japan, [6]Kanazawa University, Division of Nephrology, Department of Nephrology and Laboratory Medicine, Kanazawa, Japan, [7]Kawasaki Medical School, Department of Nephrology and Hypertension, Okayama, Japan and [8]Arbor Research Collaboration for Health, Ann Arbor, United States of America

Background and Aims: CKD progression in Japanese patients with advanced chronic kidney disease (CKD)—an estimated glomerular filtration rate (eGFR) <45 ml/min/1.73m^2—has remained largely unexamined.

Method: We conducted a nationwide cohort study of Japanese patients with advanced CKD. We recruited 2,249 advanced CKD patients (eGFR<45/ml/min/1.73m^2) receiving nephrologist care from a national sample of 31 facilities throughout Japan, randomly selected with stratification by region and facility size, aligned with the international CKD Outcomes and Practice Patterns Study (CKDopps). From baseline data, we calculated annual eGFR decline by CKD stage and causes of CKD over 4 years before enrollment. Variability of eGFR decline was calculated from standard error of the regression.

Results: The reported causes of CKD were 552(25%) had diabetic kidney diseases (DKD), 131(6%) had PKD, 591(26%) had nephrosclerosis, 299(13%) had glomerulonephritis, and 676(30%) had other renal diseases. Of 1939 eligible patients with eGFR data more than two years, median (IQR) annual eGFR declines (ml/min/1.73m^2/year) in PKD and DKD patients were 2.30 (1.16, 3.38) and 1.18 (0.23, 3.69) in G3b, 2.60 (1.81, 3.40) and 1.97 (0.20, 4.75) in G4, and 4.00 (2.00, 5.60) and 3.94 (2.05, 7.05) in G5, respectively. These eGFR declines were significantly faster than those of other kidney diseases. On the other hand, the variability of the decline in PKD patients was significantly smaller than that of DKD patients (0.43 vs 0.71, p<0.001). This trend was consistent in all CKD stages.

Conclusion: Our study clarified that, similar to DKD patients, annual eGFR decline of PKD patients was significantly faster than those of other kidney diseases throughout all stages. Furthermore, the variability of the decline in PKD patients was smaller than those of others. These data suggest that comprehensive nephrology care should be needed especially for these patients.

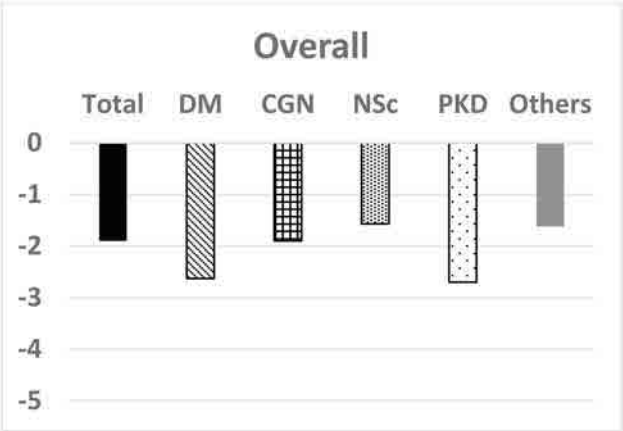


Figure: Median annual eGFR declines by causes of CKD

P0823

CHARACTERISATION OF HISTOLOGY PROVEN GLOMERULAR DISEASES IN THE MALTESE POPULATION: A NATIONAL CROSS-SECTIONAL SURVEY

Sarah Micallef[1], Deborah Balzan[1], Maria Bugeja[1], Jesmar Buttigieg[1], Emanuel Farrugia[1]

[1]*Mater Dei Hospital, Renal Division, Department of Medicine, Malta*

Background and Aims: The incidence and characterisation of glomerular diseases in Malta has not been investigated. This survey aims at determining the nationwide patterns, incidence and spectrum of biopsy-proven glomerular diseases.

Method: This is a retrospective analysis of all native kidney biopsy specimens performed in the adult population in Malta between January 2014 and December 2018. Demographic data and clinical variables were extracted from histopathology reports. Pathological diagnosis was based on findings obtained through light microscopy, immunofluorescence and electron microscopy.

Results: A total of 281 sufficiently sampled and conclusive native kidney biopsies were performed in Malta. The median age at biopsy was 52.9 years (interquartile range: 25), 58.7% were males and 93.1% were Maltese patients. The most common finding on biopsy was diabetic nephropathy (13.5%, n=38). Chronic kidney disease which was progressing faster than expected was the most common reason for performing a biopsy in these cases (65.8%, n=25/38). Ischaemic glomerulopathy was seen in 13.2% of cases (n=37). Podocytopathies accounted for 19.2% (n=54) of biopsies. Focal segmental glomerulosclerosis (FSGS) was seen in 12.8% (n=36); 58.3% (n=21/36) of which considered secondary to other conditions. Minimal change disease (MCD) accounted for 5.7% (n=16), nephrotic syndrome being the most common indication for biopsy (87.5%, n=14/16). Membranous nephropathy (MN) was identified in 11.0% of biopsies (n=31). Anti-Phospholipase A2 antibody status was available for 17 of these patients, 58.8% being positive (n=10/17). Immunoglobulin A nephropathy accounted for 11.7% (n=33). An active urinary sediment was the main indication for biopsy in 78.8% of these cases (n=26/33). Thin basement membrane was present in 2.1% (n=6). Lupus nephritis (LN) was present in 5.7% (n=16) of biopsies; class III LN in 50% (n=8/16), class IV LN in 37.5% (n=6/16); features of class V lupus were present in 31.3% (n=5/16). Only one biopsy showed isolated class V LN. Systemic involvement was present in the vast majority of patients with LN (81.3%, n=13/16). Pauci-immune glomerulonephritis was identified in 5.7% (n=16) of biopsies. Microscopic polyangiitis was the commonest type of pauci-immune ANCA-positive vasculitis (75.0%, n=12/16). Anti-glomerular basement membrane (GBM) disease accounted for only 1.1% (n=3). All patients with anti-GBM disease and 37.5% (n=6/16) of ANCA-positive vasculitis developed a rapidly progressive course requiring dialysis. Interstitial nephritis accounted for 5.7% (n=16) of biopsies; 31.2% (n=5/16) attributed to drugs. Haematological disease related glomerulonephritis accounted for 2.1% (n=6), infection related glomerulonephritis 1.1% (n=3), fibrillary glomerulonephritis 1.4% (n=4), membranoproliferative glomerulonephritis 0.7% (n=2) and other pathologies 6.4% (n=18).

Conclusion: This is the first nationwide study investigating the histopathological patterns and incidence of biopsy-proven glomerular diseases in Malta. The most common biopsy-proven glomerular disease is diabetic nephropathy, followed by focal segmental glomerulosclerosis. and ischemic glomerulopathy.

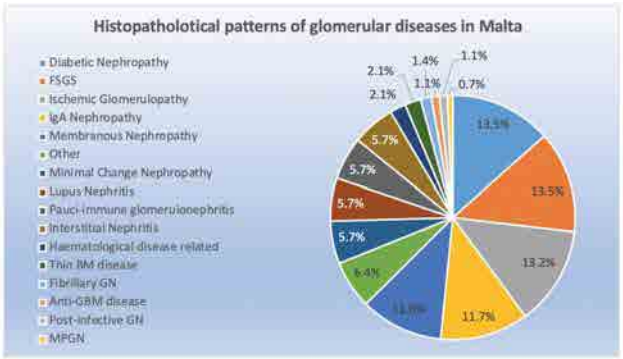


Figure:

P0824 QUALITY OF LIFE (QOL) DURING THE COURSE OF CKD: A LONGITUDINAL STUDY

Graziella D'arrigo[1], Carmela Marino[1], Daniela Leonardis[1], Patrizia Pizzini[1], Graziella Caridi[2], Giovanna Parlongo[2], F. Marino[2], Giovanni Luigi Tripepi[1], Carmine Zoccali[1], Francesca Mallamaci[2]

[1]National Research Council, Institute of Clinical Physiology, Reggio Calabria, Italy and [2]Grande Ospedale Metropolitano BMM, Nephrology, Dialysis and Transplantation Unit, Reggio Calabria, Italy

Background and Aims: Measuring QoL in CKD patients is fundamental to estimate the human cost of chronic diseases and to assess the effect of treatments. Non-medical factors play an important role in CKD progression and QoL. However, there is very limited information on the evolution of QoL over time in CKD patients and it remains unclear whether traditional and CKD specific risk factors are implicated QoL in CKD patients over CKD progression.

Method: We studied a cohort of 582 stage 2-5 CKD patients (age: 61±12 years; M: 60%, diabetics: 33%) and measured QoL by the short form of the Rand corporation questionnaire (SF36), an instrument which measures eight domains of QoL (physical functioning, role physical health, energy fatigue, pain, role emotional problem, emotional well-being, social function, and general health] and two summary scores, (the physical component score and the mental component score) which are calculated by a well validated algorithm (Taft C et al, 2001, Quality of life research). In all patients the SF36 was administered at enrolment and after one (489 patients), two (n=434) and three (n=287) years. The evolution of SF36 dimensions over-time and the predictors of SF36 changes were analyzed by the Linear Mixed Model (LMM).

Results: At baseline the median value of the Physical Component Score (PCS) was 43.7 (Interquartile range: 34.0-50.3) and the Mental Component Score (MCS) was 46.3 (37-52.9) and on average did not change over the 3 years follow up [median PCS at the 3rd year: . 46.3 (35.7-52.0), median MCS at the 3rd year 43 (33.6-50.6)]. On average the GFR at baseline was 36±13 ml/min/1.73 m2 and declined to 34±17 ml/min/1.73m2 at the 3rd year. On detailed longitudinal analysis by the LMM the PCS associated with the evolution of the GFR over time (beta=0.10; 95% CI from 0.06 to 0.13; $P<0.001$). Adjustment for time (0,1,2,3 years), age and gender did not materially modify such an association (beta=0.09; 95%CI from 0.06 to 0.13, $p<0.001$) while further adjustment for traditional (Systolic BP, diabetes, smoking, cholesterol), BMI, CV comorbidities and CKD specific (hemoglobin, albumin, calcium, phosphate) risk factors attenuated but did not cancel out the PCS-GFR link (beta=0.05, 95%CI 0.006 to 0.093, P=0.03). This finding suggests that the PCS-GFR link is either largely confounded or mediated by these risk factors but that the same risk factors do not explain in full the same link . The MCS – GFR association was weaker (beta=0.05, 95%CI from 0.008 to 0.09; P=0.02) than the PCS-GFR relationship, became non significant after simple adjustment for time, age and gender (beta=0.04 ; 95%CI -0.003 to 0.08; P=0.07) and was nullified after full adjustment (beta=-0.01; 95%CI -0.07 to 0.04; P=0.59) for the same risk factors.

Conclusion: The PCS and the MCS remain stable over the course of CKD but appear associated with the evolution of the GFR over time. Traditional and CKD specific risk factors substantially confound and/ or mediate these associations.

P0825 **ASSOCIATION OF BODY MASS INDEX CHANGES WITH CHRONIC KIDNEY DISEASE IN A JAPANESE GENERAL POPULATION**

Akiko Toda[1], Shigeko Hara[1], Hiroshi Tsuji[1], Yasuji Arase[1]
[1]*Toranomon Hospital, Health Management Center, Tokyo, Japan*

Background and Aims: Obesity is a risk factor for chronic kidney disease (CKD), but the effect of reducing body mass index (BMI) on the prevention of CKD is controversial. One of reasons for this disagreement is that part of patients with a BMI decrease may have an unfavourable health status. In such cases, the BMI decrease could be a risk factor for the development of CKD. Therefore, by analysing the data of annual health check-ups, we examined an association between BMI change and CKD development to determine whether BMI reduction helps prevent CKD development.

Method: We analysed the data of 6,959 subjects who underwent annual health check-ups in both 2013 and 2018. By a multivariate logistic regression analysis, we investigated a relationship between BMI change and CKD development within the 5 years between 2013 and 2018. The percent change in the BMI (ΔBMI) was calculated using the following equation: {(BMI in 2018 − BMI in 2013)/BMI in 2013} ×100. For analyses, we classified the subjects into five groups based on their ΔBMI value: (i) severe BMI decrease (ΔBMI $<-2.5\%$); (ii) moderate BMI decrease (ΔBMI $\geq-2.5\%$ but $<0\%$); (iii) maintained BMI (ΔBMI $\geq0\%$ but $<2.5\%$); (iv) moderate BMI increase (ΔBMI $\geq2.5\%$ but $<5\%$); (v) severe BMI increase (ΔBMI $\geq5\%$). For further analysis, we divided the subjects into non-obesity category (basal BMI <25 Kg/m^2) and obesity category (basal BMI ≥25 Kg/m^2). Subjects with an estimated glomerular filtration rate <60 mL/min./1.73 m^2 were defined as having a CKD.

Results: After adjusting several covariates, compared with the maintained BMI group, the severe BMI decrease group showed a significantly low risk of CKD development (odds ratio (OR) 0.70, 95% confidence intervals (CI) 0.54-0.91, $p<0.01$) and the severe BMI increase group had a significantly high risk (OR 1.40, CI 1.08-1.81, $p=0.01$). A farther analysis revealed that the OR of CKD development for the severe BMI increase group in the obesity category was higher than that in the non-obesity category (OR 1.75 vs. 1.29).

Conclusion: In subjects who underwent annual health check-ups, BMI reduction had a significant effect on the prevention of CKD development, whereas an increase in the BMI was a risk factor for CKD development. Moreover, by severe increase in the BMI, obesity subjects showed higher risk of CKD development than non-obesity subjects.

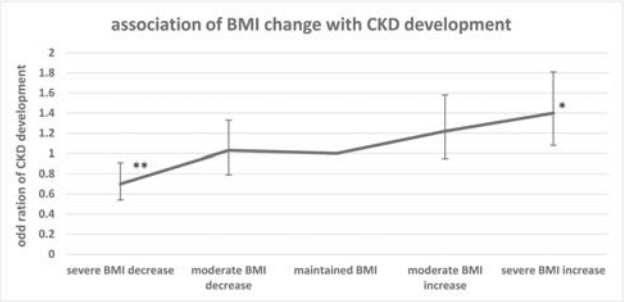


Figure:

P0826 **OBESITY AND RISK FOR CHRONIC KIDNEY DISEASE IN THE HEALTHY MIDDLE-AGED KOREAN POPULATION**

Minhae Cho[1], MI JI KIM[2], WON HEE CHO[2], Ju-Young Moon[2], Kyung Hwan Jeong[2], Sang-Ho Lee[2], Hyeon Seok Hwang[2], Jin Sug Kim[2], Yang-Gyun Kim[2]

[1]University of Memphis, School of Social work, Tennessee, United States of America and [2]KyunHee University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Although obesity is a well-known risk factor for chronic kidney disease (CKD), previous epidemiologic studies have produced mixed results. This study was purposed to investigate the relationship between obesity and CKD occurrence in the healthy middle-aged Korean population.

Method: We used a prospective, longitudinal data from the Korean Genome and Epidemiology Study (KoGES), a population-based, epidemiology study in South Korea (2001-2014). A total of 6,678 participants aged 40-69 who were free of diabetes, hypertension, and CKD at baseline were followed-up biennially. CKD was defined as at least two-time occurrence of estimated glomerular filtration rate < 60 mL/min/1.73m^2 using CKD-EPI equation during the follow-up period.

Results: A total of 433 participants (6.5%) developed CKD. We divided the participants into 5 groups by BMI: underweight (BMI < 18.5), normal-weight (BMI 18.5-22.0), overweight 1 (BMI 23.0-24.9), overweight 2 (BMD 25-29.9), and obesity (BMI >30). Compared to the normal-weight group, hazard ratio of CKD occurrence was elevated in overweight 2 (HR=1.43, p=0.01) and obesity (HR=1.73, p=0.03) in multivariate-adjusted regression analysis (variates: age, newly developed hypertension, newly developed diabetes, fasting glucose $>$ 126mg/dL, 2hours glucose $>$ 200mg/dL, systolic blood pressure $>$ 140mmHg, physical activity, alcohol consumption, smoking). When dividing the participants into three age groups: the 40s, 50s, and 60s, only the 60s group showed a significant correlation of BMI with CKD occurrence (overweight 2: HR=1.93, p=0.05, obesity: HR=3.94, p=0.03).

Conclusion: The risk of CKD was significantly high for those in their 60s who were overweight or obese despite free of underlying diseases in the Korean population.

P0827 BALKAN ENDEMIC NEPHROPATHY AND UPPER TRACT UROTHELIAL CANCER INCIDENCE - 40 YEAR FOLLOW

Stevan Glogovac[1], Zorica Dimitrijevic[1], Miomir Stojanovic[1], Danijela Tasic[1], Karolina Paunovic[1], Branislav Apostolovic[2], Miomir Prokopovic[3], Milan Pertovic[3], Stanimir Ljubenovic[1], Branka Mitic[1]

[1]Clinical Center Nis, Clinic of Nephrology, Nis, Serbia, [2]KBC Zemun, Nephrology, Beograd-Zemun, Serbia and [3]General Hospital Leskovac, Nephrology, Leskovac, Serbia

Background and Aims: Balkan endemic nephropathy (BEN) is a chronic tubulointestitial kidney disease prevalent in Serbia, Bosnia, Croatia, Bulgaria and Romania. One of its most peculiar characteristics is a strong association with upper tract urothelial carcinoma (UTUC).

The aim of the paper is to assess the basic epidemiological characteristics of UTUC, such as the incidence, sex, age geographic distribution of the diseased from Jablanica region in the 40-year period, as well as determining the linear trend of UTUC frequency in regions with BEN compared to non-endemic regions, bearing in mind those recent studies that have shown a significant decrease in the incidence of the diseased from BEN.

Method: The research period lasted from 1978 to 2017. In the analysis of the frequency of UTUC, we used the operative material of Urology Department, Health Care Center, Leskovac, and Urology Clinic, Clinical Center, Nis. The patients were divided according to the place of residence-certain areas of Jablanica region. The data from the Institutes of Nephrology and Hemodialysis were used for the classification of the area(A-endemic settlements for BEN; B-hypo-endemic; C-non-endemic urban type; and D-non-endemic rural type. The average annual incidence rate (AAIR) was calculated per 100 000 people. Finally, e jointly observed groups C and D(non-endemic areas) for UTUC. For practical reasons, this period was divided into the first(1978-1997) and the second one(1998-2017).

Results: The highest AAIR of UTUC was registered in endemic settlements(11.82) and the lowest one in non-endemic urban settlements(0.83). Association of UTUC and other tumours were observed in 39.13% in endemic regions compared to 22.53% in non-endemic regions. In endemic settlements in the first observed period, the frequency of UTUC was registered five times higher than in the second. The linear trend of UTUC in the 40-year-period shows a slow decrease($y=-0.0797x+4.2846$; $r^2=0.2028$). In addition, there was strong positive linear trend toward urinary bladder cancer occurence($y=1.6415 + 3.45$; $r^2=0.85$). However, trend of occurence of bladder cancer in endemic regions were positive, but without significance($y=0.023x+57$; $r^2=0.0004$). The results show that UTUC in endemic settlements are 2.63 times more frequent than in hypo-endemic ones; 14.24 times more frequent than in non-endemic settlements.

Our research in Jablanica region also demonstrated unexpectedly high frequency of on UTUC not only in certain endemic settlements with BEN but also in the non-endemic area-Brejanovac village-1 tumour per 99.63 people and AAIR of 40.50, Rudare village-1 tumour per 139.50 people and AAIR 28.67. This occurrence of UTUC frequency in some non-endemic settlements refers to the first observed period until no occurrence was recorded in the second observed period.

Conclusion: The high frequency of UTUC in the regions with BEN in Jablanica region possibly point to the common nephropathogenic and carcinogenic etiologic factor and confirms the existence of a positive correlation between BEN and UTUC. It is necessary that additional investigations be carried out in certain non-endemic settlements in which the frequency of UTUC and hemodialyzed patients in still high.

P0828 **CKD STAGE DISTRIBUTION IN AN ITALIAN PROVINCE; SEVEN YEARS OF FOLLOW UP.**

Alessandro Roggeri[1], Daniela Paola Roggeri[1], Carlotta Rossi[2], Marco Gambera[3], Rossana Piccinelli[3], Samanta Sonzogni[3], Ferruccio Conte[4]

[1]ProCure Solutions, Health Economics and Real World Evidence, Nembro, Italy, [2]ProCure Solutions, Statistics, Nembro, Italy, [3]ATS Bergamo, Territorial Pharmaceutical Service, Bergamo, Italy and [4]University of Milan, San Paolo Hospital, Health Sciences, Renal Division, Milano, Italy

Background and Aims: Chronic kidney disease (CKD) is a chronic illness with important implications for the health of the population and for the commitment of resources by public health services. CKD staging makes it possible to assess the severity of the disease and its distribution in the population. The distribution of the stages of CKD diagnosed through hospitalization were analyzed using administrative database of the Local Health Authority of a province with a population of about 1 million inhabitants in northern Italy.

Method: Patients with hospital discharge with a diagnosis of CKD (ICD9CM 5851, 5852, 5853, 5854) in 2011- 2012 years, without dialysis treatment, neither transplantation procedure nor acute renal failure were selected. Demographic characteristics, comorbidities, dialysis treatment, drugs prescription and nephrological follow-up were investigated. This cohort of patients was examined over a 7-year period (2011-2017). Stage five was not considered to avoid possible misunderstanding with five D stage.

Results: 1808 patients diagnosed with CKD were extracted from the 2011-2017 administrative database; of these, 1267 had a diagnosis with the CKD stage specification. The distribution of 1267 patients in the CKD stages at the first hospital discharge was as follows: 7.4% stage 1, 30.9% stage 2, 42.3% stage 3, 19.3% stage 4. The 832 patients described in the study were still alive as of Jan. 1, 2013 while 435 (34.3%) died by Dec. 31, 2012. Until Dec. 31, 2017, 503 of the 832 patients died representing the 52.8% of stage 1 patients, 62% of stage 2 patients, 58.2% of stage 3 patients, 66.4% of stage 4 patients. Males were the most prevalent gender (58.5%), without any significant difference into CKD stages. Our patients have a fairly high age as can be seen from the table 1. The presence of co-morbidities was assessed either directly for the main risk factors or by the modified Charlson index (MCI) for CKD patients. The average value of the MCI is 3.8 ± 3.1 for all patients and 3.4 ±3.0 for stage 1, 4.1 ± 3.3 for stage 2, 3.7 ± 3.1 for stage 3, 3.7 ± 2.9 for stage 4, with maximum values of 12.0, 17.0, 16.0 and 14.0 respectively. About 40% of patients had diabetes mellitus, with the highest prevalence in stage 4 (49.3%) and the lowest in stage 1 (25%). Cardiovascular disease was distributed almost equally among all patients with a value between 82% in stage 1 and 86.3% in stage 4. Cancer were present in 26.3% of patients with similar values in all stages. Just about 9% of patients underwent dialysis treatment for achieving ESRD, with a percentage of 5.6% among patients in stage 1 and 17.1% among those in stage 4. Hemodialysis represented first choice treatment (86%) compared with peritoneal one (14%). Time from the diagnosis of CKD to the first dialysis was variable with an average of 3.4 ±1.7 years; the longest interval for patients in stage 1 (5.1±1.8) and the shortest (3.0 ±1.6) for patients in stage 4. The number of nephrological visits at renal units was analyzed for an assessment of the extent of follow-up and prevention upon reaching the ESRD (table2). More than 90% of patients had prescribed drugs antagonists of the renin angiotensin system, in all stages of CKD; other antihypertensive drugs (Ca channel blockers and peripheral vasodilators) had a similar prescription level. Anemia control drugs (ESA and iron) had an incremental prescription with stages of the disease from 51.4% in stage 1 to 74% in stage 4, similarly to Ca-P metabolism control drugs ranging from 44.4% in stage 1 to 67.8% in stage 4.

Conclusion: Correct staging of CKD is very important to assess the prognosis of patients, but the major determinants of outcome are comorbidities and age of the patients. The cohort examined has a high mortality rate, far higher than reported in the literature for CKD. It should be noted that the sample was identified by hospitalization for cardiovascular diseases more than 50% complicated by diabetes and hypertension, so death represents the main outcome and not ESRD.

Table 1. Ages by CKD stage

CKD stage	N	Mean age (years ±SD)	Median age (years)
1	72	70.3 ± 18.0	75.0
2	274	77.0 ± 11.7	78.5
3	340	74.8 ± 13.7	78.0
4	146	76.0 ± 13.7	79.5
all	832	75.3 ± 13.6	78.0

Table 2. Nephrological visits by CKD stage

CKD stage	N. patients	Mean number of visits (n ±SD)	minimum	maximum
1	72	3.6 ± 7.5	0	48.0
2	274	2.4 ± 4.5	0	36.0
3	340	4.7 ± 7.7	0	61.0
4	146	7.2 ± 9.2	0	55.0
all	832	4.3 ± 7.3	0	61.0

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3	340	4.7 ± 7.7	0	61.0
4	146	7.2 ± 9.2	0	55.0
all	832	4.3 ± 7.3	0	61.0

Figure:

P0829 THE ASSOCIATION BETWEEN URINARY NGAL AND EGFR SLOPE IN PATIENTS WITH CKD

Shungo Fukuda[1], Naohiko Fujii[1], Taisuke Matsushita[1], Sayoko Yonemoto[1], Daisuke Hayashi[1], Ayako Okuno[1], Mizuho Saeki[1]

[1]*Hyogo Prefectural Nishinomiya Hospital, Nephrology, Nishinomiya, Japan*

Background and Aims: Urinary neutrophil gelatinase-associated lipocalin (uNGAL) is a new biomarker for renal tubular damage. The association between uNGAL and renal prognosis have been reported in many papers; however, it may often be affected by urinary tract infection (UTI), and its clinical value with consideration of UTI has not been well investigated in patients with chronic kidney disease (CKD). The aims of our study were to investigate the association between uNGAL and eGFR decline in CKD incorporating the effect of UTI.

Method: This was a retrospective observational cohort study at a single hospital in Japan. We included adult patients with the estimated glomerular filtration rate (eGFR) of 10 to 70 mL/min/1.73m2 from Jan 2017, who had at least one measurement of uNGAL. We used baseline uNGAL adjusted for urinary creatinine (Cr) as an exposure variable and divided the patients into quartiles. UTI was determined by a single evaluation of urinalysis at baseline. The repeated measured eGFRs were obtained from the electrical health record until dialysis initiation, loss to follow-up, or the end of the observation period whichever occurred first. We performed longitudinal analyses for eGFR decline using the mixed effects model and evaluated the longitudinal effect of uNGAL taking into account of UTI. All statistical analyses were done using STATA 13.1.

Results: In total, 281 patients with CKD were included. Mean age and eGFR at baseline were 70.2 years and 33.9 mL/min/1.73m^2, respectively. The median [interquartile range (IQR)] of baseline uNGAL and urinary protein to Cr ratio (uPCR) were 49.6 [19.4 - 171.4] ug/gCr and 0.82 [0.18 - 3.26] g/gCr, respectively. Patients with UTI (15%) showed significantly higher uNGAL at baseline than those without (219 [89 - 425] vs. 39 [16 - 131]). During the mean follow up of 229 days, nine patients developed eGFR $<$ 5 mL/min/1.73m^2. Although a higher uNGAL level was significantly associated with lower eGFR levels at baseline (-3.3 [95% confidence interval (CI): -7.6, 0.93], -9.6 [-14.2, -4.9], and -16.3 [-21.4, -11.1] mL/min/1.73m^2 in quartiles Q2-4 as compared to Q1); the eGFR trajectory did not differ with or without baseline UTI in the analytic model, while baseline proteinuria was significantly associated with a steeper slope of eGFR.

Conclusion: A higher uNGAL was significantly associated with lower eGFR levels at baseline; however, it was not associated with a steeper slope of eGFR in the longitudinal analysis, even with the consideration of the effect of UTI.

P0830

PREVALENCE OF ANXIETY IN CHRONIC KIDNEY DISEASE PATIENTS - A SYSTEMATIC REVIEW AND META-ANALYSIS OF LITERATURE

Weihao Caleb Huang[1], Poh Hui Wee[1], Lian Leng Low[2,3], Ying Leng Agnes Koong[1,3,4], Htay Htay[5], Marjorie Foo[5], Qiao Fan[6], Jun Jie Benjamin Seng[1]

[1]Duke-NUS Medical School, Singapore, Singapore, [2]Singapore General Hospital, Department of Family Medicine and Continuing Care, Singapore, Singapore, [3]SingHealth Duke-NUS Family Medicine Academic Clinical Program, Singapore, Singapore, [4]SingHealth Polyclinics - Marine Parade, Singapore, Singapore, [5]Singapore General Hospital, Department of Renal Medicine, Singapore, Singapore and [6]Duke-NUS Medical School, Centre for Quantitative Medicine, Singapore, Singapore

Background and Aims: Anxiety is a common psychopathology that affects patients with chronic kidney disease (CKD) and has been associated with poor quality of life and clinical outcomes. This review aimed to summarize the prevalence of anxiety symptoms and disorders among CKD patients.

Method: A literature search for observational studies, which reported the prevalence of anxiety in CKD patients, was performed in Medline®, Embase®, PsychINFO® and CINAHL® (through January 2019), in accordance with the PRISMA checklist. Peer reviewed, full text articles in English language were included. Studies involving kidney transplant patients were excluded. Anxiety disorders and symptoms were diagnosed and assessed using the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) or DSM-V criteria in clinical interviews, or self-administered anxiety rating scale questionnaires. To estimate the prevalence of anxiety, random effects meta-analyses were used due to the expected heterogeneity across studies.

Results: Of the 4130 reports screened, 53 studies were included. Majority of studies were conducted in Asia (n=26, 49.1%) followed by Europe (n=14, 26.4%) and North America (n=7, 13.2%). The Hospital Anxiety and Depression Scale (HADS) was the most used instrument (n=28, 52.8%) followed by the Beck's Anxiety Inventory (BAI) (n=11, 20.7%). The pooled point prevalence of anxiety across the studies involving 9,355 patients was 40.0% (95% confidence interval (CI): 33.3 – 46.7). Across continents, the prevalence of anxiety was highest in Asia (42.9%) (95% CI: 32.3 – 53.5) followed by North America (42.3%) (95% CI: 28.6 – 56.0). The prevalence of anxiety in studies that included only dialysis (n=45) or non-dialysis (n=4) patients were similar at 38.9% (95% CI: 31.8 – 46.1) and 30.5% (95% CI: 14.6 – 46.3) respectively. The prevalence of anxiety in studies that had both dialysis and non-dialysis patients (n=4) was 62.6% (95% CI: 47.1 – 78.2).

Conclusion: Given that anxiety is prevalent in 40% of CKD patients, future studies should explore developing effective anxiety screening tools and interventions as part of CKD patient management to improve clinical outcomes.

P0831

HIGH SERUM ALKALINE PHOSPHATASE PREDICTS THE RISK OF CKD PROGRESSION: EFFECT NODIFICATION BY THE GFR

Francesca Mallamaci[1], Graziella D'arrigo[2], F. Marino[1], Graziella Caridi[1], Giovanna Parlongo[1], Daniela Leonardis[2], Patrizia Pizzini[2], Sebastiano Cutrupi[2], Anna Pisano[2], Giovanni Luigi Tripepi[2], Kamyar Kalantar-Zadeh[3], Carmine Zoccali[2]

[1]Grande Ospedale Metropolitano BMM, Nephrology, Dialysis and Transplantation Unit, Reggio Calabria, Italy, [2]National Research Council, Institute of Clinical Physiology, Reggio Calabria, Italy and [3]UCLA University, Fielding School of Public Health, Orange, United States of America

Background and Aims: In the post-hoc analyses of the SUSTAIN and ASSURE trials (Kidney Blood Press Res. 2018;43:449-457), Apabetalone, an epigenetic modulator which lowers serum alkaline phosphatase (AlkPhos), stabilized the GFR in patients with cardiovascular disease and a GFR <60/ml/min/1.73m2. Analyzing the relationship between AlkPhos and renal outcomes in patients with established CKD is useful to preliminarily explore the biological hypothesis that AlkPhos is implicated in CKD progression.

Method: We investigated the relationship between AlkPhos and the risk for a combined renal end-point (30% GFR loss or dialysis/renal transplantation) in a cohort of 609 stage 3-5 CKD patients with an average GFR of 34.8±12.1ml/min/1.73 m2.

Results: Median AlkPhos levels were 91 IU/L (Interquartile range 71-117 IU/L) and in the vast majority of patients had values below 147 IU/L (the upper limit of the normal range). Over a median follow up of 3 years, two-hundred patients had the combined renal end-point. In an unadjusted analysis 1 ln increase in AlkPhos entailed a 49% risk excess for the renal end-point (HR: 1.49, 95% CI 1.11-2.01, P=0.008). Adjusting for traditional (age, gender, smoking, diabetes, total cholesterol, BMI, systolic BP, CV comorbidities) and CKD specific risk factors (hemoglobin, albumin, phosphate, and hs-CRP) did not modify the strength of this association (HR:1.48, 95% CI 1.08-2.02, P=0.016). Furthermore, In a fully adjusted analysis testing the GFR as an effect modifier of the AlkPhos - combined renal end point relationship showed a strong GFR- AlkPhos interaction (Figure). Indeed the risk for the combined renal end-point was gradually more pronounced at progressively more severe degrees of renal dysfunction, the HR being 0.94 (CI95% 0.60-1.47) at a GFR of 40 ml/min/m2 and 2.71 (CI95% 1.49-4.93) at 10 ml/min/1.73m2.

Conclusion: In patients with stage 3-5 CKD alkaline phosphatase within the normal range is associated with the risk for progression to ESRD and the GFR is an effect modifier of this relationship. Findings in this study are compatible with the hypothesis that within the normal range of this biomarker, the risk for CKD progression by alkaline phosphatase is amplified by the severity of CKD. These data are in keeping with post-hoc analyses of the SUSTAIN and ASSURE trials and provide circumstantial support to the hypothesis that interventions lowering serum alkaline phosphatase may mitigate CKD progression.

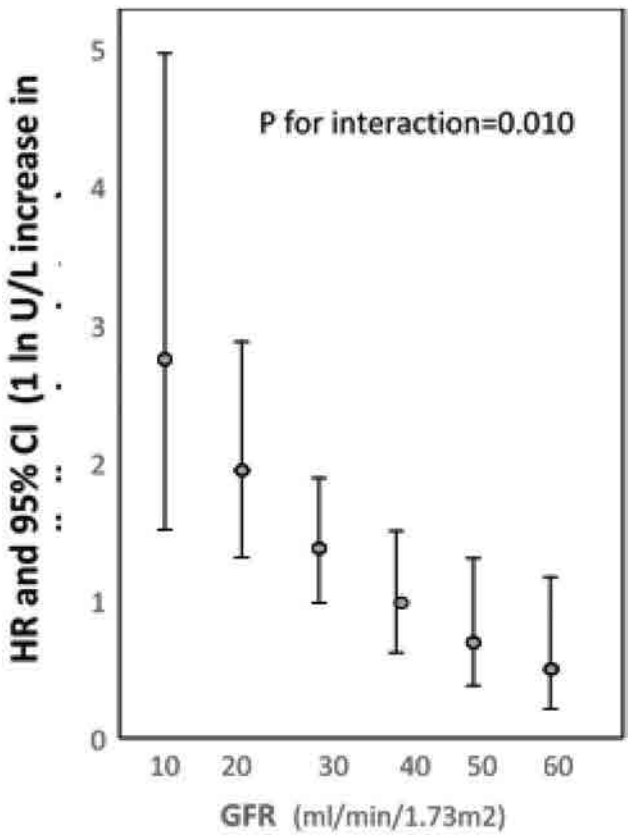


Figure:

P0832

FINAL OUTCOME OF CKD STAGE 5 PATIENTS WHO CHOSE PALLIATIVE TREATMENT-EXPERIENCE FROM ONE MEDICAL CENTER IN TAIWAN

Mei-Chuan Kuo[1,2], Lan-Fang Kung[2], Shu-Li Wang[2], Shang-Jyh Hwang[1,3], Chien-Yi Wu[4], Yi wen Chiu[1,3], Hung-Chun Chen[1,3]

[1]Kaohsiung Medical University, Faculty of Renal Care, College of Medicine, Kaohsiung, Taiwan, R.O.C., [2]Kaohsiung Medical University Chung-Ho Memorial Hospital, Department of Nursing, Kaohsiung, Taiwan, R.O.C., [3]Kaohsiung Medical University Chung-Ho Memorial Hospital, Division of nephrology, department of internal medicine, Kaohsiung, Taiwan, R.O.C. and [4]Kaohsiung Medical University Chung-Ho Memorial Hospital, Department of family medicine, Kaohsiung, Taiwan, R.O.C.

Background and Aims: Taiwan has a high incidence and prevalence of ESRD (end stage renal disease) in the world and all the medical expenses are covered by national insurance. Therefore, many old ESRD(end stage renal disease) patients received dialysis even had multiple co- morbidity. However, still some old late CKD patients withhold dialysis and chose palliative treatment. This study elucidate the experience of final outcome for those late CKD patients who chose palliative treatment in Taiwan.

Method: We enrolled 137 CKD stage 5 patients (age: 80.2±8.8 y/o, male/female:85/52) who were interested about palliative treatment since Oct, 2010 till July 2019. We reviewed their co-morbidity to calculate Modified Charlson comorbidity index by medical record and record their laboratory data at enrollment. The differences between two groups were calculated using a Chi-square test for categorical variables and a Mann-Whitney test for continuous variables. All statistical tests were two-tailed and a *P* value of less than .05 was considered a significant difference.

Results: After fully discussion, 82(59.9%) patients can accept palliative treatment, 46(33.6%) refuse palliative treatment, 9(6.6%) patients cannot decided palliative treatment or not at first. 79 patient died during study period, median survival time is 163 days. 22 death patients(27.8%) received dialysis before end of life. 10 patients (12.2%) who asked palliative treatment at first and changed their mind to received dialysis. 80% of these patients receive dialysis by double lumen catheter. For those refuse palliative treatment, 43 patient received dialysis and 24(55.8%) patients received dialysis by temporary catheter. These percentage is much higher(55.8%) than other CKD stage 5 patients (26.6%) following at our hospital. Only 13 patient(16.5%) died at home, 24 patients(30.4%) diet at hospice ward and 39(49.4%) patients diet at ordinary ward or intensive care unit. Older age, lower albumin and higher Charlson comorbidity index are found in mortality patients. The median survival time for those patients received dialysis is 467 days.

Conclusion: After fully explanation, only 59.9% patients can accept withhold dialysis and 12.2% regret later. Those who had interested in palliative treatment had higher percentage to use double lumen catheter for first dialysis. The median survival time for those patients who ever think about withhold dialysis is only 467 days even receiving dialysis. To minimize suffering before end of life and decrease medical expense burden, we still need to do more effort to popularize the concept of withhold dialysis in older and multiple comorbidity patients.

P0833 SYMPTOM BURDEN IN CHRONIC KIDNEY DISEASE : A CASE FOR STARTING KIDNEY SUPPORTIVE CARE CLINIC

Ravindra Attur Prabhu[1], Pankaj Singhai[2], Naveen Salins[2], Shankar Prasad Nagaraju[1], Indu R Rao[1], Dharshan Rangaswamy[1], Srinivas Vinayak Shenoy[1], Seema Rao[2]

[1]Kasturba Medical College Manipal, MAHE, Nephrology, Manipal, Udupi, India and [2]Kasturba Medical College Manipal, MAHE, Palliative Medicine and Supportive Care, Manipal, Udupi, India

Background and Aims Chronic Kidney Disease(CKD) is associated with a huge symptom burden which increases with progression and leads to depreciation in Quality of life both directly and indirectly through effects on functional status, health perception, and feelings of subjective well-being. Dialysis therapy does not completely improve symptoms. We studied supportive care needs of patients with CKD through assessment of symptoms using translated version of Integrated Palliative Care Outcome Scale (IPOS- Renal) in a single tertiary health setting.

Method: Patients with chronic Kidney disease having creatinine clearance less than 60 ml/min/m^2 were surveyed using IPOS Renal modified translated to vernacular language by forward- backward method. Translated version was approved by independent translator. Symptoms were classified into domains and analyzed using descriptive statistics. Scores were compared for those on maintenance hemodialysis with predialysis CKD patients.

Results: Of 184 patients, 128(69.6%) were receiving twice weekly hemodialysis, mean age was 52 years (range 20-82 year), 140(76%) were male. Average duration of dialysis was 4 years, 87 (46.9%) reported pain of which 39/87(45%) had moderate to severe pain. Other symptoms over past one week were dyspnea in 59(33.6%), Fatigue in 117(69.4%), Nausea in 53(33.6%), Vomiting in 36(20.9%), Anorexia in 90(42.4%), Constipation in 50(35.3%), Dry mouth/soreness in 62(36.4%), increased drowsiness in 63(46.6%), poor mobility in 87(55.8%), Itching in 69(39.3%), Disturbed sleep in 83(48.6%), Restless leg in75(43.6%), Skin related problems in 47(28.6%). Five patients reported presence of other severe symptoms. In Psychosocial domain 138(79.8%) patients and 126(72.8 %) family members expressed anxiety related to their disease or treatment of which one third had persistent anxiety, 140(81.6%) felt depressed and among them 58(42%) felt it most of the time or always and 145(88.6%) felt that they were not at peace, 59(35%) felt they did not have enough information about their disease and treatment and 79(47%) reported that they had unaddressed financial or personal problems, 124(77.2 %) felt they had to spend significant amount of time in healthcare facility. Patients on dialysis had significantly higher symptoms burden and Psychosocial needs.

Conclusion: CKD patients face high physical and psychosocial burden which is unaddressed in present clinical care and increases with stage. Tools such as iPOS renal are required to assess need of supportive care in CKD. Kidney supportive care clinic may be required to address this unmet need.

P0834 **IMPACT OF CKD ON MORTALITY IN HEART FAILURE**

Alexander Sarnowski[1], Rebeka Jenkins[1], Lisa Anderson[2,3], Debasish Banerjee[1,4]

[1]St George's Hospital, Renal and Transplantation Unit, London, United Kingdom, [2]St George's Hospital, Cardiology Clinical Academic Group, London, United Kingdom, [3]St George's Hospital, Department of Cardiology, London, United Kingdom and [4]St George's, University of London, Molecular and Clinical Sciences Research Group, London, United Kingdom

Background and Aims: The presence of CKD impacts short term survival of heart failure patients however impact on long term survival is not well known. The aim of this study was to investigate the impact of CKD on long term survival.

Method: Data were collected on long term survival of 845 patients (1029 admissions) admitted with diagnosis with acute heart failure. Data on mortality was collected by electronic patient records. Data were analysed using IBM SPSS 25.

Results: The baseline characteristics were: age 76 (13) mean (SD); Haemoglobin 11.8 (2), urea 37.2 (26.8), eGFR 63.3 (30.4), potassium 4.34 (0.70) and 36% diabetics, 567 patients (67%) died during follow up of median 916 days (IQR 188-1936 days).

Patients who died were older, with higher urea, creatinine, potassium and NT proBNP. In a survival analysis adjusted for diabetes and haemoglobin; age, urea, NT-proBNP baseline eGFR and potassium predicted mortality (see table).

CKD patients with eGFR <60 ml/min/1.73m2 had poorer survival compared to patients with eGFR>60 (log rank p=0.000) (see figure 1)

Conclusion: Long term mortality in patients with CKD was higher which was an independent predictor of survival

Table 1

	B	SE	Wald	df	Sig.	Exp(B)
Age at admission	.038	.004	86.434	1	.000	1.039
Urea	.016	.002	74.711	1	.000	1.016
NT-proBNP	.000	.000	42.745	1	.000	1.000
Baseline eGFR	.005	.002	7.179	1	.007	1.005
Hb	-.021	.024	.764	1	.382	.979
Na	.001	.009	.026	1	.873	1.001
K+	.194	.077	6.361	1	.012	1.214
Diabetic	-.015	.096	.024	1	.876	.985

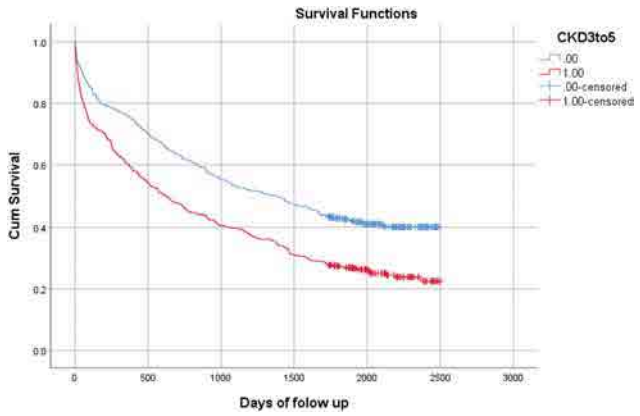


Figure 1

P0835 **IDENTIFYING THE FREQUENCY OF CHRONIC KIDNEY DISEASE OF UNKNOWN ETIOLOGY (CKDU) IN A RURAL POPULATION OF BANGLADESH**

Md M Iqbal[1,2], SC Roy[1], MAA Chowdhury[2,3], Sajal Krishna Banerjee[2,4], S Islam[2,4], RM Hossain[2,4], MS Hassan[2,5], MZ Hassan[2,6], SR Chaudhury[2,7], MI Arslan[2,4], MN Islam[2,5]

[1]SSMC, Nephrology, Bangladesh, [2]KDRG, Bangladesh, [3]NIKDU, Bangladesh, [4]BSMMU, Bangladesh, [5]Impulse Hospital, Bangladesh, [6]BUHS, Bangladesh and [7]NHFRI, Bangladesh

Background and Aims: The common etiologies of CKD are diabetes, hypertension and glomerulonephritis. Prevalence of CKD of unknown (CKDu) etiology is being increasingly considered as an emerging etiology, especially in the developing countries, with environmental predisposition to hot humid climate, dehydration and toxic metal contaminations. The aim was to identify the frequency of CKDu as an etiology in a rural population with environmental exposure.

Method: In this observational study subjects were selected from a geographically defined rural population in Bangladesh. Baseline information was recorded by the translated WHO STEP wise approach surveillance- Instrument v.3.1 (Core and Expanded). Blood Pressure was measured by digital blood pressure monitor. Serum creatinine was measured by enzymatic method using assays traceable to isotope dilution mass spectrometry (IDMS). A fasting blood sample and spot urine was collected. BP $\geq$140/90mmHg; FBS $>$ 5.6 mmol/l and HbA1c $\geq$6.5%; and eGFR$<$ 60ml/min (CKD-EPI equation) or urine ACR $>$ 30mg/g was taken as diagnostic cut-offs for hypertension, diabetes and nephropathy respectively. From diagnosed CKD patients CKDu group was further identified by stepwise approach of WHO criteria as suspected and probable stages.

Results: The mean age was 41.3 $\pm$ 12.7 years with male/female ratio 37/63 in preliminary 303 study subjects. They were 12.5% diabetic, 21% hypertensive and 75% had some form of dyslipidemia. Among all 51 subjects (16.8%) were diagnosed as CKD based on single measurement of eGFR and ACR. Of these 30 study subjects (58%) met the criteria of suspected CKDu. After repeat measures of eGFR and ACR at 3 months, prevalence of CKD came down to 10.2% persisting in 31 subjects (G1:5.3%, G2:2.3% and G3: 2.6%). Of these 7 study subjects (23%) met the criteria of probable CKDu. The main etiologies of CKD among these subjects were diabetic nephropathy (48%) followed by CKDu. The frequency of CKDu in total study population as a whole was 2.3%.The pattern of environmental exposures like types of farming, use of pesticide-fertilizer, NSAIDs intakes, water sources, amount of drinking water per day, duration of work under direct sun, pattern of fish-meat intakes, etc. were not different between subjects with CKDu versus the others.

Conclusion: The prevalence of chronic kidney disease in a rural area of Bangladesh is one in ten (10.2%). Among these nearly one-fourth (23%) of the subjects belonged to probable CKDu category. This alarmingly high frequency of CKDu needs further extensive evaluation to identify the predisposing factors responsible.

P0836 **ROLE OF THE NEPHROLOGIST AS A CONSULTANT FOR VASCULAR SURGERY SERVICE IN A UNIVERSITY HOSPITAL.**

Orlando Siverio Morales[1], Edduin Martin[1], Virginia Dominguez[1], Carlos Marin[1], Ana Aragao[1], Desirée Luis Rodríguez[1], Ana Jarque[2], Patricia Garcia[1], Maria Jose Reguera[2], Manuel Macia[1]

[1]HUNSC, Nephrology Dyalisis, Santa Cruz de Tenerife, Spain and [2]HUNSC, Nephrology, Santa Cruz de Tenerife, Spain

Background and Aims: The clinical profile and complexity of hospitalised patients from Vascular Surgery are similar to those from Nephrology. Also, the majority of patients with peripheral vascular disease has some degree of chronic kidney disease. Therefore, the collaboration of nephrologist as consultants could have a significant impact on the adequate attention of these patients.

Our aim was to analyze the epidemiological and clinical characteristics of the vascular surgery patients admitted in a public university hospital of 1000 beds that were attended by a nephrologist during their hospitalization.

Method: Observational study of a retrospective cohort of 138 patients in a 1 year period (January 1st to December 31st 2018). The following data were considered: nature of the consultation ("Urgent" LESS THAN 24 H TO BE ATTENDER OR "Standar"), reason for consultation/nephrological diagnosis, cause of admission, follow-up period, age, sex, presence of : Diabetes Mellitus (DM), Hypertension (HT) and/or Chronic Kidney Disease (CKD) presence.

Results: 138 patients, Mean age was 67,8 y (range 35-92 y). 76,81% were men and 23,19% were women. Most frequent cause for consultations were: 1. Patients on Hemodialysis treatment (66 = 47,83%); 2. Exhacerbations of CKD (29 = 21,01%); 3. Acute Kidney Failure (18 = 13,04%); 4. Kidney transplantation (11 = 7,97%); 5. Ionic alterations (7 = 5,07%); 6. Advanced CKD (6=4,35%).

Cause of admission: 1. Chronic lower limb ischemia (68=49,27%); 2. Problems related to arteriovenous fistula (Creation of vascular access: 10=7,25% and complications of vascular access: 16=11,59%); 3. Aneurysmatic complications (14=10,14%); 4. Diabetic foot (11=7,97%); 5. Infections (7=5,07%); 6. Deep venous thrombosis (6=4,35%).

About 75.35% had DM, 91.30% were hypertensive and 62.32% had both clinical conditions.

The average follow-up time was 72 days (range 1-223 days) and 92,03 % need to be follow-up more than 24 hours.

About 49,27% of the consultation were urgent.

Conclusion: The number of patients admitted to vascular surgery department requiring nephrology attention are high and represents an important percentage of the clinical activities and resources demanding to the nephrology service.

Exhacerbations of CKD, Diabetes Mellitus and Hypertension are constant clinical conditions in patients admitted to vascular surgery requiring nephrology assessment.

Based on these data is important to improve the coordination between both departments and to stablish a specific training program for nephrologist and vascular surgeons in order to optimize the management of this patients.

P0837 HYPERKALEMIA IN RENAL PATIENTS, THE GREAT FORGOT?

Wenceslao Aguilera Morales[1], JAVIER BURGOS MARTIN[2], FABIOLA ALONSO GARCIA[1], María Jesús Moyano Franco[1], Mercedes Salgueira Lazo[1]

[1]Hospital Universitario Virgen Macarena, Nefrología, Sevilla, and [2]Hospital Universitario Virgen Macarena, Nefrología, Sevilla, Spain

Background and Aims: Hyperkalemia constitutes an electrolyte imbalance that frequently appears in patients with Chronic Renal Disease (CKD) and is related to an increase in morbidity and mortality. Today, computerization of laboratory systems allows us to have access to these data to analyze the real prevalence of hyperkalemia in these patients, which we currently do not know.

Our purpose is to analyze the frequency and characteristics of nephrologic patients with hyperkalemia and identify the most prevalent areas.

Method: Using a coding established by the laboratory, we have selected all patients with potassium greater than 5.5 mEq / l in analytics requested by any nephrologist of our hospital during the months of January to March 2019. It was established as mild hyperkalemia values up to 5.5mEq / l, and up to 6.5 mEq / l, severe hyperkalemia. We retrospectively analyzed the characteristics of these patients and the prevalence according to etiology and units within our service, relating potassium levels to the prescription of hyperkalemiant or related drugs.

Results: After analyzing the data, using as a reference the total number of patients seen in each area, we obtain an estimated total prevalence of 3.5% (86/2480).

We found a distribution by sex with a predominance of men (56%), with a mean age of 62 years.

The highest prevalence is obtained in the Hemodialysis unit (39.8%), followed by Peritoneal Dialysis (11%), Transplantation (5%), Hospitalization (4.3%), Interconsultations (3.8%), ERCA (2.7%) and External Consultations (0.6%).

65% had moderate hyperkalemia (defined as potassium levels of 5.5-6.5 mEq / l).

Regarding the etiology of CKD, the most prevalent were: Vascular (29.2%), Diabetic (20.7%), Glomerular (19.5%) and Interstitial (14.6%). These etiologies also coincide with higher mean potassium levels, although without significant differences.

There is also an increase in potassium levels the lower the glomerular filtration rate. However, when performing linear regression analysis we found no significant differences.

Analyzing the drugs, it should be noted that the patients with the highest potassium levels were those taking anticoagulants, anticalcineurinics or resins (mean 6.17 mEq / l), finding significant differences only with the resins. In addition, most did not take ACE inhibitors, ARA-II or Beta blockers.

Conclusion: The prevalence of hyperkalemia in our population represents 3.5%. Being in most cases mild-moderate.

The prevalence of hyperkalemia is higher in protein and kidney nephropathies and vascular nephropathies, probably associated with increased use of antiproteinuric drugs with hyperkalemic effect.

Hyperkalemia is more prevalent in patients in patients undergoing renal replacement therapy reaching 40% in hemodialysis.

The prevalence in CKD has been lower than expected, possibly in relation to greater patient awareness and adherence to the indications.

Despite not finding a significant relationship, (due to the size of the sample) there is a relationship with the prescription of hyperkalemiant drugs. Resin prescription does not correct hyperkalemia

P0838

HYPERPROLACTINEMIA IN CKD PATIENTS AND ITS ASSOCIATION WITH STRENGHT, SEXUAL DYSFUNCTION ANS QUALITY OF LIFE

Pedro do Valle Teichman[1,2], Gabrielle Zanotto de Oliveira[1,2], Samile Sallaberry Echeverria Silveira[1,2], Carlos Alberto Angarita Jaime[1,2], Mariana Lopes De Castro[1,2], Andrea Carla Bauer[1,2]

[1]Hospital de Clínicas de Porto Alegre, Department of Nephrology, Porto Alegre, Brazil and [2]Federal University of Rio Grande do Sul, Porto Alegre, Brazil

Background and Aims: Hyperprolactinemia is a hormonal disorder associated with many diseases, including chronic kidney disease (CKD). Some studies have shown that serum prolactin (PRL) levels increase as CKD progresses, due to decreased renal clearance and increased production. This prolactin retention leads to inhibition of gonadotropic hormone production, and testosterone deficiency in male patients with CKD. Thus, this study aimed to evaluate PRL levels in male patients with different stages of CKD and its association with clinical and laboratory characteristics, strength, sexual dysfunction, and quality of life.

Method: This is a transversal study conducted in a tertiary hospital in southern Brazil. Patients with CKD stage IV and V were included and divided into three groups: 1) stage IV; 2) non-dialysis-dependent stage V and; 3) dialysis-dependent stage V (VD). Patients with prescribed hormone therapy were excluded. PRL, creatinine, testosterone, estradiol, albumin, SHBG, LH, and FSH levels were measured. Free testosterone was estimated by the Vermeulen equation. Patients were also evaluated for strength and musculoskeletal function through the "handgrip strength" test. For evaluation of the quality of life and sexual dysfunction, validated questionnaires were applied: AMS (Aging Male's Symptoms Scale), ADAM (Androgen Deficiency in the Aging Male) and SF-36 Health.

Results: In this study, 164 patients were included (IV=75; V=41; VD=48). The mean age was 64 [55-71] years and BMI 26,9 [23,3-30,04] kg/m^2. The dialysis-dependent group had higher prevalence of hyperprolactinemia (22,6% vs. 49% vs. 66%, p<0,001), higher PRL (13,4 vs. 19,43 vs. 26,13, p<0,001) and estradiol (25,6 vs. 24,4 vs. 30,5, p=0,041). PRL levels were positive correlated with CKD stage (r_s=0,482, p<0,001) and creatinine (r_s=0,467, p<0,001) and negative correlated with testosterone (r_s=-0,286, p<0,001) and free testosterone levels (r_s=-0,307, p<0,001). There was no difference in PRL levels between hemodialysis and peritoneal dialysis (p=1,000). Analyzes related to the association of PRL levels with strength, quality of life, and sexual dysfunction are still being analyzed.

Conclusion: Hyperprolactinemia is associated with the severity of CKD, with a higher prevalence in dialysis patients. The relation of PRL levels with strength, quality of life, and sexual dysfunction are being evaluated.

P0839

EVALUATION OF ECHOCARDIOGRAPHIC INDICES OF DIASTOLIC DYSFUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Alexandros Kourtinos[1], Kostas Pappas[1], Lazaros Belbasis[2], ANILA DUNI[3], Karolos Pavlos Rapsomanikis[3], Athanasios Kitsos[3], Christos Katsouras[1], Stavroula Tsiara[4], Evangelia Ntounousi[3]

[1]University of Ioannina, 2nd Cardiology, Medical School, Ioannina, Greece, [2]University of Ioannina, Dept of Hygiene and Epidemiology, Ioannina, Greece, [3]University of Ioannina, Nephrology, School of Medicine, Ioannina, Greece and [4]University of Ioannina, Internal Medicine, Ioannina, Greece

Background and Aims: The structure and function of the left ventricle (LV) are affected since the early stages of chronic kidney disease (CKD). Our cross-sectional study aimed to estimate the echocardiographic indices of the LV diastolic function and the evaluation of their potential correlation with indices of kidney injury in patients with CKD, before initiation of renal replacement therapy.

Method: 99 patients with CKD (stage 2 CKD: 31 patients (27%), stage 3 CKD: 47 patients (40.9%) and stage 4 CKD: 37 patients (32.1%)) were enrolled in the study. Anthropometric data, indices of renal function (eGFR-CKD-EPI, urinary protein excretion in mg/24h), biochemical laboratory parameters, comorbidities [hypertension (HT), diabetes mellitus (DM), coronary heart disease (CAD)] and echocardiographic indices of LV diastolic function were recorded. In specific, left atrial (LA) dimensions were measured in M-Mode and were expressed both as absolute values in mm as well as indexed to body surface area ((BSA) and expressed as the LA index in mm/m^2. The study sample, after taking into account patient gender, was further divided into separate groups according to the presence or not of LA dilation.

Results: The average patient age was 62 +/- 13 years and average eGFR (CKD-EPI) was 44.1+/-21.4 $ml/min/1.73m^2$. With regard to comorbidities, 59.3% of the sample population had arterial hypertension, 24.3% had diabetes mellitus and 10.4% had known coronary artery disease. Regarding anti-hypertensive and hypolipidemic treatment, 22.6% of the patients were on ARB and 24% on ACEi, 51.3% on CCB, 29.6% on β-blockers, 37.4% on diuretics and 28.7% of the patients were receiving statin treatment. 28.2% of the patients had dilated LA in terms of absolute value and 13.8% had dilated LA following indexing to BSA (LA index). A positive correlation was observed between the LA size and age (p=0.001), BMI (p=0.041), uric acid levels (p=0.022), PTH (p=0.029), fibrinogen (p=0.035), LV mass (p=0.006) and LV mass/BSA (p=0.005), whereas a negative correlation was observed with serum LDL (p=0.027). Additionally, there was observed a negative correlation of LA index with eGFR (p=0.05), as well as an inverse relationship between LA index and PTH (p=0.012), age (p=0.004), BMI (p=0.037) and LV mass/BSA (p=0.005). No significant correlations between LA size and LA index with proteinuria or with co-morbidities (DM, HT, CAD) were observed.

Conclusion: In a population of patients with stage 2-4 CKD, LA size correlated to indices of CKD. Larger studies are required in order to further confirm these correlations.

P0840 RENAL FUNCTION AND RISK FACTORS IN LIVER TRANSPLANT PATIENTS

Gun Woo Kang[1], Seoung Gyu Kim[1], In Hee Lee[1], Ki Sung Ahn[1]

[1]*Catholic University of Daegu School of Medicine, Internal Medicine, Daegu, Korea, Rep. of South*

Background and Aims: Advanced surgical techniques and medical managements play major roles in improving patient survival after liver transplantation (LT). At the same time, identifying the causes and risk factors for long-term survival after LT are also important. Renal dysfunction following malignancy and infection is known as an important cause of mortality after LT. Various causes such as pre/post transplantation factors are known to affect renal function. The purpose of this study is to investigate the changes of renal function in patients undergoing LT and to identify factors that can predict long-term renal dysfunction.

Method: A retrospective study was performed on 113 patients aged 15 years or older who had undergone LT at Daegu Catholic University Hospital form January 2012 to December 2013. 97 patients survived and were followed up. Changes of renal function after LT were identified using serum creatinine every year up to 4 years. And all patients were divided into groups with increased creatinine (70 patients) and non-increased creatinine (27 patients) at 4 years after LT. pre-transplantation factors were blood urea nitrogen (BUN), creatinine, protein, albumin, hemoglobin, total bilirubin, international normalized ratio. Subsequent BUN and creatinine were compared by independent t test. Statistical analysis was performed with IBM SPSS Statistics for Window, Version 19.0.

Results: 58 were male (59.7%) and the mean age was 49.5 years old. 83 patients (85.6%) received liver transplantations from living donors. There were no significant differences in the donor types and recipient's sex between the two groups with the increased and non-increased creatinine at 4 years after LT. However, the age of recipients was a significant difference between the two groups (51.3 and 45.4 years old) (p=0.018). Annual mean creatinine levels from pre-transplantation to 4 years after LT were 0.88 $\pm$ 0.39 (before transplant), 1.19 $\pm$ 0.54 (1 year after LT), 1.07 $\pm$ 0.44 (2 years), 1.12 $\pm$ 0.68 (3 years), and 1.19 $\pm$ 0.99 (4 years). Renal function decreased in 1 year after LT and improved in 2 years, then decreased again. In univariate analysis, the increased creatinine group was older than the non-increased group, and BUN and creatinine at 1 year after LT were significant differences in the two groups ($p = 0.018$, $p = 0.031$, $p = 0.013$). Multivariate analysis identified the creatinine at 1 year was an independent risk factor for long-term renal function after LT (OR 14.31, 95% CI: 1.5-133.3, $p = 0.019$).

Conclusion: This study explored that renal function was continuously decreased after LT and renal function at 1 year after LT had a significant effect on long-term renal function. Therefore, management of renal function during one year after LT is important for long-term renal function and may reduce mortality.

P0841

SPECTRUM OF RENAL DISORDERS AT A TERTIARY CARE HOSPITAL IN KARACHI, PAKISTAN: RESULTS FROM AN OUTPATIENTS DATABASE IN A DEVELOPING COUNTRY.

Sonia Yaqub[1], Safia Awan[1]

[1]*Aga Khan University Hospital, Pakistan, Karachi, Pakistan*

Background and Aims: The burden of renal diseases in developing countries is rising. However, little is known about the epidemiology and clinical pattern of various disorders in our part of the world. The objective of this study was to understand the burden of disease faced by nephrologists in a tertiary care setting.

Method: It was a prospective observational study of all presentations to nephrology clinics at Aga Khan University Hospital Karachi over a period of one year.

Results: A total of 1589 out-patients with renal diseases were seen during the study period. The mean age of the study participants were 49.9 years and 629 (53%) were male. 88.6% of patients belonged to Karachi and Hyderabad areas of Sind province. CKD was the most common diagnosis (93.5%). Diabetic kidney disease and hypertension and related disorders were causes of CKD in 29.5% and 29.1% cases respectively. In 13.1% patients, the etiology of CKD could not be determined. Among glomerulonephritis (6.67%), membranous nephropathy was the commonest disorder (32.1%) followed by FSGS (29.2%), Minimal change disease (15.1%) and IgA nephropathy (10.4%). SLE and lupus nephritis was seen in 48 patients (4.0%). Around 10% patients were suffering from various tubulointerstitial diseases (renal stones, UTIs, Acute and chronic tubulointerstitial nephritis).

Conclusion: It's a first study of its kind reporting frequency of various renal disorders from an outpatient registry at a tertiary care hospital in Pakistan. Diabetes and hypertension account for almost 60% of cases with CKD. Membranous nephropathy is the commonest glomerular disease in an urban population cohort. We need more studies on spectrum of renal diseases for better planning and available resource management.

P0842

MANAGEMENT OF RENAL RISK PATIENTS AND THERAPEUTIC CHANGES AFTER DIAGNOSIS OF KIDNEY DISEASE IN PRIMARY CARE

Emanuel Zitt[1], Hannelore Sprenger-Mähr[1], Karl Lhotta[1]

[1]*Academic Teaching Hospital Feldkirch, Internal Medicine 3 (Nephrology and Dialysis), Feldkirch, Austria*

Background and Aims: Screening for chronic kidney disease (CKD) is proposed in high risk groups. Whether a new CKD diagnosis in general practice leads to improved patient management, is largely unknown.

Method: To answer this question and evaluate the kidney disease specific pharmacological care in renal risk patients, a screening study in patients at high risk for kidney disease was performed in the primary care setting in ten general practices in the state of Vorarlberg, Austria. General practitioners were provided with guidelines for the management of CKD with a focus on blood pressure control, RAS inhibition and use of statins.

Results: In total, 434 patients between age 35 and 77 were included (61% males, mean age 56±7 years, eGFR 86±15 ml/min, body mass index 31±6 kg/m, blood pressure 135±16/83±10 mmHg), of whom 80% had hypertension, 43% had diabetes and 42% were obese. RAS-blockers were already taken by 64% of patients, statins by 39%. A diagnosis of CKD (stage ≥G3 and/or ≥A2) was established in 73 patients (17%), 60% of them had diabetes. Compared to patients without CKD, CKD patients were already treated more often with RAS-blockers (78% vs 61%, p=0.005), whereas statin usage was comparable (44% vs 38%, p=0.3347). After CKD diagnosis, medical therapy was changed in 13 patients (18%). A RAS-blocker was initiated in two out of the 16 patients without a preexisting RAS-blocker (12.5%), the dosage was increased in one patient. Antihypertensive therapy was intensified adding amlodipine in seven patients (10%), and a statin was begun in six (15%) out of 41 statin-naive patients. In those without CKD after the screening, therapy was changed in 40 patients (11%). Compared to patients with CKD, fewer patients started a statin therapy (5% vs 15%, p=0.012) and were additionally treated with amlodipine (3% vs 10%, p=0.021) to optimize blood pressure control.

Conclusion: This study shows that in the primary care setting a great proportion of CKD patients are already on RAS-blockers, whereas the prescription rate for statins is low. A diagnosis of CKD led to a moderate increase in statin therapy, which leaves further opportunity for improvement. The reasons for this rather low use of statins in CKD patients need to be determined.

P0843

EFFECT OF GROUP PSYCHO SOCIAL SUPPORT ON QUALITY OF LIFE AND MORTALITY WITH END STAGE KIDNEY DISEASE.

Zara Nisar[1], Hassan Sajjad[2], Nisar Anwar[2]

[1]Khyber Medical University, Health Research, Peshawar, Pakistan and [2]Khyber Teaching Hospital, Nephrology, Peshawar, Pakistan

Background and Aims: The patients of end stage renal disease suffer a lot of psychological trauma as well as feel a lot of social burden. They mostly show psychological distress in different forms, be it impaired quality of life, depression or anxiety. The aim of our study was to find out the effect of supportive-expressive group therapy in end stage kidney disease patients in the outcome of better health related quality of life and survival.

Method: 181 patients were recruited in the study after consent between June 2012-June 2017. They were then assigned randomly to Group A supportive-expressive group therapy or to a Group B control group (no intervention). It was a double blinded randomized control trial. 115 patients were assigned to Group A and 66 were assigned to group B. The primary outcome was the effect on health related quality of life. Secondly, if it had any impact on survival. Significant predictors of survival were not analysed. Analysis was done by intention to treat.

Results: The patients of group A showed decrease in physical pain($p=0.002$), mood elevation ($p=0.04$), compliance with treatment ($p=0.001$), reduced hopelessness ($p=0.004$), newly diagnosed depressive disorders ($p=0.01$) and better social life ($p=0.003$). Group A had 97% survival rate as compared to group B with 77%.

Conclusion: Supportive-expressive group therapy to patients with end stage kidney disease improves health related quality of life. It also has an effect on survival maybe because of compliance with treatment. We would like to further explore the role of Supportive-expressive group therapy in survival. Support groups should be provided to patients in developing countries like the setup of ours because it has a great impact on the betterment of the patient.

P0844

PREDICTION MODEL FOR RENAL FUNCTION DECLINE WITH SUGGESTING HOW TO CONTROL CLINICAL PARAMETERS TO MAINTAIN RENAL FUNCTION BY AN INTERPRETABLE MACHINE LEARNING IN JAPANESE OUTPATIENTS WITH CHRONIC KIDNEY DISEASE

Soshiro Ogata[1], Yumi Akashi[1], Takaya Sakusabe[2], Kenji Maeda[3], Shigeru Nakai[2]

[1]Fujita Health University, School of Health Science, Toyoake, Japan, [2]Fujita Health University, School of Medical Sciences, Toyoake, Japan and [3]Daiko-Sunadabashi Clinic, Nagoya, Japan

Background and Aims: Prediction models for renal function decline has already been developed. However, few prediction models can suggest how to control clinical parameters to maintain renal function. The present study aimed to develop a prediction model for renal function decline that can suggest how to control clinical parameters to maintain renal function by an interpretable machine learning in Japanese outpatients with chronic kidney disease (CKD).

Method: The present study used a retrospective cohort design. The eligible criteria of the present study were outpatients with CKD stage 3, 4, and 5, treated in Daiko-Sunadabashi Clinic in Japan between 2005 and 2019. Among the patients, we analyzed patients whose 24-hour urine samples were collected 3 times and over between 6 and 36 months. The primary outcome was renal function decline defied by glomerular filtration rate (GFR) decreased by >30% from the baseline. As predictors, we used baseline CKD stage and baseline values and change rate from the baseline to the next-to-last observations of the following clinical parameters: urine volume, GFR, quantity of protein in urine, intake of protein and salt, and body mass index (BMI). We used a random forest model with actionable feature tweaking to develop the prediction model with suggesting how to control those clinical parameters. This method has been developed recently and to improve interpretability of the random forest method. This can suggest how to alter predictor values in order to change prediction results from bad to favorable outcome (e.g., changing from predicted decline to predicted maintenance of renal function). Predictability of the prediction model was assessed by accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in training and testing datasets.

Results: We analyzed 355 participants whose mean age (SD) was 69.2 (13.0) years old. Of the participants, 65.4% were men, 37.5%, 37.2% and 25.3% were CKD stage 3, 4, and 5, respectively. Of the participants, the 80% were included in the training dataset, and the 20% in the testing dataset. Predictability of the developed prediction model was summarized in Table 1, showing the prediction model had good predictability. The developed prediction model suggested that decreasing protein in urine and salt intake, and increasing GFR could be important to change from predicted decline to predicted maintenance of renal function. The prediction model could also suggest how to control those clinical parameters at individual-level (e.g., #53 and #67 patients in Figure 1).

Conclusion: The present study developed the prediction model for renal function decline with high predictability. The prediction model suggested that decreasing protein in urine and salt intake, and increasing GFR could be important to maintain renal function.

Table 1. Predictability of the developed prediction model for renal function decline.

Dataset	Accuracy	Sensitivity	Specificity	PPV	NPV
Training	77.8%	70.5%	83.9%	78.4%,	77.4%
Testing	83.1%	79.4%	86.5%	84.4%	82.1%

Abbreviations: PPV, positive predictive value; NPV, negative predictive value.

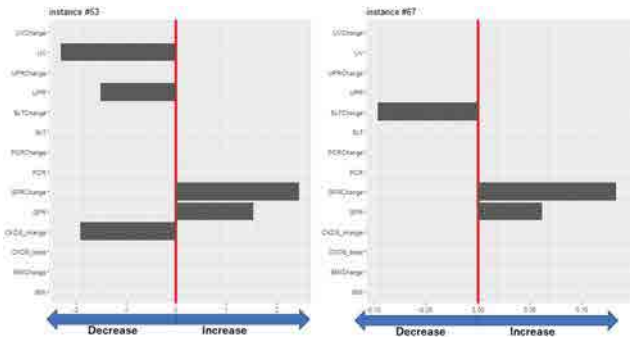


Figure 1. Clinical parameters and its controlling ways at individual-level, suggested by the developed prediction model in order to change from predicted decline to predicted maintenance of renal function.

P0845 **INCREASING TOTAL RENAL VOLUME AFTER NEPHRECTOMY FOR RENAL CELL CARCINOMA IS ASSOCIATED WITH RENAL FUNCTION EVOLUTION**

SAUL PAMPA-SAICO[1], M. Soledad Pizarro-Sánchez[1], Simona Alexandru[1], Laura García Puente-Suárez[1], María López-Picasso[1], Raquel Barba Martín[1]

[1]*Hospital Universitario Rey Juan Carlos, Mostoles, Madrid, Nephrology, Mostoles, Spain*

Background and Aims: Renal cell carcinoma is the most common form of kidney cancer. Reduction of renal mass after radical nephrectomy (RN) in these patients, results in compensatory hypertrophy of the contralateral kidney. The capacity of compensation will determine the renal function (RF) evolution. Measuring of total renal volume (TRV) of the remaining kidney pre and post RN can help assess the RF evolution.

Aims: To determine the correlation between TRV pre and post nephrectomy (a year of follow-up) with RF and the factors that modify.

Method: A retrospective cohort study was carried out in our institution, in 62 patients who had underwent RN from 2014 to 2018, due to renal cell carcinoma (confirmed by histopathology). The demographic data included age, gender, body mass index (BMI), associated comorbidities, smoking habits were collected.

Serum creatinine, estimated glomerular filtration rate (eGFR) and proteinuria were collected in the preoperative period and in the follow-up.

The TRV was calculated pre and post (a year of follow-up) RN, using ellipsoid formula equation (computed tomography scan or magnetic resonance imaging).

Renal function evolution was assessed by eGFR using the modification of diet in Renal Disease formula. Multivariate linear regression analysis was used to determine the predictor of TRV at 1 year of follow-up.

Results: The median age at the time of RN was 71 years old (range, 43-86 years). Most of them were men, 69% (43/19). The estimated glomerular filtration rate (FGe) pre and post nephrectomy was 74 (41-102) and 52.1 ml/min/ m2 (22-89) respectively (P=0.013). The TRV pre and post-nephrectomy was 165.3 (102.3-259.7) and 188.3 ml (115.3-271.2) respectively (P=0.001).

On multivariate linear regression analysis, controlling for age and sex; the pre-nephrectomy FGe ($\beta = 0.42$; $P = 0.023$) and the pre TRV ($\beta = 1.23$; $P < 0.0001$) were positively correlated with the post-nephrectomy TRV, while the FGe at year of follow-up was correlated negatively ($\beta = -1.11$; $P = 0.024$)

Conclusion: The post nephrectomy TRV was positively correlated with TRV and FGe pre nephrectomy. While with the FGe at one year post nephrectomy was negatively correlated. The increasing TRV pre and post nephrectomy can help to predict renal function at a year of follow-up in this group of patients.

CKD. ANAEMIA

P0846

ESA HYPORESPOSIVENESS AND CLINICAL OUTCOMES DURING TREATMENT WITH EPOETIN BETA PEGOL IN HEMODIALYSIS PATIENTS: A MULTICENTER PROSPECTIVE STUDY; PARAMOUNT-HD STUDY

Takayuki Hamano[1], Hideki Fujii[2], Ken Tsuchiya[3], Kuragano Takahiro[4], Nobuhiko Joki[5], Kazuhiko Tsuruya[6], Hirokazu Honda[7], Yukari Uemura[8], Yasuo Ohashi[9], Kosaku Nitta[10]

[1]Nagoya City University Graduate School of Medical Sciences, Nephrology, [2]Kobe University Graduate School of Medicine, Division of Nephrology and Kidney Center, [3]Tokyo Women's Medical University, Blood Purification, [4]Hyogo College of Medicine, Division of Nephrology and Dialysis, Department of Internal Medicine, [5]Toho University Ohashi Medical Center, Nephrology, [6]Nara Medical University, Nephrology, [7]Showa University, Nephrology, [8]National Center for Global Health and Medicine, Biostatistics Section, Department of Data Science, Center for Clinical Sciences, [9]Chuo University, Biostatistics, Department of Integrated Science and Engineering for Sustainable Society and [10]Tokyo Women's Medical University, Nephrology

Background and Aims: Hemodialysis (HD) patients hyporesponsive to erythropoiesis stimulating agents (ESAs) were reported to have poor prognosis. However, little is known regarding the association between the hyporesponsiveness to CERA and the types of outcome in HD patients. Moreover, the effect of on-line HDF on hyporesponsiveness to CERA has not been evaluated so far.

Method: In this multicenter prospective study, we enrolled 4034 maintenance HD patients receiving any kinds of ESA. Prior ESA was changed to CERA in all patients. We studied the association between erythropoietin resistance index (ERI) at 6-month after the change to CERA (baseline ERI) and such outcomes as cardiovascular events and/or mortality using Cox proportional hazards models (landmark analyses). ERI was defined as monthly CERA dose divided by hemoglobin and dry weight. Just before the enrollment of the patients, iron-based phosphate binders became available and on-line hemodiafiltration (HDF) began to be reimbursed in Japan, therefore, we examined whether oral iron-containing drugs and on-line HDF had some effects on the serial trend of ERI by mixed effects model with time-dependent ERI as a dependent variable. When ERI is found to be improved by these changes in practice patterns, we further studied the effect of time-dependent ERI on such outcomes as cardiovascular events, mortality, death due to cancer, and death due to infection by using marginal structural models to eradicate time-dependent confounding by iron parameters, C-reactive protein, iron-containing drugs, and HDF. Missing values were imputed by multiple imputations.

Results: Mean age was 65.9 years and 43.1% of patients had diabetes. The median dialysis vintage and observation period was 5.0 years and 22.1 months, respectively. The percentage of patients receiving oral iron-containing drugs increased from 11.1% at baseline to 25.0% at 24-month. As a result, mean TSAT level increased from 24.5% to 27.4% at 24-month. The percentage of patients on on-line HDF also increased from 13.5% to 22.6%. ERI gradually decreased as time went by with great improvement especially in patients with highest quintile of ERI (Q5). Mixed effects model with time-dependent ERI as a dependent variable showed that introduction of iron-containing drugs and on-line HDF had improved ERI significantly. The landmark analyses including 3001 patients failed to show significant associations between baseline ERI quintile and cardiovascular events or mortality. We only found that highest quintile of baseline ERI (Q5) was associated with significantly higher composite events of mortality and cardiovascular events as compared to the lowest quintile (Q1) (Hazard ratio [HR], 1.56; 95% CI; 1.04-2.32). However, marginal structural models showed that time-dependent ERI Q5 was significantly associated with higher cardiovascular event rate as compared to Q1 (HR, 2.11; 95% CI; 1.31-3.38). Trend toward higher rate of mortality with the increase in time-dependent ERI quintile was also observed (HR of Q5, 3.07; 95% CI; 1.95-4.83). Similar but stronger relationships were observed for death due to infection (HR of Q5, 6.70; 95% CI; 1.89-23.77) and death due to cancer (HR of Q5, 15.08; 95% CI; 4.08-55.74).

Conclusion: The prevailing use of iron-containing drugs and on-line HDF has improved hyporesponsiveness to CERA in Japan. Therefore, baseline ERI at 6-month did not predict subsequent cardiovascular events or death. However, high time-dependent ERI was a predictor of cardiovascular events, death due to infection, and death due to cancer as well as all-cause mortality. Strong association of time-dependent ERI was observed especially with death due to cancer.

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P0847 **HEPATIC ERYTHROPOIETIN SYNTHESIS IS ENHANCED IN HEMODIALYSIS PATIENTS WHO DO NOT REQUIRE ERYTHROPOIESIS-STIMULATING AGENTS**

Aki Hirayama[1], Takamoto Yanagawa[2], Yoko Kaneko[2], Yumiko Nagano[1], Shigeru Owada[3], Takashi Ishizu[2]

[1]Tsukuba University of Technology, Center for Integrarive Medicine, Tsukuba, Japan, [2]Tsukuba Central Hospital, Department of Nephrology, Ushiku, Japan and [3]Asao Clinic, Kawasaki, Japan

Background and Aims: Erythropoietin is synthesized in the liver during the fetal period and mainly in the kidney after birth. However, some patients with end-stage chronic kidney disease do not require the administration of erythropoiesis-stimulating agents (ESA) despite their damaged renal function. This study aimed to clarify the origin of extrarenal erythropoietin generation in these patients.

Method: The origin of erythropoietin was investigated by analyzing the erythropoietin glycation patterns based on the percentages of migrated isoforms (PMI). Sera of stable hemodialysis (HD) patients with (ESA group) or without (non-ESA group) ESA treatment and umbilical cord blood of newborns (UCB group), which contained erythropoietin of liver origin, were analyzed. The non-ESA group was determined as HD patients without ESA treatment for $>$ 6 months. Informed consent was obtained from all included HD patients and from the parents or guardians of the newborns. This study was performed with permission from the institutional ethical committee and was registered as a clinical trial (no. R000033462 UMIN000029335).

Results: The mean duration of no ESA treatment in the non-ESA group was 29.2 months. There were no differences in major clinical parameters, including age and HD duration. The hemoglobin concentration in the ESA group was 107 $\pm$ 5 g/L (mean $\pm$ standard error), which was significantly lower than that in the non-ESA group (123 $\pm$ 4 g/L) (P = 0.025, unpaired Student's t-test). The PMI values of the ESA, non-ESA, and UCB groups were 12.6 $\pm$ 11.4%, 61.2 $\pm$ 13.1%, and 65.0 $\pm$ 13.5%, respectively, and the PMI value of the ESA group was significantly lower than that of non-ESA or UCB group (one-way analysis of variance with Tukey-Kramer test), suggesting that the glycation pattern of erythropoietin in the non-ESA group was similar to that in the UCB group but different from that in the ESA group. No significant differences were found in the reticulocyte ratio, serum iron concentration, total iron binding capacity, and ferritin and transferrin saturation between the ESA and non-ESA groups.

Conclusion: These results suggest that patients in the non-ESA group had enhanced extrarenal erythropoietin synthesis and that their erythropoietin originated from the liver. Further analysis of the underlying mechanism may contribute to the development of internal extrarenal erythropoietin-stimulating therapy.

P0848

PROSPECTIVE OPEN-LABEL EXPLORATIVE RANDOMISED SINGLE-CENTRE COMPARATIVE STUDY TO DETERMINE THE EFFECTS OF VARIOUS INTRAVENOUS IRON PREPARATIONS ON MARKERS OF OXIDATIVE STRESS AND KIDNEY INJURY IN CHRONIC KIDNEY DISEASE (IRON-CKD)

Xenophon Kassianides[1,2], Ahmed Zeidan[1], Roger Sturmey[3], Andrew Gordon[3], Sunil Bhandari[1,2]

[1]Hull University Teaching Hospitals NHS Trust, Academic Renal Department, Kingston upon Hull, United Kingdom, [2]Hull York Medical School (HYMS), Kingston Upon Hull, United Kingdom and [3]Hull York Medical School (HYMS), Centre for Atherothrombosis and Metabolic Disease, Kingston Upon Hull, United Kingdom

Background and Aims: Iron deficiency is commonly treated with intravenous (IV) iron where oral iron is insufficient or cannot be tolerated. While IV iron is considered efficient and effective, safety concerns exist regarding the potential effect of IV iron on oxidative stress, inflammation and endothelial function. Transferrin is unable to saturate all the iron administered. Consequently, evidence has suggested differential generation of "free" or catalytic labile iron, depending on iron preparation. Labile iron stimulates lipid oxidation and free radical generation which can lead to increased oxidative stress, inflammation and endothelial dysfunction. The comparative risk of IV iron preparations has not been previ-ously extensively assessed.

The possibility of IV iron leading to changes in oxidative stress, inflammation and endothelial function is assessed in this study. The potential interplay of IV iron changes with signaling pathways may lead to renal damage depending on the iron formulation used. This may lead to tubular and glomerular injury manifested as raised Neutrophil gelatinase-associated lipocalin (NGAL) levels in patients with chronic kidney disease (CKD).

Method: IRON-CKD is a prospective open-label explorative randomized, single-centre study assessing comparative safety and efficacy of three parenteral iron preparations. Patients with established CKD stages 3-5 and serum ferritin (SF) $<$ 200microg/L and/or transferrin saturation (TS) $<$20% were recruited and randomized in a 1:1:1:1 ratio. The groups received a single infusion of 200mg Iron Dextran (Cosmofer ®), 200 mg Iron Sucrose (Venofer ®), and Iron Isomaltoside (Monofer ®) either as low (200mg) or high dose (1000mg). The patients were followed-up after IV iron at 2 hours and then at 1 day, 1 week, 1 month and 3 month intervals. Oxidative stress markers (Thiobarbituric acid reactive substances (TBARS)), inflammatory markers (Interleukin-1b, Interleukin-6, Interleukin-8, Interleukin-10) and surrogate markers of endothelial dysfunction (E-selectin, P-selectin) were measured. NGAL levels for establishment of potential acute kidney insult were measured. Free catalytic iron generation was also measured using the FeROS™ as-say. Data are presented as means and standard error of the mean (SEM). Statistical analysis was carried out using ANOVA. A p value of $<$0.05 was statistically significant.

Results: Forty patients were recruited and randomised with 10 per group. The mean age was 58.8 (±2.2) years and 23 (58%) were male. Free labile iron and TBARS increased within 2 hours of infusion (1.4 ΔFU/min (±0.5) to 7.4 ΔFU/min (±2.4)) (1083.0 nM (± 117.1) to 1552.6 nM (±156.0)) respectively with complete recovery within one week. TBARS and free labile iron were more pronounced within one day in the group receiving high dose Monofer® (TBARS: pre-infusion: 846.0 nM (±108.9) to 1865.0 nM (±203.2); Free labile iron: pre infusion: 0.3 ΔFU/min (±0.2) to 19.6 ΔFU/min (±7.1)). These were statistically significant with $p < 0.001$. These returned to predosage levels and did not translate to any detriment in markers of inflammation or endothelial function (E-selectin or P-selectin). There was a non-statistically significant increase in Interleukin-10 (an anti-inflammatory cytokine) 2-hours post-infusion which was transient. Intravenous iron cumulatively and comparatively did not lead to a significant increase in NGAL (pre-infusion 570.5 ng/ml (±52.8); post-infusion 547.8 ng/ml (SEM: ±50.5); 3 months interval 534.8 ng/ml (±52.8)) at any given time point.

Conclusion: High dose of IV iron leads to a transient increased generation of free iron which disappears within one week. Iron therapy, at least in the short term, does not adversely affect markers of acute kidney injury, endothelial function, inflammation and oxidative stress status. This mechanistic data indicates that IV iron at both low and high doses is safe in patients with chronic kidney disease.

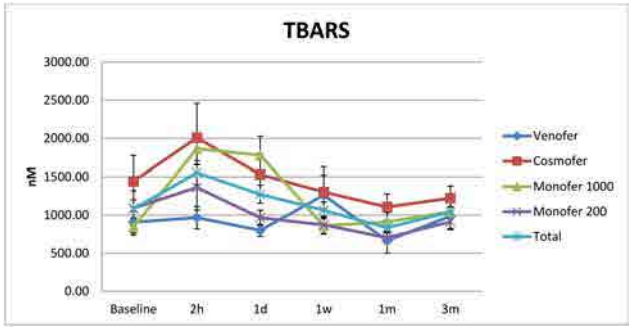


Figure:

P0849 **LOWER TRANSFERRIN SATURATION INDEX (TSAT) IS ASSOCIATED WITH WORSE HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN NON-DIALYSIS DEPENDENT CHRONIC KIDNEY DISEASE (NDD-CKD) PATIENTS AT BOTH HIGHER AND LOWER HEMOGLOBIN LEVELS**

Murilo Guedes[1], Daniel Muenz[2], Jarcy Zee[2], Marcelo Lopes[2], Sandra Waechter[3], Benedicte Stengel[4], Ziad Massy[5], Elodie Speyer[4], Fredric Finkelstein[6], Ricardo Sesso[7], Ronald Pisoni[2], Bruce Robinson[2], Roberto Pecoits-Filho[2]

[1]Pontificia Universidade Catolica do Parana, School of Medicine, Curitiba, Brazil, [2]Arbor Research Collaborative for Health, [3]Vifor Fresenius Medical Care Renal Pharma, [4]Centre for Research in Epidemiology and Population Health (CESP), Inserm UMRS 1018, [5]Institut National de la Santé et de la Recherche Médicale , [6]Department of Medicine, Yale University, New Haven, CT and [7]Universidade Federal de São Paulo

Background and Aims: Iron Deficiency (ID) is a common condition in NDD-CKD patients that is associated with poorer clinical outcomes. In different populations, such as congestive heart failure patients, treatment of ID leads to better clinical outcomes and HRQOL. However, the impact of ID on HRQOL is previously unknown among NDD-CKD individuals. We analyzed real world data from a multinational cohort of NDD-CKD stage 3 to 5 patients under nephrology care to evaluate the association between TSAT and HRQOL measures from the KDQOL-36.

Method: Patients from Brazil (N=205), France (N=2015), and the US (N=293) enrolled in the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps, 2013 to 2019) with available TSAT, ferritin, and HRQOL data were included in the analysis. We grouped patients according to their TSAT levels as ≤15%, >15-20%, >20-30% (reference group), >30-50%, and >50%. We considered the TSAT value that preceded the HRQOL measurement closest in time as the predictor. Linear mixed regression was used to estimate the mean differences (95% CI) in physical composite summary (PCS), mental composite summary (MCS), and KDQOL-36 subdomains across TSAT categories. Models were adjusted for potential confounders.

Results: 2513 patients (62% male, 44% with diabetes, mean (SD) age 67 (13) years; 48%, 44% and 8% having stage 3, 4 and 5 NDD-CKD, respectively) were included in the analysis. Mean TSAT was 25 % (10). Distribution across TSAT categories was 14%, 19%, 42%, 23, and 2%, respectively. The median [IQR] number of days between TSAT measurement and PRO collection was 24 [13, 49] days. Mean PCS was 41 (10) and MCS was 45 (11). In the multivariate analysis, TSAT ≤15% was associated with lower HRQOL scores, in particular PCS, and with less favorable effects and symptoms of kidney disease (Figure). Similarly, less favorable HRQOL scores captured in the SF-12 subdomains indicative of physical HRQOL were observed in patients with lower TSAT. The adjustment for Hb only slightly attenuated the effects, and the results were not different for subgroup of patients with hemoglobin <11.5 vs ≥ 11.5 g/dL.

Conclusion: Lower TSAT levels, indicative of iron deficiency, are associated with poorer HRQOL in NDD-CKD patients, particularly for physical domains and effects of kidney disease, even after adjustment for potential confounders and stratification for normal and low hemoglobin levels. Randomized controlled trials of iron replacement therapy aiming to evaluate its impact on HRQOL among NDD-CKD individuals are needed to confirm and integrate these findings into clinical practice.

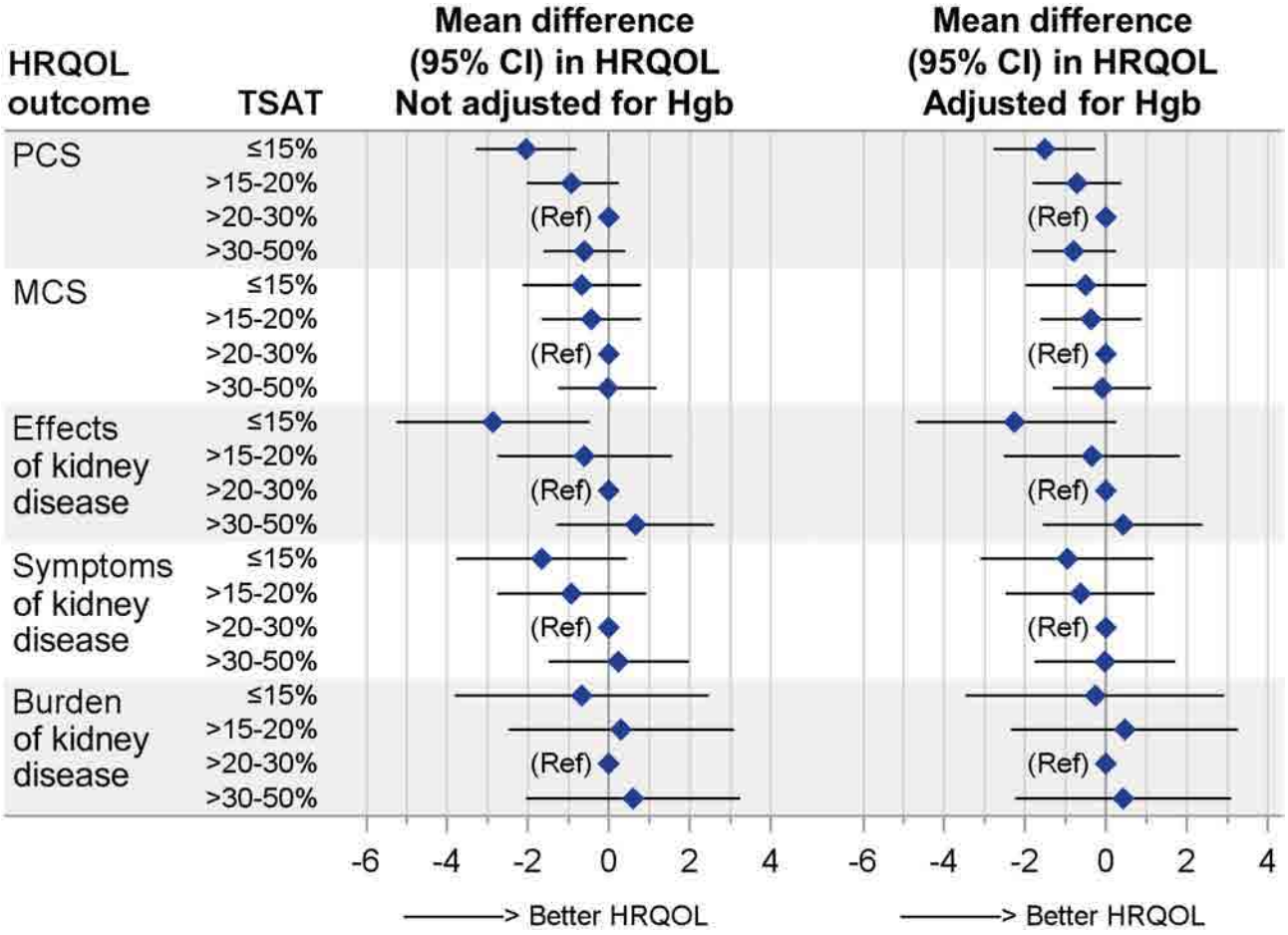


Figure. Mean differences in KDQOL-36 domains by TSAT categories, relative to TSAT >20-30%. Based on linear mixed models, adjusted for country, age, sex, race, BMI, smoking status, eGFR, albuminuria, albumin, white blood cell count, ferritin, diabetes, hypertension, atherosclerotic disease, congestive heart failure, other cardiovascular comorbidities, cancer, and history of ulcers/gangrene (left panel) and including hemoglobin (right panel). Results for TSAT>50% are not shown due to small sample size.

P0850

SERUM OSTEOPROTEGERIN LEVELS ARE ASSOCIATED WITH AN INCREASED RISK OF DEVELOPING ANEMIA IN PATIENTS WITH NON DIALYSIS CHRONIC KIDNEY DISEASE

Yooju Nam[1], Seonyeong Lee[1], Hyung Woo Kim[1], Jae Hyun Chang[2], Tae-Hyun Yoo[1]

[1]Severance hospital, Yonsei University, Department of Internal Medicine, Seoul, Korea, Rep. of South and [2]Gil Medical Center, Gachon University College of Medicine, Department of Internal Medicine, Incheon, Korea, Rep. of South

Background and Aims: Osteoprotegerin (OPG), which is an osteoclastic inhibitory factor, have been shown associated with adverse renal outcomes and progression of vascular calcification in chronic kidney disease (CKD) patients. Anemia and CKD-bone mineral disorders (CKD-MBD) are also frequently observed in these patients. Since CKD-MBD and anemia might be closely linked, therefore, we further examined whether OPG level as a marker for bone turnover can predict the future development of anemia in a large-scale prospective cohort.

Method: Among 2,238 patients with non-dialysis CKD enrolled in the KoreaN cohort study for Outcome in patients With Chronic Kidney Disease (KNOW-CKD), 2,086 patients who measured hemoglobin, hepcidin, iron profiles and OPG level were included in the analysis. Anemia was defined as a hemoglobin level of < 13.0 g/dL and 12.0 g/dL for male and female, respectively.

Results: The mean age was 53.6 $\pm$ 12.2 years and 1,270 (60.9%) patients were males. At baseline, anemia was found in 941 (45.1%) patients. Log transformed OPG levels significantly correlated with FGF23 levels, but inversely with iron profiles and hemoglobin levels at baseline. A multivariate logistic regression model showed that log OPG level was independently associated with the prevalence of anemia (odds ratio [OR], 2.22; 95% confidence interval [CI], 1.41-3.48, P=0.001). Among 1110 patients without baseline anemia, 258 (25.3%) patients developed anemia during a median follow-up duration of 34.6 (interquartile range, 23-48) months. In the fully adjusted multivariable Cox models, risk of developing anemia was significantly higher in the fourth (hazard ratio [HR], 1.99; 95% CI, 1.08-3.67; P =0.028) than in the first OPG quartile. Similar association was observed in a model when OPG was treated as a continuous variable.

Conclusion: We showed that high serum OPG levels are associated with an increased risk of developing anemia in patients with non-dialysis CKD.

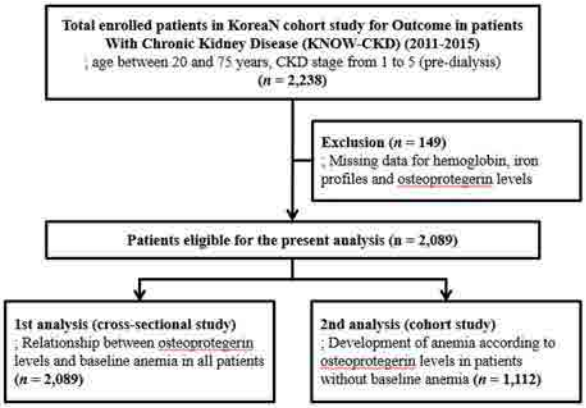


Table. Multivariable Cox regression model for the development of anemia

	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
OPG quartile								
Quartile 1	Reference		Reference		Reference		Reference	
Quartile 2	1.49 (1.05-2.13)	0.026	1.39 (0.89-2.18)	0.152	1.14 (0.70-1.84)	0.603	1.11 (0.69-1.80)	0.671
Quartile 3	1.88 (1.31-2.70)	0.001	1.58 (0.97-2.58)	0.066	1.29 (0.77-2.17)	0.336	1.25 (0.74-2.12)	0.399
Quartile 4	3.87 (2.68-5.61)	<0.001	3.10 (1.75-5.47)	<0.001	2.14 (1.18-3.94)	0.013	1.99 (1.08-3.67)	0.028
FGF23 (per 1 log)	3.89 (2.81-5.39)	<0.001	3.74 (1.16-1.36)	<0.001	2.52 (1.49-4.25)	0.001	1.17 (1.07-1.29)	0.001

Note: OPG entered as a categorical and continuous form (log transformed)

[a]Unadjusted model

[b]Adjusted for age, sex, DM, BMI, SBP, CCI, smoking status

[c]Adjusted for Model 2 + eGFR, phosphorus, iron deficiency, and proteinuria*

[d]Adjusted for Model 3 + iron replacement

* Variables are log transformed.

Abbreviations: OPG, osteoprotegrin; FGF23, fibroblast growth factor 23; DM, diabetes mellitus; BMI, body mass index; SBP, systolic blood pressure; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate

Table. Multivariable Cox regression model for the development of anemia

	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
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[d]Adjusted for Model 3 + iron replacement

* Variables are log transformed.

Abbreviations: OPG, osteoprotegrin; FGF23, fibroblast growth factor 23; DM, diabetes mellitus; BMI, body mass index; SBP, systolic blood pressure; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate

Figure:

P0851

THE DIFFERENTIAL IMPACT OF INTRAVENOUS IRON IN A MODEL OF EXPERIMENTAL URAEMIA ON TISSUE MARKERS OF OXIDATIVE STRESS

Sunil Bhandari[1], Faisal Nuhu[2], Anne.Marie Seymour[2]

[1]Hull University Teaching Hospitals NHS Trust, Renal Medicine, HULL, United Kingdom and [2]University and of Hull and Hull York Medical School, Biomedical Sciences, Hull, United Kingdom

Background and Aims: Uraemia leads to changes in cardiac structure, metabolic remodelling and anaemia, key factors in the development of heart failure in patients with chronic kidney disease (CKD). Previous studies have identified abnormalities in mitochondrial function in experimental uraemia, potentially impairing energy provision and enhancing oxidative stress. The aim of this study was to characterise oxidant status and changes in mitochondrial function in uraemia and the impact of iron therapy.

Method: Experimental uraemia was induced in male Sprague-Dawley rats via a subtotal nephrectomy and parenteral iron administration at 6 weeks post-surgery (10mg/Kg body weight). Pro-oxidant activities and antioxidant capacities (oxidised glutathione (GSSG) relative to reduced (GSH)) in both sham and uraemic animals and lipid peroxidation (thiobarbituric acid-reactive substances (TBARS) was measured. Mitochondrial function was assessed using the SEAHORSE analyser.

Results: Oxidative stress was increased in cardiac tissue (69% increase in GSSG/GSH ratio, 38% rise in TBARS and significantly (79%) upregulated NADPH oxidase activity. Glutathione peroxidase (GPx) and glutathione reductase (GR) activities were significantly increased by 30%. Iron reduced GSSG/GSH ratio and TBARS by 62% and 51% respectively. Iron therapy was also associated with significantly increased aconitase activity. Parenteral iron improved respiratory reserve in cardiac mitochondria and skeletal mitochondria suggests IV iron restores mitochondrial function.

Conclusion: Uraemia leads or oxidative stress and mitochondrial dysfunction in cardiac tissue. Iron therapy reduces oxidative stress and improves cardiac mitochondrial function. This might lead to reduced adverse cardiovascular outcomes in CKD.

P0852

PERICYTE-SPECIFIC MANIPULATION OF HYPOXIA-INDUCIBLE FACTORS REGULATES ERYTHROPOIESIS WITHOUT AGGRAVATING RENAL FIBROSIS

Pei-Zhen Cai[1], SZU-YU PAN[2,3], SHUEI-LIONG LIN[1,3]

[1] National Taiwan University College of Medicine, Taipei, Taiwan, R.O.C., [2]Far Eastern Memorial Hospital, New Taipei City, Taiwan, R.O.C. and [3] National Taiwan University Hospital, Taipei, Taiwan, R.O.C.

Background and Aims: Stabilizers of hypoxia-inducible factor (HIF) have been shown to be effective on treatment of anemia in patients with chronic kidney disease (CKD). Increased erythropoietin (EPO) production and enhanced erythropoiesis are known to be the major mechanisms responsible for the treatment effects. However, the effect of HIF stabilization on renal fibrosis is controversial. We created animal models characterized by CKD and pericyte-specific stabilization of HIF to examine the effects of HIF on renal fibrosis and erythropoiesis.

Method: *Gli1*$^{CreERT2/+}$;*Egln1*$^{F/F}$, *Gli1*$^{CreERT2/+}$;*Vhl*$^{F/F}$, and *Gli1*$^{CreERT2/+}$;*Hif1a*$^{F/F}$;*Hif2a*$^{F/F}$ mice were generated to study the effects of pericyte-specific overexpression or knockout of *Hif*. Unilateral ureteral obstruction (UUO) was used to induce CKD. The severity of fibrosis was determined by Picrosirius red stain and *Col1a1* mRNA level in the kidney.

Results: Pericyte-specific stabilization of HIF resulted in increased serum EPO level, augmented splenic erythropoiesis, and polycythemia, while the severity of renal fibrosis was not affected. In line with these findings, pericyte-specific knockout of *Hif1a* or *Hif2a* did not result in significant change of renal fibrosis.

Conclusion: Our study endorses the neutral effects of pericyte-specific HIF stabilization on renal fibrosis.

P0853 DECISION SUPPORT SYSTEM (DSS) FOR DIAGNOSTICS AND TREATMENT OF PATIENTS WITH CKD COMPLICATIONS

Egor Kondratiev[1], Vladimir Novitskiy[1,2], Aleksei Galchenkov[1,3]

[1]Nephrology Expert Council, Moskva, Russia, [2]Moscow State University of Food Production, Informatics and computing technology of food production, Moskva, Russia and [3]Moscow State University of Food Production, Moskva, Russia

Background and Aims: Some of the most common complications of CKD are anemia and bone and mineral disorders (BMD). Adequacy of treatment of patients with these complications directly affects their life quality and duration.

The goal of our work is to create medical decision support system (MDSS) that will be able to generate recommendations on diagnostics and treatment of CKD patients with anemia and BMD complications, based on clinical guidelines and control the fulfillment of corresponding prescriptions.

Method: We have developed an automated medical decision support system that generates recommendations on patient's treatment and further studies that are mandatory according to regulations, based on patient's electronic medical record. The functionality of MDSS is based on knowledge base (KB), which consists of clinical guidelines formalized as mathematical logic operators. The system is also able to control how medical staff fulfills generated diagnostic and treatment prescriptions: deadlines, duration and order of actions, mandatory studies from regulations, drug therapy, etc.

The assessment of the system was conducted on more than 2000 CKD patients on chronic dialysis from 30 "Nefrosovet" hemodialysis clinics.

Results: MDSS was developed using process-based management principles and was successfully employed on representative sample of patients with CKD on chronic dialysis from "Nefrosovet" hemodialysis clinics. The system generated recommendations for this group of patients for the duration of 6 months. Recommendations were related to diagnostics and treatment of patients, specific diagnoses, scheduled and additional studies, drug prescriptions (where dose was set by a physician), etc.

As a result of using a system, we were able to reduce average treatment cost of patient by 14% for anemia related treatment and by 36% for BMD related treatment. At the same time the treatment quality has improved from an average of 46% to 60% of patients in target ranges of key laboratory parameters after 6 months of system usage. Treatment cost has reduced due to the timely start and gradual cancelation (by indications) of drug therapy, which also allowed us to avoid overadministration of unnecessary drugs.

Conclusion: Deployment of developed MDSS for process-based management of patients with CKD on chronic dialysis with anemia and BMD complications has shown high cost efficiency. Furthermore, automated diagnostics, therapy and prescription fullfilment control is performed without loss of quality, sometimes even with the improvement of quality of treatment process.

P0854 **THE ENDOGENOUS ERYTHROPOIETIN EXPRESSION IN CKD PATIENTS AT HIGH ALTITUDE: DATA FROM TIBETAN PLATEAU**

Yan Wang[1], Zonghui Dang[2], Li Zuo[1], Lei Zhang[2]

[1]*Peking University People's Hospital, Department of Nephrology, Beijing, P.R. China and* [2]*Tibet Autonomous Region People's Hospital, Department of Nephrology, Lhasa, P.R. China*

Background and Aims: Some studies have shown that higher altitude was associated with lower EPO doses and higher hematocrit levels in HD patients. Our pre-study also confirmed that the higher the altitude, the lower the EPO resistance index [weekly weight-adjusted dose of erythropoietin (IU/kg/week) divided by Hb concentration (g/dl)]. Possible explanations included that patients at higher altitude produce more endogenous EPO or they respond more efficiently to EPO than patients at lower altitude. The aim of this study was to determine whether endogenous EPO production was up-regulated in CKD patients at high altitude.

Method: Three cohorts from different altitude were compared. Among them, 58 CKD patients were from Tibet Autonomous Region People's Hospital (3650m above sea level, recruited between March 2019 and July 2019. The other two cohorts were from the literatures. [1,2]

The exclusion criteria included patients under EPO substitution or those with acute renal failure, polycystic kidney disease, renal carcinoma or polycythemia. The subjects were then stratified into groups according to the CKD stage. EPO concentrations were determined by using electrochemiluminescent immunoassay. Change of endogenous EPO levels with altitude by CKD stage was studied.

Results: The characteristics of the Tibet cohort were shown in table 1, the other two can be found in references. In Tibet cohort, there was a significant correlation between serum EPO concentrations and CKD stages as well as eGFR. The equation derived from liner regression analysis was EPO (mIU/ml) =-1.941*CKD stage+17.67 ($r^2 = 0.093$, $P = 0.020$) and log EPO (mIU/ml) =-0.0002311*eGFR (ml/min/1.73m^2) + 1.025 ($r^2 = 0.097$, $P = 0.017$). Serum EPO concentrations dropped with decreasing of eGFR, see in Figure 1.

Normally there was an exponential relation between hemoglobin and endogenous EPO in healthy people. The correlation was attenuated and even absent in CKD patients. In Tibet cohort, there was no linear relation between hemoglobin and endogenous EPO ($r^2 < 0.001$, $P = 0.907$), see in Figure 2.

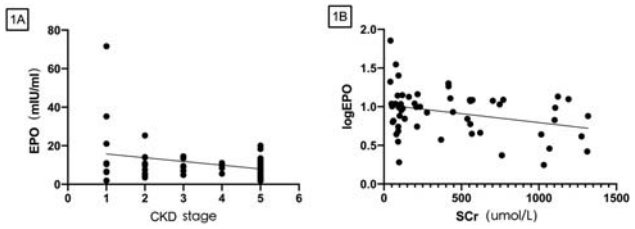


Figure 1. (**A**) Relationship between CKD stages and serum EPO concentrations. (**B**) Relationship between serum creatinine and log EPO concentrations.

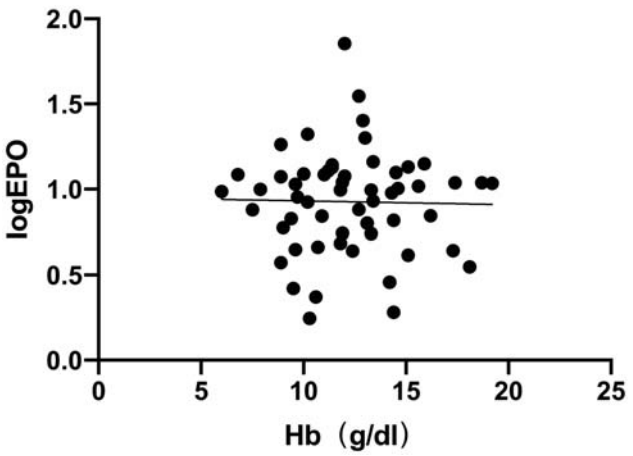


Figure 2. Relationship between Hb and serum EPO concentrations in CKD patients.

Compared with the other two cohorts at lower altitude, the average EPO concentration of Tibetan patients was higher in CKD stage one, however, it decreased quickly with increasing stages of CKD. The average EPO concentration were even lower in CKD stage two to five, see in Figure 3.

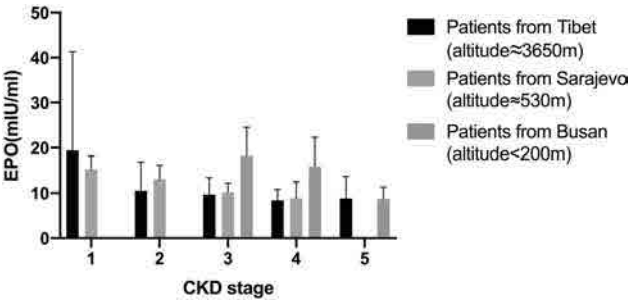


Figure 3. Comparison of serum EPO concentrations between CKD patients at high altitude and plain areas.

Conclusion: Endogenous EPO production was only up-regulated in patients with normal renal function at high altitude, those with impaired renal function failed to produce more EPO. Our results suggest that the possible explanation for CKD patients at high altitude had better EPO responsiveness is that they respond more efficiently to EPO other than they produce more endogenous EPO.

Table 1. Characteristics of the subjects from Tibet (n=58)

	CKD1(n=9)	CKD2(n=10)	CKD3(n=6)	CKD4 (n=6)	CKD5(n=27)
Male (n,%)	3(33.3)	7(70.0)	2(33.3)	1(16.7)	17(63.0)
Age(years)	39.2±14.3	56.5±10.9	47.5±15.2	56.7±10.0	46.3±16.7
Hb (g/dl)	14.3±2.7	14.9±2.7	12.8±2.3	10.9±1.6	10.6±2.4
SCr (μmol/l)	61.4±18.6	92.2±17.6	139.3±4.4	224.3±28.6	782.3±313.8
eGFR (ml/min/1.73m^2)	110.7±14.9	74.1±8.8	45.3±9.1	21.7±2.6	7.1±3.2
Albumin (g/l)	28.9±4.7	27.5±8.0	30.2±5.3	35.6±4.9	35.0±6.5
Ferritin (ng/ml)	171.5(91.2,281.9)	169.5(81.6,270.2)	475.4(348.8,570.6)	78.9(31.2,235.2)	273.4(108.7,349.2)
TSAT (%)	19.9±19.1	45.7±18.6	22.4±3.3	17.1±0.1	34.9±18.5
C-reactive protein(mg/l)	3.1±1.2	14.8±21.3	5.5±7.0	1.3±0.7	17.7±31.0
endogenous EPO(mIU/ml)	19.4±21.9	10.5±6.4	9.7±3.7	8.4±2.4	8.8±4.9

P0855

ASSOCIATIONS BETWEEN A COMPREHENSIVE PANEL OF BIOMARKERS WITH ESA HYPORESPONSIVENESS: ROLE OF IMMUNE DYSFUNCTION IN THE PATHOPHYSIOLOGY OF CKD ANEMIA

Guilherme Batalha[1], Maria Eugênia Canziani[2], Murilo Guedes[1], Ana Clara Almeida[1], Andrea N Moreno-Amaral[1], Ana Beatriz Barra[3], Américo Cuvello[4], Carlos Eduardo Poli De Figueiredo[5], Roberto Pecoits-Filho[1]

[1]Pontifícia Universidade Católica do Paraná, School of Medicine, Curitiba, Brazil, [2]Universidade Federal de São Paulo, Brazil, [3]Fresenius Medical Care, Brazil, [4]Hospital Alemão Oswaldo Cruz, Brazil and [5]Pontifícia Universidade Católica do Rio Grande do Sul, Brazil

Background and Aims: An inadequate response to the treatment of anemia with erythropoiesis-stimulating agents (ESAs) in patients with chronic kidney disease is a challenging and common clinical condition previously associated with signs of inflammation and episodic clinical events. The associations between different immune response pathways and ESA hyporesponsiveness remain poorly understood. Here we describe the associations between a comprehensive panel of inflammatory biomarkers and ESA resistance in a group of stable HD patients.

Method: This is post-hoc analysis of the baseline evaluation of patients enrolled in the HDFIT, a randomized controlled trial. A panel comprising a more general (CRP), innate (IL-1β and IL-6), adaptive (IFNγ, IFNα2) biomarkers of immune response, and also a specific vascular inflammation (MCP-1) biomarkers were simultaneously measured with the same serum sample through turbidimetry and MilliplexïŁ´Human Cytokine Magnetic Bead Panel - EMD Milipore Corporation, USA. Multivariable analysis was used to assess the association of their concentrations with the erythropoietin resistance index (ERI), defined as the weekly ESA dose divided by hemoglobin level.

Results: A total of 155 patients were included in this analysis (mean age 52 ± 6; 70% male; 32% with diabetes; mean hemoglobin 11.7 ± 1.5; median ESA dose/week 8000 IU IQR: 4000-12.000). Patients in the highest ERI tercile were mostly female, younger, more diabetic and with slightly higher proportion of iron prescription compared to those in the lowest tercile of ERI. The multivariable models adjusted for age, sex, diabetes and vascular access demonstrated that higher serum levels of IL-1β and IFN-γ were associated with higher ESA resistance, while there were no detectable associations of serum levels of IL-6 or CRP and ERI.

Conclusion: Among the biomarkers included in this comprehensive panel of biomarkers representing the multilevel nature of immune dysfunction in CKD, we observed associations between higher concentrations of innate (IL-1β) and adaptive (IFN) immune response and ESA hyporesponsiveness. Our results support the role of immune dysfunction in the pathophysiology of CKD anemia.

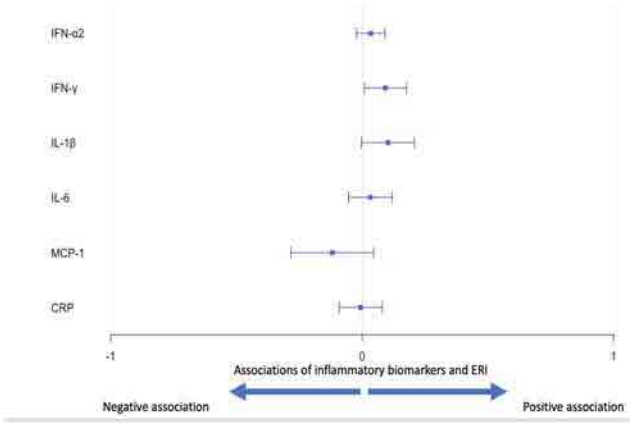


Figure 1: Estimates of linear coefficients of log-transformed concentrations of biomarkers on log-transformed ERI, adjusted for age, sex, diabetes, vascular access.

P0856 **LOW BONE MASS IS SIGNIFICANTLY ASSOCIATED WITH AN INCREASED RISK OF ANEMIA IN PATIENTS WITH CKD**

Seonyeong Lee[1], Yooju Nam[1], Hyung Woo Kim[1], Jae Hyun Chang[2], Tae-Hyun Yoo[1]

[1]College of Medicine, Institute of Kidney Disease Research, Yonsei University, Department of Internal Medicine, Seoul, Korea, Rep. of South and [2]Gil Medical Center, Gachon University College of Medicine, Department of Internal Medicine, Incheon, Korea, Rep. of South

Background and Aims: Hypoxia has been considered to be a risk factor for osteoporosis. Several studies have reported on the close associations between the anemia and an increased risk of bone loss. However, the relationship between hemoglobin levels and bone mineral density(BMD) has not been established in chronic kidney disease (CKD) patients. Therefore, the aim of this study is to investigate the relationship between BMD and anemia in a non-dialysis CKD cohort.

Method: Among 2,238 patients with non-dialysis CKD enrolled in the KoreaN cohort study for Outcome in patients With Chronic Kidney Disease (KNOW-CKD), 2,115 patients who measured hemoglobin(Hb) and BMD were included in the analysis. We defined anemia as hemoglobin(Hb) levels of $<$ 13.0 g/dL and 12.0 g/dL for males and females, respectively. The primary endpoint was the onset of a 15% decline in Hemoglobin during follow-up.

Results: The mean age was 53.6 $\pm$ 12.2 years and 1,292(61.1%) patients were males. The BMD score was positively correlated with hemoglobin levels (**β**, 0.658; 95% CI, 0.215-1.101; P 0.004). In the multivariable logistic regression model, the prevalence of anemia was significantly higher in the osteoporosis group than that in the normal BMD group (odds ratio [OR], 1.59; 95% confidence interval [CI], 1.03-2.46, P=0.038). Among 1010 patients without data of following hemoglobin levels, 396 (19.7%) patients developed 15% decline in hemoglobin level during a median follow-up duration of 36 (interquartile range, 10-60) months. In the fully adjusted multivariable Cox models, risk of developing the 15% decline of hemoglobin was significantly higher in the osteoporosis group (HR, 1.45; 95% CI, 1.03-2.05; P= 0.035) as compared to normal BMD group.

Conclusion: This study showed that low bone mass density was independently related with anemia and hemoglobin levels in patients with non-dialysis CKD. Our findings suggest that preserve bone mass be important to maintain the levels of hemoglobin with CKD patients.

P0857

BURDEN OF ANEMIA ASSOCIATED WITH CHRONIC KIDNEY DISEASE IN DIALYSIS AND NON-DIALYSIS-DEPENDENT PATIENTS IN EUROPE: A REVIEW OF PUBLISHED EVIDENCE

Tony Okoro[1], Justyna Amelio[2], Anadi Mahajan[3], Digant Gupta[3], Rodrigo Refoios Camejo[5]

[1]GSK, Value Evidence and Outcomes, Collegeville, United States of America, [2]GSK, Value Evidence and Outcomes, Stevenage, United Kingdom, [3]Bridge Medical Consulting, Richmond, United Kingdom and [5]GSK, Value Evidence and Outcomes, Brentford, United Kingdom

Background and Aims: Anaemia is a frequent complication in patients with chronic kidney disease (CKD). The aim of this literature review was to understand the prevalence and burden of anaemia associated with CKD, with a further focus on Europe.

Method: A targeted literature review was conducted to identify publications on prevalence estimates (search: January 2015 to August 2018), and a systematic literature review was performed to identify publications on humanistic and healthcare resource use (HRU) burden (search: from database inception to July 2018) using MEDLINE®, Embase®, Cochrane Library, and conference proceedings. These were complemented by grey literature searches. Citations were screened per predefined criteria to include observational studies and reviews. Case series/reports and conceptual model studies were excluded. The study population included patients with anaemia associated with CKD, irrespective of CKD stage, dialysis status, or modality. All searches were funded by GSK.

Results: After applying all inclusion and exclusion criteria, 18 publications were retained that contained prevalence data, of which 9 provided European data. Based on 9 publications, the prevalence of anaemia associated with CKD in European adults was reported to range from 12.8% to 61.5% (Figure). Prevalence was higher in older individuals (aged >60 years) and increased with more advanced CKD stages. However, the methodology used to identify anaemia was not consistent across studies. Anaemia was identified based on varying thresholds of haemoglobin (Hgb) levels per different clinical guidelines (Kidney Disease Improving Global Outcomes [KDIGO], N=4; World Health Organization [WHO], N=2; European Best Practice Guidelines [EBPG], N=3), use of anaemia treatment, or Hgb thresholds without a reference to a specified guideline. Most studies focused on later-stage CKD patients (3 – 5), with only 2 studies reporting rates for stage 1 and 2 patients. A total of 50 publications provided data on humanistic and HRU burden, 6 of which provided European data. The literature on humanistic and HRU burden showed adults with anaemia associated with CKD had significantly poorer health-related quality of life (HRQoL) compared with those without anaemia, with significantly lower Kidney Disease Quality of Life (KDQoL) scores reflecting poorer HRQoL observed in the following domains: symptoms/problems, effect of kidney disease, and burden of kidney disease. This finding was consistent irrespective of instrument used for HRQoL assessment. However, tools used were not specific to anaemia or anaemia associated with CKD, and publications did not mention whether thresholds for clinical meaningfulness had been identified and/or met. Publications on HRU in anaemia associated with CKD in Europe were sparse (N=1): this single published study reported increased HRU in CKD patients with anaemia compared with CKD patients without anaemia.

Conclusion: Prevalence rates of anaemia associated with CKD reported in Europe vary, with increased prevalence in later stages of CKD. Anaemia negatively impacts patient QoL and leads to increased HRU in patients with CKD. More data are needed to characterise anaemia in earlier stages of CKD and across different populations (e.g. patients with particular comorbidities or undergoing different types of dialysis) in European countries. Due to varied definitions of anaemia, it would be of interest to evaluate the extent of underdiagnosis and its impact on prevalence rates.

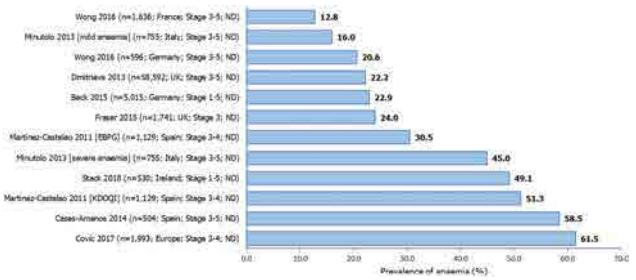


Figure: Prevalence of Anaemia Associated With Chronic Kidney Disease in Europe

ND, non-dialysis; EBPG, European Best Practice Guidelines; KDOQI, Kidney Disease Improving Global Outcomes

P0858

A MULTICENTRE PROSPECTIVE DOUBLE BLIND RANDOMISED CONTROLLED TRIAL OF INTRAVENOUS IRON IN IRON DEFICIENT BUT NOT ANAEMIC PATIENTS WITH CHRONIC KIDNEY DISEASE ON FUNCTIONAL STATUS

Xenophon Kassianides[1], Ahmed Ziedan[2], Victoria Allgar[3], Archie Lamplugh[1], Philip A. Kalra[4], Iain Macdougall[5], Sunil Bhandari[1]

[1]Hull University Teaching Hospitals NHS Trust, Renal Medicine, HUI, United Kingdom, [2]Hull University Teaching Hospitals NHS Trust, Renal Medicine, Kingston upon Hull, United Kingdom, [3]University of York (Hull York Medical School), Statistics, York, United Kingdom, [4]Salford Royal NHS Foundation Trust, Department of Nephrology, Manchester, United Kingdom and [5]Kings College Hospital NHS Foundation Trust, Renal Medicine, London, United Kingdom

Background and Aims: Iron deficiency is common in patients with CKD due to inadequate dietary intake of iron, poor iron absorption from the gut, and increased iron losses from the body. In addition to preventing anaemia, iron is also important for normal heart function, being involved in processes that generate a necessary continuous energy supply. Post hoc analysis of studies of people with iron deficiency and advanced CKD suggest treatment with intravenous iron leads to improvement in heart function and feeling of wellbeing.

The aim of the study was to investigate whether intravenous (IV) iron could improve exercise capacity in comparison to placebo over 3 months in non-anaemic CKD patients who have iron deficiency.

Method: The Iron and the Heart Study was a prospective double blinded explorative randomized, multi-centre study designed to assess the effect of IV iron supplementation (ferric derisomaltose/iron isomaltoside 1000 (FDI); Monofer®) in iron deficient but not anaemic patients with advanced CKD on functional status. Adults with established CKD stages 3b-5 and serum ferritin (SF) < 100mcg/L and/or transferrin saturation (TS) <20% were randomized in a 1:1 ratio to 1000 mg IV FDI or placebo solution. Each participant was followed up at months 1 and 3. The primary outcome was the difference in exercise capacity using the 6-minute walk test (6MWT) at 3 months. Secondary objectives included effects on haematinic profiles and haemoglobin (Hb) concentrations. Results are given as mean and standard deviations (SD). Data was analysed using ANCOVA adjusted for baseline.

Results: Between October 2016 and April 2018, 54 individuals from 3 UK centres were randomized to FDI (n=26; mean age 61.6 (10.1) years) or placebo (n=28; mean age 57.8 (12.9) years). Mean serum creatinine (167.0 (40.2) vs. 204.9 (67.3) and eGFR (32.1 (9.6) vs. 29.1 (9.6)) at baseline were similar in FDI and placebo groups respectively. Adjusting for baseline 6MWT, the 6MWT at 1-month showed no statistically significant difference between groups (p=0.736) (Figure), and no significant difference at 3 months (p=0.741). The absolute mean change from baseline to 1 month and 3 months, showed no statistically significant differences between group (p=0.952_, p=0.895). There was no statistically significant difference between groups in Hb at 3-months (p=0.152) but there were statistically significant differences in SF and TS, which both increased post FDI infusion at 1 and 3 months; p<0.001 (Table).

Conclusion: The Iron and the Heart Trial showed a significant increase in iron parameters and maintenance of Hb concentration in iron treated patients. There was a numerical increase in functional capacity at 1-month and to lesser extent at 3 months post iron infusion. This finding was not significant, which reflects the limited sample size and possible differences in population during randomisation with the large difference in 6MWT at baseline. A larger study will be required to demonstrate a possible short-term functional benefit on exercise capacity of IV iron in CKD patients with biochemical functional or absolute iron deficiency without anaemia.

Table:

		Monofer			Placebo		
		Mean	SD	n	Mean	SD	N
Hb	Baseline	131.0	7.4	26	126.5	11.8	28
	1 month	132.7	7.2	24	125.5	12.8	26
	3 months	134.7	8.9	20	126.2	12.4	25
Ferritin	Baseline	64.2	29.1	26	68.4	55.3	27
	1 month	266.0	105.8	23	70.5	55.8	26
	3 months	234.4	105.3	21	69.4	59.8	24
TSAT	Baseline	22.3	8.8	26	19.7	5.6	27
	1 month	29.6	9.5	22	19.1	7.1	26
	3 months	26.4	10.5	21	18.0	6.8	23

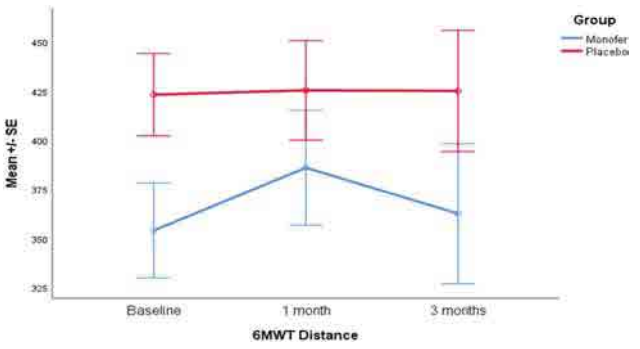


Figure:

P0859 **ACTIVATE ENDOGENOUS HYDROXYMETHYLATION TO RESTORE ERYTHROPOIETIN PRODUCTION IN FIBROTIC KIDNEYS**

AN JIE LUO[1], SHUEI-LIONG LIN[1,2]

[1]College of Medicine, National Taiwan Univ., Dept. of Physiology, Taipri, Taiwan, R.O.C. and [2]National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan, R.O.C.

Background and Aims: Our previous studies have shown that DNA methyltransferases (Dnmt) and Epo hypermethylation are upregulated in myofibroblasts in fibrotic murine kidneys. Demethylation leads to redifferentiation of myofibroblasts into pericytes. Furthermore, nontoxic doses of 5-azacytidine can restore EPO production and ameliorate anemia in mice with kidney fibrosis. Physiologic hydroxymethylation in zygotes is mediated by the 10 − 11 translocation enzymes (Tet1, Tet2, and Tet3).

Method: The mouse model of unilateral ureteral obstruction (UUO)-induced kidney fibrosis has been found to display enhanced Tet1 and Tet3 mRNA expression at day 7 and marked increase with the disease progression.

Results: According to the results, Tet expression significantly increased in fibrotic kidney. To study the effect of myofibroblast-specific Tet3 knockout in murine models of renal fibrosis. Tet3F/F mice were generated by a targeting vector with floxed region contains exons 8-9 of Tet3, which included the coding region for the conserved Fe2+-binding motif of dioxygenase. Gli1CreERT2/+;Tet3F/F mice were used to induce knockout of Tet3 in pericytes and myofibroblasts after tamoxifen administration. Tet3F/F mice were used as the control. Oral gavage of tamoxifen 8 mg/day for 3 days was used to activate Cre recombinase in Gli1+ pericytes and myofibroblasts in adult mice (6-8 week). After two-week washout period, mice were subjected to UUO for 7 or 14 days. The body weight, plasma creatinine and BUN levels showed no significant differences between groups in mice after induction and also UUO surgery. Plasma levels of BUN and creatinine were maintained within the normal range by normally functioning contralateral kidneys after UUO surgery. In UUO kidneys, knockout of Tet3 decreased renal α-SMA and Col1a1 expression. But plasma hematocrit and renal Epo mRNA level were not different between groups. In addition to Gli1CreERT2/+ mice we also used Pdgfrb-rtTATg;LC1Tg mice to breed with Tet3F/F mice for inducible knockout of Tet3. The plasma creatinine, BUN, and hematocrit were no different between groups after UUO surgery again.

Conclusion: Overall, these findings suggested increased Tet3 in myofibroblasts may play an important role in myofibroblast activation and fibrosis. Further studies need to explore the mechanisms.

P0860

INTRAVENOUS IRON ADMINISTRATION SUPPRESSES ENDOGENOUS ERYTHROPOIETIN SECRETION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Katarzyna Muras-Szwedziak[1,1], Ewa Pawlowicz[1], Michal Nowicki[1]

[1]*Łódź, Department of Nephrology, Hypertension and Kidney Transplantation, Łódź, Poland*

Background and Aims: Iron therapy may induce inflammatory response that may indirectly affect endogenous erythropoietin (EPO) production. We postulated that increased secretion of FGF-23 may provide a link between intravenous iron administration and suppression of endogenous EPO secretion.

Evaluation of a short-term effect of intravenous iron sucrose administration on the secretion of endogenous EPO in patients with chronic kidney disease (CKD).

Method: 35 non-dialysed patients with G3b-5 CKD were included. All patients received 100 mg of intravenous iron infusion (iron (III)-hydroxide sucrose complex) daily for 5 days. Plasma concentration of EPO, iFGF-23, cFGF-23, PTH, bone alkaline phosphatase (BAP), phosphorus (PO4) and calcium (Ca) were measured before and two hours after the first and third iron infusion and at the end of iron therapy.

Results: EPO concentration at the end of iron treatment was significantly lower compared to 2 h after the first iron infusion ($p<0.001$) and before the third dose ($p<0.001$) (12.6 [31.2] mIU/mL, 30.9 [38.3] mIU/mL, 33.4 [41.3] mIU/mL and, respectively). Conversely, serum iFGF-23 increased significantly after the third dose (61.1 [401.5] pg/mL; $p<0.05$) and after the treatment (92.1 [849.7] pg/mL; $p<0.01$) compared to pre-treatment value (48.4 [403.8] pg/mL). cFGF-23 concentration decreased significantly after the first dose of iron (491.8 [828.6] vs. 339.2 [875.8] RU/mL; $p<0.01$) and after the completion of the therapy (398.7 [931.9]) vs. baseline ($p<0.05$). There was no linear correlation between EPO and FGF-23.

Conclusion: Intravenous iron therapy increases the secretion of FGF-23 and supresses endogenous EPO production but these two effects do not seem to be related.

P0861

THE RELATIONSHIP BETWEEN HEPCIDIN-25 AND BONE MARROW IRON IN ANEMIC, NON-DIALYSIS, CHRONIC KIDNEY DISEASE PATIENTS

Cristina-Stela Capusa[1,2], Ana-Maria Mehedinti[1,2], Gabriela-Adriana Talimba[1], Ana Stanciu[2], Liliana Viasu[2], Gabriel Mircescu[1,2]

[1]"Carol Davila" University of Medicine and Pharmacy, Nephrology, Bucharest, Romania and [2]"Dr. Carol Davila" Teaching Hospital of Nephrology, Nephrology, Bucharest, Romania

Background and Aims: Hepcidin-25 (Hep25) is a key known regulator of iron metabolism and its interactions with inflammation, iron stores and erythropoietic activity were involved in the pathogenesis of chronic kidney disease (CKD)-associated anemia. Therefore, our aim was to assess the determinants of serum Hep25 level in non-dialysis CKD patients.

Method: In this cross-sectional, single-center study, 52 subjects (56% men, 65±13 years) with CKD [estimated glomerular filtration rate, eGFR 14.5 (95%CI 16 to 25) mL/min] and anemia [hemoglobin, Hb 9.8 (95%CI 9.2 to 9.9) g/dL], not treated with erythropoiesis-stimulating agents (ESA) or iron in the previous 6 months, were enrolled. Patients with anemia of other causes than CKD, active infectious and inflammatory diseases, malignancy, severe hyperparathyroidism, transfusions during the last 3 months, and immunosuppressive therapy were excluded.

The iron status was evaluated using both peripheral and central parameters. The iron stores were assessed by serum ferritin (Fer) and iron content in bone marrow macrophages (iMf, measured quantitively on a scale from 0 to 6). The iron available for erythropoiesis was assessed by transferrin saturation (TSAT) and the percentage of sideroblasts (%Sb). Anemia was further evaluated by a peripheral blood smear, erythrocytes indices and reticulocyte index.

Serum Hep25 and erythropoietin (Epo) were assessed by ELISA (Bachem®, and Abcam® 119522, respectively). C-reactive protein (CRP), albumin, and parameters of kidney disease (eGFR, proteinuria) were also measured.

Mann-Whitney, Kruskal-Wallis, Chi^2 tests, Spearman bivariate correlation and multiple linear regression were used for statistical analysis.

Results: The median serum Hep25 of the whole cohort was 82.1 (95%CI 68.7 to 92.1) ng/mL. According to median Hep25, subjects were clustered in Group 1 (below median - G1) and Group 2 (above median - G2).

%Sb and reticulocyte index had higher levels in G2 than in G1 [9 (95%CI 5 to 14) vs. 5 (95%CI 4 to 7) %, p=0.003 and 0.55 (95%CI 0.39 to 0.77) vs. 0.41 (95%CI 0.32 to 0.58), p=0.05, respectively], while the proportions of subjects with iMf suggestive for iron deficiency or iron overload were similar in G2 and G1 (38% vs. 50%, p=0.40, and 26% vs. 23%, p= 0.75, respectively). Peripheral blood smear, peripheral iron indices and all the other studied parameters were also alike.

In bivariate analysis, Hep25 was positively associated both with indices of iron stores, i.e. Fer (rs = 0.30, p=0.03) and iMf (rs = 0.34, p=0.01) and indices of iron available for erythropoiesis, i.e. %Sb (rs = 0.55, p<0.001) and (marginally) with TSAT (rs = 0.26, p=0.06). Meanwhile, Hep25 was not related to serum Epo, CKD parameters or inflammation markers.

In a multivariate linear regression model that explained 28% of Hep25 variation, the percentage of bone marrow sideroblasts, i.e. the tissue iron available for erythropoiesis, was the only independent determinant of Hep25:

	Beta	95%CI	*p*
Constant	41.5	21.4 to 61.6	<0.001
%Sb	2.8	1.2 to 4.5	0.001
iMf	5.1	–0.02 to 10.2	0.051

Adjusted R^2 = 0.28; p<0.001

Variables entered in the first step: reticulocyte index, percentage of medullary sideroblasts (%Sb), iron content in the bone marrow macrophages (iMf), serum ferritin, and transferrin saturation

Conclusion: In stable patients with advanced CKD, not treated with ESA or iron, with low to moderate inflammation, serum hepcidin was related only to bone marrow iron available for erythropoiesis, suggesting that in this clinical setting the need of iron for erythropoiesis prevails over inflammation in regulation of hepcidin synthesis.

P0862

DAPRODUSTAT INTERACTION WITH PHOSPHATE BINDERS HAS MINIMAL IMPACT ON HEMOGLOBIN VALUES IN HEMODIALYSIS POPULATION

Borut Cizman[1], Amy Meadowcroft[1], Nandita Biswas[3], Michael Sprys[4], Alexander Cobitz[5]

[1]GlaxoSmithKline, Clinical Science, Collegeville, United States of America, [3]GlaxoSmithKline, BioStatistics, Collegeville, United States of America, [4]GlaxoSmithKline, Biotstatistics, Collegeville, United States of America and [5]GlaxoSmithKline, Collegeville, United States of America

Background and Aims: Daprodustat is a novel hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) currently in phase 3 development for the treatment of anemia of chronic kidney disease (CKD). Phosphate binders (PB) are widely prescribed for hemodialysis (HD) patients to control for hyperphosphatemia. The coadministration of PB and HIF-PHI may potentially impact hemoglobin values thus requiring time between PB administration and HIF-PHI. The purpose of this analysis was to determine whether daprodustat interaction with PB has an impact on hemoglobin (Hgb) values in the HD population.

Method: GSK PHI113633 study (NCT01977482) included 216 subjects on maintenance HD previously treated with rhEPO. This study included daprodustat dose-ranging for the first 4 weeks, followed by a Hgb correction/maintenance phase for the next 20 weeks; daprodustat was dosed daily without regard to the timing of PB administration. The control group received placebo for 4 weeks, followed by rhEPO for the next 20 weeks as previously reported (*Clin Kidney J 2019;12(1):139-148*). Target Hgb range was 10.0-11.5 g/dL from Week 4 through Week 24. Baseline PB use was a prespecified study subgroup of interest. The difference in mean Hgb values at Week 24 between treatment groups was summarized overall and by subgroup. Comparisons were performed for the Week 24 Hgb (*post hoc*), as well as the final dose of daprodustat, for those receiving/not receiving PB.

Results: The majority of HD subjects in this 24-week safety and efficacy study received PB at baseline; 136 of 177 (77%) of subjects on daprodustat and 33 of 39 (85%) of subjects on control were taking PBs, with comparable phosphate control at baseline [mean (±SD) phosphate: daprodustat 1.76 mmol/L (0.56); control 1.67 mmol/L (0.44)].

No meaningful difference in Hgb change from baseline (CFB) at Week 24 was noted between daprodustat and rhEPO groups (Table 1).

Conclusion: These results suggest that daprodustat can be taken without regard to the timing of PB administration. Results of the large, phase 3 dialysis study of daprodustat will be important to definitively confirm these initial observations.

Table 1. Baseline Hgb and difference in CFB Hgb at Week 24 between daprodustat and rhEPO groups

Group	Mean (±SD) baseline Hgb (g/dL) for daprodustat vs control	Mean (95% CI) difference in CFB Hgb (g/dL) at Week 24
Overall population	10.39 (0.66) vs 10.55 (0.94)	-0.12 (-0.51, 0.27)
Baseline PB Use = Yes	10.38 (0.62) vs 10.48 (0.73)	-0.21 (-0.63, 0.21)
Baseline PB Use = No	10.43 (0.77) vs 10.94 (1.76)	0.25 (-0.72, 1.23)

The final median dose for subjects on daprodustat was the same for those receiving and those not receiving PB, with no meaningful difference in the mean Hgb at Week 24 (Table 2).

Table 2: Final dose and Hgb at Week 24 for daprodustat group based on baseline PB use

Baseline PB Use	Median Dose (P25, P75)	Mean Hgb at Week 24 (±SD)*
Yes	6 mg (4 mg, 10 mg)	10.40 g/dL (0.95)
No	6 mg (2 mg, 8 mg)	10.79 g/dL (0.95)

**post hoc analysis*

P0863 TYPE OF PROTON PUMP INHIBITOR AND RISK OF IRON DEFICIENCY IN RENAL TRANSPLANT RECIPIENTS

Rianne M. Douwes[1], Joanna Sophia Jacoline Vinke[1], António W Gomes-Neto[1], Hans Blokzijl[2], Stefan P. Berger[1], Stephan Bakker[1], Martin De Borst[1], Michele Freerk Eisenga[1]

[1]*University Medical Center Groningen, Nephrology, Groningen, Netherlands and* [2]*University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands*

Background and Aims: Use of proton-pump inhibitors (PPIs) is common practice in renal transplant recipients (RTRs). Emerging data suggest several adverse effects of use of PPIs, including development of iron deficiency (ID). Although the latter has been shown with respect to PPIs, specific analyses for different types of PPIs and the associated risk of ID have not been performed.

Method: We used data from the TransplantLines Biobank and Cohort study, an ongoing prospective cohort study among all types of solid organ transplant recipients. For the current study, we used data from stable RTRs with a functional graft for more than 1 year post transplantation (n=795). We excluded RTRs who used any form of iron supplementation (n=54) and EPO-stimulating agents (n=24), resulting in 728 RTRs eligible for analyses. Use of PPIs was subdivided in different types of PPIs, i.e. omeprazole, esomeprazole, pantoprazole, and rabeprazole. ID was defined as TSAT$<$20% and ferritin $<$300 μg/L. Logistic regression analysis was used to assess the associations between PPIs and ID.

Results: We included 728 RTRs (age 56$\pm$13 years, 61% males), with a mean eGFR of 53$\pm$18 ml/min/1.73m^2, a median [interquartile range] ferritin level of 96 (44 – 191) μg/L and mean TSAT of 24$\pm$10%. PPIs were used by 504 (69%) of the included RTRs, of which 398 (79%), 55 (11%), 49 (10%), and 2 (0.4%) respectively used omeprazole, pantoprazole, esomeprazole, and rabeprazole. Use of PPIs was strongly associated with ID (OR, 2.20; 95%CI 1.48 – 3.28; $P<0.001$), independent of adjustment for age, sex, BMI, eGFR, hs-CRP, smoking, alcohol use, use of calcineurine inhibitors, prednisolone, antiplatelet drugs, and antihypertensives. When subdividing the PPIs into the different types, both omeprazole (OR, 1.98; 95%CI 1.39 – 2.83; $P<0.001$) and esomeprazole (OR, 2.11; 95%CI 1.09 – 4.07; $P=0.03$) were independently associated with iron deficiency, whereas pantoprazole was not associated (OR, 0.89; 95%CI 0.47 – 1.70; $P=0.73$).

Conclusion: Omeprazole and esomeprazole, but not pantoprazole, are associated with an increased risk of ID. Our results are in line with previous reports that pantoprazole has the lowest potency with least increase in intragastric pH, thereby possibly interfering less with reduction of ferric to ferrous iron, and subsequently iron absorption. Future studies are warranted to confirm our present findings.

P0864

PHYSICIAN ATTITUDES TOWARDS DIAGNOSING ANAEMIA, TREATMENT INITIATION AND THE CURRENT UNMET NEED IN THE MANAGEMENT AND TREATMENT OF ANAEMIA: INTERIM RESULTS FROM A CROSS-SECTIONAL REAL-WORLD SURVEY IN GERMANY, ITALY AND THE UK

Madhusudan Kabra[1], Tim Hammond[1], Allison Fleetwood[1], Lewis Harrison[2], Rebecca Moon[2], James Jackson[2]

[1]Otsuka Pharmaceutical Europe Limited, Slough, United Kingdom and [2]Adelphi Real World, Bollington, United Kingdom

Background and Aims: Anaemia, a complication of chronic kidney disease (CKD), is commonly defined as serum haemoglobin (Hb) levels of <12 g/dL in women and <13 g/dL in men. Its prevalence and severity increase with the decline in renal function and it is often associated with a decreased quality of life (QoL), and an increase in number of hospitalisations and comorbidities. Traditionally, primary care physicians (PCPs) have less involvement managing patients with CKD anaemia and nephrologists have a greater role in treatment decisions. We describe current physician perception towards the diagnosis and treatment of anaemia and the current unmet need in anaemia management, in a real-world setting.

Method: Preliminary data were drawn from the Adelphi CKD Disease Specific Programme™, a point-in-time study conducted between November 2019 and January 2020 with nephrologists and PCPs from Germany, Italy and the United Kingdom. Physicians completed a detailed online survey providing information on their demographics, opinions on the diagnosis and treatment of anaemia, and the current unmet needs they believe exist in the management and treatment of anaemia. Results are based on interim data and analysed descriptively.

Results: A total of 144 physicians (n=94 nephrologists; n=50 PCPs) were included in the analysis. Among those who responded, the majority used Hb levels to diagnose anaemia in CKD patients. Over two thirds of physicians mentioned using ferritin to diagnose anaemia and over half reported using transferrin saturation (TSAT) levels. Reported use of ferritin and TSAT testing was lower among PCPs.

Three quarters of nephrologists and PCPs (76% of each respectively) reported Hb levels to be the most important factor that triggers initiation of anaemia treatment in CKD patients, followed by fatigue/weakness (53% of both nephrologists and PCPs) and overall health/QoL (29% nephrologists; 18% PCPs). Ferritin levels (24% of each respectively); TSAT levels (23% nephrologists; 24% PCPs) and shortness of breath (22% nephrologists; 24% PCPs) were also among the most important factors.

The top three unmet needs in the management and treatment of CKD anaemia, as reported by nephrologists were: treatment for refractory/resistant patients (34%), lower cost of therapy (34%) and need for more oral treatments (33%). PCPs' top three unmet needs were reported as: treatment for refractory/resistant patients (42%), fewer side effects (42%) and need for more oral treatments (34%). Differences observed between nephrologists and PCPs related to a need for alternative treatments (19% nephrologists; 26% PCPs), access to ESA treatment (17% nephrologists; 30% PCPs) and treatments with lower risk of CV events (26% nephrologists; 12% PCPs).

Conclusion: This data reinforced that Hb levels, ahead of ferritin and TSAT levels have an important role in the diagnosis and initial prescription of therapy for anaemia in CKD patients. It also highlighted an unmet need for treatment of refractory/resistant patients and the desire among both nephrologists and PCPs for safer and affordable novel treatments for anaemia patients.

P0865 A QUALITATIVE STUDY OF PATIENTS' PREFERENCE FOR THE TREATMENT OF ANAEMIA ASSOCIATED WITH CHRONIC KIDNEY DISEASE

Ana Filipa Alexandre[1], Antonia Morga[2], Kevin Marsh[3], Caitlin Thomas[3]

[1]Astellas Pharma Europe B.V., Leiden, Netherlands, [2]Astellas Pharma Europe LTD, United Kingdom and [3]Evidera, London, United Kingdom

Background and Aims: Anaemia is a common complication of chronic kidney disease (CKD) that is associated with fatigue, shortness of breath, and lethargy. CKD anaemia is commonly treated with oral or intravenous (IV) iron and IV or subcutaneous (SC) erythropoiesis-stimulating agents (ESAs). The objectives of this study were to understand patients' experiences with CKD anaemia and their preferences related to treatment.

Method: Qualitative 60-minute semi-structured interviews were conducted with ESA-treated adult CKD patients with anaemia, either non–dialysis-dependent (ND) or dialysis-dependent (DD), and with practicing nephrologists in France, Germany, Spain, the UK, and Japan. The patients' interviews, appropriately tailored for ND and DD patients, comprised three sections: 1) patients' views on the burden of the disease and its treatment; 2) discussion of vignettes describing different treatment options; and 3) non-experimental choice questions between two hypothetical treatments including mode of administration, need for iron supplement, and risk of adverse events (AEs).

Results: A total of 51 patients were enrolled (ND, n=6 per country except for France [n=7]; DD [haemodialysis or peritoneal dialysis], n=4 per country). Two nephrologists per country were interviewed. The most commonly reported symptoms associated with anaemia were tiredness (ND, 77%; DD, 85%) and shortness of breath (ND, 42%; DD, 30%); these two symptoms were also reported by nephrologists, who considered clinical efficacy the most important aspect of treatment. In Japan, dizziness was the most common (n=5/6, 83%) symptom among ND patients. Anaemia symptoms were reported to negatively affect different aspects of patients' lives, including the ability to carry out daily activities (ND, 61%; DD, 65%), work (ND, 42%; DD, 50%), and exercise (ND, 26%; DD, 30%). ESA treatments were perceived to be effective in improving patients' symptoms and quality of life. Many patients had not experienced AEs associated with treatment and were not concerned about them, however patients who had experienced gastrointestinal (GI) AEs due to oral iron were sensitive to the risk of GI effects. Out of 23 ND patients who were asked, 19 (83%) preferred an oral treatment due to the convenience of administration, and to avoid injection pain and drug storage requirements associated with SC administration. Self-administering SC ESAs was a concern among Japanese ND patients, who often had a healthcare professional administer the medication. Haemodialysis patients (n=12), who often receive IV ESAs during their dialysis sessions, were less likely to prefer oral treatments due to lack of perceived convenience. Peritoneal dialysis patients (n=8), who often receive home dialysis and SC ESAs, preferred oral treatment to avoid self-administration and storage requirements, and to make travel easier. Limitations of the study included the small number of participants and amendments to the eligibility criteria implemented during data collection, including more relaxed requirements for blood pressure, blood transfusion, and insulin use.

Conclusion: Patients considered the available treatment options to effectively treat CKD anaemia. Besides efficacy, patients' primary concern was the mode of administration of their medication, rather than safety considerations.

P0866 EVALUATION OF ERYPTOSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Mehmet Gökhan GÖK[1], Saime Paydas[2], Bülent Kaya[3], Engin Onan[4], Barış Boral[5]

[1]Siirt State Hospital, İnternal Medicine, Siirt, Turkey, [2]Cukurova University Faculty of Medicine, Department of Nephrology, Adana, Turkey, [4]Adana City Hospital, Department of Nephrology, Adana, Turkey and [5]Adana City Hospital, İmmunology, Adana, Turkey

Background and Aims: One of the many factors in the pathogenesis of renal anaemia, is eryptosis. The aim of this study is to evaluate eryptosis in patients with chronic renal disease stage 3-5 and 5 dialysis (5D).

Method: Patients with CKD who were monitored in our nephrology department were included in the study. The age range of the patient groups was 18-80 years and haemoglobin levels were <13 g / dl in men and <12 g / dl in women. As parameters of eryptosis, flow cytometric annexin V binding and intracellular calcium, and superoxide dismutase (SOD) activity with ELISA method were measured in 59 predialysis patient (eGFR<60 mL / min 1.73 m2), 26 haemodialysis patient, 21 peritoneal dialysis patient and 29 healthy volunteers with similar age (control). Haematological and biochemical tests including complete blood count(CBC), erythrocyte sedimentation rate (ESR), Parathormone (PTH), 25-OH vit D3, Blood urea nitrogen (BUN), Creatinine (Cr), C-reactive protein (CRP), Na, K, phosphor (P), ionized and total Calcium, Ferritin, B12 and Folate, were performed. IBM SPSS Statistics Version 20.0 was used for statistical analysis of the data

Results: The amount of intracellular calcium were 3.05 ± 1.66 in predialysis group, 2.24 ± 0.99 in haemodialysis group, 2.38 ± 0.87 in peritoneal dialysis group and 1.71 ± 0.46 in control group. For intracellular calcium there was statistically significant difference only between predialysis group and control group ($p < 0.000$). Annexin V binding were calculated as 1.05 ± 0.99 in predialysis group, 1.15 ± 0.56 in haemodialysis group, 1.06 ± 0.87 in peritoneal dialysis group and 0.88 ± 0.86 in control group. Comparing to control group annexin V binding in predialysis, haemodialysis and peritoneal dialysis groups, were statistically significantly increased (for all $p < 0.000$). SOD activity was 0.07 ± 0.07 in predialysis group, 0.13 ± 0.08 in haemodialysis group, 0.14 ± 0.07 in peritoneal dialysis group and 0.03 ± 0.01 in control group. The difference between the control group and dialysis group was statistically significant ($p < 0.00$). Comparing to nonusers; patients using calcium channel blockers (CCB) had low annexin V binding level ($p = 0.013$). Patients using erythropoietin (EPO) had elevated annexin V binding level ($p < 0.000$) and lower intracellular calcium ($p = 0.014$) according to non- users.

Conclusion: We determined increased eryptosis in patients with CKD stage 3-5 and 5D in our study. Inflammation and elevated parathormone were also associated with increased eryptosis. Therefore, eryptosis may be an important factor in the pathogenesis of renal anaemia. Inflammation associated CKD may increase eryptosis. In addition, this effect can be taken into consideration in the planning of treatment because of the lower incidence of eryptosis in patients using calcium channel blocker and EPO.

P0867 ANEMIA AND IRON DEFICIENCY IN NON-DIALYISIS CHRONIC KIDNEY DISEASE: A LINK WITH ADVERSE OUTOCOMES?

Sara Fernandes[1], Luis Falcao[1], Adriana Paixão Fernandes[1], Beatriz Donato[1], Ana Cortesão Costa[1], Mário Raimundo[1], Catarina Teixeira[1], Sónia Silva[1], Ana Macedo[2], Edgar Almeida[1]

[1]Hospital Beatriz Ângelo, Nephrology, Loures, Portugal and [2]Keypoint, Lisboa, Portugal

Background and Aims: Anemia is a major complication of Chronic Kidney Disease (CKD). There are few large observational studies analyzing the association between anemia and significant clinical outcomes in non-dialysis dependent CKD (ND-CKD) patients. Our aim was to evaluate the prevalence of anemia and iron deficiency and their association with mortality, cardiovascular events, need for renal replacement therapy and hospitalizations in an outpatient ND-CKD population.

Method: A patient-level, retrospective, cohort analysis of all adult ND-CKD patients evaluated in an outpatient nephrology clinic between January 2012 to December 2017 with at least one year follow up. Anemia (defined according to the WHO definition - Hemoglobin [Hb] $<$ 13.0 g/dL in men and 12.0g/dL in women), absolute iron deficiency (ferritin $<$ 100 ng/mL), other demographic and clinical data (CKD staging and etiology, comorbidities) were assessed at the first visit through individual consultation of electronic medical records.

Results: During the 6-year period, 3008 patients were identified (mean age 70.9$\pm$14.1 years; 54.5% male; 91.7% white) with a mean follow-up of 3.3$\pm$2.0 years. The most frequent cardiovascular comorbidities were arterial hypertension (81.9%), obesity (58%), diabetes mellitus (57.9%) and dyslipidemia (43.9%). The mean Hb was 11.8 $\pm$1.9 g/dL. Anemia was present in 49.9 % of patients, with similar distribution between genders (50.4% in men vs 49.6% in women) and more frequent in white patients (92% vs 8% p= 0.019). Anemia prevalence increased across CKD stages - 12.9%, 25.9%, 57.2%, 72.7% and 86.4% for stages 1 to 5, respectively (p$<$0,001 for the trend). Anemia was associated with cardiovascular comorbidities, such as diabetes (52% vs 32%, p$<$0.001), hypertension (86.7% vs 77.7%, p$<$0.001), obesity (65.5% vs 60.8 %, p=0.012) and dyslipidemia (46% vs 41.2%, p=0.01). Among patients with ferritin levels available (1638), 41.7% had absolute iron deficiency. Anemia was associated with increased mortality (74% vs 26%, p $<$0,001) and hospitalization (61,8% vs 38.2%, p $<$0.001). In multivariate logistic regression analysis, anemia (OR 1,923; 95%IC 1,362-2.716; p$<$0,001) and absolute iron deficiency (OR 0.531 95% IC 0.348-0.809; p=0.003) emerged as independent predictors of death. Cardiovascular events were more prevalent in the group of patients with Hb levels 10-12 g/dL (4.1 vs2.3% 2p=0.006).

Conclusion: As expected, anemia prevalence increases across CKD stages and, as well as absolute iron deficiency, is independently associated with adverse clinical outcomes in ND-CKD patients, including death. Future studies should be developed to investigate if correction of these factors improves adverse outcomes.

P0868

ZONULIN AS A THERAPEUTIC POTENTIAL BIOMARKER OF ANEMIA IN PATIENTS WITH MULTIPLE MYELOMA AND CHRONIC KIDNEY DISEASE

Karolina Woziwodzka[1], Jolanta Malyszko[2], Małgorzata Banaszkiewicz[1], Ewa Koc- Żorawska[3], Paulina Dumnicka[4], Marcin Krzanowski[1], Krzysztof Batko[1], Paulina Gołasa[1], Joanna Tisonczyk[4], Marcin Zorawski[5], Jacek Małyszko[6], Ryszard Drozdz[4,4], Marek Jan Kuznieswki[1], Katarzyna Krzanowska[1]

[1]Jagiellonian University Collegium Medicum, Department of Nephrology and Dialysis Unit, Kraków, Poland, [2]Medical University of Warsaw, Department of Nephrology and Dialysis Unit, Warsaw, Poland, [3]Medical University of Bialystok, Second Department of Nephrology and Hypertension with Dialysis Unit, [4]Jagiellonian University Collegium Medicum, Department of Medical Diagnostics, Kraków, Poland, [5]Medical University of Bialystok, Department of Clinical Medicine, Poland and [6]Medical University of Bialystok, Nephrology and Dialysis Unit, Poland

Background and Aims: Zonulin is a haptoglobin 2 precursor, that regulates the intestinal permeability. As a double-chain form it takes part in scavenging haemoglobin. Chronic inflammation is common complication of chronic kidney disease which affects iron metabolism. The most frequent manifestation of multiple myeloma is anaemia in up to 73% of patients. Serum concentrations of zonulin are associated with inflammation process, age, kidney failure and iron status and anaemia.

The aim of the study was to analyse zonulin as a marker of anaemia in MM patients and investigate its relationship with acclaimed parameters of renal failure, inflammation, bone metabolism and stages of MM.

Method: The studied group of seventy-three patients with MM (67 symptomatic, 6 smoldering) included 35 women and 38 man, with mean age 69 ± 10 years. Median (IQR) of time from initial MM diagnosis was 36 (17; 69) months. Forty patients were in ISS stage 1, 15 in stage 2, and 12 in stage 3 at the time of blood collection. Remission of MM was diagnosed in 52 patients and stable or progressive disease in 21. Twenty-six patients had eGFR <60 ml/min/1.73 m^2. The examined parameters included creatinine, urea, serum monoclonal protein, albumin, ferritin, blood hemoglobin and NT-proBNP. The association between zonulin, markers of MM stages and renal and bone markers were determined by the Pearson's test and multivariate stepwise regression analysis. The p-value <0.05 was considered statistically significant.

Results: Median (IQR) serum zonulin in the studied group was 23.9 (19.9; 27.4) ng/ml. There were no differences in zonulin concentrations between patients with smoldering versus symptomatic MM (p=0.4), with ISS 1 to 3 (p=0.7), with remission versus stable or progressive MM (p=0.9), or with eGFR <60 ml/min/1.73 m^2 versus those with higher eGFR (p=0.6). Also, zonulin did not differ between subjects with and without anemia (Hb< the lower reference limit) (p=0.4). In whole studied group, significant correlations were observed between zonulin and serum albumin (R=0.30; p=0.009), creatinine (R=-0.28; p=0.018), eGFR (R=0.26; p=0.025), ferritin (R=0.34; p=0.013), NT-proBNP (R=-0.32; p=0.006). Moreover, in patients with symptomatic MM, zonulin correlated with monoclonal protein in serum (R=-0.29; p=0.046), blood hemoglobin (R=0.27; p=0.027), and age (R=-0.24; p=0.044). In multiple regression, serum concentrations of monoclonal protein (beta=-0.48 ± 0.16; p=0.006) and ferritin (beta=0.34 ± 0.14; p=0.023) as well as ISS stage 3 (beta=0.40 ± 0.18; p=0.034) were identified as independent predictors of zonulin concentrations.

Conclusion: Zonulin as a biomarker may promote diagnosis of etiology and management of MM-associated anaemia, which can contribute to biomarker-targeted therapeutic interventions. Early treatment may result in improved life expectancy in patients with MM and increase their quality of life.

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CKD. BONE DISEASE

P0879 EARLY STEROID WITHDRAWAL HAS A POSITIVE EFFECT ON BONE KIDNEY TRANSPLANT RECIPIENTS: A PROPENSITY SCORE STUDY WITH INVERSE PROBABILITY-OF-TREATMENT WEIGHTING

Benjamin Batteux[1,2], Valérie Gras-Champel[1,2], Mathilde Lando[3], François Brazier[3], Isabelle Desailly-Henry[4], Amayelle Rey[1,2], Youssef Benis[1,2], Kamel Masmoudi[1], Gabriel Choukroun[2,3], Sophie Liabeuf[1,2]

[1]Amiens University Medical Center, Clinical Pharmacology, Amiens, France, [2]Jules Verne University of Picardie, MP3CV Laboratory, EA7517, Amiens, France, [3]Amiens University Medical Center, Department Of Nephrology Internal Medicine Dialysis Transplantation, Amiens, France and [4]Amiens University Medical Center, Rheumatology, Amiens, France

Background and Aims: Long-term corticosteroid use after kidney transplantation is associated with a decrease in bone mineral density and a high fracture risk. We hypothesized that patients with early steroid withdrawal (ESW) would display a gain in bone mineral density in the year following kidney transplantation, when compared with patients on long-term corticosteroid therapy (LTCT).

Method: In a cohort of kidney transplant recipients, 317 patients were included between 2012 and 2018. Dual-energy X-ray absorptiometry was performed 1 and 12 months after transplantation. The data were analyzed using linear regression with inverse probability-of-treatment weighting based on a propensity score.

Results: One year after transplantation, the gain in bone mineral density was significantly greater in recipients with ESW than in recipients on LTCT for the lumbar spine (+0.027 g/cm, $P < 0.001$) and the femoral neck (+0.021 g/cm, $P = 0.035$). Among patients with ESW, (i) none had osteoporosis, (ii) the percentage with normal bone mineral density increased from 35.0% at month 1 to 56.4% at month 12, and (ii) the percentage with osteopenia fell from 52.5% to 43.6%. In patients undergoing LTCT, the fracture incidence was 14.5 per 1000 person-years. None of the patients in the ESW group experienced a fracture. Cardiovascular risk factors were more prominent in the LTCT group relative to the ESW group: patients in LTCT group (i) were more likely to have high blood pressure ($p<0.001$), (ii) gained more weight gain ($p=0.032$) and (iii) displayed a greater increase in serum triglyceride levels ($p=0.004$).The acute rejection rate was similar in the two groups.

Conclusion: Early steroid withdrawal is associated with a spontaneous increase in bone mineral density at 12 months post-transplantation (relative to patients on long-term steroid therapy), with a reduction in several cardiovascular risk factors and does not appear to harm the graft.

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P0880

EFFICACY AND SAFETY OF SEVELAMER CARBONATE IN NON-DIALYSIS HYPERPHOSPHATEMIA PATIENTS: A RANDOMIZED, DOUBLE BLIND, PARALLEL GROUP STUDY FOR THE TREATMENT OF HYPERPHOSPHATEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE NOT ON DIALYSIS IN CHINA

Xueqing Yu[1]

[1]*Guangdong Provincial People's Hospital, Nephrology, Guangzhou, P.R. China*

Background and Aims: Hyperphosphatemia in chronic kidney disease (CKD) patients is associated with adverse outcomes, including vascular calcification, increasing risks of disease progression and even death. Sevelamer carbonate have been approved in Europe for phosphate lowering treatment in pre-dialysis CKD patient, its efficacy and safety in Chinese CKD hyperphosphatemia patients are not previously reported.

Method: This was a phase III, multi-center, randomized, double blind, placebo-controlled, balanced (1:1, sevelamer: placebo) parallel-group study to evaluate the efficacy and safety of sevelamer carbonate versus placebo over 8 weeks' duration in hyperphosphatemic CKD patients not on dialysis in China (Registration number NCT03001011). The primary objective of this study is to demonstrate efficacy of sevelamer carbonate tablets in the reduction of serum phosphorus in hyperphosphatemia in patients with chronic kidney disease (CKD) not on dialysis.

Results: In all, 202 patients were randomized (sevelamer, n=101; placebo, n=101); mean age was 50.7 years, 53.5% were male and the mean time of CKD diagnosis was 3.4 years with mean eGFR 7.5 ml/min/1.73 m^2. The baseline phosphorous were 2.13±0.35 mmol/L and 2.12±0.37 mmol/L in sevelamer and placebo group, respectively. The mean serum phosphorous decreased significantly in patients treated with sevelamer carbonate (-0.22±0.47 mmol/L) compared with placebo (0.05±0.44 mmol/L) (mean difference between sevelamer carbonate and placebo was -0.26 mmol/L, P<0.0001). When compared with placebo, sevelamer carbonate significantly reduced serum total cholesterol (-0.90±0.85 vs. -0.06±0.68 mmol/L, P<0.0001), low-density lipoprotein cholesterol (-0.94±0.72 vs. -0.04±0.58 mmol/L, P<0.0001) and calcium-phosphorous product (-0.48±0.97 vs. 0.05±0.81 $mmol^2/L^2$) from baseline to week 8. Serum iPTH was not significantly changed in sevelamer carbonate group compared with placebo group (-9.60±136.00 vs. 7.61±141.92 ng/L, P=0.83). Sevelamer carbonate was well tolerated with 83.27% compliance compared with 82.19% compliance in placebo arm. Average dose of sevelamer carbonate was 7.51 g/d at the end of study and 4.52 g/d across the study. Adverse events experienced by patients in sevelamer carbonate and placebo group were similar.

Conclusion: This study demonstrated that sevelamer carbonate has produced a significant reduction of serum phosphorous, and is safe and tolerated in Chinese pre-dialysis CKD patients with hyperphosphatemia.

P0881

ANEMIA SIGNIFICANTLY INCREASES RISK OF OSTEOPOROSIS IN PATIENTS WITH NON-DIALYSIS CHRONIC KIDNEY DISEASE

Seonyeong Lee[1], Yooju Nam[1], Hyung Woo Kim[1], Jae Hyun Chang[2], Tae-Hyun Yoo[1]

[1]Institute of Kidney Disease Research, Yonsei University, Department of Internal Medicine, Seoul, Korea, Rep. of South and [2]Gil Medical Center, Gachon University College of Medicine, Department of Internal Medicine, Incheon, Korea, Rep. of South

Background and Aims: Anemia was frequently observed in chronic renal failure patients. The risk of osteoporosis is higher in patients with chronic anemia. Chronic anemia also showed a close relationship with bone mineral density. However, few studies have been done whether anemia affects bone mineral density with chronic kidney disease(CKD) patient. Therefore, the aim of our study is to evaluate the relationship between anemia and bone mineral density(BMD) in a large sample of non-dialysis CKD cohort.

Method: We performed an observational study in 2,089 patients who measured hemoglobin and BMD with non-dialysis CKD enrolled in the KoreaN cohort study for Outcome in patients With Chronic Kidney Disease (KNOW-CKD). Anemia was defined as hemoglobin(Hb) levels of < 13.0 g/dL for males and 12.0 g/dL for females, respectively. BMD was estimated by dual energy x-ray absorptiometry system. The observed variable was decline of BMD during follow up.

Results: The mean age was 53.6 $\pm$ 12.2 years and 1,292(61.1%) patients were males. The BMD score was positively correlated with hemoglobin levels (**β**, 0.007; 95% CI, 0.003-0.012; P 0.002), but inversely with prevalence of anemia (**β**, -0.03; 95% CI, -0.042–0.008; P 0.004). In the multivariable logistic regression model, the prevalence of osteoporosis was significantly higher in the anemia group than that in the normal hemoglobin levels (odds ratio [OR], 1.67; 95% confidence interval [CI], 1.11-2.51, P=0.014). Among 881 patients except unavailable following BMD, 396 (19.7%) patients developed the decline of BMD during a median follow-up duration of 48 (interquartile range, 46-49) months. In the fully adjusted multivariable Cox models, risk of developing the decline of BMD was significantly higher in the anemia group (HR, 1.38; 95% CI, 1.02-1.87; P= 0.036) as compared to normal hemoglobin group.

Conclusion: We found that anemia is independently and significantly correlated with an increased risk of osteoporosis with non-dialysis CKD. Our study suggests that prompt correction of anemia in CKD patients could be beneficial to preserving bone mineral density.

P0882 **STUDY ON MECHANISM OF PTH SECRETION IN SECONDARY HYPERPARATHYROIDISM BY OPTOGENECTICS**

NAN HU[1], XINZHOU ZHANG[1]

[1]*Department of Nephrology and Key Laboratory of Shenzhen Renal Diseases, Shenzhen People's Hospital, SHENZHEN,GUANGDONG, P.R. China*

Background and Aims: Hyperparathyroidism (SHPT) which caused by disorders of PTH metabolism is one of the most common complications in CKD patients. In the progression of SHPT, expression of CaSR in the parathyroid gland decreases, which impairs the regulation of PTH secretion. It is technically challenging to precisely manipulate PTH secretion in hyperplastic human parathyroid tissue. As an emerging technology, optogenetics allows the reversible control of neuronal activity and cellular precesses using lights. In this study, we establish an optogenetic approach that bypasses CaSR to regulate the level of PTH secretion in human parathyroid cells. It is hoped to provide a new idea for the prevention and treatment of SHPT.

Method: First, we isolated and identified human parathyroid gland by SHPT patients. The primary cell culture of chief cells were performed and identification. After that, the cells were transfected with the lentivirus carrying ChETA-eYFP or eYFP gene. Lights stimulation of the cultured human parathyroid cells was performed after ChETA expression. The PTH level was measured by ELISA before and after stimulation. Meanwhile, Fura-2/AM was loaded to normal or ChETA expressing chief cells for calcium imaging by microscope.

Results: The parathyroid glands of three SHPT patients were obtained after total parathyroidectomy (Fig.1A). Hematoxylin & Eosin (HE) staining was performed. The tissue showed typical histological characteristics of SHPT: asymmetric enlargement of the chief cells and the nodular distribution (Fig.1B).

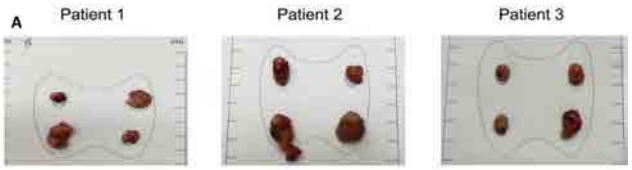


Fig.1 Parathyroid gland were obtained from SHPT patients and HE staining

Parathyroid cells were cultured by primary culture method. By the 7th day of cultivation, the chief cells were grown in uniform size and aggregation state (Fig. 2A). The cells were stained with immunofluorescence, results showed that most of the isolated cells expressed parathyroid hormone (PTH), calcium-sensing receptors (CaSRs) and Vitamin D receptors (VDR) (Fig. 2B).

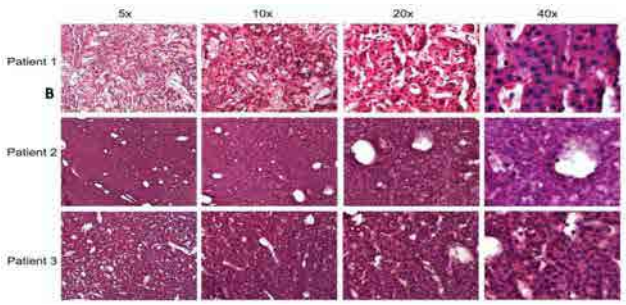


Fig. 2 Culture and immunofluorescence identification of parathyroid cells

We used lentivirus carrying the CMV-ChETA-eYFP construct to transfect cultured human parathyroid cells. Comparing with eYFP, most of the chief cells were labeled and expressed green fluorescence successfully after 48 hours (Fig.3).

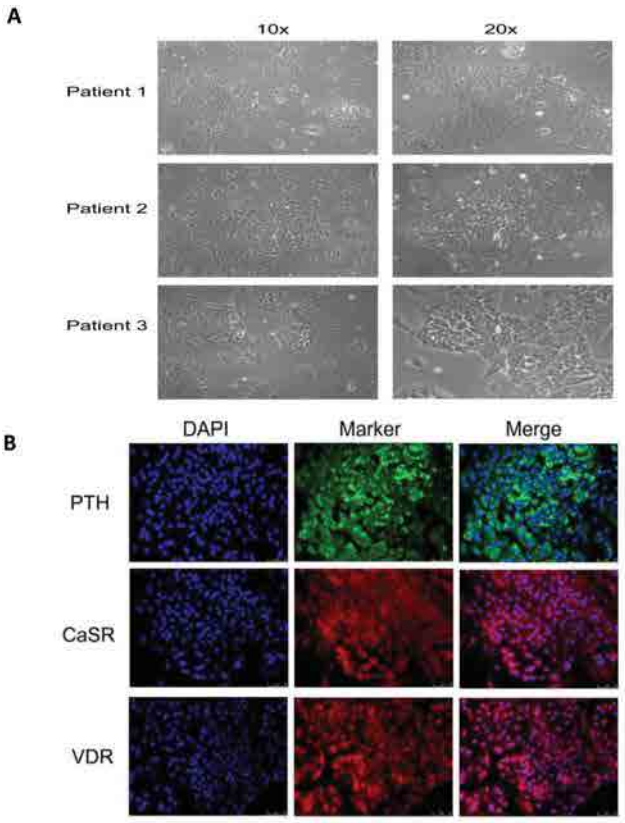


Fig. 3 Construction and identification of lentivirus vectors with CMV-ChETA-eYFP

We constructed a blue light-emitting diode to stimulated the transfected human parathyroid chief cells for 0.5h (20 Hz with stimulus intervals of 50 ms). Culture medium was collected before and after stimulation for 1h and 6h, and PTH was determined by ELISA. The results showed that there was no significant difference in PTH level between ChETA group and eYFP group before stimulation, however, PTH decreased significantly after 1 hour of stimulation in ChETA group, and gradually returned to the control group after 6 hours (Fig.4).

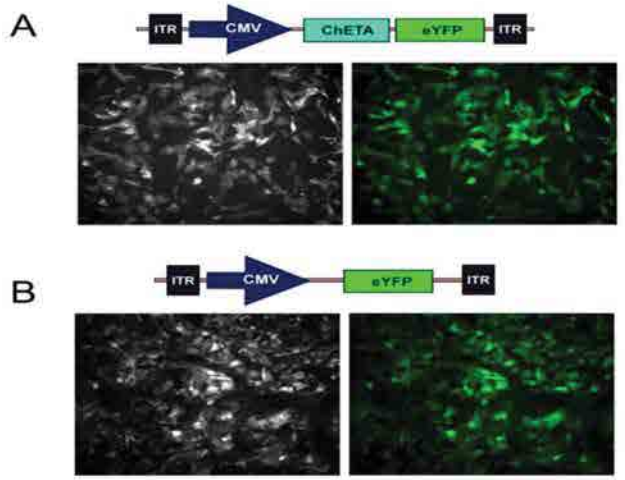


Fig. 4 The level of PTH before and after blue light stimulation.

After that, we used a calcium fluorescence assay to reveal light-induced changes of intracellular Ca2+. In ChETA group, blue light stimulation led to a significant increase in fluorescent signals, but a significant decrease when turned off, and the signal strength increased again when it was turned on in a rhythmic manner. But the fluorescent signal of eYFP group remained stable throughout the whole process (Fig.5).

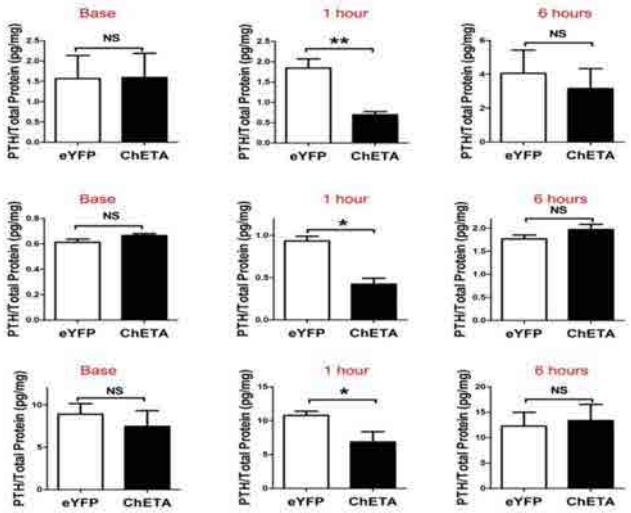


Fig. 5 Calcium fluorescence assay was used to reveal light-induced changes of the intracellular Ca^{2+}.

Conclusion: We used optogenetics to bypass CaSR rhythmic suppression of PTH secretion in human parathyroid cells. It is hoped that this study will provide new strategies for the treatment and prevention of SHPT

P0883 HEALTHY FEMALES EXCRETE MORE PHOSPHATE THAN MALES IN RESPONSE TO AN ORAL CHALLENGE

Mandy Turner[1], Christine White[2], Patrick Norman[3], Corinne Babiolakis[2], Michael Adams[1,2], Rachel Holden[1,2]

[1]Queen's University, Biomedical and Molecular Sciences, Kingston, Canada, [2]Queen's University, Medicine, Kingston, Canada and [3]Kingston General Hospital, Clinical Research Services, Kingston, Canada

Background and Aims: There are disparities in the diagnosis, treatment and prognosis for cardiovascular disease (CVD) between sexes and these differences are rooted, in part, in biology. Abnormalities in phosphate regulation and vascular calcification are important risk factors for CVD, even in the setting of preserved kidney function. Elevations of serum phosphate within the normal range are a risk factor for CVD. Abnormalities and differences in phosphate regulation are often not reflected in single circulating measurements of serum phosphate, but can be revealed by the acute circulating and mineral response to an oral phosphate challenge. The aim of this study was to assess the differences between sexes in the hormonal response and excretion capacity of an oral phosphate challenge.

Method: Healthy people (N=78) free of type 2 diabetes (T2D) and symptomatic CVD (~10 males and ~10 females from each decade between 40 and 80 years) were recruited from Kingston, Ontario, Canada. Following a 12-hour fast, participants consumed a 1250 mg phosphate drink (sodium phosphate) where blood and urine were collected hourly from baseline to 4 hours following the oral challenge.

Results: In the cohort, 43 of the participants were female and the average age for males and females was 58.4±10.8 and 60.0±9.6, respectively. Kidney function was normal, with eGFR measurements of 88±12ml/min/1.73m^2 and 93±14ml/min/1.73m^2, in males and females respectively. There was no difference in fasting baseline levels of phosphaturic hormones, fibroblast growth factor 23 (FGF-23) or parathyroid hormone (PTH) between sexes, nor was there an impact of age on either of these measures. Females had a similar fasted urinary phosphate-to-creatinine ratio as males, but higher circulating serum phosphate (1.2±0.1 mM v 1.0±0.1 mM, $p<0.01$). In response to the phosphate challenge, females increased their phosphate excretion more than males, significant for all measured time points (Figure 1A). There was a substantial increase in urinary excretion of calcium in females only (Figure 1B). Circulating calcium was not altered by the challenge nor different between the sexes. After adjustment for sex and age, testosterone was inversely correlated with fasted serum phosphate (r=-0.20) and urinary phosphate-to-creatinine ratio (r=-0.28), but not to measures of acute response to the oral challenge. Estradiol was not correlated to any measure of phosphate homeostasis, but correlated negatively to serum calcium (r=-0.30) and positively with post-challenge urinary calcium excretion (r=0.22), after adjustment for age and sex.

Conclusion: Females have greater capacity to excrete a phosphate load than males and also excrete calcium in response to phosphate. Impaired acute phosphate response may lead to increased exposure to circulating phosphate, and in that way may contribute to the initiation or propagation of vascular calcification. Improved acute handling of phosphate may contribute to the lower prevalence of coronary artery calcification and lower risk of developing CVD in females. Phosphate as a stimulus for acute calcium excretion, as well as its correlation to estradiol, has potential importance in relation to dietary phosphate exposure and osteoporosis. These observed differences in mineral homeostasis between females and males may be important as, to date, there has been no attempt to identify sex-specific targets or sex-specific treatment approaches.

P0884

MYO-INOSITOL HEXAPHOSPHATE PEGYLATION IMPROVES BIOAVAILABILITY BUT REDUCES ITS ANTI-VASCULAR CALCIFICATION EFFECT IN RATS

M. Mar Pérez[1], Miguel David Ferrer Reynes[1,2], Joaquín Ortega-Castro[2], Firas Bassissi[1], Joan Perelló[1], Carolina Salcedo[1]

[1]Sanifit Therapeutics, Palma, Spain and [2]University of the Balearic Islands, Palma, Spain

Background and Aims: Vascular calcification (VC) is a major contributor to increased morbidity and mortality in End Stage Kidney Disease (ESKD) patients undergoing dialysis. SNF472, a salt of inositol hexaphosphate (InsP6), is a selective calcification inhibitor that interferes in the formation and growth of ectopic hydroxyapatite (HAP). SNF472 is currently in Phase 3 clinical trials for the treatment of calciphylaxis in ESKD patients on dialysis. Inositol-1,2,3,5-tetraphosphate-4,6-bisPEG100 (InsP4bisPEG or INS3001) results from the PEGylation of inositol tetraphosphate (InsP4) with polyethylene glycol (PEG) 100. Our aim was to compare the relative bioavailability of SNF472 and InsP4bisPEG and their efficacy in the inhibition of calcification in silico, in vitro and in vivo.

Method: Subcutaneous (10 mg/kg) pharmacokinetics of InsP4bisPEG and SNF472 were assessed in Sprague Dawley (SD) rats. To evaluate the adsorption binding affinity (Eads) of SNF472, InsP4bisPEG and other inositol phosphates to the HAP crystal surface, computational studies were performed using Density Functional Theory calculations with DMOL3 (MS2016). The in vitro efficacy of the compounds was evaluated using a pharmacodynamic assay to measure the calcification potential of human plasma. An in vivo efficacy study (calcification induced by 3 consecutives daily s.c. administrations of 150 kIU/kg vitamin D3) was performed with SD rats receiving s.c. vehicle, or equimolar doses (36 μmol/kg) of SNF472 or InsP4bisPEG once daily.

Results: The PEGylation of inositol tetraphosphate in positions 4 and 6 increased the exposure and $t_{1/2}$ of the compound when given subcutaneously compared to SNF472. Molecular modelling revealed that SNF472 binds to the HAP surface with higher affinity than InsP4bisPEG and INSP4 (ΔEads=-352 kcal/mol for SNF472, ΔEads=-177 kcal/mol for InsP4bisPEG and ΔEads=-146 Kcal/mol for InsP4, taking inositol as reference). These results were correlated with the inhibition of calcium phosphate crystallization in plasma in vitro. SNF472 treated animals presented significantly lower calcium levels in aorta, which were 38% and 55% lower than placebo and InsP4bisPEG treated animals, respectively.

Conclusion: The differential pharmacokinetic profile of InsP4bisPEG (INS3001) does not translate into higher, but lower, efficacy than SNF472 against vascular calcification when comparing equimolar doses.

P0885 **THE RELATIONSHIP BETWEEN BONE REGULATORY MARKERS AND BONE TURNOVER IN RENAL OSTEODYSTROPHY**

Syazrah Salam[1,2], Orla Gallagher[2], Fatma Gossiel[2], Arif Khwaja[1], Richard Eastell[2]

[1]Sheffield Teaching Hsopitals NHS Foundation Trust, Sheffield Kidney Institute, Sheffield, United Kingdom and [2]University of Sheffield, Oncology and Metabolism, Medical School, Sheffield, United Kingdom

Background and Aims: Renal osteodystrophy is common in advanced chronic kidney disease (CKD) patients and is characterized by abnormal bone turnover and mineralization. Parathyroid hormone (PTH) increases bone turnover through osteoblast and osteoclast activation. Osteoprotegerin (OPG) is a decoy receptor of receptor activator of nuclear factor kappa-β ligand and thus, inhibits osteoclast maturation. Meanwhile, sclerostin is an inhibitor of the Wnt signalling pathway and thus, inhibits osteoblast maturation. We aimed to assess the relationship between these bone regulatory markers and bone turnover as assessed by bone histomorphometry and bone turnover markers (BTMs).

Method: We recruited 43 CKD patients with eGFR<30ml/min/1.73m^2 or on dialysis. Fasting serum samples were analysed using Immunodiagnostic Systems automated assays (Boldon, UK) for intact PTH (iPTH) and BTMs such as bone alkaline phosphatase (bALP) and intact procollagen type 1 N-terminal propeptide (intact PINP) which are bone formation markers, and tartrate-resistant acid phosphatase 5b (TRAP5b) which is a bone resorption marker. OPG and sclerostin were analysed using manual ELISA by Biomedica (Vienna, Austria). Trans-iliac bone biopsy was performed after tetracycline labelling. Bone samples were analysed using quantitative histomorphometry. Normal bone turnover was defined as bone formation rate/bone surface (BFR/BS) of 18 - 38μm^3/μm^2/year. Spearman rank correlation was used to test the relationship between the variables.

Results: Median BFR/BS was 32.12 (IQR 17.76 – 48.25) um^3/um^2/year. 26% of patients had low and 40% had high bone turnover. iPTH and OPG were positively correlated with BFR/BS (rho = 0.42, p<0.01 and rho = 0.36, p<0.05 respectively). Sclerostin was not correlated with BFR/BS. Furthermore, sclerostin did not correlate with bALP and intact PINP whereas OPG correlated with TRAP5b (rho = 0.43, p<0.01). iPTH correlated with bALP (rho = 0.62, p<0.001), intact PINP (rho = 0.62, p<0.001) and TRAP5b (rho = 0.50, p = 0.001).

Conclusion: Circulating levels of iPTH and OPG were modestly associated with bone turnover but sclerostin was not. There are likely to be bone regulators other than iPTH, OPG and sclerostin which regulate bone turnover in renal osteodystrophy.

P0886 **EFFICACY AND SAFETY OF EVOCALCET IN PERITONEAL DIALYSIS PATIENTS: A SINGLE CENTER LONGITUDINAL STUDY IN JAPAN.**

Hiroki Uchida[1], Motoyasu Kurahashi[1], Kenji Harada[1], Hidetoshi Kanai[1]

[1]*Kokura Memorial Hospital, nephrology, Kitakyushu kokurakita ku asano, Japan*

Background and Aims: Calcimimetic agent is used for secondaryhyperparathyroidism (SHPT), but it might cause gastrointestinal side-effects. These side effects are severe problem for PD patients with gastrointestinal symptoms due to dialysis fluid storage. Evocalcet is a new calcimimetic agent for SHPT, and expected to reduce gastrointestinal related symptoms. There have been some reports about switching from cinacalcet to evocalcet or administered for HD patients. However, there have been few reports on PD patients. Here, we reported the efficiency and safety of evocalcet in PD patients.

Method: PD patients who had newly started to treat for SHPT with evocalcet, between August 2018 to August 2019 were selected. Patients who died or transferred to HD within 6 months after administered evocalcet were excluded. We compared the changes in whole PTH level, serum phosphorus level and serum corrected calcium level with baseline and after administration. Moreover, we investigated adverse events of gastrointestinal related symptoms.

Results: Overall, 34 PD patients were included, (mean age: 67.5 years old, male/female: 23/11, average PD vintage: 39.6 months, serum phosphorus level: 5.1 $\pm$ 1.0 mg/dl). There was a significant reduction in whole PTH at week 16 from baseline (346 $\pm$ 187 pg/ml vs 258 $\pm$ 196 pg/ml, $p < 0.001$), and this relation was continued at week 32. There was no significant change in serum phosphorus level during this study. Serum corrected calcium level was the lowest at week 12 from baseline (9.4$\pm$0.7 mg/dl vs 9.0$\pm$0.1 mg/dl: p=0.004), thereafter, serum calcium level was not decline with adjustment of vitamin D receptor activators and calcium preparation. Adverse events were observed in 6 patients (18.2 %), nausea occurred in 3 patients, decreased appetite occurred in 2 patients, and diarrhea occurred in 2 patients. Although some adverse events had occurred, all patients continued study.

Conclusion: These results suggested that evocalcet might be efficient and safety in PD patients with SHPT.

P0887

MAJOR OSTEOPOROTIC FRACTURES AFTER KIDNEY TRANSPLANTATION: INCIDENCE, PREDICTORS AND ASSOCIATION WITH MORTALITY

Ken Iseri[1,2], Juan Jesus Carrero[3], Marie Evans[1], Li Felländer-Tsai[4], Hans Berg[4], Björn Runesson[1], Peter Stenvinkel[1], Bengt Lindholm[1], Abdul Rashid Tony Qureshi[1]

[1]Karolinska Institutet, Divisions of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, [2]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Japan, [3]Karolinska Institute, Department of Medical Epidemiology and Biostatistics and [4]Karolinska Institutet, Division of Orthopaedics and Biotechnology, Department of Clinical Science, Intervention and Technology

Background and Aims: Major osteoporotic fractures (MOF) are associated with increased morbidity and mortality in ESRD patients. We investigated incidence, predictors and clinical outcomes associated with first MOF (MOF_{first}) following kidney transplantation (KT).

Method: In Swedish Renal Registry of 3992 first KT recipients (2005 -2016) (age 53 years, 65% men), we identified all MOF_{first} in hip, spine, humerus and forearm following KT. We estimated incidence rates and predictors of MOF_{first} using flexible parametric hazard models and Fine-Gray analysis accounting for competing risk of death, and risk of all-cause mortality following MOF_{first} using Cox proportional hazards models with fracture as time-varying exposure.

Results: During median follow-up of 4.8 years (IQR 2.2-7.9 years), there were 279 fractures of which 139 were forearm fractures. The crude incidence rate of MOF_{first} (n=279) was 14/1000 patient-years and that of hip fractures (n=69) 3/1000 patient-years. The multivariate-adjusted fracture incidence rates were highest during the first 6 months following KT, and two-fold increased among women. High age, female sex, previous history of MOF, diabetes nephropathy, pretransplant dialysis therapy and acute rejection were associated with increased risk for MOF_{first}, whereas pre-emptive KT was associated with lower risk of MOF_{first}. Spline curves showed that impact of age in women on MOF_{first} was markedly higher than in men. MOF_{first} (including all cases) independently predicted increased all-cause mortality (hazard ratio, HR, 1.78(95%CI 1.35-2.36)). Among MOF_{first}, hip fracture (HR, 4.68(95%CI 1.56-14.06)) and spine fracture (HR, 4.02(95%CI 1.19-13.54)) were significantly associated with increased all-cause mortality.

Conclusion: The initial six months following kidney transplantation is a high-risk period for major osteoporotic fractures, especially forearm fractures. MOFs, especially hip and spine fracture, are associated with increased mortality.

P0888 **FIBROBLAST GROWTH FACTOR 23 PRODUCES ARTERIAL STIFFNESS THROUGH CHANGES IN VASCULAR SMOOTH MUSCLE CELL PHENOTYPE.**

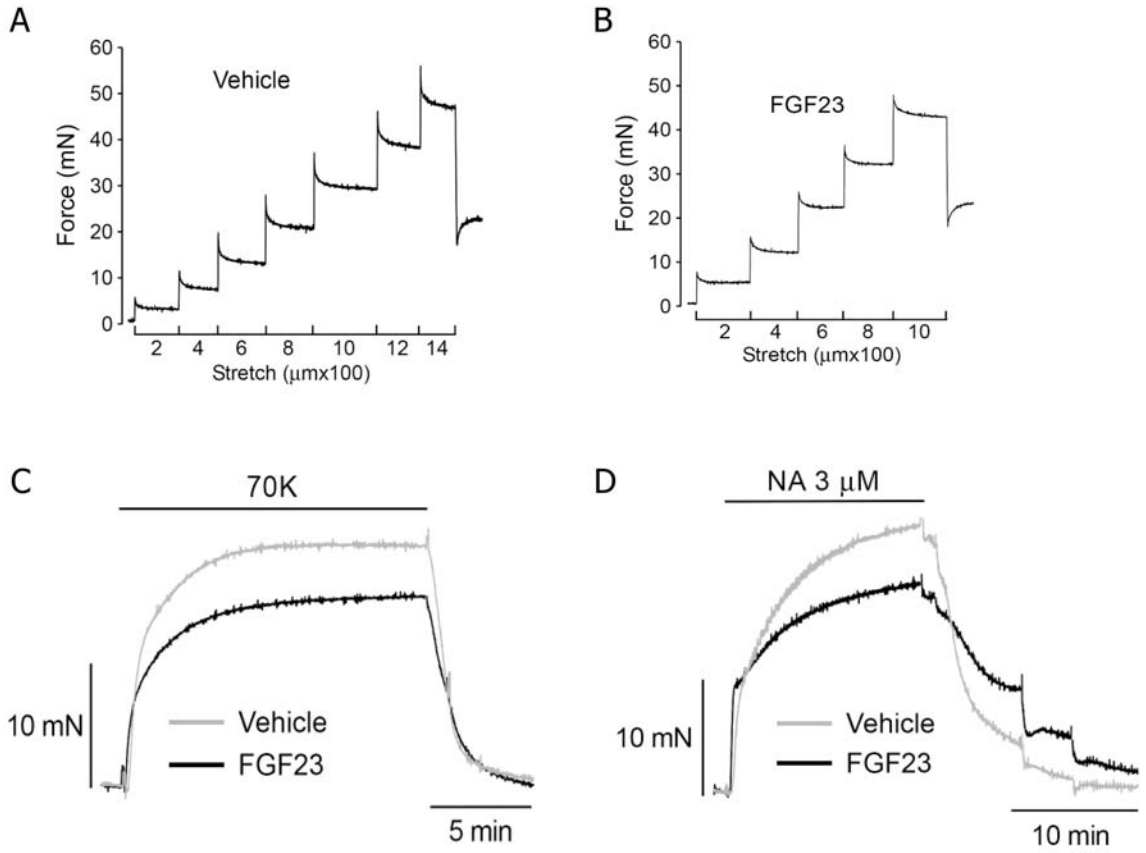
Juan. R Muñoz-Castañeda[1], Cristian Rodelo-Haad[1], M. Victoria Pendon-Ruiz de Mier[1], Noemi Vergara[1], Gonzalo Revilla-Gonzalez[2], Juan Migueo Diaz-Tocados[1], Cristina Membrives[1], Rodrigo Lopez-Baltanas[2], Sagrario Soriano Cabrera[1], Alejandro Martin-Malo[1], Juan Ureña[2], Rafael Santamaria[1], Mariano Rodriguez[1]

[1]1Maimonides Institute for Biomedical Research (IMIBIC), Cordoba, Spain. 2University of Cordoba, Spain 3Nephrology Service, Reina Sofia University Hospital, Cordoba, Spain., Cordoba, Spain and [2]Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Dpto. de Fisiología Médica y Biofísica, Sevilla, Spain., Sevilla, Spain

Background and Aims: In patients with chronic kidney disease (CKD), high levels of c-terminal fibroblast growth factor 23 (FGF23) are associated with cardiovascular disease and mortality. Vascular smooth muscle cells (VSMC) may present two clearly differentiated functional phenotypes, contractile and synthetic. The abundance of synthetic phenotype is associated with vascular dysfunction and it is unknown whether in FGF23 may promote transition from a contractile to a synthetic phenotype in VSMC causing vascular stiffness. The present study was conducted to evaluate whether FGF23 affects VSMC phenotype and arterial stiffness.

Method and Results: High levels of FGF23 promoted VSMC transition from a contractile to a synthetic phenotype. These effects were mediated through FGFR1 and Ras/MAPK signaling activation. Inhibition of both pathways enhanced contractile phenotype of VSMC. The pro-contractile microRNAs, miR-221 and miR-222 were reduced by FGF23 and miR-221 transfection recovered the contractile phenotype of VSMC decreased by FGF23. In experimental rats, exogenous infusion of FGF23 produced an increase in vascular wall thickness with VSMC exhibiting synthetic phenotype and reduction of plasma levels of miR-221. Functional studies performed on aortic arterial rings revealed that passive and active forces were altered in rats treated with FGF23. In a group of CKD stage 2-3 patients with rather high levels of FGF23 it was observed an increased in pulse pressure reflecting vascular stiffness together with low plasma levels of miR-221 and miR-222.

Conclusion: FGF23 favors the transition of VSMC from contractile to synthetic phenotype causing vascular dysfunction and arterial stiffness; this may be a mechanism by which FGF23 contribute directly to the development of vascular disease in CKD patients.



Representative records during the normalization process in aortic arterial rings from rats treated with vehicle (A) or FGF23 (B). Representative records of arterial contraction induced by 70K^{+} (C) or noradrenaline (D) in aorta rings of rats treated with FGF23 and vehicle. Number of animals for 70K: vehicle, 4 (15 rings); FGF23, 4 (16 rings). Number of animals for NA: vehicle, 3 (10 rings); FGF23, 3 (11 rings).* P<0.05, **P<0.01. Data representing mean ± SE.

Figure:

P0889

TO WHAT EXTENT CAN WE ACHIEVE MINERAL BONE METABOLISM TREATMENT TARGETS AS SUGGESTED BY UPDATED 2017 KDIGO GUIDELINES IN PATIENTS WITH PREDIALYSIS CHRONIC KIDNEY DISEASE

Mevlut Tamer Dincer[1], Şeyda Gül Özcan[2], Selma Alagoz[3], Cebrail Karaca[1], Sibel Gulcicek[4], Sinan Trabulus[1], Meltem Pekpak[1], Nurhan Seyahi[1]

[1]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Nephrology, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Istanbul, Turkey, [3]Bagcilar Training and Research Hospital, Department of Nephrology, Istanbul, Turkey and [4]Istanbul Training and Research Hospital, Department of Nephrology, Istanbul, Turkey

Background and Aims: The mineral bone disorder is an essential problem in chronic kidney disease (CKD). It is an independent modifiable risk factor for renal damage progression and CKD related mortality. Therefore, it is important to treat chronic kidney disease mineral bone disorder (CKD-MBD) according to international guidelines. Data on the management of mineral bone disorders in predialysis patients is scarce. We aimed to investigate the proportion of CKD-MBD patients reaching targets suggested by the updated 2017 KDIGO guidelines.

Method: We performed a multicenter cross-sectional study. We recruited consecutive adult (>18 years of age) CKD 3-5 patients who were on regular nephrology outpatient clinic follow up. Patients who have GFR loss over 30% in the last six months, patients with malignancy, and decreased life expectancy due to severe comorbid disease and patients on renal replacement therapy were excluded. Data were collected in two-time points: one during the recruitment (second data point) and one, three to six months prior to the current visit (first data point). Persistent laboratory abnormalities were defined by out of normal range values in both time points. Therapeutic inertia was calculated for hyperphosphatemia. It was defined as a lack of using phosphate binders despite hyperphosphatemia.

Results: We examined a total of 213 patients for 3 different nephrology outpatient clinics. Of these patients, 49.5 % were male, with a mean age of 64,9 ± 12,0 years. 51.7 % of the patients were diabetic, 78 % were hypertensive, and 20.1 % had a history of coronary artery disease. Laboratory values related to MBD are shown in Table 1. KDIGO guideline targets were not reached in 14.8%, 18.4%, 59.0%, 71.0% patients regarding Ca, P, PTH, and vitamin D in the first visit. The targets were not reached in 15.0%, 19,2%, 61,2%, 81% patients regarding Ca, P, PTH, and vitamin D in the second visit. Persistence of out of target values were observed in 5.8%, 9.9%, 49.2% and 65.4% of the patients for Ca,P, PTH and Vitamin D respectively. The prevalence of therapeutic inertia for hyperphosphatemia was 34,4 % in the second visit

Conclusion: Regarding KDIGO guidelines, MBD is not optimally managed in predialysis CKD patients. Clinicians should have an active attitude regarding the correction of MBD even at the earlier stages of CKD.

Table: Laboratory values related to MBD

	1° visit	2° visit	
	Mean ± SD	Mean ± SD	p
CKD-EPI (ml/min/1.73m^2)	33.9 ± 14.4	33.9 ± 14.8	0.873
Calcium (mg/dl)	9.3 ± 0.6	9.4 ± 0.6	0.011
Phosphorus (mg/dl)	3.8 ± 0.70	3.7 ± 0.8	0.405
PTH (ng/dl)	112.1 ± 90.7	123.9 ± 137.2	0.158
25(OH)-vitamin-D3	25.8 ± 13.6	23.7 ± 13.6	0.070

P0890

EFFICACY AND SAFETY OF CINACALCET IN CHINESE MAINTENANCE HEMODIALYSIS PATIENTS WITH DIFFERENT STAGES OF SECONDARY HYPERPARATHYROIDISM: INTERIM ANALYSIS RESULTS OF ACTIVE STUDY

Aili Jiang[1], Ping Fu[2], Guanqing Xiao[3], Jian-ming Ye[4], Zhang-suo Liu[5], Xiao-Nong Chen[6], Zhaohui Ni[7], Yisheng Ling[8], Qiang He[9], Jing Chen[10], Chaosheng Chen[11], Li Hao[12], Jizhuang Lou[13], Shixiang Wang[14], Guohua Ding[15], Hong Liu[16], Yonghui Mao[17], Li Zuo[18], Junwei Yang[19], Aihua Zhang[20], Jianying Niu[21], Xuemei Li[22], Yunyan Zhang[23], Hui Jin[24], Liu Zhi-hong[25]

[1]the Second Hospital of Tianjin Medical University, Department of Kidney Disease & Blood Purification Treatment, Tianjin, , [2]West China Hospital of Sichuan University, Division of Nephrology , Chengdu, P.R. China, [3]The First People's Hospital of Foshan , Nephrology Department, Foshan, P.R. China, [4]The First People's Hospital of Kunshan, Department of Nephrology, Kunshan, P.R. China, [5]The First Affiliated Hospital of Zhengzhou University , Department of Nephrology, Zhengzhou, P.R. China, [6]Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Department of Nephrology, Shanghai, P.R. China, [7]Renji Hospital, School of Medicine, Shanghai Jiaotong University, Department of Nephrology, Shanghai, P.R. China, [8]Zhongshan Hospital, Xiamen University, Department of Nephrology, Xiamen, P.R. China, [9]Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Nephrology Division, Chengdu, P.R. China, [10]Huashan Hospital, Shanghai Medical College, Fudan University , Division of Nephrology, Shanghai, P.R. China, [11] The First Affiliated Hospital of Wenzhou Medical University, Department of Nephrology, Wenzhou, P.R. China, [12]The Second Affiliated Hospital of Anhui Medical University, Department of Nephrology, Hefei, P.R. China, [13]Nanjing First Hospital, Nanjing Medical University, Division of Hemodialysis, Nanjing, P.R. China, [14]Beijing Chao-Yang Hospital, Capital Medical University, Nephrology Faculty, Capital Medical University , Department of Blood Purification, Beijing, P.R. China, [15]Renmin Hospital of Wuhan University, Division of Nephrology, Hubei, P.R. China, [16]The Second Xiangya Hospital, Central South University, Key Lab of Kidney Disease and Blood Purification in Hunan, Department of Nephrology, Changsha, P.R. China, [17]Beijing Hospital, National Center of Gerontology, Department of Nephrology, Beijing, P.R. China, [18]Peking University People's Hospital, Department of Nephrology, Beijing, P.R. China, [19]Second Affiliated Hospital of Nanjing Medical University, Center for Kidney Diseases, Nanjing, P.R. China, [20]Peking University Third Hospital, Division of Nephrology, Beijing, P.R. China, [21]The Fifth People's Hospital of Shanghai, Fudan University Department of Nephrology, Department of Nephrology, Shanghai, P.R. China, [22]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Nephrology, Beijing, P.R. China, [23]Kyowa Hakko Kirin China Pharmaceutical Co., Ltd , Department of Medical Affairs, Shanghai, P.R. China, [24]Kyowa Hakko Kirin China Pharmaceutical Co., Ltd, Department of Medical Affairs, Shanghai, P.R. China and [25]Jinling Hospital, Nanjing University School of Medicine National Clinical Research, Center of Kidney Diseases, Nanjing, P.R. China

Background and Aims: Chronic kidney disease (CKD) is a major public health issue worldwide including in China. One of the most common complication in advanced Chronic kidney disease (CKD) is secondary hyperparathyroidism (SHPT). Reports show higher risk of bone fracture, cardiovascular events and all-cause mortality is associated with uncontrolled SHPT in patients with CKD. Cinacalcet, a calcimimetic agent was reported to reduce iPTH levels without Ca increase in patients with SHPT previously. However there has been no large-cohort study and stratified analysis of cinacalcet based on the level of iPTH in China. Moreover, the optimal therapeutic doses of cinacalcet with mild-to-severe SHPT is remaining unknown. ACTIVE study is an IV, open-label, multicenter clinical trial aimed to: (1) evaluate the efficacy and safety of cinacalcet in maintenance hemodialysis patients with mild-to-severe SHPT; (2) explore optimal combinations therapy with cinacalcet and other agents for treating patients with CKD-mineral and bone disorder. (3) investigate the benefit of long-term, continuous medication with cinacalcet in the real-world setting.

Method: The study design was reported on 2019 ASN. Key inclusion criteria were a baseline iPTH ≥300 pg/mL with life expectancy of ≥2 years, and ≥12 weeks of maintenance dialysis (three dialysis sessions per week) prior to enrollment. The enrollments were grouped based on their iPTH level as having mild (300-600 pg/mL), moderate (600-900 pg/mL) or severe (≥900 pg/mL). Patients initiated treatment with cinacalcet orally at a starting dose of 25 mg once daily (qd). The primary efficacy endpoint is the proportion of patients achieving iPTH targets (iPTH between 150-300pg/mL) at 20 and 32 weeks after the initiation of cinacalcet treatment. Adverse events and serious adverse events were recorded. An interim analysis was scheduled as 375 patients completed 32 weeks visit.

Results: 911 patients were recruited and of 750 eligible patients, 275 were identified as mild, 224 were considered as moderate and left 251 were grouped as severe SHPT. The study flowchart of 375 patients including mild(127), moderate(106) and severe(142) SHPT for interim analysis was shown in Fig 1. The baseline results including demographic and biomarkers level were reported on 2019 ASN. After 4 weeks' cinacalcet treatment, serum PTH decreased in all three group, while extremely remarkable in the severe SHPT group. Interim analysis results revealed that the proportion of patients achieving iPTH target (150-300 pg/mL) at 20 wk visit among mild, moderate and severe groups were 38.61% (39/101), 30.11% (28/93) and 10.91% (12/110) respectively. The proportion of patients achieving iPTH target at 32 wk visit in 3 groups increased to 44.68% (42/94), 27.27% (24/88) and 14.56% (15/103) respectively (Table.1). The trends of the proportion of patients achieving iPTH target increased in all 3 different groups (Fig.2). The safety analysis showed the most common treatment-related AE in top 3 including hypocalcemia, hyperlipidemia, and loss of appetite. In vital signs, electrocardiogram (ECG) and laboratory examination of descriptive analysis, found no obvious safety tips. This study is sponsored by Kyowa Hakko Kirin (China) Pharmaceutical Co., Ltd. The analysis is still ongoing and results will be released at EDTA meeting this year.

Conclusion: Oral cinacalcet HCl was effective and safe in reducing iPTH in patients receiving HD with mild-to-severe SHPT.

Table 1. Proportion of patients achieving iPTH targets in 3 groups

	20 weeks (n,%)			32 weeks (n,%)		
	Achieved	Failed	P	Achieved	Failed	P
Mild	39 (38.61)	62 (61.39)	<0.001	42 (44.68)	52 (55.32)	<0.001
Moderate	28 (30.11)	65 (69.89)		24 (27.27)	64 (72.73)	
Severe	12 (10.91)	98 (89.09)		15 (14.56)	88 (85.44)	

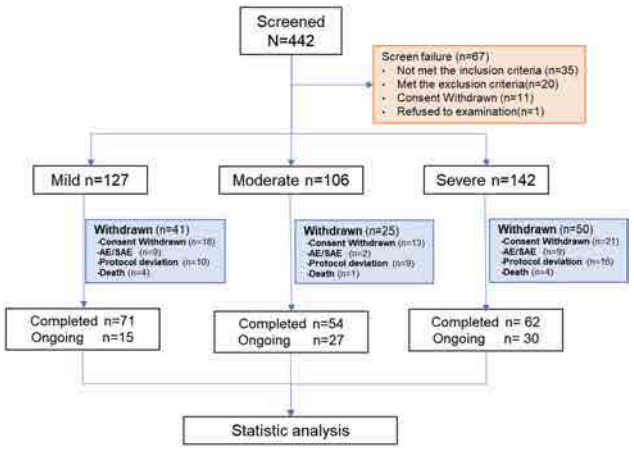


Fig 1. Study flowchart

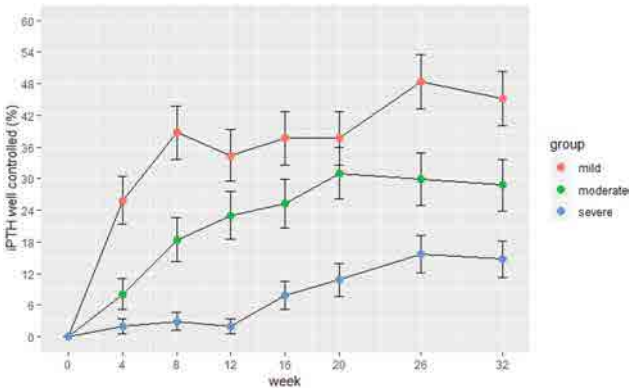


Fig 2 Trends of the proportion of patients achieving iPTH target in 3 groups

P0891

META-ANALYSIS OF NUTRITIONAL VITAMIN D FOR THE TREATMENT OF SECONDARY HYPERPARATHYROIDISM IN PATIENTS WITH NON-DIALYSIS CHRONIC KIDNEY DISEASE

Joel Gunnarsson[1], Rosa Lauppe[1], Edelgard Kaiser[2], Marco Soro[2], Philipp Csomor[2]

[1]Quantify Research, Stockholm, Sweden and [2]Vifor Pharma, Glattbrugg, Switzerland

Background and Aims: Chronic kidney disease (CKD) is commonly associated with mineral and bone disorder (CKD-MBD). Secondary hyperparathyroidism (SHPT) is a critical component of CKD-MBD characterized by excessive PTH secretion and parathyroid hyperplasia. SHPT develops in CKD because of disturbances in CKD-MBD parameters such as increases in serum phosphate and fibroblast growth factor 23, and reductions in 25-hydroxyvitamin D (25(OH)D), 1,25-dihydroxyvitamin D (1,25(OH)2D) and serum calcium. Low vitamin D levels play a critical role in the development and progression of SHPT. Nutritional vitamin D (NVD) supplements are being frequently used to address SHPT, especially in early CKD. The objective of this meta-analysis (MA) was to evaluate the effectiveness of the NVDs cholecalciferol and ergocalciferol in reducing PTH and increasing 25(OH)D in patients with non-dialysis CKD (ND-CKD).

Method: A systematic literature search was performed in PubMed to identify relevant randomized control trials (RCTs) to be included in the MA. All analyses were performed using both random and fixed effects models with inverted-variance weighting. Comparisons were made between the effects of NVDs relative to placebo-treated or untreated patients and between the baseline and end-of-study values of the patients treated with the NVDs, i.e. the effects in treated patients only.

Results: A total of 14 RCTs comprising 974 patients were included in the analyses. Overall reductions in PTH were small when compared to baseline (reduction of 10.95 pg/ml, 95 % confidence interval (CI): -15.99 to -5.91 pg/ml), while reductions in PTH were approximately three times larger when compared to placebo-treated or untreated patient groups (reduction of 34.35 pg/ml, 95 % CI:-47.47 to -21.24 pg/ml). This indicated a limited potential to actively lower PTH with NVDs as the relative effect on PTH when compared to placebo-treated or untreated patient groups was driven to a large degree by increases in PTH in the comparator arms. Treatment with NVDs tended to increase levels of 25(OH)D both when compared to placebo-treated or untreated patients (increase of 26.54 ng/ml, 95 % CI: 24.62 to 28.46 ng/ml) and when only the changes in treated patients were considered (increase of 21.49 ng/ml, 95 % CI: 20.54 to 22.44 ng/ml). However, large variations in effect sizes on levels of 25(OH)D were observed, making judgements about the size of any true treatment effect difficult. Average levels of 25(OH)D in treated patients at the end of the study period were >30 ng/ml in all but two RCTs and >50 ng/ml in only five of the included RCTs. No clear relationship was observed between study length (range: 4 to 144 weeks) or doses administered (range: 14 000 to 75 000 UI weekly average) and effects on 25(OH)D or PTH.

Conclusion: Our results suggest that treatment with NVDs is not efficacious to reliably and consistently lower PTH in ND-CKD patients with SHPT. Although treatment with NVDs can potentially be used to correct vitamin D insufficiency, our results suggest that the potential of NVD treatment to raise 25(OH)D levels to >50 ng/ml, a level needed to reduce PTH, is limited.

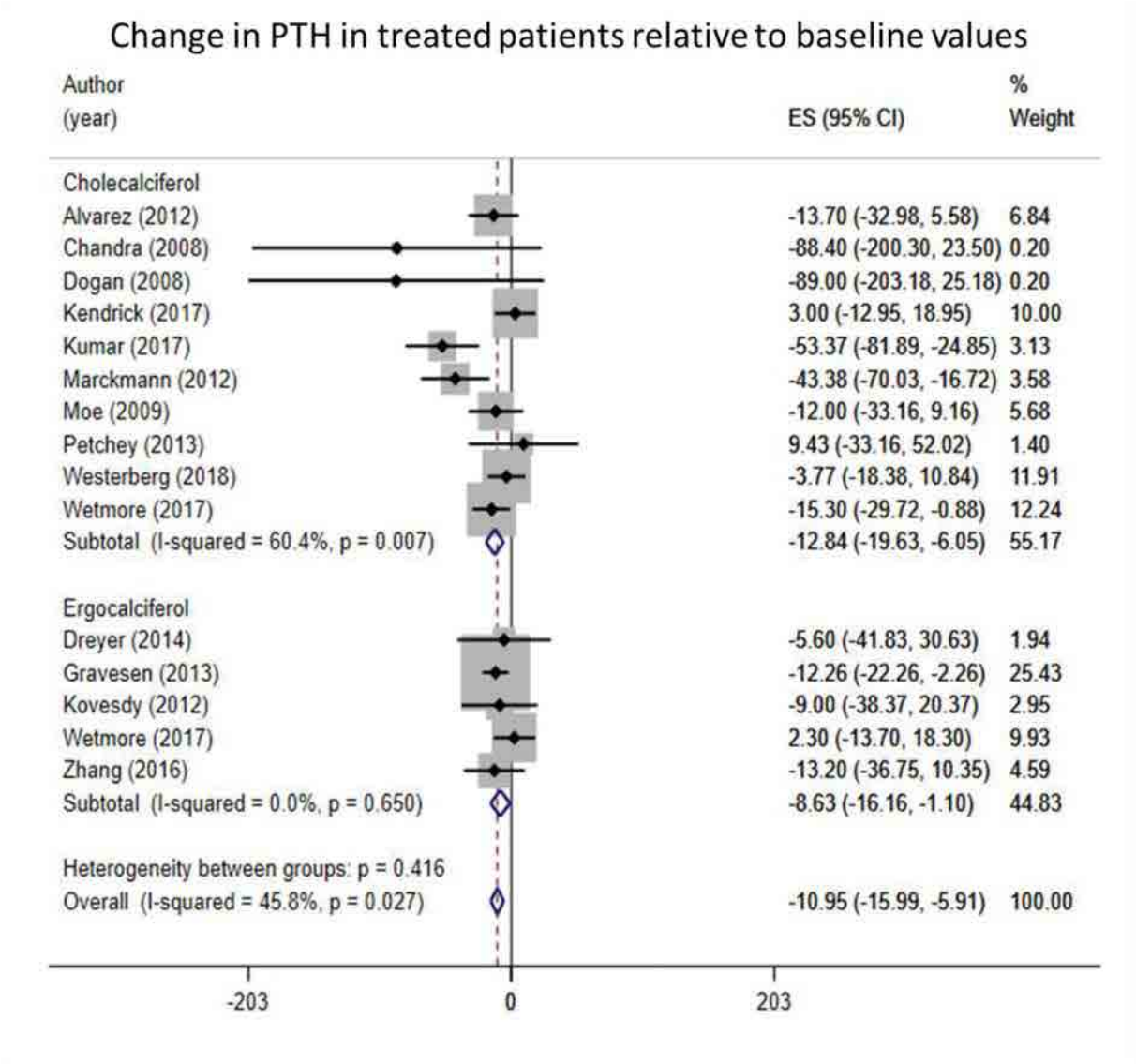


Figure:

P0892 PROFILE OF FIBROBLAST GROWTH FACTOR 23 IN CHRONIC KIDNEY DISEASE IN INDIAN POPULATION

SAMEER MAHAJAN[1], RAJEEV ANNIGERI[2]

[1]Kamalnayan Bajaj Hospital, NEPHROLOGY, Aurangabad, India and [2]Apollo Hospital Chennai, NEPHROLOGY, Chennai, India

Background: Chronic kidney disease (CKD) is a complex disease. Recent discovery that fibroblast growth factor 23 (FGF23) play a major role in development of CKD related bone mineral disorder (BMD) indicated a paradigm shift in our understanding of CKD–BMD. Recent research indicates that higher levels of FGF23 are associated with rapid progression of CKD and higher mortality in CKD patients. It is found that FGF23 level in blood is elevated significantly early in the course of CKD, even before a rise in parathyroid hormone (PTH) level which could contribute directly to tissue injury in heart, blood vessels and kidneys, apart from just being a marker of adverse outcome, and this needs further research.

The dietary habits, especially phosphate intake is likely to be different in Indian CKD population compared to western CKD population.

Aims and objectives:

1. To study prevalence of high FGF23 in CKD stage 3 to stage 5 in our hospital.
2. To study correlation of FGF23 with serum calcium, phosphorus, 1,25-dihydroxy vitamin D3 and PTH level in CKD stage 3 to 5.
3. To study the correlation of high FGF23 with clinical features associated with CKD-BMD.

Method: This is an observational study on 75 consecutive patients visiting Apollo hospital nephrology OPD in Chennai, India from June 2015 to Nov 2015. FGF23 level were determined simultaneously with serum creatinine, albumin, Vitamin D level, serum calcium, phosphate and serum PTH level done on enrolment. Serum samples when not immediately processed, were stored at -20°C.

Results: The age of the patient population varied from 19 to 80 years, mean 53.33 yrs with a SD of 15.49. 57(76%) were males and 18(24%) females. In our study, 46.7%patients belonged to CKD stage 4 while CKD stage 3 and 5 had 25.3% and 28% among the study population respectively.

The mean FGF23 level in study population was 154.82pg/ml (Normal range 11-48.6 pg/ml). Though the FGF23 values in stage 5 CKD were higher than those in stage 3 and 4 CKD, the difference was not statistically significant (p=0.74). In our study, 63 patients (84%) had high FGF23 level and 56(74.7%) patients were already on phosphate binding drugs and PTH suppressing drugs like vit D or cinacalcet for at least 2 months. 48(85.7%) patients of those on medications and 15 (79%) of those not on medications had high FGF23 level (P value -0.48, Yates P value-0.739).

In our study, PTH had an inverse correlation with eGFR and the association was statistically significant (P value 0.001). Serum Phosphorus level had an inverse correlation with eGFR and the association was statistically significant (P value 0.0001). Correlation of FGF23 values with eGFR was negative which was expected as the FGF23 levels increased with decreasing eGFR, but the association was not statistically significant. Similar results were obtained when FGF23 values were studied for association with serum calcium levels where the P value was 0.359 which was not statistically significant. Similarly, vit D levels had a negative association with P value of 0.077 and PTH levels had a positive association with P value of 0.987 (No statistical significance). Similarly, FGF23 levels and phosphate levels had a positive association without statistical significance(p= 0.224).

Conclusion: In conclusion, our data indicate that the rise of serum FGF23 levels in progressive Indian CKD patients is a common finding in CKD stage 3 and beyond.

P0893

BONE EFFECTS AND SAFETY OF ONE YEAR DENOSUMAB THERAPY IN A COHORT OF RENAL TRANSPLANTED PATIENTS: AN OBSERVATIONAL MONOCENTRIC STUDY

Carlo Maria Alfieri[1,2], Valentina Binda[1], Maria Teresa Gandolfo[1], Donata Cresseri[1], Maria Rosaria Campise[1], Silvia Malvica[1], Evaldo Favi[3], Piergiorgio Messa[1,2]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Nephrology, dialysis and renal transplantation, Milano, Italy, [2]University of Milan, Department of Clinical Sciences and Community Health, Milano, Italy and [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Renal Transplantation, Italy

Background and aims: Bone and mineral metabolism (MM) disorders are relevant problems in renal transplanted patients (RTxp). In our observational monocentric study, we evaluated the effects on femoral and lumbar bone mineral density (BMD) and on MM parameters, and the safety of one year-treatment with Denosumab (DB) in a cohort of RTxp.

Method: We recorded data about 32 RTxp treated with DB in our Center in the last year. RTxp were evaluated for BMD and T-score (Ts) before the start (T0) and after 12 months (T12) of treatment. Osteopenia was defined, at femoral (F-OPN) and lumbar (L-OPN) sites as Ts:-1>Ts>-2.5 whereas osteoporosis, in the same sites (F-OPS and L-OPS) as Ts<-2.5. X ray evaluation for spontaneous vertebral fractures (sVF) was made at T0 and, in 25 RTxp repeated at T12. MM and renal function parameters (serum creatinine, sCr and daily urinary protein excretion, ProtU) were recorded at T0 and after 1,3,6, and 12 months of therapy. The clinical indications for DB therapy, in the presence of Ca>9.0 mg/dL were the finding at T0 of: 1) F-OPS and/or V-OPS; 2) sVF. During the year of treatment, hypocalcemic (HpCa=Ca<8.0 mg/dL) episodes, infections, graft rejections and loss and RTxp survival were monitored.

Results: The cohort was composed mainly by females (n=21). The time of RTx was 144[59-232]mths. Steroid therapy was prescribed in 30 RTxp (93%), 22(68%) and in 2 (6%) RTxp were taking 25OHD and 1-25OH. Three RTxp (9%) were receiving Ca supplements. Bisphosphonate therapy was reported in 15 RTxp (46%) in the year before DB start. At T0, 25(78%) and 7 (22%) RTxp had F-OPS and F-OPN. Twenty-three (71%) and 6 (20%) RTxp had L-OPS and L-OPN. In 3 RTxp normal lumbar T-score was found. sVF were present in 17 RTxp (53%). Ca and P were 9.6±0.6 mg/dL and 3.1±0.6 mg/dL whereas PTH, ALP and 25OHD were 64±32 pg/mL, 80±37 U/L and 28±16 mg/dL. SCr and Prot-U were 1,32±0,4 mg/dL and 0,23±0,16 g/24h. At T12, F-Ts increased significantly (T0: -3.0[-3.5/-2.5] vs T12:-2.8[-3.5/-2.4) as like as V-Ts (T0: -3.0[-3.7/-1.9] vs T12:-2.8[-3.0/-1.6) both p<0.0001. A significant increase was found also in BMD: F-BMD +2.4%[-1.1%/+13%] (p<0.0001), V-BMD +2.6%[-3.4%/+12%] (p=0.009). The prevalence of F-OPS reduced from 78% to 73% (p<0.0001) and 4 RTxp ameliorated their Ts category. Prevalence of V-OPS reduced to 53% at T12 from 71% (p<0.001), and 4 RTxp ameliorated their Ts category. In 2 RTxp were found novel sVF. During the treatment no significant modifications of Ca were found, with only a slight but significant difference between T0 and T12 (T12 Ca: 9.22±1.17, p=0.01). PTH and ALP were significantly higher at T3, T6 and T12 respect T0. No differences in 25OH, sCr and ProtU were found. During the year of treatment, in 3 RTxp 25OHD supplementation was started. No one required novel Ca supplementation. DB therapy wasn't associated to HpCa episodes. Four RTxp had infections during the time of treatment (mean time of DB treatment:114 days). They had positive pathologic anamnesis for urinary tract infections (UTI). Two of them had symptomatic UTI and 2 required hospitalization for sepsis. No biopsy proven graft rejections were observed during the time of treatment and no graft loss or RTxp death were reported.

Conclusions: The preliminary results presented in our study, limited by the monocentric, not randomized design and by the smallness of the cohort, reported a good bone efficacy of DB in RTxp, especially at lumbar level. The therapy was characterized by a good general safety. Future longer and randomized studies, involving more RTxp might elucidate the possible primary role of DB in the treatment of bone disorders in RTxp.

P0894 **OBESITY IMPAIRS THE ACUTE RESPONSE TO AN ORAL PHOSPHATE CHALLENGE**

Mandy Turner[1], Christine White[2], Patrick Norman[3], Corinne Babiolakis[2], Michael Adams[1,2], Rachel Holden[1,2]

[1]Queen's University, Biomedical and Molecular Sciences, Kingston, Canada, [2]Queen's University, Medicine, Kingston, Canada and [3]Kingston General Hospital, Clinical Research Services, Kingston, Canada

Background and Aims: T Obesity is an increasing health problem world-wide. People who are overweight or obese are at greater risk of developing chronic diseases including cardiovascular disease (CVD). Factors associated with dysregulated phosphate metabolism have been linked to the presence of vascular calcification in people with type 2 diabetes (T2D) with normal kidney function. Insulin resistance and abdominal obesity are associated with increased circulating levels of phosphaturic hormones including fibroblast growth factor 23 (FGF-23) and parathyroid hormone (PTH). Abnormalities in phosphate regulation may not be reflected in single circulating measurements of serum phosphate, but can be revealed by the acute circulating and mineral response to an oral challenge of phosphate. The aim of this study was to determine if obesity and insulin resistance impact the acute capacity to excrete an oral phosphate challenge.

Method: Community-dwelling people (N=78) free of T2D and symptomatic CVD (~10 males and ~10 females from each decade between 40 and 80 years) with normal kidney function were recruited from Kingston, Ontario, Canada. Following a 12-hour fast, participants consumed a 1250 mg phosphate drink (sodium phosphate) where blood and urine were collected at baseline, 1, 2 and 3 hours following the oral challenge. Participants with a high-risk metabolic profile characterized by an elevated waist-to-height ratio (WHtR) (> 0.58) were matched by age and sex to participants with a low risk WHtR (<0.5).

Results: The results reveal a significant impact of obesity on phosphate excretion in response to an oral phosphate challenge. There was an association between WHtR ratio and the level of iFGF-23 (R=-0.34 $p<0.01$) but not PTH. After adjustment for age and sex, WHtR ratio was inversely correlated with urinary phosphate excretion in response to the phosphate challenge (R=-0.29, p=0.02) and the change in fractional excretion of phosphate (r=-0.34, p=0.007).

From the larger cohort, an age- and sex- matched subset was selected for 12 high risk and 12 low risk metabolic profiles with WHtR of 0.66±0.02 and 0.46±0.01, respectively. Kidney function was the same between the two groups (eGFR 92.3±13.1 versus 95.8±13.6 ml/min/1.73m^2 respectively) but high risk participants had significantly higher homeostatic model assessment of insulin resistance (HOMA-IR) (1.61±0.81 versus 0.68±0.3, $p<0.01$). Participants with a high risk metabolic profile had a greater increase in serum phosphate from baseline (29% increase in the area under the curve, p=0.04) and a significantly blunted increase in the fractional excretion of phosphate in response to the oral phosphate challenge (35% reduction in area under the curve [AUC], p=0.03) compared to the matched low risk profile participants.

Conclusion: Overweight/obese individuals demonstrate impaired response to an oral phosphate challenge, whereby phosphate excretion was impaired and there was increased exposure to new circulating phosphate. An impaired acute phosphate response may contribute to the initiation or propagation of vascular calcification. Dysregulated phosphate homeostasis may be an under-recognized cardiovascular risk factor in obese people that could be modified by diet and weight loss. Whether insulin enhances renal phosphate reabsorption requires further study.

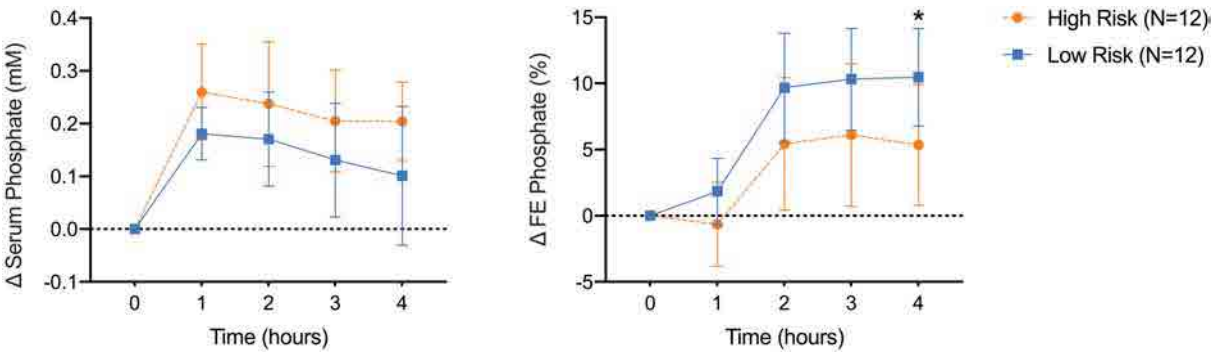


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P0894A

EFFECTS OF DENOSUMAB ON BONE MINERAL DENSITY AND LOW ENERGY FRACTURES IN KIDNEY TRANSPLANT PATIENTS: SAFE AND EFFECTIVE

Davide Rolla[1], Michela Ardini[1], Matteo Trezzi[1], Paola Bizzoni[2], Francesca Lauria[1], Andrea Casabella[3]

[1]Ospedale Sant'Andrea, Divisione di Nefrologia e Dialisi, La Spezia, Italy, [2]Ospedale Sant'Andrea, Servizio di Medicina Nucleare, La Spezia, Italy and [3]Ospedale Policlinico San Martino, Clinica Reumatologica, Genova, Italy

Background and Aims: Fractures are a disabling clinical outcome after kidney transplantation (KTx), with incidence 5 to 34 times higher expected in males and females, respectively. Denosumab, a fully human monoclonal antibody that binds to RANKL with high affinity and specificity, blocking the interaction of RANKL with RANK, mimicking the endogenous effects of osteoprotegerina, increase bone mineral density; however, its effects to reduce the risk of vertebral fractures and ameliorate BMD remain undefinite in the KTx.

Method: Thirteen kidney recipients (aged from 50 to 79 yy, 6.2 + 5.5 (SD) yy after KTx), 6 M and 7 F (all postmenopausal) with nearly normal renal function (creat. 1.1+-0.31 mg/dl), affected by low energy vertebral fractures (21 dorsal and 1 lumbar vertebrae), evaluated by morphometric X-ray absorptiometry (Hologic DQR-4500A), were treated with denosumab (four 60-mg doses of denosumab Q6M) over 24 months. Data for vertebral heights and height ratios (P-A), covering 9 vertebral bodies were obtained, besides the data of vertebral, femural and radius BMD.The immunosuppressive regimen consisted of CNI (TAC or CsA), MMF and 8 out of 13 patients were still taking prednisone. Bone mineral metabolism parameters (whole-PTH, 25OHD3 and alcaline phosphatase) were also evaluated.

Results: No sides effects were observed, and all Patients concluded the study.After two years of denosumab treatment, we observed a significative reduction of vertebral T-score (from -2.12 +- 0.35 (SE) to -1.67+-0.35; $p < .02$), while T score of femural and radius did not show significative variation (-1.86+-0.21 versus -1.84+- 0.23 and -3.04+-0.42 versus -3.19+-0.45, respectively). The number of low energy vertebral fractures, basal versus two years control, had increased for only two dorsal vertebral fractures. However, to one of two subjects, with new dorsal vertebral fractures, was administered high dose of methylprednison for a severe kidney reject. No variations were observed in whole-PTH (89.31+-19.9 versus 68.38+-9.8 pg/ml), 25OHD3 (24.02+-2.75 versus 26.67+-2.29 ug/dl) and alcaline phosphatase (78.46+-12.73 versus 56.77+-7.14 UI).

Conclusion: Treatment with denosumab improve BMD at vertebral site in KTx, despite continuous steroid therapy and reduce the risk of new low energy vertebral fractures

P0895 **THE RELATIONSHIP OF ARTERIAL CALCIFICATIONS IN CHRONIC KIDNEY DISEASE PATIENTS WITH INDIRECT ANTICOAGULANT INTAKE AND HEART MORBIDITY**

Asen Kamenov[1], Stoyanka Georgieva[2], Dobrina Mlachkova[3], Daniela Valentinova Monova[4]

[1]Medical Institute of Ministry of Interior, Clinic of Internal Medicine, Nephrology, Dialysis and Rheumatology, Sofia, Bulgaria and [2]Medical Institute of Ministry of Interior, Clinic of Image Diagnostics, Sofia, Bulgaria

Background and Aims: In patients with chronic kidney disease (CKD), arterial calcification (AC) is a potential mechanism for the progression of cardiovascular disease. AC is common in CKD patients and is a consequence of mineral-bone disorders. Indirect anticoagulants or vitamin K deficiency lead to matrix γ-carboxyglutamate decarboxylation, which may potentiate vascular calcification formation. The impaired renal function and indirect anticoagulants intake may lead to vitamin K deficiency and increased AC. The aim of this study is to determine if oral intake of Acenocoumarol has influence on abdominal aorta calcium score (AACS) and the AC relation with atrial fibrillation (AF) and / or ischemic heart disease (IHD) morbidity.

Method: We observe 129 patients with CKD (glomerular filtration rate below 44 ml/min/1,73 m^2, MDRD formula calculated). X - ray of the lateral abdominal aorta is performed for the AACS assessment according to L. I. Kauppila et al. method. The assessment of calcium score is formed by the involvement grade of each segment on the anterior and posterior wall of the vessel along the first four lumbar vertebrae. Calcification affecting less than 1/3 of the anterior wall of the aorta along the lumbar vertebral body receives 1 score and calcification extending over 1/2 of the vertebral body length receives 3 scores (total score - 24). The patients are distributed into three groups: I group with calcium score from 0 to 7, II - from 8 to 15 and III group - from 16 to 24. The data from assessed AACS are compared with Acenocoumarol intake and the presence/absence of AF and/or IHD. The results are processed with $\chi 2$ statistical analysis.

Results: One hundred twenty nine patients with CKD (95 males and 34 females) are included in the study. The patients data (mean, percentages, degrees, etc.) are summarized in tabl.1 and tabl. 2.

Clinically significant is the correlation between the grades of AACS and Acenocoumarol intake ($p < 0,05$). With the calcium score increasing, the patients percentage treated with Acenocoumarol also increases (fig. 1). There is a moderate correlation (Cramer's coefficient is 0,39) between the AACS grades and heart morbidity from AF and / or IHD ($p < 0,05$). The data shows that the higher calcium score is related with increased patients percentage with AF and / or IHD morbidity (fig. 2).

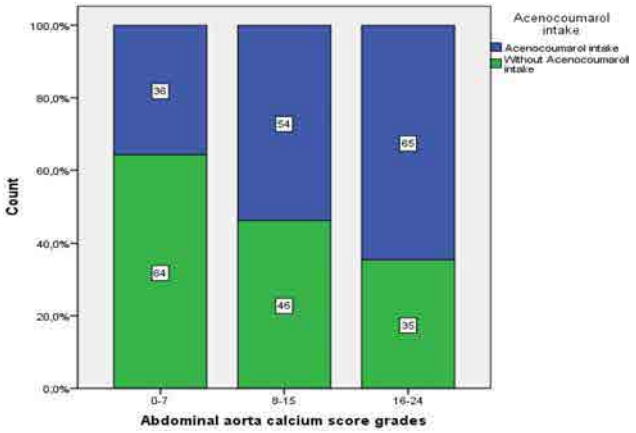


Fig. 1. Relationship between the AACS grades and Acenocoumarol intake.

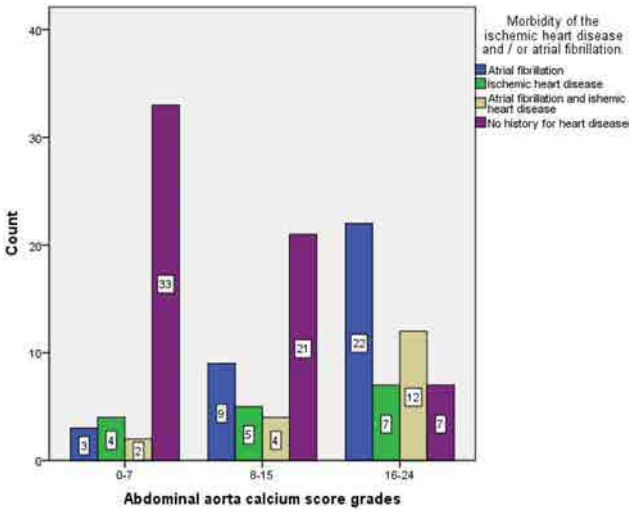


Fig. 2. Correlation between the AACS grades and atrial fibrillation and/or ischemic heart disease morbidity.

In our study, vascular calcifications are found in the abdominal aorta walls in all of the observed patients. We found that a higher AACS is associated with an Acenocoumarol intake in CKD patients and corresponds to an increased morbidity of AF and / or IHD. Acenocoumarol intake may lead to increased AACS. The higher calcium score is associated with a higher incidence of AF and / or IHD morbidity.

Conclusion: The study outcome supported the hypothesis that the increased AC formation and cardiovascular morbidity high risk could be a reason for the limited vitamin K antagonists (acenocoumarol) use in CKD patients. Furthermore, vitamin K2 supplementation is reasonable and may reduce the progression of AC.

Table. 1. Mean summarized data (age, glomerular filtration rate, CKD and Acenocoumarol duration.

Patients mean age in years	Average glomerular filtration value ml/min/1.73 m^2 (5 - 44 ml/min/1,73 m2)	Average duration of the CKD before enrollment in the trial in months	Average duration Acenocoumarol intake in months
67,7 ± 11	21,76 ± 9,5	82,7 ± 53,4	39,6 ± 16

Table. 2 Patient's distribution according the AACS and heart morbidity.

Mean AACS	Patient's groups according abdominal aorta calcium score			Patient's distribution according the morbidity of AF and / or IHD			
	I group	II group	III group	AF	IHD	AF and IHD	No history for heart disease
11,6 ± 7	42 patients (32,6%)	39 patients (30,2%)	48 patients (37,2%)	34 patients (26,4%)	16 patients (12,4%)	18 patients (14%)	61 patients (47,3%)

P0896 **TRABECULAR BONE SCORE PREDICTS OSTEOPOROTIC FRACTURE IN CHRONIC KIDNEY DISEASE PATIENTS**

Eunjin Bae[1], Tae Won Lee[1], Ha Nee Jang[2], Hyun Seop Cho[2], Hyun-Jung Kim[2], Se-Ho Chang[2], Dong Jun Park[1]

[1]Gyeongsang National University Changwon Hospital, Internal medicine, Korea, Rep. of South and [2]Gyeongsang National University Hospital, Korea, Rep. of South

Background and Aims: Chronic kidney disease and mineral bone disease (CKD-MBD) is a common complication of CKD and this is associated with higher risk of fracture, morbidity and mortality. Current guidelines recommend measurement of bone mineral density (BMD) in CKD patients. However, the focus is only on bone turnover and bone density, and there is no guideline for trabecular bone score (TBS) for trabecular bone microarchitecture in CKD patients. We aim to evaluate the role of TBS in predicting osteoporotic fracture in CKD patients

Method: We retrospectively enrolled 125 patients with CKD between 2016 and March 2019. Lumbar spine TBS was extracted from dual-energy X-ray absorptiometry, and we categorized the TBS into three groups as lowest ($\geq$ 1.31), moderate (1.31-1.23), and highest risk group ($\leq$ 1.23). The logistic regression analysis was used to assess osteoporotic fracture risk.

Results: Of 125 patients, mean age was 65.9 $\pm$ 14.2 years, 49.6% were on dialysis, 11.2% was highest risk group by TBS. Patients with highest risk group by TBS were significantly older, had lower height, weight, serum 25-OH vitamin D, serum sodium level, BMD *T*-score (lumbar spine, femur neck and total hip) than lower risk group. TBS significantly correlated with BMD *T*-score (lumbar spine, femur neck and total hip), height, weight and serum creatinine level ($P < 0.001$). Osteoporotic fracture was identified in 20 (16.0%) patients. In univariate analyses, old age, women, lower weight, TBS tertile group, lower potassium level were significantly associated with osteoporotic fracture. In multivariate analyses, only highest risk group by TBS was significantly associated with increased osteoporotic fracture risk after adjustment for demographic, comorbid, medication use, and previous fracture.

Conclusion: Lumbar spine TBS significantly correlated with BMD *T*-score and predicts osteoporotic fractures in patients with CKD.

P0897 RISK FACTORS FOR AVASCULAR BONE NECROSIS IN PATIENTS WITH LUPUS NEPHRITIS

Daniela Monova[1], Simeon Monov[2], Assen Kamenov[3], Vladislava Milenova[3]

[1]Medical University - Sofia, Medical Institute, Department of Internal Medicine, Nephrology and Rheumatology, Sofia, Bulgaria, [2]Medical University - Sofia, Department of Internal Medicine, Clinic of Rheumatology, Sofia, Bulgaria and [3]Medical Institute-MVR, Department of Internal Medicine, Nephrology and Rheumatology, Sofia, Bulgaria

Background and Aims: Avascular necrosis of bone (AVN) is an important complication of systemic lupus erythematosus (SLE) and often causes serious physical disability. The aim of this study was to investigate the risk factors for symptomatic avascular necrosis of bone (AVN) in lupus nephritis (LN) patients.

Method: The records of 374 patients (43 males, 331 females) with kidney biopsy-proven LN were reviewed retrospectively. Symptomatic AVN cases were defined as those with at least one diagnosis of AVN. The patients with LN who did not have AVN were evaluated as a control group. To determine risk factors for AVN, clinical, laboratory and therapeutic variables were analyzed by logistic regression.

Results: Symptomatic AVN was present in 17 patients (4 males, 13 females, mean age of 27,4±6,7 years). Among the 17 patients, 28 joints presented AVN. 12 occurred in hips (2 bilateral), 6-in ankles, 4-in knees, 3-in shoulders and 1- in lumbar spine. In 9 patients AVN involved 2 or more joints. 14 patients were on steroids at the time of presentation of AVN. 2 patients were not on CS and 1 patient did not has documentation of steroid use. Meta-analysis demonstrates a significant increased risk of AVN in patients with high disease activity and class IV LN ($p<0,005$). LN patients with AVN showed an earlier onset age ($p<0,05$) and received significantly higher total cumulative corticosteroid dose. AVN was not significantly associated with use of immunosuppressive agents. Serositis, coagulation disorders, vasculitis, cigarette smoking were higher incidence in male with LN and AVN. Raynaud's phenomenon, autoimmune thyroiditis, arthritis, Sjögren's syndrome, IgM anticardiolipin antibodies, antiphospholipid syndrome, Cushingoid body habitus were higher incidence in female with LN and AVN.

Conclusion: Many risk factors have been involved in the development of AVN in LN patients. AVN is prevalent in class IV LN and in younger patients. Since asymptomatic osteonecrosis may remain undetected, its true prevalence could be much higher than we reported. Multifocal lesions involving more than three anatomical sites are unusual. Corticosteroids are the principal risk factor, although some cases of AVN occur in relatively steroid naïve patients. Early detection of AVN is important because the prognosis depends of the stage and location of the lesion. An individual risk assessment for AVN development should be made prior to and during treatment for LN, especially in patients high dose corticosteroids.

P0898

VITAMIN C STATUS MODIFIES PARATHYROID HORMONE SECRETION IN NON-DIALYZED CHRONIC KIDNEY DISEASE PATIENTS

Ryuta Fujimura[1], SHOGO SHIBATA[1], Takechiyo Tokuda[1], Ayako Tanaka[1], Aya Mizumoto[2], TAMAKI HARADA[1], Nakata Hiroto[1]

[1]Higashiosaka City Medical Center, Division of Nephrology, Osaka, Japan and [2]Nippon Life Hospital, Division of Nephrology, Osaka, Japan

Background and Aims: Among patients with chronic kidney disease (CKD) at predialysis stage, there is a high incidence of secondary hyperparathyroidism. Metabolic changes associated with secondary hyperparathyroidism lead to renal osteodystrophy, including osteitis fibrosa, ectopic calcification, cardiovascular disease, and the risk of death, and serum parathyroid hormone levels are influenced by nutritional variables. Non-dialyzed CKD patients are especially prone to vitamin C deficiency because of dietary restrictions and malnutrition. Vitamin C is an important antioxidant and relates to the development and maintenance of bone tissues. However, the contribution of vitamin C deficiency to parathyroid hormone secretion is unknown. Here, we performed a single-center cross-sectional study in order to assess association of serum vitamin C and parathyroid hormone in non-dialyzed CKD patients.

Method: We had 280 consecutive patients who underwent serum vitamin C and serum intact parathyroid hormone (iPTH) measurement for screening purposes from January 1st, 2013 to November 30th, 2017. We analysed a total of 128 patients (71.3±11.6 year-old, 80 males) who had an estimated glomerular filtration rate (eGFR) that remained less than 60 mL/min/1.73m^2 after 152 patients were excluded because of vitamin C or vitamin D supplementation, age <20 years, dialysis, positive serostatus for HIV, hepatitis B or hepatitis C, chronic infection, or cancer.

Results: Twenty-three percent of the patients (n=29) had vitamin C levels< 2.0 μg/mL (a range seen in very deficient subjects), 53% (n=68) had levels between 2.0 and 5.5 μg/mL, and 31 patients (24%) had vitamin C levels >5.5 μg/mL, which is considered the upper limit of normal for the healthy population. Log(iPTH) significantly correlated with age (r=-0.238, p=0.00672), log(eGFR) (r=-0.625, p<0.0001), serum calcium (r=-0.609, p<0.0001), and serum phosphate (r=0.41, p<0.0001), and had a tendency to correlate with serum albumin (r=-0.146, p=0.101). Low serum vitamin C was associated with higher serum iPTH (P=0.0005, one-way analysis of variance). In a multiple linear regression model with log(iPTH) as the dependent variable, and age, gender, log(eGFR), serum levels of calcium, phosphate, albumin, and vitamin C as independent variables, the inverse relationship of log(iPTH) and serum vitamin C was confirmed (R^2 = 0.568, adjusted R^2 = 0.543, P<0.0001), along with other parameters influencing iPTH levels, including age, log(eGFR), serum calcium, and serum phosphate. Low vitamin C levels were also associated with increased serum alkaline phosphatase (r=-0.209, p=0.0179), a further indicator of the impact of vitamin C status on bone metabolism.

Conclusion: Vitamin C deficiency is prevalent in a significant proportion of non-dialyzed CKD patients. Low vitamin C levels contribute to secondary hyperparathyroidism, leading to increased bone turnover. This novel observation may result from effects of vitamin C on vitamin D metabolism, vitamin D binding in target tissues, and cAMP-linked signalling pathways in bone and parathyroid gland. Therapeutic intervention with supplemental vitamin C for secondary hyperparathyroidism might be a good strategy.

P0899 BIOMARKERS OF CKD-MBD IN CHILDREN

Altynay Balmukhanova[1], Assiya Kanatbayeva[1], Kairat Kabulbayev[1], Abay Shepetov[1], Aigul Balmukhanova[2]

[1]Asfendiyarov Kazakh National Medical University, Nephrology, Almaty, Kazakhstan and [2]Asfendiyarov Kazakh National Medical University, Science and research, Almaty, Kazakhstan

Background and Aims: In recent years there has been a growth in the number of patients with chronic kidney disease (CKD). As it is known, one of the most severe complications of CKD is mineral and bone disorder (MBD). MBD, which develops in childhood, contributes not only to the development of degenerative bone disease, but also to the growth of vascular morbidity and mortality in adulthood. Therefore, adequate control of bone and mineral metabolism is one of the goals in the treatment of children with CKD. Due to the recently discovered FGF-23, a significant role in the pathogenesis of MBD is given to hyperphosphatemia as the initiator of the process. However, changes in value of phosphorus and parathyroid hormone (PTH) are revealed only on the last stages of the disease. FGF-23 is a protein, which produced in bone cells and nowadays it is considered to be the central regulator of mineral-bone metabolism. It increases the loss of phosphorus in the urine due to the blockade of the sodium-phosphorus transporter in the proximal tubule of the nephron. FGF-23 also inhibits 1α-hydroxylase and stimulates 24-hydroxylase, leading to accelerated degradation of the active form of vitamin D.

Thus, **the aim of our study** was to investigate the relation between FGF-23 and other markers of bone metabolism such as phosphorus and parathyroid hormone.

Method: The study was conducted on 73 children (38 boys and 35 girls) with different stages of CKD. An average age of the patients was 9.89 ± 0.57 years. Exclusion criteria: active inflammatory, bone, infectious, oncological, immunological diseases; taking steroids and vitamin D supplements. We performed further laboratory tests: phosphorus, PTH, vitamin D and FGF-23. Serum concentration of intact FGF-23 was assessed by using the kit for ELISA method (Biomedica Medizinprodukte GmbH, Austria). This study was approved by the local scientific ethics committee of National medical university. Ethical standards and rights of patients were not violated. Descriptive statistics and correlation analysis were performed in MS Excel 2016 and SPSS 18.0.

Results: The laboratory tests results revealed that the mean value of phosphorus was 1.77±0.04 mmol/l among all patients with different stages of CKD. There were 29 (33.3%) children with hyperphosphatemia. The most of these patients were ESRD and they needed a renal replacement therapy. No patients with CKD 1-3 stages had high level of phosphorus. The values of PTH increase as CKD progresses. The patients with the first and second stages had absolutely normal PTH value and only 2 patients with the third stage had slightly elevated level. Only 1 out of 17 patients on dialysis (both hemodialysis and peritoneal dialysis) had an acceptable PTH value. By contrast, there was a vitamin D deficiency (a mean value was 22.4±1.64 ng/ml).

The results of identification FGF-23 by the ELISA kit showed that there was also a gradual increase in its level depending on the stage of the disease. Moreover, there were 14 (19.2%) children with elevated FGF-23 concentration though other markers of bone metabolism were normal.

The correlation analysis revealed positively significant associations between FGF-23 and phosphorus (r=0.60, p=0.00), FGF-23 and PTH (r=0.68, p=0.00).

Conclusion: Overall, our investigation proved that FGF-23 is positively correlated to phosphorus and PTH. Furthermore, in most cases, FGF-23 responds much sooner than other markers of mineral and bone metabolism and its increased value might be an early predictor of mineral and bone disorder. However, more research is required in this area.

P0900 **EXPLORE THE MECHANISM OF BEAUVERICIN ON THE OSTEOBLAST CELLS.**

Chien-Lin Lu[1], Kuo-Cheng Lu[2]

[1]Division of Nephrology,, Department of Medicine, Fu Jen Catholic University Hospital, School of Medicine, Fu Jen Catholic University, New Taipei City, Taiwan, Taiwan, R.O.C. and [2]Division of Nephrology,, Division of Nephrology, Department of Medicine, Fu Jen Catholic University Hospital, School of Medicine, Fu Jen Catholic University, New Taipei City, Taiwan, Taiwan, R.O.C.

Background and Aims: In chronic kidney disease (CKD), dysregulation in mineral and bone metabolism cause abnormal bone turnover disease. Over the past years, we focus the dysregulation of osteoblast and osteoclast in CKD. Numerous evidences have shown beauvericin (BEA), a cyclic hexadepsipeptide from Codyceps cicadae, possesses anti-convulsion, anti-arrhythmia, sedation, and anti-tumor activities. The mechanism of the BEA cytotoxicity on osteoblast remains fully unclear. During bone formation and fracture healing, osteoblasts and chondrocytes undergo an orderly developmental progression that ultimately ends in apoptosis. It is still unclear what signal transduction pathways are used of beauvericin in programmed cell death in osteoblasts and its effect on bone turnover.

Method: 7F2 cell line is cultured in Dulbecco's modified eagle medium (DMEM). To induce osteoblast differentiation, a total of 1×10^5 7F2 cells were plated in a 6-cm dish containing 100 μg/mL ascorbic acid, and 10 mM β-glycerol phosphate in the absence or presence of a 0-3μM dose of Beauvericin overnight. The cytotoxic effect of BEA was first determined using the MTT method. Cell lysates were prepared by extracting proteins with lysis buffer, and western blots were developed with a peroxidase-conjugated secondary antibody, and then proteins were visualized by enhanced chemiluminescence (ECL) procedures.

Results: To clarify the rational of inhibitory effect of beauvericin on osteoblast, preosteoblast 7F2 cells were treated with 0-3μM beauvericin overnight. The extent of cell viability after 5-day culture period and observed through microscopy and MTT assay. Figure 1 showed Beauvericin can significantly decrease the number of differentiated osteoblasts in a dose dependent manner. Figure 2 in MTT assay showed the 7F2 osteoblast cells survival rate was significant reduced under beauvericin treatment, especially in high dose of beauvercin. Western blot analysis in Figure 3 showed that under 2 μM Beauvericin dose treatment, the expression of Bax protein was increased and conversely the expression of BCl-2 was decreased.

Conclusion: Taken together, we thought Beauvercin induce 7F2 osteoblast cells death and might be in a relation to apoptosis. However, the further detail mechanism is need further investigated.

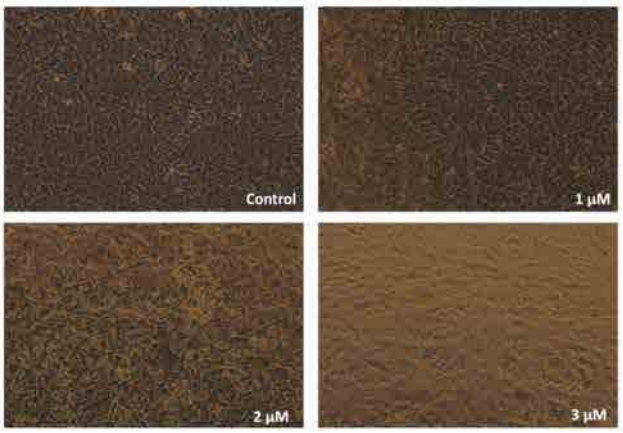


Figure 1. Effect of beauvericin on the cell cytotoxicity in 7F2 osteoblast cells by microscopy. The cell number of osteoblast cell was significant decrease as the increase of beauvericin dose.

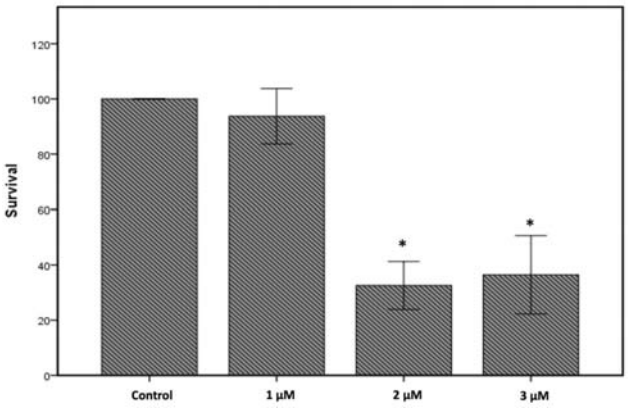


Figure 2. Cell survival rate of 7F2 osteoblast cells under beauvercin treatment overnight. The survival of differentiated osteoblast was significantly decreased in dose dependent manner, esp. 2-3μM beauvericin. Data are mean number ± 95%CI. (* $p<0.05$ versus control group, n=3).

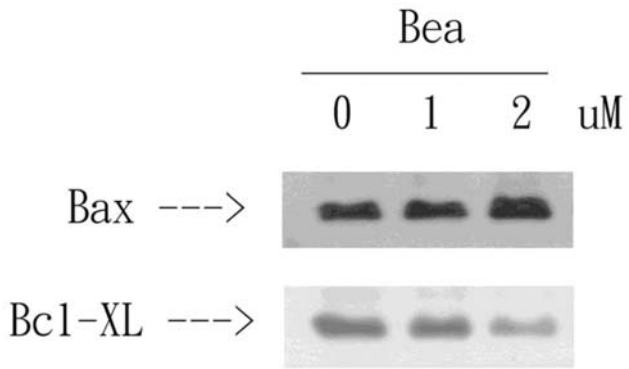


Figure 3. Apoptosis related protein expression in 7F2 osteoblast cells under beauvercin treatment. (Upper) The expression of Bax protein in beauvercin-treated osteoblast is increased in a dose- dependent manner. (Lower) Conversely, the expression of BCl-2 protein in beauvercin-treated osteoblast is decreased in a dose-dependent manner.

P0901

REAL-WORLD ASSESSMENT: CLINICAL EFFECTIVENESS AND SAFETY OF VITAMIN D THERAPIES IN ND-CKD PATIENTS

Michael J Germain[1], Subir K Paul[2], Varshasb Broumand[3], George Fadda[4], Andy Nguyen[5], November McGarvey[5], Matthew Gitlin[5], Akhtar Ashfaq[6]

[1]Renal and Transplant Associates of New England, PC, Springfield, United States of America, [2]Shoals Kidney & Hypertension Center, Florence, United States of America, [3]South Texas Renal Care Group, San Antonio, United States of America, [4]California Institute of Renal Research, San Diego, United States of America, [5]BluePath Solutions, Los Angeles, United States of America and [6]Opko Health Inc, Miami, United States of America

Background and Aims: Extended-release calcifediol (ERC), active vitamin D analogs (VDA), and nutritional vitamin D (NVD) are the predominant vitamin D therapies (VDTs) commonly used for treatment (Tx) of secondary hyperparathyroidism (SHPT) in adults with stage 3 or 4 non-dialysis chronic kidney disease (ND-CKD) and vitamin D insufficiency (VDI). Clinical trials have demonstrated varying efficacy on serum total 25-hydroxyvitamin D (25D) and intact parathyroid hormone (iPTH) across VDTs. This study aimed to descriptively assess the real-world experience of various VDTs in increasing 25D, reducing iPTH, and modifying serum calcium (Ca).

Method: Medical records of the first 376 adult patients with stage 3 or 4 CKD and a history of SHPT and VDI who met study criteria from 18 geographically representative United States nephrology clinics were reviewed from 1 year before through 1 year after initiation of VDT. Key study variables included patient demographics, medication usage, and laboratory results. The study population had a mean age of 69.5 years with gender and racial distributions representative of the US ND-CKD population. Patients were stratified into cohorts based on their index therapy at index date: ERC (n=174), VDA (n=55) and NVD (n=147).

Results: Patients treated with NVD were predominantly CKD Stage 3 (69.4%), while CKD Stage 4 were the majority of those treated with ERC (53.4%) and VDA (61.8%). The ERC Tx'ed subjects demonstrated an increase in 25D by 23.7 ± 1.6 ng/mL ($p<0.001$) and a decrease iPTH by 35 ± 6.2 pg/mL ($p<0.001$) without statistically significant impact on serum calcium (Ca) and phosphorus (P) levels. The VDA Tx'ed group demonstrated an increase in 25D by 5.5 ± 1.3 ng/mL ($p<0.001$) without statistically significant impact on iPTH and serum phosphorus levels. Additionally, serum Ca increased by 0.2 ± 0.1 pg/mL ($p<0.001$) among VDA recipients. The NVD Tx'ed group demonstrated an increase in 25D by 9.7 ± 1.6 ng/mL ($p<0.001$) without statistically significant impact on iPTH and serum Ca and P levels (Table 1).

Conclusion: Clinical effectiveness and safety varied across VDTs. ERC was the only VDT which significantly reduced mean iPTH in the real world setting despite highest mean levels at baseline among the three cohorts. Additionally, subjects treated with ERC demonstrated the largest mean increase in 25D and ERC was the only VDT which raised mean 25D to the normal range (>30 ng/mL). Patients treated with ERC and NVD saw no statistically significant impact on serum Ca and P levels; however, those treated with VDAs saw a small, but statistically significant increase in serum Ca levels.

Table 1

	ERC (n = 174)				VDA (n = 55)				NVD (n = 147)			
Lab Value	Pre	Post	Δ	$Mean_{FU}$	Pre	Post	Δ	$Mean_{FU}$	Pre	Post	Δ	$Mean_{FU}$
25D, ng/mL*	20.3	44.0	23.7[a]	24.6	23.5	29.0	5.5[a]	21.3	18.8	28.5	9.7[a]	21.1
Mean (SE)	(0.7)	(1.7)	(1.6)		(1.0)	(1.2)	(1.3)		(0.6)	(1.6)	(1.5)	
iPTH, pg/mL*	181.4	146.8	-34.6[a]	23.4	156.9	149.9	-7.0	21.6	134.8	144.4	9.6	20.7
Mean (SE)	(7.4)	(7.2)	(6.6)		(9.7)	(11.1)	(9.8)		(6.8)	(9.5)	(6.0)	
Ca, mg/dL	9.9	9.7	-0.2	-	9.1	9.3	0.2[a]	-	9.4	9.7	0.3	-
Mean (SE)	(0.4)	(0.3)	(0.3)		(0.1)	(0.1)	(0.1)		(0.1)	(0.3)	(0.3)	
P, mg/dL	4.0	4.1	0.1	-	3.8	3.9	0.1	-	3.7	3.8	0.1	-
Mean (SE)	(0.2)	(0.2)	(0.1)		(0.2)	(0.2)	(0.1)		(0.1)	(0.1)	(0.1)	

FU = follow-up in weeks

*Sites had varying truncation points for 25D levels and differing reference ranges for iPTH

[a]$P<0.001$

P0902 DAILY TERIPARATIDE TREATMENT AND PHARMACOKINETICS IN HEMODIALYSIS PATIENTS WITH LOW BONE MASS

Rikako Hiramatsu[1]

[1]*Toranomon Hospital, Nephrology Centre, Minato City, Japan*

Background and Aims: Daily 20μg teriparatide (PTH1-34) is an osteoanabolic agent approved for use treating osteoporosis. However, there are few reports about concerning use of this agent in hemodialysis patients.

Method: We conducted an observational study, single centre study on 5 patients with low bone mineral density (BMD) and low iPTH levels defied as iPTH below 60 pg/mL, who were treated with recombinant human PTH1-34; teriparatide 20 μg 3 times per week between January 2012 and January 2015. All patients were 20 years of age or older, had undergone regular hemodialysis treatment and were without skeletal malignancies and bone metastasis. Low BMD in this study was defined either as BMD T-score -2.5 at the lumbar spine (LS) or /and femoral neck (FN) and distal one –third radius (RS) analyzed by dual-energy X-ray absorptiometry (DXA), or BMD T-score of -2.5 to -1.0 with history of fragility fractures. We analyzed the biochemical data including bone metabolic makers (intact amino-terminal propeptide of type I collagen (iP1NP), bone alkaline phosphatase (BAP), and tartrate-resistant acid phosphatase-5b (TRACP-5b) at baseline, and after 3, 6, and 12 months of teriparatide treatment. BMD at LS and FN were evaluated at 6months of treatment.

Results: Data from five patients (mean age: 69.2±7.4years; mean hemodialysis time: 23.2±6.2years) were reviewed. Laboratory data at baseline were iPTH: 34.2±24.2 pg/mL, BAP: 13.0±4.9 μg/L, iP1NP: 45.3±14.3 ng/mL, TRACP-5b: 350±201 mU/dL, corrected Ca (cCa): 9.7±0.3 mg/dL, and P:4.1±0.7 mg/dL. Baseline BMD T-score at LS and FN were -2.8±1.7 and -3.0±0.6, respectively. During a 12 month- teriparatide treatment, mean cCa levels significantly decreased from 9.7±0.3 to 9.1±0.2 mg/dL at 3 months ($P < 0.05$) and returned to 9.5±0.4 mg/dL at 12 months. As for bone metabolic markers, BAP and iP1NP significantly increased from baseline by 31.3±12.9 ($P < 0.05$) and 47.4±14.5% ($P < 0.05$) at 6 months of teriparatide treatment, while TRACP-5b significantly decreased by 10.5±2.5% at 3 months, which did not reach a statistical significance. BMD changes from baseline at LS and FN were 2.1±2.5% and 1.2±1.5% at 6 months of treatment with a significant change at LS.

Pharmacokinetics of Teriparatide The time-course of changes in plasma teriparatide acetate concentration was evaluated in one patient who had undergone parathyroidectomy 20 years before enrollment in this study and her serum endogenous iPTH level was undetectable at baseline. After teriparatide injection, serum teriparatide acetate levels peaked at 30 minutes at 157.2 pg/mL, and then rapidly decreased to undetectable levels at 240 minutes.

Conclusion: We report that teriparatide improved LS and FN BMD in hemodialysis patients with low iPTH. Pharmacokinetics showed this agent might not accumulate in dialysis patients and can be used safely. Adequate Ca supplementation might be needed to adjust serum Ca levels.

P0903 **EFFECTS OF OSTEOPOROSIS MEDICATIONS ON BONE FRACTURE IN PATIENTS WITH CHRONIC KIDNEY DISEASE**

Chih-Chin Kao[1], Pei-Chen Wu[2], Ming-Tsang Chuang[3], Mai-Szu Wu[1], Tzu-Hao Chang[3]

[1]Taipei Medical University, Internal medicine, Taipei, Taiwan, R.O.C., [2]Mackay Memorial Hospital, Taiwan, R.O.C. and [3]Taipei Medical University, Taiwan, R.O.C.

Background and Aims: To evaluate the association of osteoporosis medications and outcomes of patients at risk of CKD.

Method: We included patients with stage 3-5 CKD from three Taipei Medical University-affiliated hospitals between January 1, 2011 and August 31, 2016. Patients were divided into two groups based on whether they received osteoporosis medications (bisphosphonates, raloxifene, teriparatide, or denosumab) and then matched at a 1:1 ratio by using propensity scores. The outcomes of interest were bone fractures, cardiovascular (CV) events, and all-cause mortality. Cox proportional hazard regression models were applied to identify the risk factors.

Results: A total of 39128 patients with CKD were included. After propensity score matching, 763 patients were in the study and control groups, respectively. The mean age of patients was 71.9 ± 12.5 years, and 34.4% of patients were men. After a median follow-up of 2.9 years, the incidence rates of bone fracture, CV events, and all-cause mortality were 10.4%, 7.5%, and 7.5%, respectively. Multivariate analysis results indicated that osteoporosis treatment was note associated with reduced risks of bone fracture (HR 0.85; 95% CI 0.43–1.68; $P = 0.65$), CV events (HR 0.82; 95% CI 0.56–1.20; $P = 0.30$), and all-cause mortality (HR 0.74; 95% CI 0.51–1.08; $P = 0.12$). Subgroup analysis demonstrated only patients with CKD stage 3 who received osteoporosis medications associated with better survival.

Conclusion: Osteoporosis medications did not reduce bone fractures, CV events or mortality in patients with CKD. Improved overall survival was observed in patients with CKD stage 3.

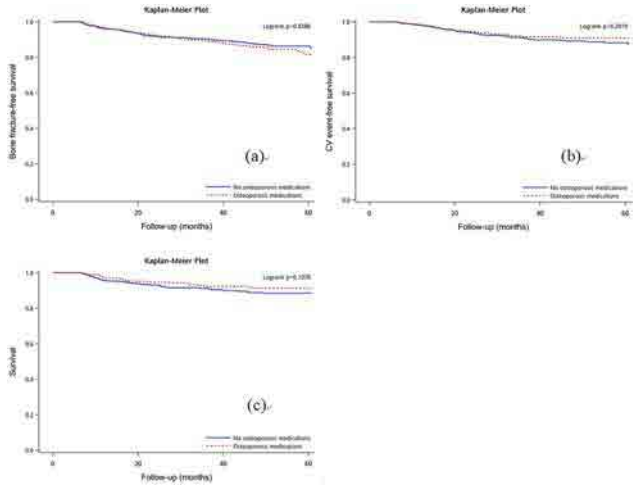


Figure. Risk of adverse outcomes according to whether patients received osteoporosis medication (Kaplan–Meier curve): (a) bone fracture (b) CV events, and (c) mortality.

P0904

EFFECT OF EMPAGLIFLOZIN ON SERUM MARKERS OF OSTEOCYTE AND OSTEOBLAST FUNCTION AND ALBUMINURIA IN DIABETIC AND NON-DIABETIC PATIENTS WITH CHRONIC KIDNEY DISEASE

Anna Masajtis-Zagajewska[1], Katarzyna Pä™czek[1], Tomasz Holub[1], Michal Nowicki[1]

[1]*Medical University of Lodz, Department of Nephrology, Hypertension and Kidney Transplantation, Lodz, Poland*

Background and Aims: Sodium-glucose co-transporter 2 (SGLT2) inhibitors are new class of oral antidiabetic drugs that show potent cardio- and nephroprotective actions. Despite having a favorable safety profile the treatment with SGLT2 inhibitors has been associated with several side-effects including increased risk of fractures. Although the pathomechanism of this complication has not been elucidated these drugs may inhibit tubular reabsorption of phosphate which may stimulate a secretion of fibroblast growth factor 23 (FGF23).

The study was designed to assess the effect of SGLT2 inhibitor on markers of calcium-phosphate metabolism, bone turnover and early glomerular injury in diabetic and non-diabetic patients with stage 3 chronic kidney disease (CKD).

Method: 41 patients with chronic kidney disease including 23 without diabetes (13 M, 11F, age 52.9±0.7 years, estimated glomerular filtration rate (eGFR) 38.6±10.8 ml/min/1.73 m^2) and 18 with type 2 diabetes (12 M, 6F, age 58.8±1.4 years, eGFR 38.8±7.7 ml/min/1.73 m^2) were recruited. Main inclusion criteria were CKD stage 3 and urine albumin secretion >100 mg/g creatinine. All subjects received oral empagliflozin 10 mg once daily for 7 days.

Serum calcium, phosphorus, parathormone (PTH), calcitriol, bone alkaline phosphatase (BAP), FGF23 and urine calcium, phosphate and albumin were measured at baseline and after 7 days of empagliflozin treatment.

Results: Plasma calcitriol, serum and urine calcium, phosphorus and BAP did not change significantly during the administration of empagliflozin. Urine phosphate/creatinine ratio was similar in both subgroups at baseline and did not change during empagliflozin administration. Plasma PTH was higher in non-diabetics than in diabetics both at baseline and after empagliflozin. The increase of PTH after empagliflozin tended to be higher in diabetic patients (p=0.07). There was only a trend towards an increase of serum FGF23 in both non-diabetic and diabetic subgroup (by 4.2±0.2 vs. 9.3±1.1 pg/mL, ns). BAP was significantly higher at baseline in diabetic patients but did not significantly change after empagliflozin in the subgroups.

Albumin/creatinine ratio decrease after empagliflozin administration was significant only in non-diabetic patients (-62±17 vs. -2±8 mg/g in diabetic patients, p=0.03 for difference).

Conclusion: Our study showed no effect of short-time administration of empagliflozin on calcium-phosphate and bone metabolism markers in patients with both diabetic and non-diabetic CKD. Empagliflozin decreased albuminuria significantly only in non-diabetic CKD that may suggest a potentially greater nephroprotective effect of this SGLT2 inhibitor in non-diabetic than in diabetic nephropathy.

P0905 **INFLUENCE OF TUMOR NECROSIS FACTOR ON MINERAL BONE DISEASE IN ESRD PATIENTS**

Jelena Tosic Dragovic[1], Nada Dimkovic[1,2], Jovan Popovic[1], Petar Djuric[1], Radomir Naumovic[1,2]

[1]University Hospital Center Zvezdara, Nephrology, Belgrade, Serbia and [2]Faculty of Medicine, Belgrade University, Belgrade, Serbia

Background and Aims: Serum levels of parathyreoid hormone is the main cause of mineral disorders in patients on chronic hemodialysis, and it well known that this hormone acts as an uremic toxine and contributes to oxidative stress and overall mortality rate. However, there are many observations which imply that the protean manifestations of renal bone disease cannot be explained simply by abnormalities of PTH or vitamin D metabolites. For example, levels of PTH correlate relatively poorly with various parameters of bone histology. It has been shown that uremia leads to cytokijne imbalance with overbalance of proinflammatory citokines such as TNF. Also, studies showed that calcimimetic therapy decreases not only PTH levels, but also levels of TNF. The aim was to analyse tumor necrosis factor (TNF) gene polymorphisms in group of hemodialysis patients and to correlate the findings with presence of secondary hyperparathyroidism.

Method: This cross sectional study included 202 patients on regular hemodialysis for more than six months in University Medical Centar Zvezdara. Venous blood for genotyping and for PTH analysis was collected on midweek dialysis session from each patient. Genetic analysis was performed by using polymerase chain reaction. Patients are diveded in two groups regarding the level of PTH, so that first group had normal PTH levels or mild SHPT, while patients in second group had sever SHPT. We analysed influence of genetic polymorphism for TNF on apperance of SHPT.

Results: The results have shown 3 fold lower risk for developing SHPT in GG homozygots for TNF gene with statistical significance (p=0,01)- Table 1.

Conclusion: Parathyreoid gland hyperfunction is multifactorial disorder and there are emerging evidence that cytokines as endogenous modulators have an important impact on its pathogenesis.

TNF	OR	p	95%CI
GG	0.721	0.403	0.335-1.552
GG+AA	1	0.01	——

P0906

SALUBRINAL IMPROVES OSTEOCLAST DIFFERENTIATION AND VASCULAR CALCIFICATION IN UREMIC MILLENNIUM THROUGH INHIBITION OF THE ENDOPLASMIC RETICULUM (ER) STRESS CONDITION

Cai-Mei Zheng[1,2,3], Hui-Wen Chiu[1,3], Kuo-Cheng Lu[4], Chien-Lin Lu[4], Mai-Szu Wu[2,3], Yung-Ho Hsu[1,2,3]

[1]Graduate Institute of Clinical Medicine, College of Medicine, Taipei Medical University, Taipei, , [2]School of Medicine, College of Medicine, Taipei Medical University, Division of Nephrology, Department of Internal Medicine, Taipei, Taiwan, R.O.C., [3]Shuang-Ho Hospital, Taipei Medical University, Division of Nephrology, Department of Internal Medicine, NEW TAIPEI CITY, and [4]Fu Jen Catholic University Hospital, School of Medicine, Fu Jen Catholic University, Division of Nephrology, Department of Internal Medicine, NEW TAIPEI CITY, Taiwan, R.O.C.

Background and Aims: Chronic kidney disease (CKD) is a globally increasing health problem especially in aged era. CKD-mineral and bone disorder (CKD-MBD) becomes a principal consequence of CKD, which includes mineral abnormalities, vascular calcifications (VC) and renal osteodystrophy (ROD), and patients eventually present with fractures and cardiovascular disease (CVD) (Figure 1). Thus, bone loss in CKD patients relates closely with cardiovascular calcification. The endoplasmic reticulum (ER) stress is triggered by many clinical conditions unique to CKD, including uremic toxins, chronic inflammation, metabolic acidosis, proteinuria, malnutrition, etc. In our study, we hope to evaluate the ER stress inhibitor, salubrinal as targeted therapy for CKD related bone loss and vascular calcification.

Methods: **Isolation of primary osteoclasts from long bone primary cell culture:**

Femoral and tibia bone from 8-week-old Sprague–Dawley rats were removed and used as primary osteoclast cultures. Osteoclast precursor cells were seeded in 96-well plates (2.0 x 104 cells/well) and cultured for 6 days in alpha minimum essential medium (α-MEM) supplemented with 10% FBS, 50 ng/ml M-CSF and 50 ng/ml RANKL in the absence or presence of uremic toxins. The whole process of osteoclast development in cell cultures was divided into first M-CSF–dependent growth of osteoclast progenitor's phase and latter phase is RANKL induced terminal differentiation phase. The experiment is performed with the approval of the Laboratory Animal Center of the Taipei Medical University in Taipei, Taiwan.

Primary Human Aorta Vascular Smooth Muscle Cell Culture:

Primary human aorta vascular smooth muscle cells (VSMC) were isolated by ScienCell Research Laboratories, Inc. (Carlsbad, CA) and purchased through Innoprot (Derio, Spain).

We examined the role of uremic toxin on ER stress and autophagy using osteoclasts and vascular smooth muscle cells cultured with uremic toxins including PTH, p-cresyl-sulfate (pCS) and p-cresylglucuronide (pCG), indoxyl sulfate, asymmetric dimethylarginine (ADMA), and homocysteine. The cells are treated with salubrinal with or without toxins and see how ER stress and autophagy effects on survival and differentiation of osteoclasts and VSMC cells.

Results: We found that ER stress and autophagy related mRNA were increased in osteoclasts using GEO database analysis, revealed that ER stress and autophagy play an important role in osteoclast differentiation. Further, we revealed that uremic toxins increased the autophagy and ER stress status and increased the osteoclasts differentiation. Treatment of the osteoclasts under uremic millennium with salubrinal, an ER stress inhibitor, inhibited the ER stress and osteoclast differentiation. Uremic toxins also increased the ER stress in human vascular smooth muscle cells (VSMCs). After treated with salubrinal, the calcification and proliferation improved in these cells.

Conclusion: ER stress increases osteoclast differentiation and vascular calcification in uremic millennium, and salubrinal improves these conditions through inhibition of ER stress. Thus, salubrinal probably might be used as targeted therapy for vascular calcification and bone loss in CKD patients.

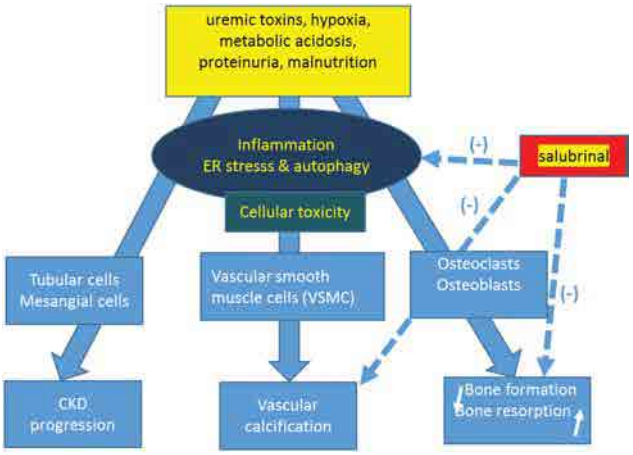


Figure: The proposed relationships between ER stress in CKD, vascular, bone disorders and possible protective effects of salubrinal in CKD-MBD.

P0907

STRIKING NOVEL MULTI-MISMUTATIONS ON GNAS1,FGF23,FGFR3 GENES IN CKD WITH SECONDARY HYPERPARATHYROIDISM.(SH).SAGLIKER SYNDROME(SS).SS IS A COMBINATION-COMPULSION OF BONE DYSPLASIAS-HEREDITARY OSTEODYSTROPHİES AND SH AND CKD.

Yahya Sagliker[1], Osman Demirhan[2], Hasan Sabit Sagliker[2], Piril Sagliker Ozkaynak[2], Nuray Paylar[2], Cemal Sagliker[2], Idris Emir[2], Isıl Ozkaynak[2]

[1] and [2]Sagliker Hypertension and Nephrology Unit, Adana, Turkey

Background and Aims: Sagliker Syndrome seems to be related to CKD and the consequent SH.SS starts and develops particularly before puberty while CKD reaches stage III level with overt SH. Since it occurs in some patients, it is plausible to think SS is genetically predisposed.GNAS1, FGF23 and FGFR3 genes' mismutations on the genesis of SS is unclear, and no data are available.

Method: We conducted clinical, radiological, laboratory studies and screening for mutations in GNAS1 gene in 23 patients, FGF23 and FGFR3 genes in 17 patients.DNA isolations were performed from blood samples and mutations regions were amplified by Polymerase Chain Reaction (PCR).

Results: In 73.9% (17/23) patients, 17 different genetic abnormalities in GNAS1 were detected.Seven (58.3%) of the 12 nucleotide alterations comprised novel missense mutations in different manners. There were also 6 heterozygous tranversion polymorphism in exons.Six of them were introngenic mismutations found in exons (introns; 65626, 70387 and 70817).We found 10 different mismutations in FGF23 gene. 8 were novel mismutations and are defined first in our study. 3 of them were in intronic region near exon 2.In FGFR3 gene we also found 22 different mutations. 16 were novel mismutations defined first in our study.8 of them were in intronic region near exon 11,last 2 were in non-coding exonic region of exon 18. Twelve mismutations were found in exons, 8 were found in introns and 2 were found in non-coding exonic regions. One was in the exon-exon junction region between exon 11 and 12 Therefore this mutation might be preventing splicing of this intron.

Conclusion: There are plenty of mutations on those three genes in Sagliker Syndrome and are consistent with an insufficiency of those three genes playing a role in the clinical phenotype of loss of function mutations and with functional alleles having predominant roles in preventing the hormonal resistance.Since the incidence of

CKD late stage III is around 8% in the world but the incidence of Sagliker Syndrome is around 0.5% in CKD patients, these gene mismutations might be responsible for bone Displasias– Hereditary Osteodystrophies such as Mc Cune- Albright syndrome, achondroplasias etc.., although our patients were not resembling any of them but they could be in between and Sagliker Syndrome might be a combination-compulsion of Bone displasias-Hereditary Osteodystrophies and SH and CKD.

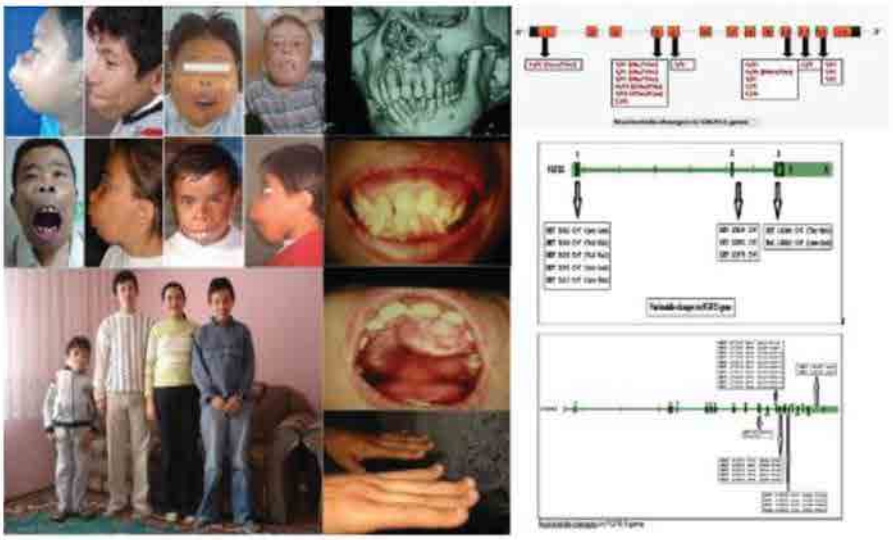


Figure:

P0908 FGF-23, MBD AND INFLAMMATION IN CKD

Mariana Chaikovska[1], Liliya Martynyuk[1], Butvyn Sergii[2]

[1]*Ternopil State Medical University, Internal Medicine #3, Ternopil, Ukraine and* [2]*Educational and Scientific Institute of Postgraduate Education of Ternopil State Medical University, Therapy And Family Medicine, Ternopil, Ukraine*

Background and Aims: Systemic inflammation, as well as Mineral and Bone Disease, are seen to be inherent complications of CKD, tightly related to cardio-vascular disease, protein-energy wasting and general mortality. It remains an actual problem to study relation between systemic inflammation and CKD-MBD. The aim of the study was to evaluate serum concentrations of c-terminal FGF-23 as an early marker of CKD MBD, Il-1 β, Il-6, Il-8 as inflammatory markers, and to establish relationships between FGF-23 and IL-1 β, Il-6, Il-8.

Method: The study involved 106 patients with CKD stages from 1 to 4, 47 women (44%) and 59 men (56%) aged from 35 to 72, mean (49.6± 13.9) years. The C-terminal FGF-23 fragment was determined using a set of reagents for the enzyme immunoassay «Biomedica». Concentration of IL-1β, IL-6 and IL-8 was determined using an assay «Vector BEST». The glomerular filtration rate (GFR) was calculated using the CKD EPI formula (KDIGO 2012).

Results: A progressive growth in FGF-23 levels was observed simultaneously with GFR decrease in patients with CKD. IL-1 concentration increased from CKD stage 1 ((12.64±4.30) pg/ml) to 4 ((32.06±7.86) pg/ml) ($p < 0.05$) accordingly GFR fall, as well as the level of IL-6 ((7.25±2.14) pg/ml to (46.27±10,06)pg/ml) and Il-8 ((9.39±1.62) pg/ml to (33.00±9.17)pg/ml). The existence of a strong direct association ($r = 0.84$, $p < 0.05$) between the level of Il-6 and FGF-23 in CKD stages 1-4 was established. IL-1 and Il-8 were found to have a medium strength assotiation ($r=0.45$, $p < 0.05$ and $r=0.57$, $p < 0.05$, accordingly) with FGF-23 concentration in patients with CKD stages 2-4.

Conclusion: The increase in the concentration of inflammatory factors along with progression of chronic renal failure was revealed. The existence of a strong link between the level of IL-6 and the C-terminal fragment of FGF-23 in CKD was established. Finding out the issue of the primary stimulation factor of FGF-23 production in CKD requires further research.

P0909 **HYPOCALCAEMIA MANAGEMENT POST PARATHYROIDECTOMY IN RENAL PATIENTS - A REVIEW OF PRACTICE.**

Tricia Tay[1], Rajkumar Chinnadurai[2], Tina Chrysochou[2], Helen Doran[3], Smeeta Sinha[2]

[1]University of Manchester, Manchester Medical School, Manchester, United Kingdom, [2]Salford Royal NHS Foundation Trust, Renal Department, Manchester, United Kingdom and [3]Salford Royal NHS Foundation Trust, Department of Endocrine Surgery, Manchester, United Kingdom

Background and aims: Hypocalcaemia is a common post-parathyroidectomy complication in renal patients with secondary hyperparathyroidism. This is due to reduced parathormone (PTH) mediated calcium absorption in the kidneys and increased influx of calcium to bones. Our initial study in January 2015 showed preloading patients with one alfacalcidol 2 microgram once a day for 5 days preoperatively was ineffective in reducing hypocalcaemia related complications. We re-investigated the outcomes in patients following a change in practice to use one alfacalcidol 5 microgram once a day for 5 days preoperatively.

Method: All patients with pre-existing chronic kidney disease (CKD) who underwent parathyroidectomy by a single surgeon in our centre between March 2016 and October 2017 were included (12 patients). The outcomes (length of hospital stay and hypocalcaemia requiring IV calcium replacements) were compared with a previous study on patients operated on by the same surgeon between April 2008 and September 2014 (24 patients). Statistical analysis was conducted using Microsoft excel and SPSS version-22.

Results: Twelve patients were included in this study; 5 were females. Mean age at surgery was 54 (range 45-61) years. Eight patients were on long-term haemodialysis, 3 had a functioning renal transplant and 1 had CKD stage 5. Eight patients had been receiving cinacalcet for more than one month preoperatively.

Mean length of stay (LoS) was 5.3 days (range 3-10), half (n=6) were discharged four days post-op. Ten had a total parathyroidectomy, of which half (n=5) were discharged after post-op day 4. Four patients were not preloaded with 5mcg as per protocol; reasons for non-adherence to the protocol included regular prescription of alfacalcidol and physician discretion to utilise a lower dose. Patients with lower pre-op corrected calcium levels (2.4-2.6 mg/dL) stayed for a mean of 6.74 days after surgery. This was a longer LoS compared to other calcium ranges. No hypercalcemia related complications were recorded. The need for post-operative intravenous calcium use decreased from 10/24 to 2/12. Despite more patients having total parathyroidectomy and being on dialysis, a smaller proportion required IV calcium in the post-operative phase, although this was not statistically significant due to the small sample size (p=0.26).

Conclusion: Our study highlights that the current practice of preloading one alphacalcidol 5 mcg once a day for 5 days preoperatively in renal patients undergoing parathyroidectomy appears to be a safe and effective approach. Ongoing monitoring and further studies on a larger cohort of patients is needed to strengthen these observations.

Table

Variable	InitialN=24	Re-auditN=12	p-Value
Gender, male	18 (72%)	7 (58%)	0.46
Age, years	54 (47-60)	54 (45-61)	0.96
Modality in groups, HD	9 (36%)	8 (66%)	0.16
Total parathyroidectomy	13 (52%)	10 (83%)	0.08
Patients needing IV calcium	10 (40%)	2 (17%)	0.26

P0910

CLINICAL-LABORATORY AND CYTOMORPHOLOGICAL CHARACTERISTICS OF HYPERPARATHYROIDISM IN PATIENTS WITH CRONIC KIDNEY DISEASE

Maria Ivanova[1], Olga Vetchinnikova[2], Natalia Zakharova[3]

[1]M.F. Vladimirsky Moscow Regional Research and Clinical Institute, Department of Endocrinology Faculty of Postgraduate Education, Moscow, Russia, [2]M.F. Vladimirsky Moscow Regional Research and Clinical Institute, Department of Transplantology Nephrology and Artificial Organs Faculty of Postgraduate Education, Moscow, Russia and [3]Federation Medical and Biology Agency, Clinical and diagnostic laboratory, Russia

Background and Aims: Secondary hyperparathyroidism (HPT) is a serious complication of chronic kidney disease (CKD), which decrease the medical and social rehabilitation of patients, increases cardiovascular morbidity and mortality. The aim of the study is analysis the clinical and laboratory manifestations of secondary HPT and cytomorphological signs of parathyroid glands (PG) tissue in patients with CKD.

Method: 51 patients (age 24-66 years) with CKD G5D (on hemodialysis – 30 patients and peritoneal dialysis – 21 patients) and HPT were examined. Clinical and laboratory examination included determination of laboratory parameters of mineral and bone metabolism, an ultrasound study of the PG, a fine needle aspiration biopsy of the visualized lesions in the projection of the PG, and light microscopy of the material obtained (x400). The method of logical-semantic analysis (program "Consilium") is used.

Results: All patients had severe HPT with high turnover bone disease: bone pain and deformity, increase of serum PTH to 2200±817 pg/ml, calcium and phosphorus of blood, respectively 2.4±0.2 and 2.2±0.4 mmol/l, alkaline phosphatase activity 489±205 u/l (norm 30-117), a decrease in bone mineral density according to dual energy X-ray absorptiometry in the distal forearm – 100% patients, proximal femur and lumbar spine – 50% patient. An ultrasound procedure visualized from two to four enlarged PG with a diameter of more than 1 cm and a heterogeneous ultrasound structure. A large number of epithelial elements were determined in the puncture material of the PG tissue, multicellular clusters of major dark parathyrocytes in combination with groups of major light parathyrocytes, the presence of pronounced intercellular contacts and the absence of macrophages and fat cells (fig).

Conclusion: Severe HPT in patients with CKD is characterized by an increase in PG by more than 1 cm with a heterogeneous ultrasound structure and pronounced proliferative activity in the parenchyma of glands tissue.

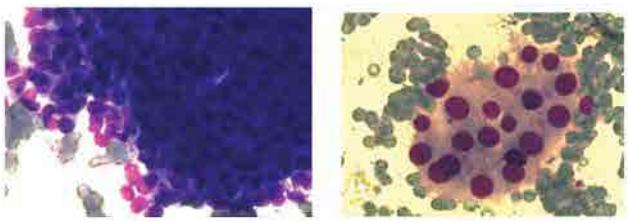


Figure: Cytogram fragment of PG in patient C. with CKD and severe secondary HPT (azur-eosin stain x400): a. multi-layer cluster of major dark parathyrocytes; b. accumulation of light parathyrocytes.

P0911 **TO STUDY CHANGES IN BONE MINERAL DENSITY POST RENAL TRANSPLANTATION**

PRASHANT MALVIYA[1], Soma Sekhar Mudigonda[1]

[1]*Apollo Hospital Jublihills, NEPHROLOGY, Hyderabad, India*

Background and Aims: Chronic kidney disease patients get affected by mineral bone disease in view of changes in various biochemical parameters. After transplantation there are changes in these parameters with additional effect of immunosuppression on bone mineral density. My study was to observe changes in biochemical parameters like calcium, phosphorus, vitamin D, parathyroid hormone, alkaline phosphatase and compare bone mineral density with the help of DEXA scan post renal transplantation after 3 and 6 months. It was a prospective observational comparative study.

Aim of my study is to evaluate changes in Bone Mineral Density post renal transplantation

Method: Study was conducted at Apollo Tertiary care Hospital, Hyderabad which caters to rural as well as urban population in southern parts of India. This study was carried out form June 2017 to Dec 2018. Total 40 patients were included in study and they were followed up for the period of 6 months and underwent sets of investigations to assess their bone mineral density. Biochemical variables consist of calcium, phosphorus, alkaline phosphatase, vitamin D level and iPTH. Biochemical variables were classified into hypo, normal or hyper based on their lab values. iPTH values were considered high if value was nine times the upper limit of normal or low if value was less than two times the upper limit of normal. DEXA scan results were classified into normal, osteopenia and osteoporosis based on their t value.

Results: Study showed that patients who got admitted for transplant belong to age group of 31 – 50 yrs (39.8 +/- 12.8 yrs) predominantly male patients 30 (75%). In 25% patients (10) we were unable to find out native kidney disease shown as CKD (u). Other common causes were DM, ADPKD, CGN or CIN. Most patients were undergoing dialysis for more than 1 year, 47.5% (19) had significant loss of BMD as compared to patients whose dialysis was <1 year (p value 0.498 and 0.05). Hypocalcemia was predominantly seen in pretransplant period 26 (65%) but as the patient followed up level improved with few developing hypercalcemia 4 (10%) after 6 months. Hyperphosphotemia was seen in 19 (47.5%) patients before transplant while hypophosphatemia in 4 (10%) patients 6 months post transplantation, others had normal phosphorus level. Patients were on calcium and vitamin D supplements developed sufficiency to high level of vitamin D 33 (82.5%) patients 6 months post renal transplant. In iPTH around 12 (30%) of patients were having iPTH >150 pg/dl after 6 months of transplant. Majority presented for transplant detected to have osteoporosis and osteopenia at lumbar spine 31 (77.5%) and hip joint 27 (67.5%) with fracture risk 4 to 8 times of normal population. There was 8% and 10% increase in number of patients having osteoporosis at lumbar spine and hip joint respectively post-transplant. There was loss of 5.5% (mean t score at 0 month -1.98 and at 6 month -2.09) BMD at lumbar spine and 1.7% (mean t score at 0 month -1.83 and at 6 month -1.9) BMD at hip joint. Net loss of BMD was 3.6% over the period of 6 months. This accounts to increased risk of fractures post renal transplant. Biochemical variable in the form of iPTH has shown to have significant association with DEXA scan at lumbar spine (p value 0.01) and hip joint (p value 0.00) before and after transplant (p value of 0.01 and 0.00) though there was fall in iPTH level.

Conclusion: Pretransplant bone disease remains predominant cause of post-transplant bone disease with significant association with iPTH. Hypophosphatemia, hypercalcemia and high Vitamin D level are common findings in post-transplant period upto 6 months. Early use of DEXA scan along with follow up of biochemical variables can help to prognosticate and decide treatment strategies to reduce fracture risk in renal transplant recipients.

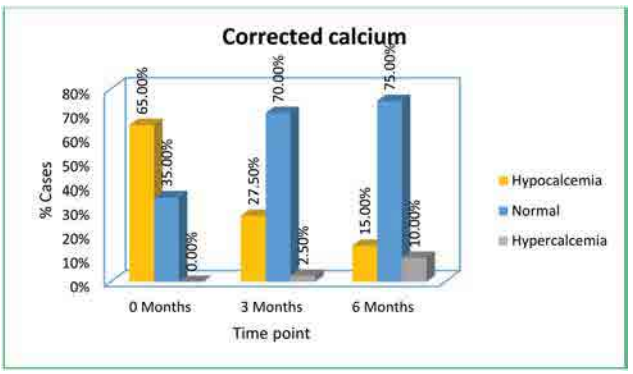


Figure:

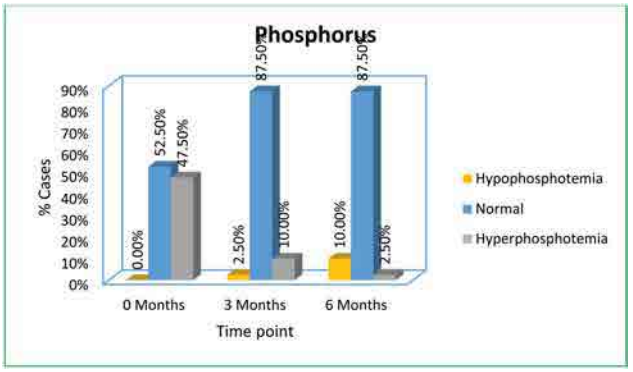


Fig 1: Calcium levels

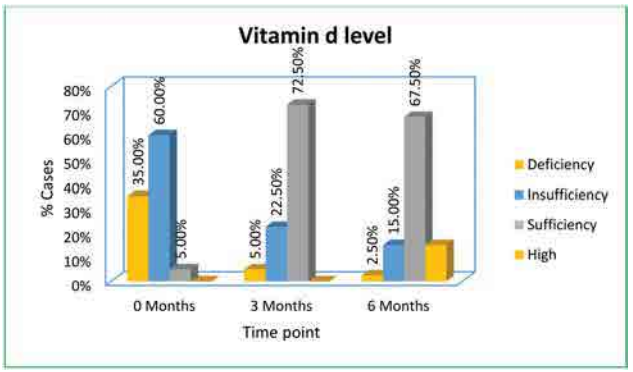


Fig 2: Phosphorus levels

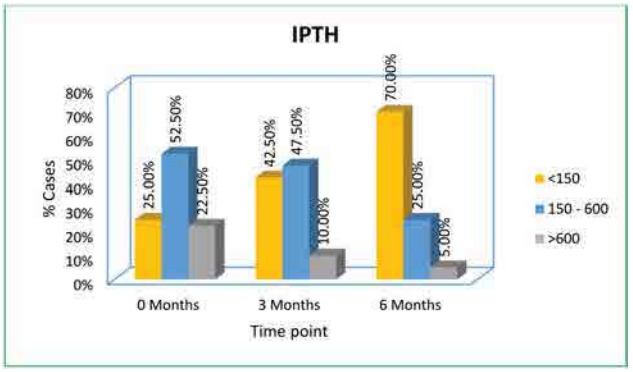


Fig 3: Vitamin D levels

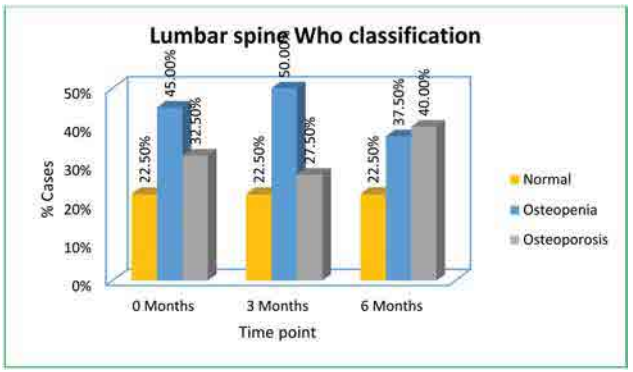


Fig 5: Lumbar spine BMD

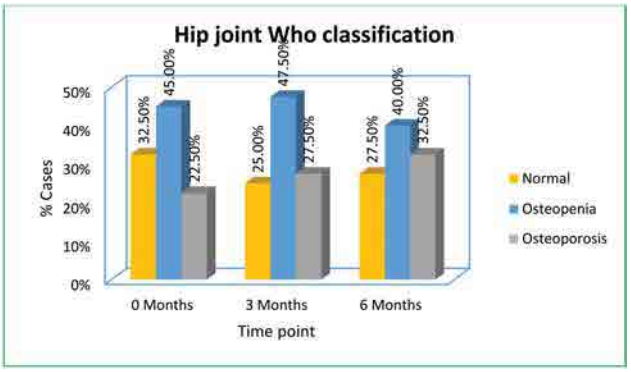


Fig 6: Hip joint BMD

CKD. NUTRITION, INFLAMMATION AND OXIDATIVE STRESS

P0912 **THE SERUM CREATININE TO CYSTATIN C RATIO AND CLINICAL OUTCOMES IN PATIENTS WITH NON-DIALYSIS CHRONIC KIDNEY DISEASE: THE KNOW-CKD COHORT**

Kyu-Beck Lee[1], Young Youl Hyun[1], Kook-Hwan Oh[2], Curie Ahn[1]

[1]Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Division of Nephrology, Department of Internal Medicine, Seoul, Korea, Rep. of South and [2]Seoul National University Hospital, Department of Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Muscle wasting leads to poor outcomes in patient with chronic kidney disease (CKD). The serum creatinine to cystatin C (Cr/CysC) ratio has been reported as marker for muscle mass and may predict outcomes in chronic diseases. We hypothesized that the Cr/CysC ratio would be a predictor of outcomes in CKD.

Method: We investigated a total of 2142 patients (male 61%, aged 54±12 year) with CKD followed for a median of 3.74 years. We assessed the factors associated with Cr/CysC ratio and the relationship between Cr/CysC ratio and outcomes of end-stage renal disease (ESRD), cardiovascular event (CVE), and mortality.

Results: The Cr/CysC ratio significantly correlated with age (r=-0.18), estimated glomerular filtration rate (eGFR) (r=-0.21), serum albumin (r=0.11), 24-hour urine creatinine (r=0.38), and moderate to vigorous physical activity time (r=0.07). After adjusting for age, sex, eGFR, and log urine albumin creatinine ratio (model 1), the hazard ratios for ESRD, CVE, and mortality were 0.96 (95% CI, 0.86-1.07), 0.78 (95% CI, 0.61-0.99), and 0.72 (95% CI, 0.53-0.97) per 1 standard deviation Cr/CysC increase (0.21), respectively. After full adjustment for model 1 variables plus lifestyle factors, laboratory factors, and comorbidities (model 2), the hazard ratios for ESRD, CVE, and mortality were 0.99 (95% CI, 0.88-1.10), 0.84 (95% CI, 0.65-1.07), and 0.75 (95% CI, 0.55-0.99) per 1 standard deviation Cr/CysC increase (0.24), respectively. In subgroup of the elderly (age>65 year) and early stage CKD (eGFR>60 ml/min/1.73m2), the hazard ratios for CVE were significantly lower in patients with high Cr/CysC ratio.

Conclusion: Cr/CysC ratio correlates with muscle biomarkers and physical activity. A higher Cr/CysC ratio is associated with low CVE and mortality, but not ESRD in CKD.

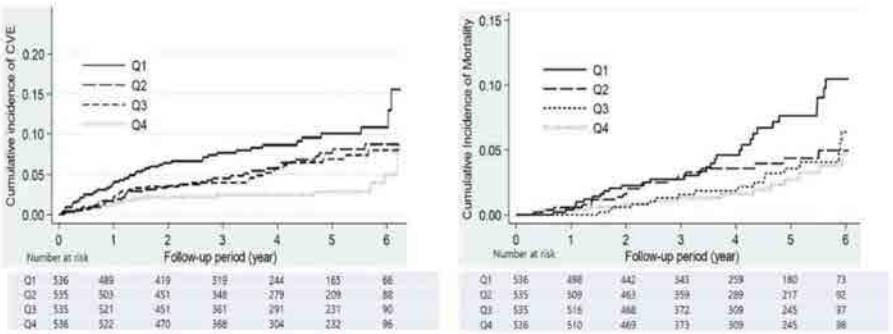


Figure. Kaplan-Meier curve: time to cardiovascular events (CVE) and mortality according to creatinine/cystatin C ratio sex-specific quartile

Figure:

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P0912A

KIDNEY AGING CONSTITUTES INFLAMMATORY PROCESS THAT CONTRIBUTES TO EXACERBATION OF KIDNEY INJURY

Su Woong Jung[1], Ju-Young Moon[1], Yang-Gyun Kim[1], Kyung Hwan Jeong[2], Sang-Ho Lee[1]

[1]Gangdong Kyung Hee University Hospital, Korea, Rep. of South and [2]Kyunghee University Hospital, Korea, Rep. of South

Background and Aims: Aging is a natural process accompanied by decline of regenerative potential. Some argue that aging process is just an irreversible physiologic process, whereas some advocate that it should be viewed as disease.

Method: To determine the nature of kidney aging and kidney disease at transcriptional level, whole kidney RNA sequencing was performed on young (2-month-old), middle-aged (12-month-old), and old (24-month-old) mice and young mice with adenine-induced nephropathy. In addition, young and old mice were fed with either standard or adenine-enriched diet for 4 weeks, and then the degree of renal injury was compared.

Results: The transcript profile of the old kidneys was mostly involved in inflammation and activation of innate and adaptive immune system and almost same to the transcript alterations of adenine-induced nephropathy. The genes implicated in fibrosis were downregulated until middle-age period, and then upregulated with the advance of age. The old kidneys showed augmented inflammatory response in a model of adenine-induced nephropathy compared with young kidneys, leading to more widespread fibrosis.

Conclusion: These findings showed that the pathophysiologic process of kidney aging and adenine-induced kidney injury shows similar natures in the context of inflammation and immune response. When kidney injury is superimposed on the aged kidneys, age-related inflammation potentiates inflammatory response and results in increased renal damage.

P0913 HYPERPHOSPHATEMIA INCREASE INFLAMMATION PROMOTING SENESCENCE AND MUSCLE DYSFUNCTION

Patricia Sosa[1], Elena Alcalde-Estévez[1], Ana Asenjo-Bueno[2], Patricia Plaza[2], Gemma Olmos[1,3], María Angeles Caballero[4], Manuel Rodríguez-Puyol[1,3], Susana López-Ongil[2,3], Maria Piedad Ruiz[1,3]

[1]Facultad de Medicina, Universidad de Alcalá, Biología de Sistemas, Alcalá de Henares, Spain, [2]Hospital Príncipe de Asturias, Fundación para la Investigación Biomédica, Alcalá de Henares, Spain, [3]Instituto Reina Sofía de Investigación Nefrológica (IRSIN) y Red Renal (REDinREN) del ISCIII, Madrid, Spain and [4]Hospital General Universitario de Ciudad Real, Servicio de Geriatría y Unidad de fragilidad, Ciudad Real, Spain

Background and Aims: Hyperphosphatemia has been associated with aging and chronic kidney disease (CKD). Sarcopenia, which is a related condition of these pathologies, is defined by loss of force and muscular mass. During aging, chronic systemic inflammation appears, termed inflammaging, due to changes in immune system function. Inflammaging has been associated with many age-related diseases including Sarcopenia and CKD. The work aimed to evaluate the effect of hyperphosphatemia on proinflammatory profile of cultured myoblast cells and to analyze, in old mice, the effect of a dietary restriction in the phosphate intake on the aging-related sarcopenia.

Methods: Culture murine myoblast C_2C_{12} cells were used for in vitro experiments. Cells were treated with 10 mM beta-glycerophosphate (BGP) as phosphate donor for 24, 48 or 72h. Inflammation was assessed through IL6, TNFα and MCP-1 expression by RT-qPCR. Twenty-four months old, C57BL6 mice were used for in vivo studies. Mice were fed with a normal diet containing 0.6% of phosphate until 21 months, after that, one group of mice continued with a normal diet and the other group was fed with a hypophosphatemic diet, containing a 0.2% of phosphate, for the following 3 months. Old mice were compared with 5 months old mice. Muscle force was measured by a grip strength test. Serum phosphate concentration was evaluated with a commercial kit and inflammation was assessed through IL-1β expression levels by RT-qPCR.

Results: Results showed that BGP treatment augmented pro-inflammatory cytokines levels, in myoblast, at 72h. On the other hand, old mice had a 40% increase in serum phosphate concentration regarding young mice, and, in parallel, they showed a reduction in forelimb strength. Old animals feeding with a hypophosphatemic diet showed a decreased level of phosphate serum linked to a better muscle function. Pro-inflammatory cytokines expression was higher in old mice compared to young mice; those values were reduced in 24-month-mice fed with a low phosphate diet. Furthermore, there was a positive correlation between IL-1β expression levels and serum phosphate levels, suggesting that high levels of serum phosphate were increasing inflammation in vivo and a negative correlation between IL-1β and grip strength test, which shows that high levels of inflammation decrease muscular function

Conclusion: In this work, we propose that high levels of phosphate are related to inflammation in vitro and in vivo. This increase of proinflammatory cytokines decreases muscle function whereas dietary restriction of phosphate decreases inflammation and improves muscle function. These results could point to a direct link between elevated serum phosphate levels and inflammaging presented in sarcopenic people such as CKD patients and aged people.

P0914 NEUTROPHIL EXTRACELLULAR TRAPS FORMATION IN HEMODIALYSIS PATIENTS

Adi Litmanovich[1,2], Khaled Khazim[1], Kamal Hassan[1,2], Batya Kristal[2]

[1]Galilee Medical Center, Nephrology, Nahariya, Israel and [2]Bar Ilan University, Faculty Of Medicine, Safed, Israel

Background and Aims: Hemodialysis (HD) patients suffer from devastatingly high rates of morbidity and mortality due to infections. Neutrophils isolated from HD patients were shown in the past to exhibit impaired phagocytosis in a mechanism yet to be completely elucidated. In 2004, Brinkmann et al. were the first to describe a new form of cell death which they termed Neutrophil Extracellular Trap Formation, or NETosis, in which neutrophils expulse batches of DNA and proteins in response to bacterial or chemical stimuli in order to trap and remove the stimulus. NETosis is further divided into two pathways, NADPH oxidase (NOX)-dependent and NOX-independent, induced *in vitro* by phorbol 12-myristate 13-acetate (PMA) and Calcium Ionophore (CI), respectively. In this research, we aim to assess the capacities of HD neutrophils to engage in NETosis, hypothesizing they might be diminished similarly to their phagocytic capacities, and to elucidate the underlying mechanism behind this impairment.

Method: Neutrophils were isolated from whole venous blood of normal controls and from the arterial line of HD patients before the onset of a dialysis session using EasySep™ direct human neutrophils isolation kit. Then, NETosis was induced with either PMA, Calcium Ionophore A23187 or Phosphate-buffered saline (PBS) as negative control. cfDNA released from the cells was quantified by measuring SYTOX™-green nucleic acid stain fluorescence levels in the supernatant after stimulation using Elisa plate reader and morphological analysis was done under fluorescence microscope. Reactive oxygen species levels were quantified using flow cytometry and superoxide dismutase (SOD) activity was measured using the SOD Assay Kit (Sigma-Aldrich). Protein arginine deiminase 4 (PAD4) expression was assessed by western blotting. Hydrogen peroxide (H_2O_2) was added exogenously in order to restore NETosis.

Results: HD isolated neutrophils exhibit decreased NETosis compared with normal controls in response to both PMA in the NOX-dependent pathway and CI in the NOX-independent pathway, as measured by immunofluorescence and cfDNA quantification. In the NOX-dependent pathway SOD activity was found to be 14% decreased in HD patients, resulting in the accumulation of superoxide radicals and decreased production of H2O2. In the NOX-independent pathway, PAD4 expression was found to be significantly decreased as well. NET formation was restored in vitro in HD neutrophils by the addition of exogenous H_2O_2.

Conclusion: To date, impaired NETosis was described only in congenital conditions such as chronic granulomatous disease and myeloperoxidase deficiency. To our knowledge, our research is the first to describe an acquired defect in NETosis in end stage renal disease patients undergoing chronic hemodialysis. An intervention aimed to improve neutrophil function in these patients may reduce the morbidity and mortality due to infection-related disease.

P0915

PROTEIN ENERGY WASTING IS ASSOCIATED WITH A DECLINE IN MUSCLE PROTEIN SYNTHESIS IN CKD PATIENTS

Michela Saio[1], Antonella Sofia[1], Rodolfo Russo[1], Leda Cipriani[1], Giacomo Garibotto[1], Daniela Verzola[1]

[1]*Opsedale Policlinico San Martino, Nephrology, Genoa, Italy*

Background and Aims: Skeletal muscle is a highly adaptive tissue, however even small imbalances between protein synthesis and degradation can lead to substantial protein loss. Althought proteolysis plays a major role in the development of cachexia in CKD (chronic kidney disease), the responses of muscle protein metabolism to malnutrition had not been completely elucidated.

We evaluated retrospectively the results of kinetic studies of protein turnover estimated by the forearm perfusion method associated with H2phenylalanine kinetic, obtained in CKD patients and controls in the last 25 years.

Method: We analyzed 59 forearm H^2phenylalanine kinetic studies obtained in 14 controls (C) (M 11, F 3) and 45 patients with CKD, of whom 15 (M 10, F 5) were on conservative treatment (CKD stage IV-V), 16 (M 14, F 2) under maintenance hemodialysis (HD), 14 (M 12, F 2) in peritoneal dialysis (DP); all subjects were on non-restricted protein/calorie (0.8-1.1 g/kg and 28-32 kcal/kg, respectively) diets. Ten (M 9, F 1) HD patients had Protein Energy Wasting. Acidosis was corrected in all patients (HCO3 24.2 ± 1.9 mmol/L) and studies were performed in the post-absorptive overnight fasted state at rest.

Results: Overall, Muscle protein synthesis and degradation were similar (p=NS) in patients and controls. Protein net balance was reduced in patients with PD and those with CKD Stage IV-V ($p < 0.003$ - $p < 0.014$) indicating a reduced catabolic state and nitrogen conservation. However PEW HD patients showed reduced rates of protein synthesis and degradation ($p < 0.048$ and $p < 0.04$ respectively). In addition the efficiency of muscle protein turnover, a parameter expressing muscle's ability to reuse amino acids derived from degradation into protein synthesis, was significantly reduced in HD PEW patients vs. controls (55.5 vs. 61.2 %, $p < 0.018$, respectively) and vs. not malnourished patients in conservative treatment (70.1 % $p < 0.0025$) or in PD (74.6 % $p < 0.005$).

Conclusion: In CKD patients, in absence of acidosis, muscle is able to increase the efficiency of protein metabolism for the maintenance of nitrogen balance. However, in PEW patients, combined alterations of protein synthesis and degradation proceed together to a reduced efficiency of amino acids recycled into protein synthesis and contribute to maintaining wasting. These data also suggest that calorie/protein requirements of CKD patients with PEW may be higher than currently theorized.

P0916

OLIVE LEAF EXTRACT IMPROVES RENAL ANTIOXIDANT DEFENSE WITHOUT ALTERING THE HEME OXYGENASE-1/ BILIVERDIN REDUCTASE PATHWAY IN HYPERTENSIVE RATS WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS

Danijela Karanovic[1], Nevena Mihailovic-Stanojevic[1], Zoran Miloradovic[1], Milan Ivanov[1], Jelica Grujic-Milanovic[1], Una-Jovana Vajic[1], Dragana Dekanski[2], Djurdjica Jovovic[1]

[1]University of Belgrade, Institute for Medical Research, Group for Cardiovascular Physiology, Belgrade, Serbia and [2]R & D Institute, Galenika a.d., Belgrade, Serbia

Background and Aims: Oxidative stress is implicated in the pathophysiology of chronic kidney disease. Previously, we showed that adriamycin (anticancer agent, enhances reactive oxygen species production) induced focal segmental glomerular sclerosis (FSGS) with massive proteinuria in spontaneously hypertensive rats (SHR). The heme oxygenase (HO) system plays an important role in regulating oxidative stress and is protective in chronic kidney disease. HO-1 is a cytoprotective enzyme that catalyzes the conversion of highly reactive free heme molecules into biliverdin, carbon monoxide, and iron. Biliverdin is subsequently converted to bilirubin by biliverdin reductase and has potent antioxidant effect. Olive leaf extract (OLE, Olea europaea L.) is rich in phenolic compounds that are known to possess powerful antioxidant properties. Here, we aimed to investigate the effects of OLE, focusing on its modulatory role on oxidative stress and HO-1/BVR pathway in the kidney of SHR with adriamycin-induced FSGS.

Method: Adult females SHR were divided into three groups. Control rats received vehicle. Two other groups, FSGS and FSGS+OLE, received adriamycin (2 mg/kg body weight i.v.) twice in 3-week-interval. After the second injection, FSGS+OLE group received OLE (80 mg/kg/day) by gavage for 6 weeks. Mean blood pressure (MAP), urine albumin-to-creatinine (Ualb/cr), renal HO-1 and biliverdin reductase protein expressions (Western Blot), protein carbonyl content (PCOs), and antioxidant capacity (ABTS) were analyzed.

Results: In FSGS group albuminuria was significantly increased in comparison to the level in control. Chronic consumption of OLE markedly, but not significantly decreased Ualb/cr compared to that in control. Analysis of renal PCOs revealed that significant enhancement of protein oxidation in the kidney of model group was reduced after OLE treatment to the level as in control. The ABTS level in kidney homogenates significantly decreased in FSGS group in comparison to the level in control. OLE significantly increased renal antioxidant capacity in FSGS+OLE group compared to that in model group. Western blot analysis of HO-1, and biliverdin reductase in the kidney revealed that protein expressions of both enzymes were significantly decreased in FSGS group compared to that in control. Following OLE treatment in FSGS+OLE group protein expressions of HO-1, and biliverdin reductase remained at similar level as in model group. No change in MAP values were observed between control and model groups. OLE significantly decreased MAP in FSGS+OLE group in comparison to the value of model group, and nearly significant reduction of MAP compared to the value of control.

Conclusion: Collectively, our results showed that OLE expressed its antioxidant property and improved oxidative status in the kidney of SHR with ADR-induced FSGS, independently of the HO-1/BVR pathway.

P0917

N-ACETYL CYSTEINE FAILS TO IMPACT ON PLASMA ANTIOXIDANT CAPACITY IN BOTH A PLACEBO CONTROLLED CROSSOVER STUDY AND A PARALLEL GROUP TRIAL OF PATIENTS WITH CKD STAGE III: IMPLICATIONS FOR ITS USE AS A PROPHYLACTIC FOR CONTRAST INDUCED NEPHROPATHY

Khuram Raja[1], Kirsty Hickson[1], Andrew Treweeke[1], Gordon Rushworth[2], Emma Morrison[3], Euan Sandilands[3], James Cobley[1], David McEneaney[4], Michael Eddleston[3], Ian Megson[1]

[1]University of the Highlands and Islands, Institute of Health Research and Innovation, Inverness, United Kingdom, [2]NHS Highland, Highland Pharmacy Education & Research Centre, Inverness, United Kingdom, [3]University of Edinburgh, Pharmacology, Toxicology and Therapeutics, Edinburgh, United Kingdom and [4]Craigavon Area Hospital, Dept. Of Cardiology, Craigavon, United Kingdom

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Background and Aims: N-acetyl-L-cysteine (NAC) has been proposed as a prophylactic for the prevention of contrast induced nephropathy (CIN), a serious, adverse complication following administration of contrast media in patients with diabetes and chronic kidney disease (CKD). However, clinical trial results have failed to demonstrate consistently the beneficial qualities of NAC in this setting. The suggested mechanism by which NAC has been proposed to be effective is via antioxidant activity, but NAC itself appears not to be a powerful antioxidant; intracellular conversion of NAC to glutathione (GSH) is essential for antioxidant effects. We tested the hypothesis that oral or intravenous NAC fails to increase antioxidant activity in the plasma of healthy volunteers or CKD stage III patients undergoing elective coronary angiography.

Method: 16 healthy volunteers (8 receiving contrast media) and 8 patients with chronic renal failure were recruited to 3 separate groups as a part of a crossover design study. 66 patients with CKD stage III undergoing elective coronary angiography were recruited to a parallel group randomized controlled trial. Each volunteer or patient was randomised to receive NAC (i.v.; 50 mg/kg/hr infusion for 2 h, followed by 20 mg/kg/hr infusion for a further 5 h), or NAC (oral; 1200 mg twice daily, commencing the day before the study visit) or placebo. Participants attended the Clinical Research Facility on three occasions for the crossover groups, but only once in the parallel group trial. Patients were infused with para-aminohippurate (PAH) and inulin to enable measurement of renal function parameters. Plasma and paired buffy coat samples were collected at several time points for 2 hours before contrast infusion and for 6 hours after. Samples were used to measure various clinical parameters, along with intracellular and plasma thiol concentrations and the plasma antioxidant capacity (oxygen radical antioxidant capacity; ORAC).

Results: Plasma NAC concentrations peaked at 222 μM (healthy volunteers), 354 μM (CKD patients), 271 μM (healthy volunteers receiving contrast) and 348 μM (CKD patients undergoing elective coronary angiography) following infusion of NAC. The corresponding peak concentrations were ∼2 μM following oral NAC across all groups. No comparable increase in the plasma compartment ORAC antioxidant capacity was measured in any of the treatment groups. Equally, contrast infusion itself did not significantly reduce antioxidant capacity in plasma, even in the placebo group. Buffy coat measures showed that there was a significant increase of intracellular GSH in some patients. Also, no clear additional benefit was witnessed by increasing plasma NAC ∼100-fold through infusion of NAC over oral administration.

Conclusion: NAC fails to influence ORAC antioxidant capacity in the plasma compartment of CKD stage III patients receiving contrast media. Our results question the importance of oxidative stress in contrast-induced nephropathy. Furthermore, the findings fail to demonstrate a direct antioxidant impact of NAC in the plasma compartment and question the antioxidant hypothesis related to contrast-induced nephropathy and NAC.

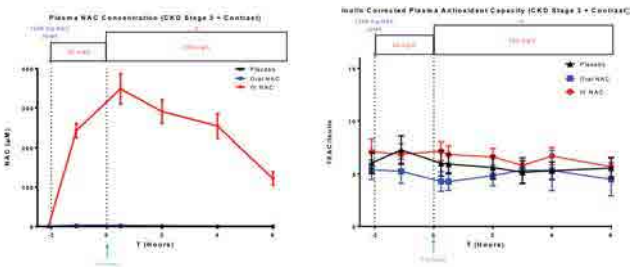


Figure:

P0918

LONGITUDINAL TRAJECTORIES OF NUTRITIONAL PARAMETERS WITH ORAL NUTRITIONAL SUPPLEMENT USE AMONG NON-DIALYSIS CHRONIC KIDNEY DISEASE PATIENTS

Michelle Wong[1,2], Dani Renouf[3], Sophia Zheng[4], Zainab Sheriff[5], Adeera Levin[4,6]

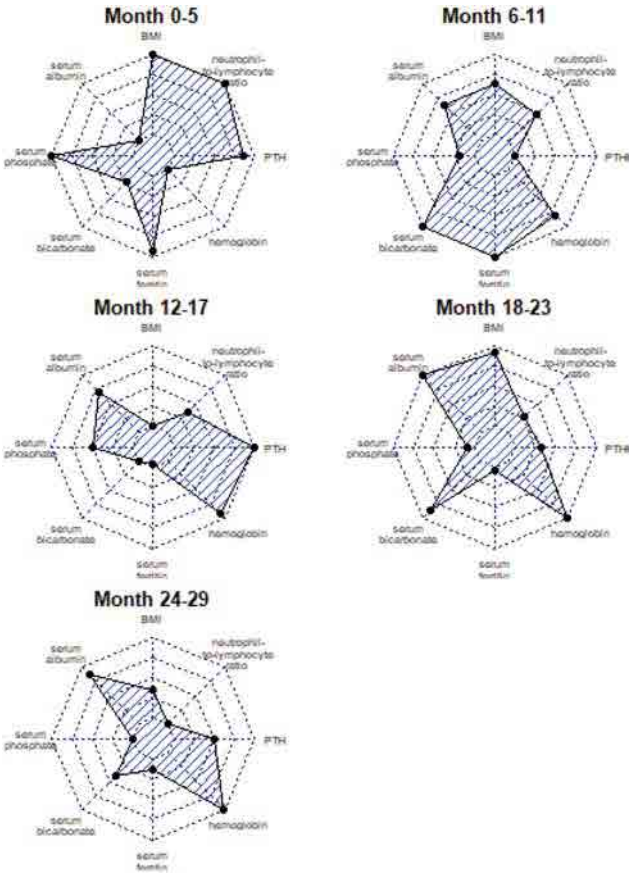
[1]BC Renal, Vancouver, Canada, [2]University of British Columbia, Department of Medicine, Vancouver, Canada, [3]St. Paul's Hospital, Vancouver, Canada, [4]BC Renal, Vancouver, BC, Canada, [5]University of British Columbia, Vancouver, Canada and [6]University of British Columbia, Vancouver, BC, Canada

Background and Aims: Malnutrition and protein-energy wasting are complications of advanced CKD associated with increased risk of mortality and morbidity. In the province of British Columbia, Canada, a Nutritional Supplement Policy stewarded by renal dietitians guides prescription of oral nutritional supplements (ONS). To date, there have been a lack of studies assessing the effects of ONS among non-dialysis CKD patients (CKD-ND). The aim of the study was to assess longitudinal trajectories of nutrition, inflammation and associated biochemical parameters following initiation of ONS among CKD-ND patients.

Method: In this retrospective cohort study of adult CKD-ND patients who initiated follow-up at multidisciplinary Kidney Care Clinics during 2013-2015, we used radar charts to examine longitudinal trajectories of nutritional, inflammation and related parameters over 2 years, among patients who had at least one ONS prescription and who had available lab data for the following 8 parameters within any given time interval: body mass index (BMI), serum albumin, bicarbonate, phosphate, parathyroid hormone, ferritin, neutrophil-to-lymphocyte ratio (NLR) and haemoglobin. Mean values of each parameter were plotted at 6-month intervals from the first prescription of ONS, up to 29 months.

Results: There were 963, 692, 569, 481, 425 patients with available data during the intervals at month 0-5, 6-11, 12-17, 18-23 and 24-29 following the first ONS prescription, respectively. Mean serum albumin increased from a mean of 37 to 40 g/L over the 29-month period after ONS initiation, while mean NLR declined from 4.5 to 3.6 (Figure). Mean serum ferritin also declined slightly from 293 to 261 µg/L at 3 months and remained stable thereafter. There were small fluctuations in mean BMI (range 24.5 to 25.1 kg/m^2), bicarbonate (range 24 to 25 mmol/L), PTH (range 15.5 to 18.0 pmol/L). Mean haemoglobin rose from 108 g/L in the first interval to 116 g/L in the last interval. Mean serum phosphate changed minimally from 1.4 to 1.3 mmol/L.

Conclusion: Among CKD-ND patients who had at least one ONS prescription, serum albumin increased, while there was a decrease in inflammation parameters (NLR and ferritin), and other variables had small fluctuations over the 2+ year follow-up. Future analyses will include multivariable-adjusted models to assess the associations of ONS treatment with nutritional variables and with clinical outcomes, including progression to end-stage kidney disease.



Radar charts of nutritional parameters among CKD-ND patients. The mean values of each variable are plotted along the respective spoke; the innermost ring represents the minimum and the outermost ring represents the maximum value of that variable across all data points. A line connects the data values on each spoke.

P0919 CALORIC RESTRICTION DOES NOT PROTECT AGAINST THE DEVELOPMENT OF VASCULAR CALCIFICATION

Rafael Ríos-Varo[1], Ángela Vidal[1], Ana Isabel Raya[1], Carmen Pineda[1], Ignacio López[1], J. Mariano Rodriguez-Portillo[2], Escolástico Aguilera-Tejero[1]

[1]Universidad de Córdoba, Medicina y Cirugía Animal, Córdoba, Spain and [2]Instituto de Investigación Maimónides (IMIBIC), GC13. Metabolismo del Calcio, Córdoba, Spain

Background and Aims: Vascular calcification (VC) is an important contributor to the high rate of cardiovascular mortality associated to chronic kidney disease.

The inability to eliminate phosphorus (P) and the subsequent P retention promotes CV. P metabolism and uremic VC are influenced by obesity and by the caloric content of the diet.

Caloric restriction (CR) has been shown to have multiple beneficial effects on health, for example, CR has been reported to improve vascular health and retard vascular ageing. However, to our knowledge the effect of CR on the development of uremic VC has not been explored.

We hypothesize that CR may be beneficial to prevent the development of uremic VCs. Thus, the objective of the present study was to determine if rats subjected to CR were protected against VC.

Method: 48 Wistar rats were divided in four groups. The control diet provided Metabolizable Energy = 3.528 kcal/g and contained 0.6% Calcium (Ca) and 0.6% P. Additional diets of identical composition to the control diet but containing varying levels of Ca and P: 0.9% Ca, 0.9% P; 0.6% Ca, 1.2% P; and 0.9% Ca, 1.8% P, were also used in the experiments.

Rats in Group 1 and 3 were fed 15 g/day of the control diet. Rats in Group 2 and 4 were calorie restricted and fed 10 g/day of diet with Ca/P = 0.9%/0.9%. Thus the daily P intake should be identical in the four groups.

Uremia was induced by 5/6 nephrectomy (Nx). After Nx rats in Group 1 and 2 were fed ad libitum a diet with 0.6% Ca and 1.2% P. While rats in Group 3 and 4 were fed ad libitum a diet with 0.9% Ca and 1.8% P. Rats were supplemented with calcitriol.

At the end of the experiment, rats were sacrificed to obtain blood samples and tissue samples (thoracic and abdominal aortas).

After blood collection, plasma was separated by centrifugation and stored at –20° C until assayed. Plasma creatinine, Ca and P were measured by spectrophotometry. Energy intake was calculated based on food intake. VC was studied by histology and by measuring the tissue Ca content.

Values are expressed as mean ± standard error (SE), the difference between groups was assessed by ANOVA. Fisher LSD test was used as a post-hoc procedure. $p<0.05$ was considered significant.

Results: Before Nx, caloric intake was significantly lower in calorie restricted rats (35.4 ± 0.1 and 35.8 ± 0.1 kcal/day) than in rats eating normal calories (52.7 ± 0.1 and 52.8 ± 0.2 kcal/day); however, P intake was almost identical in the four groups and ranged between 89.8 and 91.6 mg/day.

After Nx, rats in all groups reduced food intake and, consequently, caloric intake. Thus, although the P content of the diet was increased after Nx, daily P intake was not increased in Groups 1 and 2; however, P intake was significantly increased in Groups 3 and 4 (120.9 ± 4.6 and 122.2 ± 6.2 mg/day, respectively).

In all groups, rats had high plasma concentrations of creatinine and P, and low plasma concentrations of Ca. Also, all rats had elevated Ca content in the aorta. No significant differences between the study groups were found in any of these parameters (Table 1).

Table 1. Plasma metabolites (mg/dl) and aortic mineral deposition (mg/g of tissue) in the study groups.

	Group 1	Group 2	Group 3	Group 4
Plasma Creatinine	7.8 ± 1.2	7.7 ± 1.2	7.8 ± 1.0	6.8 ± 1.1
Plasma Phosphate	20.7 ± 3.6	20.5 ± 2.0	24.8 ± 4.7	30.9 ± 2.4
Plasma Calcium	2.3 ± 0.12	2.8 ± 0.24	2.7 ± 0.24	2.6 ± 0.43
AORTIC CALCIUM	11.5 ± 1.7	10.9 ± 2.1	12.5 ± 2.3	12.0 ± 2.9

Von Kossa staining of the aortas showed abundant mineral deposition in the four groups.

Conclusion: This study shows that, contrary to what was expected, CR did not prevent or ameliorate uremic calcifications.

P0920 **THE METHIONINE RESTRICTION DIET ATTENUATES CHRONIC KIDNEY PROGRESSION IN MICE.**

Jihyun Yang[1], Hyeon-jin Min[1], Bong Gyun Sun[1], Young-Bin Son[1], Eunho Choi[1], Se Won Oh[1], Myung-gyu Kim[1], Sang-Kyung Jo[1], Won-Yong Cho[1]

[1]*Korea University Anam Hospital, Seoul, Korea, Rep. of South*

Background and Aims: The clinical usefulness of protein-restricted diets is known to slow the progression of obesity, fatty liver, aging and cancer. Protein-restricted diet in chronic kidney disease is known to alleviate the deterioration of the renal function. The purpose of this study is to confirm whether the reduction in new function can be improved when methionine restricted (MR) diet is supplied in the chronic kidney disease (CKD) animal model and to study the its renoprotection mechanism.

Method: We used four-week-old C57L/B6 to make a CKD model by administration 0.025% adenine chow mixed with R3 diet for four weeks for the control group. For the MR diet group, we supplied the mixture of 0.025% adenine with methionine/Choline Deficient Diet. We measured serum blood urea nitrogen (BUN), serum creatinine, gut permeability, stool short chain fatty acid (SCFA), kidney α-SMA and renal pathology. This study was approved by Korea University Institutional Animal Care and Use Committee (KOREA-2019-0047).

Results: The principal coordinates analysis of the microbiome showed the two groups have distinctive component features. The stool SCFA, especially butyrate was increased in the MR diet group. However, gut permeability using FITC-dextran showed no significant change. The kidney α-SMA and MT stain area showed that the MR diet could improve renal fibrosis. The kidney inflammation including neutrophil and macrophage infiltration was also improved in histology analysis. The macrophage phenotype was more favorable to M2 type. Serum BUN and creatinine were significantly attenuated in the MR diet group.

Conclusion: In conclusion, the MR diet has a reno-protective effect in adenine induced CKD. The MR diet increased butyrate production and decreased renal inflammation and fibrosis. These results shed light on the role of protein restriction diet for CKD management in the real world.

P0921

ROLE OF UREMIC TOXIN, INDOXYL SULFATE IN SARCOPENIA OF NONDIALYSIS DEPENDENT-CHRONIC KIDNEY DISEASE PATIENTS

Jun Chul Kim[1], Seok Hui Kang[2], Miyeun Han[3], Su-Hyun Kim[4], Ran-Hui Cha[5], Won Suk An[6], Jun Young Do[2]

[1]CHA Gumi Medical Center, Internal Medicine, Gumi-si, Korea, Rep. of South, [2]Yeungnam University Medical Center, Internal Medicine, Daegu, Korea, Rep. of South, [3]Pusan National University Hospital, Internal Medicine, Pusan, Korea, Rep. of South, [4]Chung-Ang University Hospital, Internal Medicine, Seoul, Korea, Rep. of South, [5]National Medical Center, Internal Medicine, Seoul, Korea, Rep. of South and [6]Dong-A University Hospital, Internal Medicine, Pusan, Korea, Rep. of South

Background and Aims: Sarcopenia in patients with chronic kidney disease (CKD) is highly prevalent and leads to high rate of morbidity and mortality. The role of indoxyl sulfate (IS) to develop muscle wasting has been researched and proved in several animal model studies. However, there is no human data showing this relationship in CKD population. The aim of the present study was to evaluate the association between serum IS levels and each component of sarcopenia in nondialysis dependent-CKD (NDD-CKD) patients.

Method: We enrolled 150 NDD-CKD adult patients from 6 medical centers and collected data of demographics, blood chemistry such as indoxyl sulfate, interleukin (IL)-6, and estimated glomerular filtration rate using MDRD equation (eGFR), and body mass index (BMI, kg/m^2). We also measured hand-grip strength (HGS, kg), walking speed (WS, m/s), skeletal muscle mass (SMM, kg) by bioelectrical impedance analysis (BIA).

Results: The numbers of male sex was 97 (64.7%). Mean age was 63.7±10.8 years old. The numbers of patients with diabetes mellitus was 77 (52.0%). Charlson comorbidity index (CCI) score was 3.9 ± 1.9. The stage of CKD ranged from 3 to 5 (eGFR=33.7±12.0 ml/min/1.73m^2, mean±SD). Correlation coefficients with indoxyl sulfate levels were 0.211 for serum IL-6 level ($P = 0.010$), -0.212 for HGS ($P = 0.009$), -0.188 for WS ($P = 0.021$), -0.237 for SMM ($P = 0.004$), and -0.168 for BMI ($P = 0.041$), respectively. Correlation analysis showed that indoxyl sulfate levels had inverse association significantly with HGS, WS, SMM, and BMI and were positively associated with serum IL-6 levels.

Conclusion: Our study shows that higher serum indoxyl sulfate level was significantly associated with lower levels of muscle mass, strength, and physical performance function and higher inflammation status in non-dialysis dependent CKD patients. We suggest that the role of AST120 in prevention or treatment of sarcopenia be studied in this CKD population.

P0922

A LOW AROMATIC AMINO-ACID DIET IMPROVES RENAL FUNCTION AND PREVENTS KIDNEY FIBROSIS IN MICE WITH CHRONIC KIDNEY DISEASE

Christophe Barba[1,2], Christophe Soulage[2], Griet Glorieux[3], Cecile PICARD[4], Denis Fouque[1,2], Laetitia Koppe[1,2]

[1]Hospices Civils de Lyon, Centre Hospitalier Lyon-Sud, Department of Nephrology, Pierre-Bénite, France, [2]Univ. Lyon, CarMeN lab, INSA-Lyon, INSERM U1060, INRA, Université Claude Bernard Lyon 1, VILLEURBANNE, France, [3]Ghent University Hospital, Nephrology Section, Department of Internal Medicine, Ghent, Belgium and [4]Hospices Civils de Lyon, Groupement Hospitalier Edouard Herriot, Department of Pathology, Bron, France

Background and Aims: Despite decades of use of low protein diets (LPD) in the management of chronic kidney disease (CKD), the mechanisms through which it delays the progression to end-stage renal disease (ESRD) remain controversial. A reduced production of uremic toxins could contribute to the benefits of the LPD. Aromatic amino-acids are precursors of major uremic toxins such as p-cresyl sulfate (PCS), indoxyl sulfate (IS), indole-3-acetic acid or phenol. We investigated the hypothesis that a low aromatic amino acid diet (LAA, namely low intake of tyrosine, tryptophan and phenylalanine) while being normoproteic, could be as effective as a LPD, through the specific diminution of uremic toxins production.

Method: Renal failure was chemically induced in mice with a diet containing 0.25% (w/w) of adenine. Thereafter, they received 3 different diets for 6 weeks: normoproteic diet (NPD: 14.7% proteins, aromatics 0.019%), LPD (5% proteins, aromatics 0.007%) and LAA (14% proteins, aromatics 0.007%).

Results: LAA and LPD had no significant effect on body weight. Plasma creatinine was significantly lower in LPD and LAA groups compared to NPD group (72 $\pm$ 4 and 73 $\pm$ 4 µmol/L vs 127 $\pm$ 6 µmol/L, $p<0.0001$), as well as proteinuria (1.3 $\pm$ 0.3 and 1.2 $\pm$ 0.1 mg/24h vs 3.8 $\pm$ 0.9 mg/24h, $p<0.05$). Kidney fibrosis was more severe in NPD group vs LPD and LAA groups (17 $\pm$ 1% vs 10 $\pm$ 1 % and 13 $\pm$ 2 %, $p<0.0001$ and $p=0.01$). Kidney inflammation was also reduced with LPD and LAA. Free PCS and IS were lower in LPD and LAA groups compared to NPD group.

Conclusion: These results suggest that LAA confers similar benefits as compared with those of LPD to delay the progression of CKD through reduction of uremic toxins production, with lower risk of malnutrition.

Renal function and urinary protein excretion in control and CKD mice

Serum creatinine (A), blood urea nitrogen (B) and urinary proteins (C) in control and CKD mice fed with normoproteic diet (NPD), low protein diet (LPD) or low aromatic amino-acid diet (LAA). Data are expressed as mean $\pm$ SEM for n = 5-11 animals in each group.

$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$ vs CKD-NPD; (two-way ANOVA and Dunnett post hoc test).

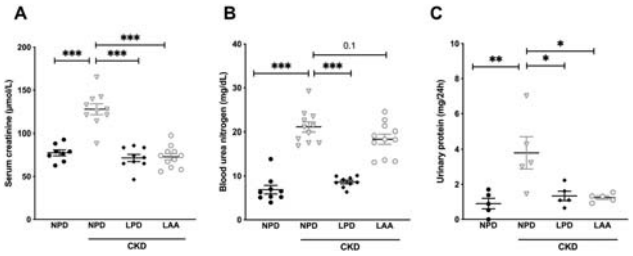


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P0923

5-AMINOLEVULINIC ACID PREVENTS LIPID-INDUCED ER STRESS AND APOPTOSIS BY INDUCING HEME OXYGENASE-1

Yukari Mae[1], Yui Kobayashi[1], Tomoaki Takata[1], Kohshiro Hosokawa[1], Takaaki Sugihara[1], Tsutomu Kanda[1], Hajime Isomoto[1]

[1]*Tottori University Faculty of Medicine, Division of Medicine and Clinical Science, Yonago, Japan*

Background and Aims: A growing number of evidence indicates the association with dyslipidemia and the progression of chronic kidney disease. Endoplasmic reticulum (ER) stress and apoptosis in renal tubule are suggested to be linked to the pathophysiology of toxic lipid-induced kidney injury. 5-aminolevulinic acid (ALA) is a precursor of heme oxygenase (HO)-1, which plays an important role in protecting cells from various stresses. In the present study, we aimed to investigate the therapeutic effect of ALA, on toxic lipid-induced ER stress and apoptosis in the renal tubule.

Method: Renal proximal tubular epithelial cells (RPTECs) were treated with palmitic acid to induce ER stress and apoptosis. ALA was also added with palmitic acid (PA). The gene and protein expressions of NF E2-related factor 2, HO-1, glucose-regulated protein (GRP)78, and C/EBP-homologous protein (CHOP) were quantified. Apoptotic cells were evaluated by caspase-3/7 assay. An HO-1 inhibitor, Zn-protoporphyrin IX, was added to investigate the involvement of HO-1 in ALA-mediated therapeutic effect on the ER stress and apoptosis.

Results: The expressions of GRP78 and CHOP increased in cells treated with PA. Apoptotic signals also increased with PA treatment. ALA induced a significant increase in the HO-1 expression and that led to the suppression of ER stress response. Apoptotic signals in PA-treated cells also decreased with ALA and the effect of ALA disappeared when combined with Zn-protoporphyrin IX.

Conclusion: PA-induced ER stress and apoptosis in RPTECs. ALA has a therapeutic effect by suppressing ER stress, possibly through HO-1 induction.

P0924

IMMUNE DISTURBANCES INDUCED BY HYPERVOLEMIA DO NOT ACTIVATE THE NLRP3 INFLAMMASOME IN HAEMODIALYSIS PATIENTS

Christof Ulrich[1], Annegret Wilke[1], Nadja Schleicher[1], Matthias Girndt[1], Roman Fiedler[1]

[1]*Martin Luther University Halle-Wittenberg, Internal Medicine II, Halle (Saale), Germany*

Background and Aims: Hypervolemia is frequent in haemodialysis (HD) patients and is linked to inflammation, which may be further enhanced by endotoxemia. The impact of hypervolemia on immune cells i.e. a main monocytic defence mechanism - the NLRP3 inflammasome, has not been studied in detail. Therefore, we hypothesized that endotoxinemia putatively present in hyper- but normovolemic patients can trigger the activation of caspase-1 and thus increasing IL-1ß secretion.

Method: 45 HD patients were included in the observational study, measuring immune parameters (cell counts, caspase-1, oxidative stress, cytokine gene expression and serum analysis (IL-1ß) at two time points (directly after dialysis BS1) and three days later after the long dialysis free interval (BS2). Fluid status was evaluated by electrical bioimpedance vector analysis, defining hypervolemia (H) as >75 vector percentile. Data collected after the long dialysis interval is presented in this paper.

Results: Seventeen patients were classified as hyper-(H-HD), 19 as normovolemic (N-HD), 9 failed to meet the inclusion criteria. Monocytes were elevated and lymphocytes decreased by hypervolemia. Oxidative stress was slightly elevated in H-HD. However, neither caspase-1 frequency (H: 77.9±4.2% vs. 79.2±6.9%, p=0.916) nor caspase-1 expression (MFI, H: 42.8±13.3 vs. 43.6±17.1, p=0.880) were different. In vitro stimulation of PBMC's by specific NLRP3 inflammasome stimulation significantly increased caspase activity in both cohorts to the same extent (89.9±22.6 vs. 88.0±23.3, p=0.900). As a result of it both IL-1ß mRNA expression (1.7±1.9 vs N: 1.1±0.8, 0.306) and serum IL-1ß (pg/ml) did not differ between the groups (H: 1.99±0.2 vs. N: 1.98±0.6, p<0.135).

Conclusion: The NLRP3 inflammasome is not activated thus refuting the hypothesis that endotoxemia is a main driver for inflammation in H-HD.

P0925 **EFFECTS OF A NUTRITION INTERVENTION IN ADDITION TO AN INTRADIALYTIC EXERCISE PROGRAM IN HEMODIALYSIS PATIENTS**

Ana Valente[1], Cristina Caetano[1], Inês Ramos[1], Joana Sebastião[1], Mariana Pinto[1], Telma Oliveira[1], Pedro Martins[2], Cristina Garagarza[1]

[1]Nephrocare Portugal, Nutrition Department, 1750-233, Portugal and [2]Nephrocare Portugal, Physical Exercise Programme, 1750-233, Portugal

Background and Aims: Physical inactivity and low protein intake are related with protein-energy wasting syndrome. This is a very common condition in hemodialysis (HD) patients and is related with poor survival. Both, intradialytic exercise programmes (IEP) and nutrition interventions, are proposed as strategies to increase lean tissue mass in these population. The aim of this study was to analyze the effect of specific nutritional counseling in nutrition, body composition parameters and in eating habits, in patients undergoing HD with an IEP.

Method: This was a multicenter longitudinal intervention study with 3 months of follow-up. We enrolled 88 patients already performing intradialytic exercise (aerobic and strength training) for more than 3 months. These patients had an appointment with the dietitian and received specific nutritional counseling (NC) and a flyer with focus on nutrition recommendations for exercise. Eating habits were obtained through a questionnaire and body composition with bioimpedance spectroscopy (Body Composition Monitor®). Potassium and phosphorus were collected at baseline and 3 months after. Statistical tests were performed with SPSS, version 26.0. A $p < 0.05$ was considered significant.

Results: Patient's mean age was 63.5±1.5 years and median HD time was 34 (Interquartil range (IQR): 20-58) months. 61.4% (n=54) were male and 26.1% (n=23) were diabetics. Results pre and pos intervention for the parameters studied were, respectively: Body Mass Index (BMI) 25.4[IQR: 23.7-28.4] Kg/m^2 vs. 25.6[IQR: 23.4-28.9] Kg/m^2; Fat Tissue Mass 12.6±5.0 Kg/m^2 vs. 12.5±4.8 Kg/m^2; Lean Tissue Mass 13.5[IQR: 11.5-15.3] Kg/m^2 vs. 13.4[IQR: 12.1-15.3] Kg/m^2; Body Cell Mass 20.1[IQR: 15.7-25.1] Kg/m^2 vs. 20.4[IQR: 16.4-24.8] Kg/m^2; % Interdialytic Weight Gain 2.7±1.1 Kg/m^2 vs. 2.8±1.1 Kg/m^2; potassium 5.1±0.7 mEq/L vs. 5.2±0.8 mEq/L and phosphorus 4.6±1.3 mg/dl vs. 4.8±1.2 mg/dl. No statistically significant differences were observed between baseline and follow-up. Concerning eating habits, the intake of protein sources from meat and fish before the HD session increased after the 3 months (17% vs. 20.5%; p=0.002). About 23% of the patients reported having made changes in their diet after the NC and 60% felt positive changes in performance and fatigue.

Conclusion: We can conclude that NC contributed to increase the consumption of high biological value protein-rich foods and to improve the patient's perception of fatigue and performance. Moreover, this intervention did not have a worrying effect on potassium and phosphorus levels. Longer follow up studies are needed to analyze the effect on body composition.

P0926

ASSOCIATION OF HIGH-SENSITIVE C-REACTIVE PROTEIN WITH CARDIOVASCULAR EVENTS, MORTALITY, AND ADVERSE KIDNEY OUTCOMES IN KOREAN PATIENTS WITH CHRONIC KIDNEY DISEASE: RESULTS FROM KNOW-CKD

Changhyun Lee[1], Keun Hyung Park[2], Young Su Joo[3], Ki Heon Nam[2], Tae-Ik Chang[1], Ea Wha Kang[1], Joongyub Lee[4], Yun Kyu Oh[5], Ji Yong Jung[6], Curie Ahn[7], Kyu-Beck Lee[8], Jung Tak Park[2], Tae-Hyun Yoo[2], Shin-Wook Kang[2], Seung Hyeok Han[2]

[1]NHIS Ilsan Hospital, Internal medicine, Goyang-si, Korea, Rep. of South, [2]Yonsei university Medical school, Internal medicine, Seoul, Korea, Rep. of South, [3]Myongji Hospital, Internal Medicine, Goyang-si, Korea, Rep. of South, [4]Inha University Hospital, Prevention and Management, Incheon, Korea, Rep. of South, [5]SMG-SNU Boramae Medical Center, Internal medicine, Seoul, Korea, Rep. of South, [6]Gacheon University Medical Campus, Internal medicine, Incheon, Korea, Rep. of South, [7]Seoul National University Hospital Medical Research and Innovation Center, Internal medicine, Seoul, Korea, Rep. of South and [8]KANGBUK SAMSUNG HOSPITAL, Internal medicine, Seoul, Korea, Rep. of South

Background and Aims: High-sensitivity C-reactive protein (hs-CRP) level is lower in East Asians than in the Western people and its clinical significance needs to be further explored. We aimed to investigate whether hs-CRP could function as a biomarker in Korean CKD patients.

Method: We studied the association of hs-CRP with adverse clinical outcomes in 2,018 patients from the KoreaN cohort study for Outcome in patients With Chronic Kidney Disease (KNOW-CKD). The primary outcome was a composite of extended major cardiovascular events (MACE) or all-cause mortality. Extended MACE (eMACE) included non-fatal cardiovascular events, symptomatic arrhythmia, and cardiac death. The secondary endpoints were separate outcome of eMACE, all-cause death, and adverse kidney outcome. We also evaluated predictive ability of hs-CRP for the primary outcome.

Results: The median hs-CRP level was 0.60 mg/L (IQR 0.2-1.7), and the mean eGFR was 53.6 ml/min/1.73 m^2. During the mean follow-up of 3.9 years, there were 125 (6.2%) eMACEs and 80 (4.0%) deaths. The primary composite outcome occurred more frequently in patients with higher hs-CRP level than in those with lower hs-CRP level. In multivariable Cox analysis after adjustment of confounders, there was a graded association of hs-CRP with the primary outcome. The HRs (95% CI) for hs-CRP of 1.0 to 2.99, and $\geq$ 3.0 mg/L were 1.37 (0.89-2.12) and 2.20 (1.36-3.56), compared with hs-CRP of $<$1.0 mg/L. In analyses of secondary outcomes, this association was consistent for eMACE and all-cause death; however, hs-CRP was not associated with adverse kidney outcomes. Finally, prediction models failed to show improvement of predictive performance of hs-CRP compared to conventional factors.

Conclusion: In Korean CKD patients, serum hs-CRP level was low and significantly associated with higher risk of eMACEs and mortality. However, a low serum hs-CRP level was not predictive of adverse kidney outcome, and the predictive performance of hs-CRP was not strong.

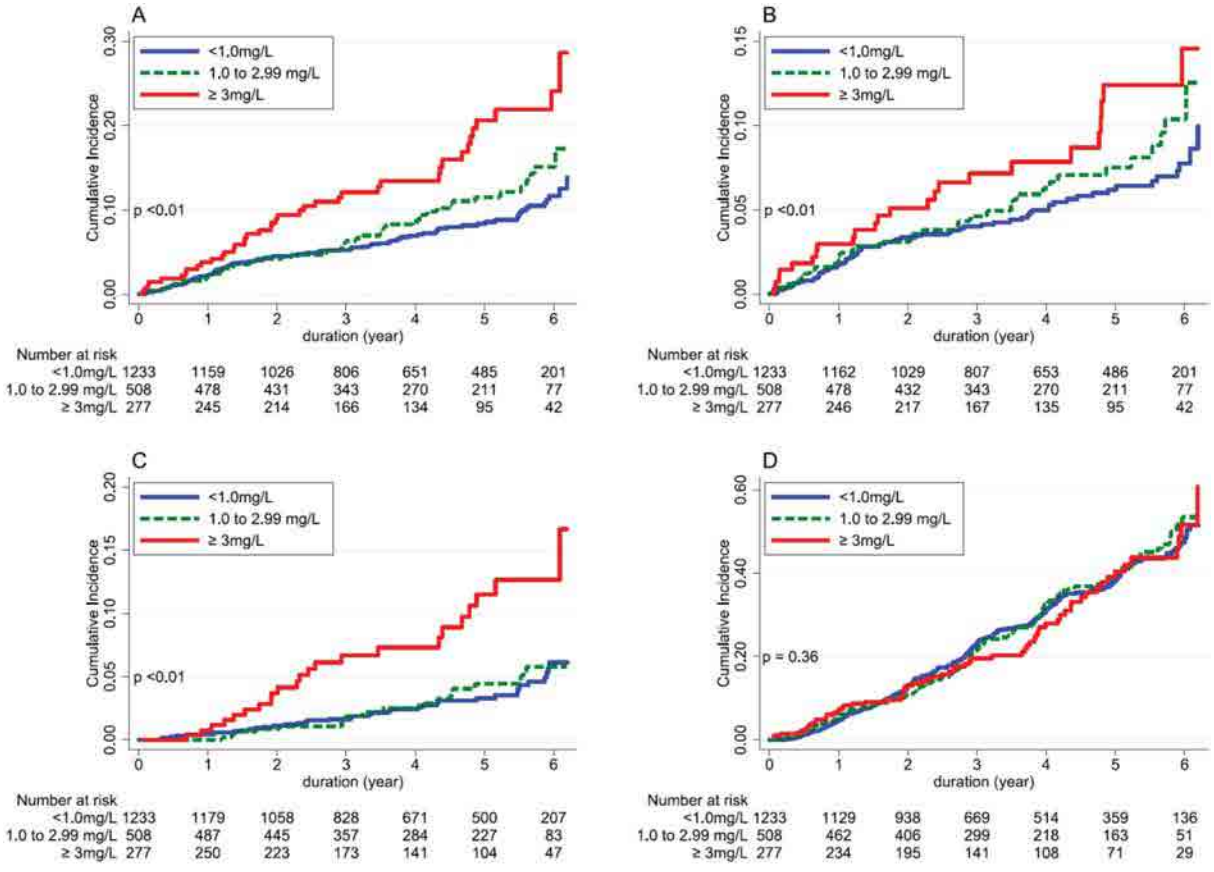


Figure 1. Cumulative incidence curve for (A) the primary and individual secondary outcomes of (B) eMACE, (C) all-cause mortality, and (D) composite renal outcome according to hs-CRP group.

Table 1. Hazard ratios for the primary composite outcome according to hs-CRP groups

	Model 1		Model 2		Model 3	
hs-CRP category	HR [95% CI]	*P*	HR [95% CI]	*P*	HR [95% CI]	*P*
<1.0 mg/L	1.00 [Reference]		1.00 [Reference]		1.00 [Reference]	
1.0 to 2.99 mg/L	1.28 [0.90-1.81]	0.16	1.31 [0.87-1.99]	0.20	1.37 [0.89-2.12]	0.15
≥3.0 mg/L	2.10 [1.46-3.03]	<0.01	2.24 [1.43-3.51]	<0.01	2.20 [1.36-3.56]	<0.01

Note: Model 1 without adjustment

Model 2 ; adjusted for age, sex, alcohol intake, smoking status, Charlson comorbidity index, socioeconomic status, educational status, BMI, SBP, use of renin-angiotensin system blockers, beta blockers, diuretics, and use of statin

Model 3 ; adjusted for Model 2 plus laboratory parameters such as eGFR, urine protein-to-creatinine ratio, HDL-C, serum calcium, serum phosphate, serum albumin, fasting glucose, and ferritin.

Abbreviations: BMI, body mass index; CI; confidence interval; eGFR, estimated glomerular filtration rate; HDL-C, High-density lipoprotein-cholesterol**;** HR, hazard ratio; hs-CRP, High sensitive C-reactive protein; SBP, systolic blood pressure

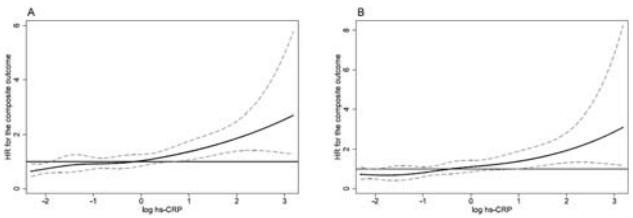


Figure 2. Cubic spline curve for the association between hs-CRP and the primary outcome. Univariable (A) and fully-adjusted restricted models (B) adjusted for age; sex; alcohol intake; smoking status; Charlson comorbidity index; socioeconomic status; educational status; use of renin-angiotensin system blockers, beta blockers, diuretics, and statins; baseline body mass index; systolic blood pressure; and laboratory parameters of eGFR, urine protein-to-creatinine ratio, HDL-C, serum calcium, phosphate, albumin, fasting glucose, and ferritin.

P0927 **THE IMPACT OF NUTRITIONAL EDUCATION ON PHOSPHORUS CONTROL IN HEMODIALYSIS PATIENTS**

Kariem Mohamed Salem[1], Mohammed Kamal Nassar[2], Doaa Hamed El-Sabakhawi[3], Ousama Elshahat[4], Malak Nabil Amin[1], Nagy Sayed-Ahmed[2], Hussein Sheashaa[6]

[1]Theodor Bilharz Research Institute, Nephrology Department, Cairo, Egypt, [2]Mansoura University, Mansoura Nephrology and Dialysis Unit (MNDU), Internal Medicine Department, Mansoura, Egypt, [3]National Nutrition Institute Cairo Egypt, Cairo, Egypt, [4]New Mansoura General Hospital, Nephrology Department, Mansoura, Egypt and [6]Urology and Nephrology Center, Mansoura University, Nephrology Department, Mansoura, Egypt

Background and Aims: Hyperphosphatemia is frequently encountered in hemodialysis patients and is an important risk factor of cardiovascular diseases. It is usually difficult to be managed by phosphate binders and hemodialysis. This study was carried out to assess the effect of nutritional education (NE) on the control of serum phosphorus level in hemodialysis patients.

Method: An open label, single center randomized controlled trial was conducted in the nephrology department, New Mansoura General Hospital, Egypt. One hundred hemodialysis patients were randomized into two groups; intervention Group (IG) (n=50) subjected to NE program for 3 months and Control group (CG) (n=50) received the usual care. Nutritional education was applied for the intervention group, by a trained renal dietitian, in the form of educational sessions, booklets, procures, audio visual teaching aids and patient-tailored counselling. Nutritional evaluation was done for all patients using dietary history, 24 hour diet recall sheet and malnutrition inflammation score (MIS) in addition to assessment of anthropometrics measurements and routine laboratory tests before randomization and at the end of the study.

Results: Three months after randomization, body mass index, waist circumference and midarm muscle circumference (MAMC) were significantly lower among IG versus the CG (p=0.04, 0.04 and 0.004 respectively). MIS score was significantly lower among the IG compared to the CG (p=0.02). Regarding laboratory tests, serum phosphorus level and calcium X phosphorus product were significantly lower among IG compared to the CG at the end of the study (p<0.001 and =0.04 respectively) with a percent change of serum phosphorus of -13.8 ± 21.41 after NE. The percentage of patients with hyperphosphatemia (> 5.5 mg/dl) were significantly lower in the IG at the end of study (p=0.04). Other laboratory tests including serum albumin, hemoglobin level, iron status and urea reduction ratio did not show any significant difference between both groups.

Table

	Intervention Group"n=50"	Control Group"n=50"	P
BMI:			
Before	25.3±4.21	26.8±2.98	0.21
After	24.6±3.85	26.1±3.11	0.04*
Waist circumference (cm):			
Before	101.02±19.12	103.00±18.68	0.21
After	97.34±18.68	105.80±20.45	0.04*
MAMC:			
Before	256.32±30.05	253.25±46.65	0.46
After	261.34±36.25	242.50±31.68	0.04*
MIS:			
Before	12.00±2.10	12.72±2.47	0.61
After	9.01±3.84	10.88±3.29	0.02*
Phosphorus (mg/dl):			
Before	4.38±1.60	4.35±1.24	0.46
After	3.56±0.95	4.50±1.40	<0.001*
Percent change of phosphorus:			
	-13.8 ± 21.41	8.43±35.89	0.006*
Calcium X phosphorus product:			
Before	37.77±15.59	36.93±12.27	0.38
After	33.78±12.04	38.13±16.27	0.04*
Serum phosphorus at the end of the study:			
< 5.5 mg/dl: n (%)			
>5.5 mg/dl: n (%)			
46 (92)			
4 (8)			
39(78)			
11 (22)			
0.04*			

Conclusion: NE applied to dialysis patients added to the control of hyperphosphaemia without exposing the patients to the risk of malnutrition, resulting from injudicious dietary restrictions.

P0928

PHYSICALLY ACTIVE PATIENTS IN HEMODIALYSIS: DO THEY HAVE A DIFFERENT EATING PATTERN AND BODY COMPOSITION?

Cristina Garagarza[1,2], Ana Valente[1], Cristina Caetano[1], Inês Ramos[1], Mariana Pinto[1], Telma Oliveira[1], Manuel Anibal A. Ferreira[3,4,5,6], Catarina Sousa Guerreiro[2]

[1]Nephrocare Portugal, Nutrition Department, 1750-233, Portugal, [2]Faculdade de Medicina da Universidade de Lisboa, Laboratório de Nutrição, Lisbon, Portugal, [3]Nephrocare Vila Franca de Xira, Dialysis Unit, Vila Franca de Xira, Portugal, [4]Dialverca, Dialysis Unit, Forte da Casa, Portugal, [5]NIDAN, Lisbon, Portugal and [6]Faculdade de Ciências Médicas, NOVA Medical School, Lisbon, Portugal

Background and Aims: Body composition influences outcomes in hemodialysis (HD) patients. These patients need to follow specific nutritional recommendations and physical activity has been highly encouraged. The aim of this study was to evaluate if there are differences in body composition and in dietary patterns between physically active and no physically active HD patients.

Method: This was a multicenter observational cross-sectional study where 582 HD patients from 38 dialysis centers were enrolled. Clinical parameters were recorded and body composition analysis was performed with the Body Composition Monitor®. Dietary intake and physical activity were obtained respectively from the Food Frequency Questionnaire and from the International Physical Activity Questionnaire, both validated for the Portuguese population. For the analysis, patients were divided in 2 groups: physically active (PA), if they follow the World Health Organization recommendations, and no physically active (NPA). T-student and non-parametric tests were performed to compare means and medians respectively. A $p<0.05$ was considered significant.

Results: Mean age was 67.8 ±17.7 years, 41.4% were female, 31.6 % had diabetes mellitus and median HD vintage was 65 (Interquartil range:43-104) months. PA patients were younger ($p<0.001$) and had a higher energy intake ($p= 0.017$), protein ($p=0.016$), total fat ($p=0.023$) and omega 3 fatty acids ($p=0.006$). Regarding body composition; higher total body water ($p=0.027$), intracellular water ($p=0.002$), lean tissue index ($p=0.002$), % lean tissue mass ($p=0.001$), body cell mass ($p=0.001$) and lower % fat ($p=0.003$) was found in PA patients. Urea pre-dialysis ($p=0.013$), albumin ($p=0.026$), creatinine ($p< 0.001$) and 6 months weight gain ($p=0.047$) were higher in PA patients whereas age-adjusted Charlson comorbidity index ($p<0.001$) was lower in these patients. No statistically significant differences were observed among other nutrients or parameters studied nor in body mass index, HD vintage or overhydration.

Conclusion: These data shows that, after comparing PA patients with NPA, differences were observed in body composition and clinical parameters related to a better nutritional status. Moreover, the PA patients̀ dietary intake was more approximated to the existing recommendations for this population, namely for energy and protein daily intake.

P0929 LOW PROTEIN DIET, BLOOD PRESSURE CONTROL AND NATRIURESIS IN PATIENTS WITH ADVANCED DIABETIC KIDNEY DISEASE AND HEAVY PROTEINURIA

Andreea Mihalache[1], Liliana Garneata[2], Carmen-Antonia Mocanu[3], Tudor Petrisor Simionescu[3], Gabriel Mircescu[3]

[1]"Carol Davila" Univesity of Medicine and Pharmacy, Cardiology Department, "Saint John" Emergency Clinical Hospital, Bucharest, Romania, [2]"Carol Davila" Univesity of Medicine and Pharmacy, Internal Medicina and Nephrology, "Dr C Davila" Hospital of Nephrology, Bucharest, Romania and [3]"Carol Davila" Univesity of Medicine and Pharmacy, Internal Medicine and Nephrology, "Dr C Davila" Hospital of Nephrology, Bucharest, Romania

Background and Aims: Recent data suggest the possibility to optimize blood pressure control by low protein diet (LPD) in patients with diabetic kidney disease (DKD). We aimed to assess the effects of a low protein diet (LPD) supplemented with keto-analogues on urinary sodium excretion and blood pressure control.

Method: Prospective, uni-center study with a total duration of 15 months.The study was conducted in a tertiary Nephrology Clinic and included a total of 92 diabetic patients with advanced CKD (eGFR < 30 mL/min) and heavy proteinuria (> 3 g/g creatininuria). Intervention consisted in a LPD (0.6 g/kg-day) supplemented with keto-analogues of essential amino acids with nutritional counselling and adjustment of anti-hypertensive therapy.

The primary efficacy parameter was proteinuria during intervention as compared to pre-enrolment. Blood pressure (BP), urinary sodium excretion, eGFR and blood glucose control were secondary end-points.

Results: Mean arterial pressure (MAP) decreased from baseline (Bs) to end of study (EOS) with -11 (-17 to -7) mmHg despite a reduction with 22% of patients needing antihypertensive medication. Independent predictors of a lower than median MAP (90mmHg) were a lower protein intake (HR 0.00 (0.00; 0.04; p=0.002), treatment with furosemide (HR 1.06 [1.06; 3.85]; p=0.03) but not with angiotensin-aldosterone system inhibitors (RAASi) [HR 0.17 (0.17; 0.90); p=0.03)] and was not influenced by natriuresis.

Natriuresis decreased from 130 (121-135) to 80 (71-86) mmol/day (p<0.0001). A lower than median natriuresis (100mmol/day) was directly related to proteinuria [HR 0.0003 (0.00; 0.004); p=<0.0001], eGFR [HR 0.0001 (0.00; 0.14); p=0.01] and to diuretic therapy [0.21 (0.05; 0.83); p=0.03] but not to protein intake.

Cardiovascular events were observed in 20% of patients and their occurrence was related to a lower MAP [0.97 (0.95; 0.99}; p=0.001]. No renal adverse were noted and the diet was nutritionally safe.

Conclusion: A low protein diet supplemented with ketoanalogues of essential amino acids on top of anti-hypertensive therapy (mostly loop diuretics) allows for a good control of blood pressure, unrelated to natriuresis in heavy proteinuric patients with advanced DKD.

P0930 **SERUM LEVELS OF OSTEOPROTEGERIN ARE ASSOCIATED WITH OBESITY IN CHRONIC KIDNEY DISEASE**

Yooju Nam[1], Seonyeong Lee[1], Hyung Woo Kim[1], Jae Hyun Chang[2], Tae-Hyun Yoo[1]

[1]Severance Hospital, Yonsei University, Department of Internal madcine, Seoul, Korea, Rep. of South and [2]Gil Medical Center, Gachon University College of Medicine, Department of Internal Medicine, Incheon, Korea, Rep. of South

Background and Aims: Osteoprotegerin (OPG), which is an osteoclastic inhibitory factor, is associated with type 2 diabetes mellitus, severity of vascular calcification, coronary artery disease, and chronic kidney disease. Obesity is a risk factor for diabetes, and cardiovascular disease, however there are few studies about the relationship between OPG and obesity, especially in patients with CKD. This study aimed to investigate association between OPG level and obesity in a large-scale prospective cohort.

Method: Among 2,238 patients with non-dialysis CKD enrolled in the KoreaN cohort study for Outcome in patients With Chronic Kidney Disease (KNOW-CKD), 1,970 patients who measured body mass index (BMI), waist circumference (WC) and OPG level were included in the analysis. Obesity were defined as having a BMI >25 kg/m2 and WC > 90 cm in male, > 85 cm in female.

Results: The mean age was 53.6 ± 12.2 years and 1,196 (60.7%) patients were males. At baseline, obesity by BMI, WC, and composite of BMI and WC were found in 814 (41.3%), 208 (26.9%) and 1,137 (57.7%) patients. A multivariate logistic regression model showed that log transformed OPG level was independently associated with the prevalence of obesity by BMI, WC, composite of BMI and WC (odds ratio [OR], 0.33; 95% confidence interval [CI], 0.16-0.65, P<0.001 and OR, 0.37; 95% CI, 0.18-0.75, P=0.006, and OR, 0.33, 95% CI, 0.16-0.69, P=0.003, respectively). Among patients without baseline obesity, 207 (19.3%) patients developed obesity by BMI, 202 (21.7%) by WC, and 194 (23.3%) by composite of BMI and WC. In the fully adjusted multivariable Cox models, risks of developing obesity by BMI, WC and composite of BMI and WC were significantly higher with increased level of OPG (hazard ratio [HR], 0.59; 95% CI, 0.38-0.92; P=0.019, HR, 0.63; 95% CI, 0.41-0.98; P=0.001).

Conclusion: We showed that serum OPG levels are associated with obesity in patients with non-dialysis CKD.

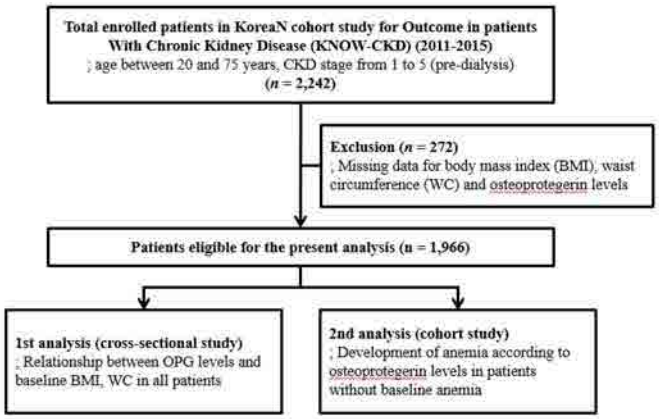


Table 1. Multivariable Cox regression model for the development of obesity

	Obesity by BMI		Obesity by WC		Obesity by composite of BMI and WC	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
OPG (per 1 log)	0.59 (0.38-0.92)	0.019	0.63 (0.41-0.98)	0.039	0.48 (0.31-0.74)	0.001

Note: OPG entered as a continuous form (log transformed)

Adjusted for age, sex, HTN, DM, BMI, SBP, eGFR, log transformed CRP, log transformed total cholesterol

* Variables are log transformed.

Abbreviations: OPG, osteoprotegrin; HTN, hypertension; DM, diabetes mellitus; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; eGFR, estimated glomerular filtration rate

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Figure:

P0931

PROTEIN ENERGY WASTING ON MORTALITY IN HEMODIALYSIS PATIENTS IN DIFFERENT SERUM ALBUMIN AND CHOLESTEROL LEVELS: A POPULATION STUDY IN TAIWAN

YEN-CHUNG LIN[1,2], Cai-Mei Zheng[2,3]

[1]Taipei Medical University Hospital, Division of Nephrology; Department of Internal Medicine, Taipei, Taiwan, R.O.C., [2]Taipei Medical University, Department of Internal Medicine; School of Medicine; College of Medicine, Taipei, Taiwan, R.O.C. and [3]Taipei Medical University Shuang Ho Hospital, Division of Nephrology; Department of Internal Medicine, New Taipei City, Taiwan, R.O.C.

Background and Aims: Protein-energy wasting, hypoalbuminemia and hypercholesterolemia play an important role in mortality among hemodialysis (HD) patients. How hypoalbuminemia and hypercholesterolemia influence the nutrition (normalized protein catabolic rate (nPCR)) related mortality among HD patients is still unclear.

Method: Using the nationwide data from the Taiwan Renal Registry Data System (TWRDS) between 2005 and 2012, we divided the HD patients into nPCR$<$1.2 and nPCR$\geq$1.2 groups. The relation of nPCR with three-year all-cause and cardiovascular mortality were determined. The influence of serum albumin (Alb) and cholesterol (TC) on nPCR related mortality were further analysed.

Results: Of 88,330 HD patients, 58122 (85.6%) patients were among nPCR $<$1.2 group and 30,208 (14.4%) in nPCR$\geq$1.2 group. Both all-cause and cardiovascular mortality were increased in nPCR $<$1.2 group. In the nPCR $<$1.2 subjects, Alb $\geq$ 3.7 was associated with increased risk of both overall and CV mortality (adjusted hazard ratio [HR]; 95% confidence interval [CI]: 1.16; 1.07–1.25, p=0.0003 and 1.15; 1.02–1.13, p=0.03) compared to the those with Alb $<$ 3.7 (adjusted hazard ratio [HR]; 95% confidence interval [CI]: 1.00; 0.90–1.08, p=0.74 and 1.15; 1.02–1.31, p=0.03). Further analysis revealed that in nPCR $<$ 1.2 and Alb $\geq$ 3.7 group, TC $\geq$ 150 had increased risk of both all-cause and CV mortalities (adjusted hazard ratio [HR]; 95% confidence interval [CI]: 1.14; 1.04–1.25, p=0.005 and 1.17; 1.02–1.35, p=0.026). No significant relation was found betweent mortality and nPCR among patients with Alb $<$ 3.7 irrespective of TC levels.

Conclusion: From this nationwide study, we found the close relation between dietary protein intake and mortality among those with Alb $\geq$ 3.7 and TC $\geq$ 150 group. Thus, we need to emphasize the importance of cholesterol control and dietary protein intake even among HD patients with normal serum albumin levels.

P0932

CLINICAL EVALUATION OF DISTURBANCES GASTROINTESTINAL TRACT IN PATIENT WITH CHRONIC KIDNEY DISEASE

Marufjon Salokhiddinov[1,1], Faxriddin Umarov[1]

[1]*Tashkent Medical Academy, Nephrology, Tashkent, Uzbekistan*

Background and Aims: Chronic kidney disease (CKD) affects gastrointestinal function and results in numerous adaptive and maladaptive responses. Disruption of the colonic microbiome and its attendant consequences - the loss of gut barrier integrity and increased generation of uremic toxins - has become well-recognized. However, less attention has been paid to characterizing the mechanisms behind the dysfunction of the upper gastrointestinal (GI) tract, largely owing to the difficulty of studying small bowel function in vivo

Method: The study included 72 people, of whom 52 made up the main group (CKD group) and 20 people - the comparison group (healthy volunteers without a kidney and cardiovascular disease). The main group consisted of patients with CKD stage 3 (RCGF creatinine 30-59ml / min / m2). The criterion for the inclusion of patients in the study, in addition to reducing the eGFR (estimated glomerular filtration rate), was the presence of arterial hypertension. The renal filtration function was the preserved comparison group and was reduced in the CKD group ($p < 0.001$), which served as a criterion for the inclusion of patients in the study. To assess the state of the gastrointestinal tract, all patients underwent an endoscopic study with an assessment of the acidity and evacuation function of the stomach

Results: The study showed that 75% of patients had complaints of a dry and unpleasant taste in the mouth, poor appetite, aversion to meat food, nausea. These symptoms were directly related to the level of eGFR. There was also a difference in the frequency and nature of the erosive, erosive-ulcerative, ulcerative lesions of the esophagus and formation of erosions and ulcers in patients with CKD occurred significantly more often against the background of chronic gastritis and with the severity of the inflammatory process with severe dyspeptic disorders. The frequency of erosive, erosive-ulcerative and ulcerative lesions of the mucous membrane of the upper GI tract among CKD patients was 72%, which were manifested by nausea, decreased appetite, heaviness in the stomach after eating, belching, heartburn, epigastric pain (in 50% of patients), meteorism, pain in the epigastric region during palpation. Endoscopic examination of patients with CKD noted the presence of erosive esophagitis, erosive gastritis, erosive bulb it, erosive duodenitis, mixed erosive lesions, erosive-ulcerative gastritis, gastric ulcer, ulcer of duodenal ulcer. Among them, the leading place is occupied by erosive gastritis and mixed erosive lesions, which account for 22% and 27%, respectively. Hemorrhagic erosions were more common in the stomach (41%) and 12: duodenal ulcer (47%) in patients with CKD

Conclusion: Erosive, erosive-ulcerative, ulcerative lesions of the upper gastrointestinal tract occur in 76% of patients with CKD. The frequency, nature, prevalence of these lesions are associated with the treatment of CKD - active (hemodialysis) and conservative, the stage of chronic renal failure. In patients with chronic renal failure, the endoscopic picture of erosive, erosive-ulcerative, ulcerative lesions of the upper GI tract is diverse.

P0933

PROTECTIVE EFFECT OF AN SGLT2 INHIBITOR ON ER STRESS THROUGH REDUCTION OF ECTOPIC LIPID DEPOSITION IN RENAL TUBULES IN OBESE MICE

Tomoaki Takata[1], Kohshiro Hosokawa[1], Takaaki Sugihara[1], Tomomitsu Matono[1], Masahiko Koda[1], Tsutomu Kanda[1], Masaya Ogawa[1], Ayami Ida[1], Yukari Mae[1], Marie Yamamoto[1], Takuji Iyama[1], Satoko Fukuda[1], Hajime Isomoto[1]

[1]Tottori University Faculty of Medicine, Division of Medicine and Clinical Science, Yonago, Japan

Background and Aims: Chronic kidney disease (CKD) is a major health issue closely related to metabolic syndrome. Although a potential link between ectopic lipid-induced ER stress and the progression of CKD has been suggested, the underlying mechanism has not yet been fully elucidated. SGLT2 inhibitors have been reported to be effective in reducing fat accumulation. However the effect on lipid-associated kidney disease remains unclear. The aim of this study was to investigate the role of ectopic lipid and ER stress in the development of CKD, and evaluate the efficacy of an SGLT2 inhibitor.

Method: FLS-ob/ob mice, a model that shows significant ectopic lipid deposition and closely imitate the pathophysiology of non-alcoholic steatohepatitis, were treated with vehicle or an SGLT2 inhibitor, Ipragliflozin (1 mg/kg body weight) for 12 weeks. Metabolic characteristics, histology of the kidney, ER stress and apoptotic signals were evaluated.

Results: Ipragliflozin significantly reduced the serum triglyceride level. Ectopic lipid deposition in renal tubules found in FLS-ob/ob mice was prevented by Ipragliflozin, accompanied by reduced interstitial fibrosis. Both GRP78, a master regulator or ER stress, and CHOP, a downstream mediator of ER stress, were significantly downregulated in mice treated with Ipragliflozin. Apoptotic signal in kidney tissue was also reduced.

Conclusion: Ipragliflozin improved the pathogenesis of CKD by reducing ER stress through preventing ectopic lipid deposition in the kidney. SGLT2 inhibitors may have therapeutic effect on lipid-associated kidney disease.

P0934

THE IMPACT OF HAEMODIALYSIS INITIATION ON CKD-ASSOCIATED MYELOID CELL DYSREGULATION

Sarah Cormican[1,2], Serika Diane Naicker[1], Denise Connolly[2], Gemma Prendergast[2], M. Conall Dennedy[3], Matthew Dallas Griffin[1,2]

[1]National University of Ireland, Galway, REMEDI, School Of Medicine, Galway, Ireland, [2]Galway University Hospitals, Saolta University Healthcare Group, Nephology Services, Galway, Ireland and [3]National University of Ireland, Galway, Discipline of Pharmacology, School of Medicine, Galway, Ireland

Background and Aims: Abnormalities of the myeloid immune cell lineages are well described in people with both Chronic Kidney Disease (CKD) and End Stage Renal Disease (ESRD). Increased numbers and proportions of the intermediate ($CD14^{++}CD16^{+}$) and nonclassical ($CD14^{+}CD16^{+}$) monocyte subsets and increased neutrophil numbers have been reported in both settings. These changes are one aspect of the chronic inflammatory state which exists in people with CKD and ESRD and which contributes to complications including cardiovascular disease and protein-energy malnutrition.

The effects of transition from advanced CKD to dialysis on myeloid cell populations has not been well studied. We investigated these changes by measuring major leucocyte population numbers and monocyte subset numbers and proportions in adults with Stage 5 CKD prior to and after haemodialysis initiation.

Method: Adults with stage 5 CKD and a non-emergent indication for dialysis initiation (in-centre haemodialysis) were recruited after informed consent. Blood samples were collected within the week prior to dialysis initiation and follow-up samples were collected prior to a dialysis session at one week and one month after haemodialysis initiation. Major leucocyte population numbers were determined by two-colour flow cytometric analysis of whole blood on an Accuri™ Flow Cytometer. Peripheral blood mononuclear cells were isolated and stained for multi-colour flow cytometric analysis on a Canto II™ flow cytometer. The absolute number of each monocyte subset/ml blood was calculated based on the above values.

Results: Ten individuals (six male, four female) with a mean age of 78 ± 6.4years were enrolled and completed all follow-ups. The mean eGFR was 9 ± 1.9ml/min at the time of haemodialysis initiation.

Total monocyte numbers had not changed after one month of haemodialysis (**Figure 1A**) ($3.6x10^5 \pm 1.6x10^5$cells/ml) compared to initiation ($5.2x10^5 \pm 3.2x10^5$, p=0.11). However, the proportion of nonclassical monocytes was markedly increased after one week of haemodialysis (16.8% (IQR 12.8-21.0%) compared to 11.2% (IQR 9.3-12.3%) at initiation, p=0.007) (**Figure 1B**). At one month the proportion of nonclassical monocytes was maintained (17.1% (IQR 14.5-20.5%)) but had not increased further compared to the one week timepoint (p=0.97). This proportionate change was not reflected in the absolute nonclassical count. There were no significant changes in the proportion of classical or intermediate monocytes.

Neutrophil numbers were reduced at one month ($3.6x10^6 \pm 1.3x10^6$cells/ml) compared to initiation ($4.8X10^6 \pm 1.6x10^6$cells/ml, p=0.04) (**Figure 1A**). Total lymphocyte numbers did not change significantly after dialysis initiation.

Conclusion: Haemodialysis initiation is associated with an increase in the proportion of nonclassical monocytes without significant increases in the absolute number of any monocyte subset. A reduction in total neutrophil number also occurs one month after dialysis initiation. It has been previously been shown that progression of CKD results in increasing abnormalities of the myeloid cell lineages. Here we have demonstrated that transition from advanced CKD to haemodialysis results in further modulation of myeloid cell numbers and myeloid cell subset proportions.

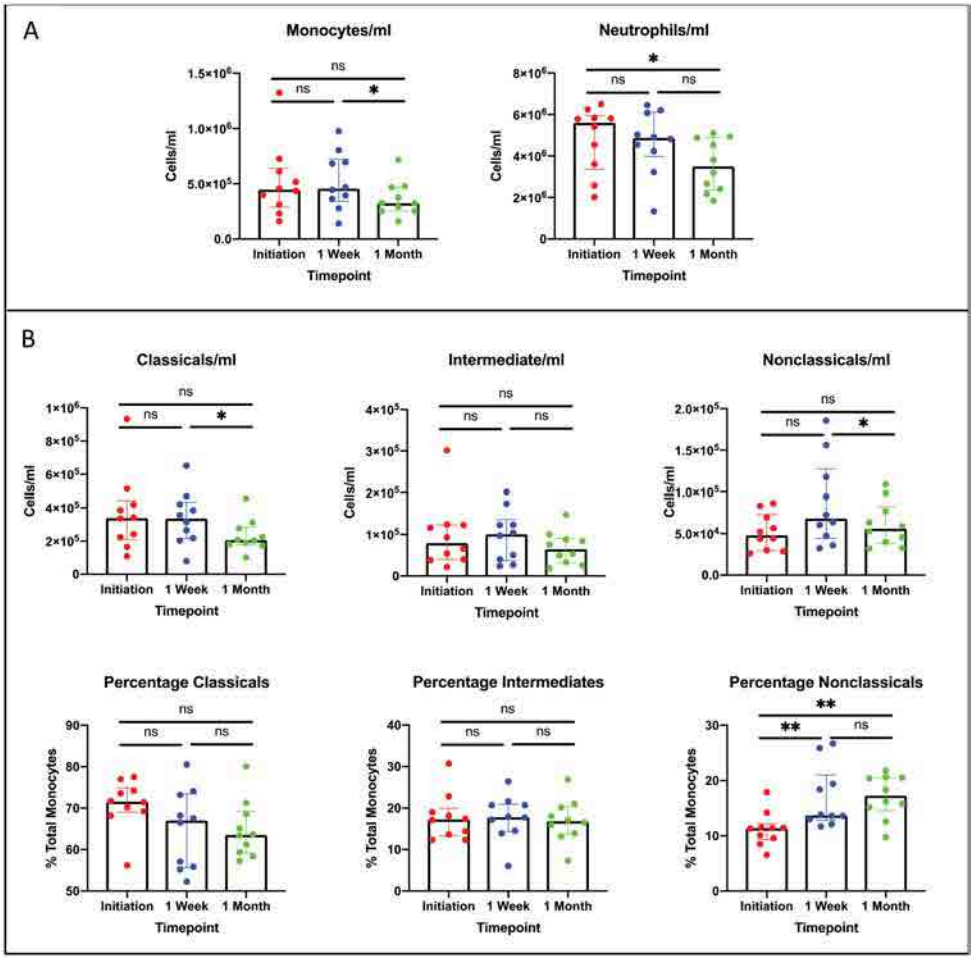


Figure 1: Changes in the number of total monocytes and neutrophils at one week and one month after dialysis initiation **(A)** and changes in the numbers and proportions of monocyte subsets at one week and one month after dialysis initiation **(B)**

P0935

ASSOCIATION OF DIETARY INTAKE WITH SERUM LEVELS OF PHOSPHORUS AND POTASSIUM IN KOREAN HEMODIALYSIS PATIENTS USING NEWLY DEVELOPED SEMI QUANTITATIVE FOOD FREQUENCY QUESTIONNAIRE(SEMI-FFQ)

Jung-Hyun Kim[1], Dong-Ryeol Ryu[2], Hyun-Jung Kim[3], Min-Sook Kyung[4]

[1]PaiChai University, Home Economics Education (Major of Food and Nutrition), Daejeon, Korea, Rep. of South, [2]Ewha Womans University, Internal Medicine, Korea, Rep. of South, [3]Ewha Womans University, College of Nursing, Korea, Rep. of South and [4]YonSei University, Food and Nutrition, Korea, Rep. of South

Background and Aims: Dietary intake patterns in hemodialysis (HD) patients in Korea are diverse and unique comparing with those of other countries. Hyperphosphatemia and hyperkalemia are closely related to intake of dietary phosphorus and potassium. Dietary intake of Korean HD patients was analyzed using newly developed semi-FFQ for Korean food in order to get the baseline data for improving a dietary management guide for Korean HD patients.

Method: We investigate the effects of consumed food on serum phosphorus and potassium levels of 128 HD patients(74 males and 54 females) in 6 tertiary referral hospitals using semi-FFQ consisting of 23 food meal items based on the Korean usual diets.

Results: The mean age was 59.7±11.6 years for males and 58.9± 9.3 years for females and the hemodialysis duration was 5.4±5.6 years for men and 5.4±3.9 years for women, respectively. Mean serum phosphorus level was 4.50±1.52 mg/dl and mean serum potassium level was 4.74±0.73 mEq/L. Hyperphosphatemia was found in 45.8% of the subjects, and hyperkalemia in 35.4%. Energy, protein and other nutrients intake were significantly lower than the recommended intakes for HD patients ($p<0.05$). Serum phosphorus levels showed positive correlation with intake of mixed grain meals ($p<0.05$). There was a significant difference in the daily intake frequency of cooked rice between males (2.5±0.76/day) and females (2.15±0.86/day)($p<0.001$). The noodle intake frequency also showed a significant difference between males (0.09±0.14/day) and females (0.04±0.06/day) ($p<0.001$). Serum potassium level showed positive correlation with intake of potatoes, high-potassium vegetables & fruits and Kimchi ($p<0.05$). There was a significant gender difference in the daily intake frequency of Kimchi between males (1.28±0.11/day) and females (1.07±0.99/day)($p<0.05$). In case of medium and high potassium vegetables & fruits, consumption was higher in females than in males ($p<0.05$). Intake of white rice showed negative correlation with serum potassium levels ($p<0.05$).

Conclusion: Intake of white rice meals rather than mixed grains meals is an important factor for maintaining normal serum phosphorus and potassium levels. Intake of potatoes, medium and high potassium vegetables & fruits is recommended to be reduced to less than three serving per week. Considering abundance of potassium and phosphorus in Korean food pattern, customized dietary management as well as medical treatment is essential in all HD patients.

P0936 INJURY OF NEUTROPHILS DURING HAEMODIALYSIS AND ITS INVOLVEMENT FOR DEVELOPMENT OF CHRONIC MICROINFLAMMATION

Masaaki Nakayama[1,2], Mariko Miyazaki[1,3], Tae Yamamoto[1], Taro Fukushi[3]

[1]Tohoku University, Research division of CKD and Dialysis Treatment, Sendai, Japan, [2]St Luke' International Hospital, Kidney center, Tokyo, Japan and [3]Tohoku University Hospital, Division of blood purification, Sendai, Japan

Background and Aims: Owing to the quality developments of membrane material and dislysis water, it is believed that the biocompatibility of haemodialysis (HD) system has been considerably improved. However, mortality and morbidities of dialysis patients have remained unacceptably high, which raises a question as to the biocompatibility improvement of current HD systems.

Method: Seventy-one patients on regular HD (male/female: 52/19, mean age: 63 years old, median HD duration: 19 months, HD session 3 times a week for 3 to 4 hours each by using high performance synthetic membrane) at Tohoku University Hospital were examined. Blood samples were obtained from all patients before and after the HD session, to measure followings; number of white blood cell fraction, and apotosis cells, plasma levels of following molecules; myeloperoxidase (MPO), pentraxin 3, angiogenin, lactoferrin, complement (C3a, C5a, C5b-9), and 17 cytokines. Apoptosis (positive for Annexin-V-FITC and negative for propidium iodide) was measured in 100,000 cells by flow cytometer, and plasma molecules were measured by ELISA kit.

Results: The main findings of this study were as follows (changes in the values after HD as compared to the pre HD); the significant decrease of leukocytes counts (neutrophil and lymphocyte), significant increases of apoptosis positive cells of leukocytes (neutrophiles and monocytes), significant increases of plasma MPO and pentraxin3 levels, significant decrease of angiogenin, and, no or only marginal changes in plasma pro-inflammatory cytokine levels and complement products. There was a significant positive correlation between the change in MPO and apoptosis before and after HD.

Conclusion: Bio-incompatibility of HD has remained a crucial issue even in the current systems. Among the several pathologies, process of neutrophile apoptosis accompanying MPO degranulation, may plays a central role for developing microinflammation. In this regard, change of plasma MPO could be a clinical marker for the biocompatibility of HD system. And in order to achieve better patients' outcomes, innovative HD systems which fully improve biocompatibility are needed.

P0937 **IMPACT OF TANNINS AS FOOD SUPPLEMENT IN A CKD POPULATION WITH RECURRENT URINARY TRACT INFECTIONS: PRELIMINARY DATA.**

Annalisa Noce[1], Giulia Marrone[1,2], Roberta Bernini[3], Margherita Campo[4], Manuela Di Lauro[1], Anna Pietroboni Zaitseva[1], Annalisa Romani[4], Nicola Di Daniele[1]

[1]University of Tor Vergata, Department of Systems Medicine, Rome, Italy, [2]University of Tor Vergata, PhD School of Applied Medical, Surgical Sciences, Rome, Italy, [3]University of Tuscia, Department of Agriculture and Forest Sciences (DAFNE), Viterbo, Italy and [4]University of Firenze, PHYTOLAB (Pharmaceutical, Cosmetic, Food Supplement, Technology and Analysis)-DiSIA, Sesto Fiorentino (FI), Italy

Background and Aims: Urinary tract infections (UTIs) are estimated to account for over 7 million office visits *per* year. UTIs are about 50 times more frequent in women than in men, however, in men the incidence steeply increases after 50 years of age for prostate involvement. UTI diagnosis is based on symptoms and urinalysis. Antibiotic therapy is often required in subjects with relapsing UTIs. Therefore, it would be useful to develop a therapeutic strategy based on natural active compounds, free from side effects (such as on renal function), that could counteract UTIs recurrence. For this purpose, tannins (TNs) could represent a valid therapeutic alternative. TNs are polyphenolic compounds known for their anti-inflammatory, antimicrobial and antioxidant effects. Recent studies highlighted how TNs intake can counteract UTI recurrence, improving the quality of life. The aim of our study was to evaluate the beneficial action of chestnut TNs administered as oral food supplement (OFS) in recurrent UTI patients.

Method: OFS was characterized by HPLC/DAD/MS analysis for its content in secondary polyphenolic metabolites and by Folin-Ciocalteau *in vitro* tests for its antioxidative and anti-free radical activity with stable radical DPPH•. For *in vivo* tests, 16 chronic kidney disease (CKD) patients (8 female and 8 males) who suffered from recurrent UTIs, were recruited. The OFS was administered in 2 cps/ day, for 9 weeks. Patients were evaluated at T0= baseline and T1= after 9 weeks of OFS treatment. We performed laboratory and urinary tests, and the quality of life (SCL-90R questionnaire) and body composition (bioimpedentiometry) assessment. All parameters and questionnaires were evaluated at T0 and T1. At the same time, oxidative stress (OS) and antioxidant defenses were monitored using CR4000 (FORD and FORT tests).

Results: HPLC/DAD/MS quali-quantitative analysis allowed for an in depth chemical characterization of the individual polyphenols present in the OFS: total tannins amount is 10.542mg/g, whereas total anthocyanins are 1.885mg/g. The Folin Ciocalteu assay results show a total polyphenols content of 68.7mg/g GAE; the antiradical activity by DPPH assay is 94% for a solution 0.519mg/mL of powder. The epidemiological features of the population were reported in Table 1 and it was divided into two subgroups, according to gender. Laboratory parameters were reported in Table 2. During the study, we observed a drop out of three female subjects because of gastrointestinal (GI) disorders (nausea, gastric heartburn). We did not find any significative change in body composition parameters after OFS treatment. We highlighted a significant reduction (Table 3) of ESR only in male patients (16,7 ± 2,2 mm/h *vs* 11,3 ± 1,5 mm/h, p=0,0062). The urinalysis, showed a significant reduction of leukocytes in both subgroups (male: 43,5 (1-450) n/uL *vs* 15 ± 5,7 n/uL p = 0,0391; female: 28,5 (1-990) n/uL *vs* 7 (1-91) n/uL p= 0,0625) but urinary bacterial flora, after OFS supplementation significantly decreased only in male subjects (428 ± 143,4 n/uL *vs* 34 (0- 450) n/uL p= 0,0156).

Interestingly we observed a significant reduction of OS parameters after OFS treatment as reported in Table 4. We also observed a reduction of the anxious and depressive components in male subjects in the SCL-90R questionnaire.

Conclusion: TNs seem to exert an antimicrobial action in a gender dependent manner, useful to counteract the recurrence of UTIs. OFS contains *Serenoa repens*, a substance with peripheral, antispastic and antiandrogenic action that could induce nausea and vomiting. Female patients dropped out for GI disorders had lower body weight and SR probably were overdosed for their body mass. In male subjects, the decrease in anxiety and depression at the end of the study, could be linked to the improvement of the urinary symptomatology. A randomized clinical trial conducted a larger population is needed to confirm these findings and explain the correlation with gender.

P0938 HEALTH-RELATED QUALITY OF LIFE IN A CHILEAN POPULATION OF DIALYSIS PATIENTS

Caterina Tiscornia[1], Francisca Peña[2], Lucia Del vecchio[3], Samuel Duran[4], Hugo Poblete[5], Valeria Aicardi[5]

[1]Universidad Finis Terrae, Santiago, Chile, [2]Universidad San Sebastian, Santiago, Chile, [3]Lecco, Nephrology and Dialysis, Lecco, Italy, [4]Universidad San Sebastian, Santiago, Chile and [5]Centro de Dialisis Sermedial, Valparaiso, Chile

Background and Aims: A growing number of patients treated with maintenance dialysis are older, frail and have functional impairment. In many instances, functional impairment is a more powerful predictor of adverse outcomes than traditional disease-based measures. The Kidney Disease Quality of Life 36-item short form survey (KDQOL-36) is widely used in dialysis patients; its scores are important predictor of outcome. Aim of the study is to evaluate the associations of KDQOL-36 scores with diabetes, dialysis modality, nutritional status and age in a cohort of dialysis patients from Chile.

Method: observational, multicenter, cross-sectional study performed in the region of Valparaiso, Chile. 207 adult patients on dialysis from more than 3 months (140 in HD, 67 in PD: mean age 58.9 ± 14.5 years with 37% >= 65 years, M/F 119/88) were asked to fill in the Spanish translation of the KDQOL-36 questionnaire (administered by a trained caregiver). The responses to the SF-36 questions were used to determine scores for the mental component summary (MCS), physical component summary (PCS), burden of kidney disease (BKD), symptoms and problems of kidney disease (SPKD), effects of kidney disease (EKD). The scores went from 0 to 100; the higher scores the better the quality of life. 50 was set as a cut-off level. Nutritional parameters were collected (BMI; mean 27.16 ± 4.7 kg/m^2, brachial muscular or fat areas (< 25th percentile for age and sex defined as malnourished). All the patients signed an informed consent.

Results: Overall, mean scores and percentage of patients with values <50 on the PCS, MCS, BKD, SPKD, and EKD subscales were 45.54 ± 18.82 (60.9%), 57.38 ± 19.41 (36.2%), 73.43 ±18.33 (65.2%), 79.03 ±11.59 (1.9%), and 36.02 ± 34.74 (11.6%), respectively. The mean score of the combination of MCS and PCS was 51.46 ± 16.77 (52.2%).

Compared to younger patients, those who were 65 or more years old had significantly higher score of EKD (79.91 ± 16.63 vs 69.59 ± 18.26, p<0.0001), with only 12% of older patients having a score below 50 (X^2 7.79, p=0.005); the other subscales did not differ significantly.

Ninety-one (43.5%) patients were diabetics. They were more likely of being older, having a higher BMI and lower signs of malnutrition (borderline significance). In comparison to non-diabetics, they had lower mean scores on BKD scale (30.42 ± 35.12 vs 40.4 ± 33.87, p=0.04) with a higher number having BKD scores < 50 (66/91 vs 69/116, X^2 3.82, p=0.035). Moreover, they were more likely of having scores < 50 for the SPKD and EKD subscales.

A significant reduction of the muscular and fat brachial areas (<25th percentile) were found in 88 (42.1%) and 49 (23.4%) of the patients, respectively. Mean scores of all subscales did not differ significantly between the groups of muscular and fat brachial areas.

The dialysis modality had a significant impact on some subscales. in comparison to PD, a higher number of HD patients had scores < 50 for BKD (X^2 18.24, p < 0.0001). On the other hand, PD patients were more likely of having lower MNS scores (X^2 5.69, p < 0.013) and of the combination of PCS and MCS subscales (X^2 12.82, p < 0.0001). Similar findings were obtained when analysing the scores as continuous variables.

Conclusion: This is the first formal evaluation of the performances of the KDQOL-36 questionnaire in a cohort of dialysis patients in Chile. Overall, the mean scores of PCS and EKD were well below the reference value of 50. General and kidney-related subscales were affected differently by age, dialysis modality and diabetes. In particular diabetic patients were more likely to perform poorly at kidney-related subscales, with no significant difference for general ones. Interestingly, dialysis modality had an impact on both BKD and MCS with opposite trends. The nutritional status seems to little affect patient quality of life.

P0939

THE ASSOCIATION BETWEEN MUSCULAR STRENGTH, MUSCLE MASS AND DEPRESSION IN KIDNEY TRANSPLANT RECIPIENTS: A CROSS-SECTIONAL ANALYSIS

Marijana Vučković[1], Hrvoje Raos[1], Katja Kovačević[2], Josip Orešković[2], Andrea Gelemanović[3], Marija Rogulјić[2,4], Josipa Radic[1,5]

[1]University of Split, School of Medicine, Split, Croatia, [2]University of Split, School of Medicine, Study of Dental Medicine, Split, Croatia, [3]MedILS - Mediterranean Institute for Life Sciences, Split, Croatia, [4]Study of Dental Medicine, Department of Oral Medicine and Periodontology, Split, Croatia and [5]University Hospital Center Split, Split, Croatia

Background and Aims: While kidney transplantation (Ktx) offers several advantages in terms of improved clinical outcomes and quality of life compared to dialysis modalities, depressive symptoms are still present in approximately 25% of patients, rates comparable to that of the hemodialysis population. Correlates of depressive symptoms include marital status, income, and kidney function, history of affective illness, malnutrition, and inflammation. The aim of this study was to evaluate possible correlations between nutritional status evaluated through body mass composition parameters, muscle strength and depression in kidney transplant recipients (KtR).

Method: 115 KtR, 61 (53 %) men and 54 (47 %) women, aged 59.3 (range 25 - 83) years were included. For each patient data about duration after Ktx, duration of dialysis before Ktx, age, gender, body weight and height were collected and body mass index (BMI) was calculated. Tanita MC780 Multi Frequency segmental body composition analyser was used to measure content of body fat, muscle mass, and visceral fat each study subject measured in kilograms (kg) and percentage (%.) Peripheral muscle strength of KtR was measured by using a standardized handgrip dynamometry protocol. The Beck Depression Inventory-Second Edition (BDI-II) was used as an indicator of the severity of depression.

Results: Out of all 115 KtR patients, according BDI-II score 25 (21.7 %) were depressed; 15 (13 %) had mild, 6 (5.2 %) moderate and 4 (3.5 %) severe depression. Significantly negative correlations between BDI-II scores (higher score – more depressive symptoms) and muscle mass (kg and %) was found (R=-0.205, P=0.032), (R=-0.278, P=0.003), respectively. Therefore, significantly positive correlations between BDI-II scores (higher score – more depressive symptoms), fat mass (%) and age was found (R=-0.24, P=0.012), (R=-0.231, P=0.013), respectively. Those KtR patients with more depressive symptoms (higher BDI-II score) had statistically lower muscle strength (R=-0.205, P=0.032). Significantly correlation between duration after Ktx and duration of dialysis before Ktx with BDI-II score was not found.

Conclusion: Prevalence rates for depression in this study is similar with previous reports and results have shown that depressive KtR patients were older and had significantly lower muscle mass and muscle strength and significantly higher fat mass content. Possible explanation for this findings might be that depression in KtR is associated with unhealthy behaviours including lower activity levels and worse dietary habits, which may in turn impact body mass composition parameters and upon transplant-related outcomes. Efforts to detect and treat depression should be a priority if one is to improve treatment and dietary adherence, quality of life, and outcomes in KtR.

P0940 **CLINICAL ASSOCIATION BETWEEN SEVERE INFECTION AND HYPOZINCEMIA IN INCIDENT PATIENTS ON HEMODIALYSIS**

Yosuke Saka[1], Akihisa Kato[1], Tomohiko Naruse[1]

[1]*Kasugai Municipal Hospital, Department of Nephrology, Japan*

Background and Aims: Hypozincemia can arise in patients with advanced chronic kidney disease (CKD) due to low protein intake and urinary or dialytic loss. Several studies have confirmed an association between hypozincemia and infection. Because infections comprise a major complication in patients with advanced CKD, we investigated whether hypozincemia is associated with infection risk in incident patients on dialysis.

Method: We prospectively analyzed 380 consecutive patients aged 20 years old or more who started hemodialysis between January 2013 and December 2018. Six patients who were receiving zinc supplementation at the time of the study were excluded. Serum zinc values were obtained at the time of dialysis initiation. We followed up the remaining patients after enrollment. The endpoint was severe infection defined as infection-related death or bacteremia confirmed by the detection of microorganisms in two sets of culture bottles. The patients were equally divided into groups with low, middle or high serum zinc concentrations. Data were analyzed using Kaplan-Meier curves and Cox hazards models. The local ethics committee approved this research. Informed consent was obtained from each individual participant included in the study.

Results: The rate of severe infection events over a follow-up of one year was the highest in the group with low zinc ($p = 0.030$). Cox hazards models adjusted for age, sex, diabetes mellitus, serum albumin and serum zinc, selected hypozincemia as an independent risk factor for severe infection events (HR, 10.76; 95% CI, 1.28–90.41; $p = 0.029$).

Conclusion: Hypozincemia is associated with risk of subsequent severe infection in incident patients on dialysis.

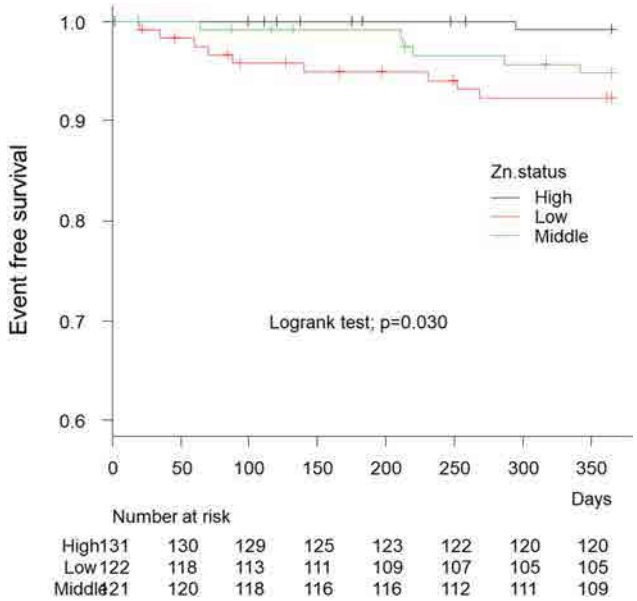


Figure:

P0941

HEALTHY K-RICH DIET IN CHRONIC KIDNEY DISEASE (CKD) PATIENTS USING SODIUM ZIRCONIUM CYCLOSILICATE (SZC) TO CONTROL HYPERKALEMIA: A FEASIBILITY STUDY (HELPFUL)

Carla Avesani[1], Zoya Lagunova[2], Helen Lönnberg[3], Gerd Faxen Irving[4], Abdul Rashid Tony Qureshi[1], Olof Heimbürger[1], Samiha Benedek[1], Bengt Lindholm[1], Peter Stenvinkel[1]

[1]Karolinska Institutet, Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden, [2]AstraZeneca Nordic Baltic, Medical Department, Södertälje, Sweden, [3]Karolinska Institutet, Clinical Nutrition, Karolinska University Hospital, Stockholm, Sweden and [4]Karolinska Institutet, Department of Neurobiology, Care Sciences and Society, Huddinge, Sweden

Background and Aims: Preventing hyperkalemia - a potentially fatal complication in advanced CKD - by prescribing diets low in K (=limited intake of healthy components such as vegetables, fruits, whole grains and nuts) leads to poor dietary quality. K-restricted unhealthy diets may affect quality of life, patient satisfaction with treatment, achievement of nutritional targets, and increase risk of obstipation, gut dysbiosis and progression of CKD. We designed a feasibility study to test if a low-protein healthy K-rich diet with fruits, vegetables, whole grains and nuts with concomitant use of new potassium binder (SZC) can be safely prescribed to patients with CKD stages 4 and 5 with hyperkalemia.

Method: A feasibility descriptive single arm open-label interventional trial lasting 6 weeks will enroll 36 CKD patients at the outpatient clinic with: age 18 - 85 years; glomerular filtration rate < 29 ml/min/1.73 m^2 and not on dialysis; serum K > 5.1 mmol/L or in previous use of sodium polystyrene sulfonate (SPS) to decrease serum K levels, and who develops hyperkalemia after SPS is ceased. Patients with serum K > 6.5 mmol/L and those likely to start dialysis within 2 months, with inflammatory bowel syndrome or with a history of hypokalemia (<3.0 mmol/L) will not be included. Primary end points will be changes in patient satisfaction with treatment, patient symptom list, and intake of energy and protein before and after the stabilization and healthy diet phase. Secondary outcomes will include changes in quality of life, obstipation and circulating gut microbiota-related uremic toxins. Intervention: In the first 3 weeks, representing *stabilization phase*, SZC will be prescribed to normalize serum K to 3.5 to 5.0 mml/L, and a diet with energy 25-35 kcal/kg/day and protein 0.6 to 0.8 g/kg/day and with low K content will be prescribed by a renal dietitian. At the end of the first 3 weeks, the patients will be instructed to keep the same content of energy and protein and initiate a healthy diet containing 3700 to 4000 mg/potassium for 3 weeks (*healthy diet phase*). In order to increase adherence, a food basket containing fruits, vegetables, whole grains, nuts, white meat, fish and eggs in amounts adequate for the patient and the family will be provided. Serum K will be monitored to promote serum K between 3.5 to 5.0 mmol/L and adjustments in the dose of SZC will be performed according to the drug label. Blood measurements, quality of life and intestinal obstipation questionnaires and measurements of nutritional intake will be performed in the beginning and at the end of the stabilization phase and again in the beginning and end of the healthy diet phase. Additionally, during stabilization and healthy diet phases, serum K will be measured every 72 hours until serum K is normalized and after that, once per week. The protocol is registered at www.clinicaltrials.gov (identifier NCT04207203).

Results: NA

Conclusion: This interventional feasibility pilot study will test the hypothesis that - with precautions aiming at reducing risk of hyperkalemia - a K-rich healthy diet in patients with CKD stage 4 may improve patient satisfaction with treatment and patient symptoms. Depending on the results, a larger randomized controlled longitudinal trial will be considered to investigate if K-rich diet in CKD stage 4-5 patients is safe and beneficial.

P0942 **HYPOXEMIA AND UREMIA INDUCE OXIDATIVE IMBALANCE IN ENDOTHELIAL CELLS.**

Andrea N Moreno-Amaral[1], Caroline Carvalho Silva[1], Gabriela Bohnen Andrade[1], Julia Monteiro[1], Nadja Grobe[2], Roberto Flavio Silva Pecoits Filho[1], Andréa E. M. Stinghen[3], Peter Kotanko[2,4]

[1]Pontifícia Universidade Católica do Paraná, PPGCS, Curitiba, Brazil, [2]Renal Research Institute, New York, United States of America, [3]Universidade Federal do Paraná, Curitiba, Brazil and [4]Icahn School of Medicine at Mount Sinai, New York, United States of America

Background and Aims: Intradialytic hypoxemia is associated with oxidative stress, endothelial dysfunction, inflammation, higher erythropoietin requirements, and higher all-cause hospitalization and mortality in hemodialysis (HD) patients (Meyring-Wosten, et al., 2016). The aim of the present study was to further expand our insights into the hypoxia-uremia axis by investigating the oxidative balance in endothelial cells (EC) under hypoxic and uremic conditions.

Method: Human umbilical EC were incubated with DMEM medium supplemented with 10% of fetal bovine serum (FBS; control) or with sera obtained from healthy subjects (S-CON) or HD patients (S-HD, 1:10), respectively, for 40 minutes, 4 hours, and 24 hours under normoxic (21% O_2) or hypoxic (5% O_2) conditions (Culture Chamber ProOx, Biospherix). EC were analyzed by flow cytometer (BD Accuri^{TM} C6 Plus) to assess a) intracellular production of reactive oxygen species (ROS, DCFH-DA probe, Abcam); b) reduced glutathione (GSH) content (ThiolTracker Violet probe, Thermo Fisher Scientific).

Results: S-HD increased intracellular ROS production at all time points compared to S-CON. Moreover, ROS production was higher under hypoxic conditions. ROS production declined after 24 hours. S-HD induced slightly higher GSH content when compared to S-CON in normoxia (Table 1).

Conclusion: In our in vitro experiments, hypoxia and uremia jointly favor EC oxidative imbalance. This effect is particularly pronounced after 4 hours. Translational studies are warranted to explore the clinical relevance of our findings.

Table:

	Baseline (of 100%): EC incubated in DMEM medium supplemented with 10% FBS + antibiotics					
	Normoxia (21% O2)				Hypoxia (5% O2)	
ROS production [%]	28.9±2.4				52.3±7.2	
GSH content [%]	8.4±1				8.1±0.8	
	Values after Incubation with S-CON or S-HD					
	40 minutes		**4 hours**		**24 hours**	
ROS production	**Normoxia**	**Hypoxia**	**Normoxia**	**Hypoxia**	**Normoxia**	**Hypoxia**
S-CON [%]	102±5.2	121±6.32&	102.5±7.3	109.2±9.2	34.2±7.3	50.5±14.5
S-HD [%]	130.7±8.7*	146.2±8.3*&	150±13.9*	190.3±37.6*	71.8±11.4*	94.8±19.3*&
GSH content	**Normoxia**	**Hypoxia**	**Normoxia**	**Hypoxia**	**Normoxia**	**Hypoxia**
S-CON [%]	8.9±1.3&	6.5±2.3	7.6±1.2	7.4±1.6	7.9±1.5	8.1±1.2
S-HD [%]	12.7±1.8*&	6.3±0.9	9.3±1.6*	9.8±1.8*	10.4±1.3*&	7.5±0.8

*p <0.05 compared to control for the same O_2 concentration. & p<0.05 normoxia vs hypoxia.

P0943

FAT MASS/FAT FREE MASS RATIO AS A CARDIOVASCULAR RISK FACTOR. SURVIVAL STUDY

Guillermina Barril[1], Angel Nogueira[1], Nuria Garcia[2], Paloma Sanz[3], Graciela Alvarez[1], Leydy Yohana Gil Giraldo[1], Patricia Muñoz[1], Martin Giorgi[1], Almudena Nuñez[1], Jose Antonio Sanchez Tomero[1]

[1]Hospital de La Princesa, Nephrology, Madrid, Spain, [2]Clinica Universitaria de Navarra, Nephrology, Pamplona, Spain and [3]Clinica Ruber Juan Bravo, Hemodialysis, Madrid, Spain

Background and Aims: Excess fat mass correlates with cardiovascular risk and if the increase in BMI is at the expense of fat mass it can increase mortality.

Aims- To evaluate the Fat Mass/Fat Free Mass ratio (FM/FFM)in 195 CKD patients and establish a correlation with nutrition-inflammation parameters, body composition and hand grip strenght

Method: We have studied 195 patients aged 67.01 ± 14.52 years, 126 (64.6%) men and 69 (35.4%) women. 41% in HD and 59% with advanced CKD. We have determined FM/FFM ratio using BIA monofrequency Bodigram Plus (Akhern) and hand grip stengh (baseline).We determine biochemical nutrition-inflammation parameters also.

Results: xRatio FM/FFM = 0.499 ± 0.2304, in men = 0.41 ± 0.16 and in women = 0.64 ± 0.26 (both less than published 0.57 men and 0.867 in women). Median 0.4558 and percentils (p) with cut-off points 0.3868 and 0.5574. In HD 31 in P1, 23 in P2 and 26 in P3. In advanced CKD 32 in P1, 41 in P2 and 42 in P3. Anova significant according to percentiles: SMI, age, TBW% BCMI, albumin, waist circunference, and Hand grip strenght.

Correlations

Men: FM / FFM ratio direct sig correlation with weight, AEC% and Trasferrin%, inverse with MIS, SMI, Na / K, BCM%, TBW%, IBW%, BCMI and right dynamometry. Do not continue with BMI, Phase Angle, Hb, lymphocytes, prealbumin, PCR.

Women: FM/FFM ratio direct sig correlation wih: weight, Na / k, BMI, prealbumin, CRP, MIS, inverse with: TBW. No sig: SMI, BCM%, EBW%, IBW%, MAMC, BCMI, Hb, hand grip strenght, lymphocytes or transferrin.

In the 24-month mortality study we found no significant differences in Kaplan Meier overall mortality using the 3 percentiles. They died 7/63 in P1, 1/64 in P2 and 8/68 in P3. If we make the union of 1 and 2 vs percentil3 we find significant differences in mortality between strata, especially in HD with Long Rank 0.05.

Conclusions:

1.-The FM /FFM ratio is a useful tool for diagnosis of sarcopenic obesity

2.-It correlates significantly with parameters of CRP (direct) inflammation, muscle strength (inverse) and CV risk (direct waist circumference and tricipital fold)

3.- In a survival study joining P1 + P2 vs P3 we found greater survival in P1 + P2, mainly in HD.

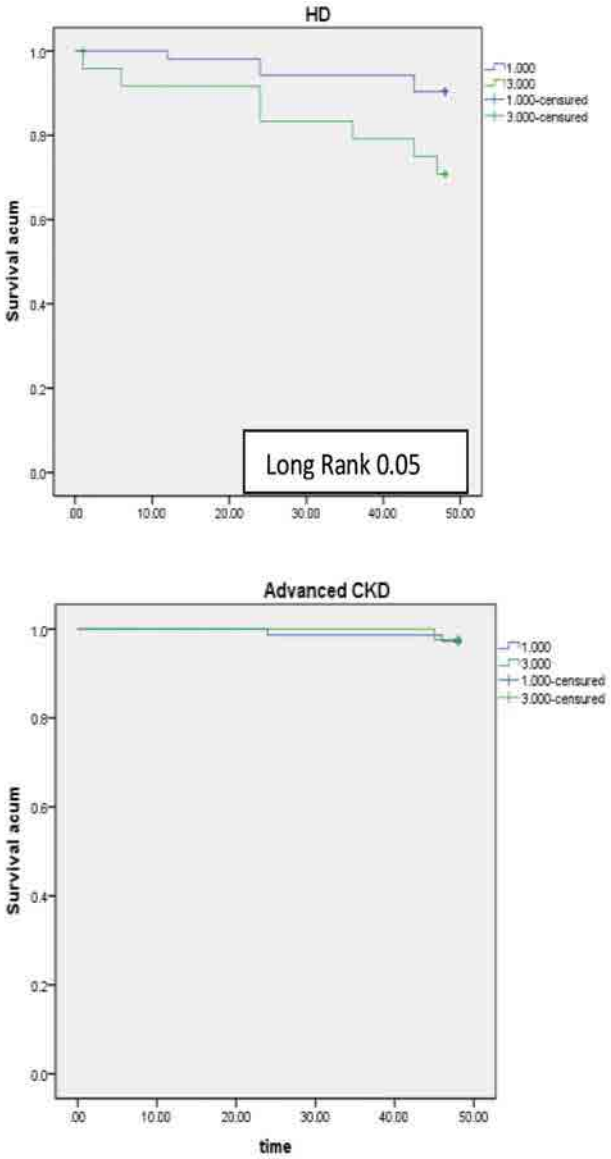


Figure: Kaplan Meier curves in HD and ACKD patients

P0944

UREMIC SARCOPENIA IN THE ELDER: PRELIMINARY RESULTS OF A PRECISION MEDICINE APPROACH IN A COHORT OF UREMIC PATIENTS

Rocco Baccaro[1,2], Wanda Lattanzi[3], Francesca Maria D'Ascenzo[1], Patrizia Silvestri[1], Giovanni Gambaro[4], Pietro Manuel Ferraro[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Nefrologia, Roma, Italy, [2]Università Cattolica del Sacro Cuore, Roma, Italy, [3]Università Cattolica del Sacro Cuore, Dipartimento di Scienze della Vita e Sanità Pubblica, Roma, Italy and [4]University of Verona, Renal Unit, Division of Nephrology and Dialysis, Department of Medicine, Verona, Italy

Background and Aims: Sarcopenia is defined as a chronic condition of "muscle failure", characterized by reduced muscular strength, mass and performance. End-stage renal disease (ESRD) and sarcopenia have several complications in common including inflammation, low sexual hormones, reduced levels of Vitamin D, and low satellite cells proliferation rate.

Sarcopenic and uremic patients have higher risk for fracture, cardiovascular events, cognitive impairment, low quality of life, hospitalization and death.

The European Working Group on Sarcopenia in Older People (EWGSOP2) 2019 guidelines standardize the diagnostic criteria and recommend a systematic approach for sarcopenia assessment.

The aim of our study is to evaluate the prevalence of sarcopenia in ESRD patients not yet on dialysis and to characterize their clinical, laboratory and behavioral features.

Method: This is a pilot cross-sectional study. ESRD patients expected to initiate replacement therapy (hemodialysis or peritoneal dialysis), age $\geq$60 years, free mobility and hemoglobin levels $\geq$9.5 g/dL were enrolled. Exclusion criteria were: use of steroids $>$3 months during the previous year, previous renal replacement treatments.

Enrolled patients were screened for sarcopenia following the three diagnostic criteria: muscle strength (through "handgrip strength" and "chair stand-up test"), muscle mass (with dual X-ray absorptiometry and bio-electrical impedance analysis), and muscle performance (with "4m gait speed test"). Clinical data were collected as well as anthropometric measures. Patients also underwent an abdominal ultrasound and a hematology, chemistry, urinary and inflammation laboratory panel. Finally, they filled questionnaires for sarcopenia identification (SARC-F), quality of life (SF-36), daily activity (ADL and iADL) and nutritional status. GFR was estimated according to CKD-EPI formula.

Results: We evaluated 9 patients (2 females and 7 males), mean age 72 $\pm$ 7 years, mean GFR 10.2$\pm$1.5 mL/min/1.73 m^2 (range 7.3, 11.8). 7/9 reported hypertension history, 4/9 were diabetic.

The prevalence of sarcopenia was 44% (4 patients) according EWGSOP2 criteria.

Table 1 reports diagnostic exam results from our cohort. Taking individually EGWSOP2 criteria 4 patients showed low muscle strength, 5 reached the threshold for a low DXA muscle mass while 3 patients had a low gait speed performance, marker for sarcopenia severity.

Compared with controls, sarcopenic patients (Table 2) showed a significantly lower handgrip strength (15.0$\pm$4.3 vs 23.0$\pm$6.7 Kg respectively, p-value 0.03), a lower but not significant appendicular lean mass (ALM) index normalized for squared height (European criteria) or for BMI (American criteria). Moreover, sarcopenic patients were more anemic (p 0.05), with a lower hematocrit (p 0.04).

Finally, SF36 questionnaire describes sarcopenic patients as more jaded about physical activity, with impaired social activity and higher bodily pain.

Conclusion: Sarcopenia has a complex and diversified background, and ESRD represents an important risk factor. Sarcopenic patients with ESRD might need more carefulness on daily activity, anemia management, physical functioning and muscle recovery.

Patient	Gender	HandGrip (Kg)	ALM/h²	ALM/BMI	Gait Speed m/s	Sarcopenic EWGSOP2	SPPB (max 12)
1	M	35,6	6,74*	0,90	1,00	No	10
2	M	19,1*§	5,74*	0,62§	0,45#	Yes	1
3	M	24,3*§	7,64	0,62§	1,15	Yes	8
4	F	21,7	6,15	0,59	1,33	No	8
5	M	26,1*	6,66*	0,73§	1,15	Yes	12
6	M	34,5	7,39	0,64§	0,92	No	7
7	M	30,7	6,49*	0,93	1,76	No	11
8	M	33,7	5,85*	0,83	0,77#	No	7
9	F	14,5*§	4,33*	0,42§	0,50#	Yes	3

Table 1: Diagnostic Data for study patients. * sarcopenic patients according to EWGSOP2 criteria; § sarcopenic patients according to FNIH criteria. # marks severe sarcopenic patients.

Figure:

P0945

STUDY PROTOCOL: ADIPOSE TISSUE CONTENT OF N-3 POLYUNSATURATED FATTY ACIDS AND THE RISK OF CHRONIC KIDNEY DISEASE

Bahram Hashemi[1], Erik Berg Schmidt[2], My Svensson[3], Søren Lundbye-Christensen[2], Christian Bork[2], Jeppe Hagstrup Christensen[1]

[1]Aalborg University Hospital, Nephrology, Aalborg, Denmark, [2]Aalborg University Hospital, Cardiology, Aalborg, Denmark and [3]Akershus University Hospital, Nephrology, Oslo, Norway

Background: Chronic kidney disease (CKD) is associated with life style diseases such as hypertension and type 2 diabetes. However the role of diet is not yet clearly defined for development of CKD.

Recent studies have shown that n-3 polyunsaturated fatty acids (PUFAs) may exert favourable effects on several processes that may inhibit the development and progression of CKD.

A gold standard biomarker for long-term intake and metabolism of n-3 PUFAs, is their content in adipose tissue; because these fatty acids are essential and not endogenously produced.

Aims: The primary aim of this study is to investigate the association of adipose tissue content of marine and plant-based n-3 PUFAs to the risk of incident CKD.

This study will also examine associations between the content of n-3 PUFAs in adipose tissue and the risk of main subtypes of CKD: Proteinuria with unknown cause, Hypertensive nephropathy, Glomerular diseases, Diabetic nephropathy and Chronic renal failure of unknown cause.

Method: In this case-cohort study based on data from the prospective Danish Diet, Cancer and Health cohort (DCH), information concerning diet and other lifestyle factors was obtained from 57,053 Danish men and women aged 50 to 65 years, using questionnaires and interviews. Anthropometric measurements were undertaken, and adipose tissue biopsies were taken from the buttocks of all participants at baseline.

The follow-up period was from December 1993 to September 2017. The outcome CKD is defined as having a diagnosis of one of the CKDs causes in the Danish National Patient Registry (DNPR). Cases of CKD will be identified and included together with a randomly drawn subcohort, representative for all participants of the cohort. Adipose tissue samples will be analyzed by gas chromatography in all incident CKD cases and in 5,000 randomly drawn participants from the whole cohort.

The outcome will be adjusted for age, sex, body mass index, physical activity, energy intake, alcohol consumption, fermented dairy products, education, smoking status, hormone replacement therapy and comorbidity.

The study is approved by the Danish National Committee on Health Research Ethics (N-20180074) and the Danish Data Protection Agency (2018-139).

Results: No results are available yet.

Conclusion: Our hypothesis is that the content of total n-3 PUFAs, as well as both marine and plant-based n-3 PUFAs, in adipose tissue is inversely associated with the risk of CKD and its subtypes.

P0946 **OXIDATIVE STRESS AND HEME METABOLISM IN RED BLOOD CELLS FROM HEMODIALYSIS PATIENTS**

Gabriela Ferreira Dias[1,2], Gabriela Bohnen[2], Nadja Grobe[1], Xia Tao[1], Roberto Pecoits-Filho[3], Peter Kotanko[1], Andrea N Moreno-Amaral[2]

[1]Renal Research Institute, New York City, United States of America, [2]Pontificia Universidade Catolica do Parana, Curitiba, Brazil and [3]Arbor Research Collaborative for Health, Ann Arbor, United States of America

Background and Aims: We have previously described that indoxyl sulfate promotes red blood cells (RBC) ROS generation through organic anion transporter 2 as well as NADPH oxidase activity-dependent and GSH-independent mechanisms (Dias et al., 2018). However, there is little information regarding pathways of antioxidant balance to protect RBC from extensive oxidative stress that occurs during hemodialysis (HD). Intracellular free heme is degraded by Heme Oxygenase 1 (HO-1), which is regarded as the major cytoprotective enzyme (Maines, 1988; Gozzelino et al., 2010). In the current study, we assessed HO-1 activity and ROS production in RBC from healthy subjects and hemodialysis (HD) patients before and after HD.

Method: Blood was drawn from 6 healthy individuals (CON-RBC) and 6 HD patients (HD-RBC) before (pre/HD-RBC) and after high flux HD (post/HD-RBC). Isolated RBC were stained with DCFH-DA (Abcam) for ROS measurements. To quantify HO-1, RBC were incubated with anti-HO-1 antibody (Abcam) and m-IgGκ BP-CFL 488 (Santa Cruz Biotechnology) as a secondary antibody. Samples were analyzed by flow cytometry.

Results: Our results show a 4-fold increase in ROS levels in pre/HD-RBC compared to CON-RBC. ROS levels were even further increased by 1.65-fold after HD treatment in post/HD-RBC (Figure 1). Both pre/HD-RBC and post/HD-RBC showed a similarly significant increase of 3.3-fold in HO-1 compared to CON-RBC. (Figure 1).

Conclusion: High levels of HO-1 may represent a defense against oxidative stress that occurs in ESKD and particularly during the HD session. Further research is needed to evaluate whether HO-1 overexpression could accelerate heme degradation and contribute to renal anemia.

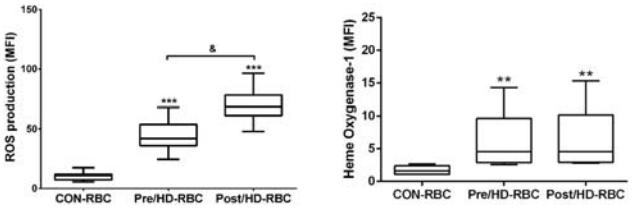


Figure 1. Reactive oxygen species (ROS) and Heme Oxygenase-1 levels in red blood cells (RBC) from healthy individuals (CON-RBC) and patients pre (Pre/HD-RBC) and post (Post/HD-RBC) hemodialysis. Data are shown as median and interquartile range of the Mean Fluorescence Intensity (MFI). ***$p<0.001$ and **$p<0.01$ represent the difference compared to CON-RBC. &$p<0.001$ represents the difference between pre- and post/HD-RBC.

P0947

DIETARY HABITS, BODY COMPOSITION AND MUSCULAR STRENGTH ARE CORRELATED TO COGNITIVE IMPAIRMENT IN DALMATIAN HYPERTENSIVE KIDNEY TRANSPLANT RECIPIENTS (KTRS)

Katja Kovačević[1], Josip Orešković[1], Marijana Vučković[2], Hrvoje Raos[2], Andrea Gelemanović[3], Marija Roguljić[1,4], Josipa Radić[2,5]

[1]University of Split, School of Medicine, Study of Dental Medicine, Split, Croatia, [2]University of Split, School of Medicine, Split, Croatia, [3]MedILS - Mediterranean Institute for Life Sciences, Split, Croatia, [4]Study of Dental Medicine, Department of Oral Medicine and Periodontology, Split, Croatia and [5]University Hospital Center Split, Split, Croatia

Background and Aims: Cognitive impairment is correlated with increased mortality of chronic kidney disease patients and hypertension is a well known comorbidity. While transplantation offers various general health and cognitive function improvement over dialysis, kidney transplant recipients (KTRs) still show greater cognitive impairment than healthy control. Researched pathophysiological mechanisms in KTR population include infection and immunosuppressive induced neurotoxicity. The aim of this study was to determine what impact do body composition, dietary habits and muscular strength have on cognitive impairment of hypertensive KTRs.

Method: 48 (52.17 %) men and 44 (47.83%) women, aged 59.7 (range25-83) years were included. For each patient data about duration after Ktx, duration of dialysis before Ktx, age, gender, body weight and height were collected and BMI and waist-to-height ratio (WHtR) were calculated. Tanita MC780 Multi Frequency segmental body composition analyser was used to measure content of body fat, muscle mass, and visceral fat each study subject measured in kilograms (kg) and percentage (%.) Peripheral muscle strength of KtR was measured by using a standardized handgrip dynamometry protocol. The Mini Mental State Exam (MMSE) was used as an indicator of cognitive impairment. Mediterranean Diet Serving Score (MDSS) questionnaire was used to determine adherence to Mediterranean Diet (MeDi) considering the consumption of foods and food groups per meal, day or week.

Results: Out of 92 KTR patients with hypertension, 5 of them scored $\leq$ 24 points on MMSE scale implying serious cognitive dysfunction. Mean score of MMSE was 28.2, (range 22-30) Regarding MDSS score, 11 patients scored $\geq$ 16 meaning highest adherence, while 67 KTRs scored $<$ 16 meaning low adherence to MeDi, (results range 2-18) . Positive correlations were found between MMSE score (higher score meaning better cognitive functioning) and MDSS score (higher score implying better adherence to MeDi)(R=0,282, p=0,012), consuming 1-2 portions of fruits(R=0,266,p=0,016) or $\geq$ 2 portions of vegetables (R=0,241,p=0,03) per main meal, skeletal muscle mass (%) (R=0,278, p=0,008), peripheral muscular strength(R=0,325,p=0,003) and fat free mass (kg)(R=0,212,p=0,045). On the other hand we found statistically significant negative correlation between MMSE score and WHtR (R=-0,255, p= 0,023) . as well as PWV(R=-0,244, p=0,022).

Conclusion: Cognitive impairment correlations in this study are similar to ones in general population specially regarding Mediterrranean diet and muscle mass . Possible explanation of positive MeDi impact on cognitive function in KTRs could be its low phosphate intake which prevents vascular calcification and negative effects of hyperparatiroidism. Although benefits of MeDi in CKD patients can be argued due to high pottasium levels, after kidney Tx it should not be an obstacle anymore. These results suggest that lifestyle interventions such as following MeDi, building more muscle and reducing fat could provide hypertensive KTR patients with longer preservation of cognitive function.

P0948

ASSOCIATION OF PHASE ANGLE WITH NUTRITION, MORTALITY, MAJOR ADVERSE CARDIOVASCULAR EVENTS AND SARCOPENIA IN MAINTENANCE HEMODIALYSIS PATIENTS.

Eunjin Bae[1], Tae Won Lee[1], Ha Nee Jang[2], Hyun Seop Cho[2], Hyun-Jung Kim[2], Se-Ho Chang[2], Dong Jun Park[1]

[1]Gyeongsang National University Changwon Hospital, Internal medicine, Changwon, Korea, Rep. of South and [2]Gyeongsang National University Hospital, Jinju, Korea, Rep. of South

Background and Aims: Nutrition has been consistently important in end stage renal disease patients. However, it is difficult to obtain adequate nutritional status while avoiding fluid overload, hyperphosphatemia and hyperkalemia in hemodialysis patients. In addition, there is no golden standard for diagnosing protein energy wasting (PEW) in maintenance hemodialysis patients. We studied the clinical significance of phase angle using bioelectrical impedance analysis (BIA), one of the PEW diagnostic tools, to predict various clinical outcomes in maintenance hemodialysis patients.

Method: We retrospectively enrolled patients who received hemodialysis for more than 3 months from 2016 to March 2019, excluding patients had active cancer, or died within 30 days, had no BIA data. We evaluated the factors related phase angle and the role of phase angle as predictors of all-cause mortality and major adverse cardiovascular events (MACE), sarcopenia.

Results: Of 191 patients, 63.4% were men, mean age was 64.2 ± 12.4 years, mean body mass index (BMI) was 23.8 ± 6.9 kg/m2, and the most common underlying disease were hypertension and diabetes mellitus. Lower phase angle group (phase angle ≤4°) patients had older age, higher portion of women, malnourished, and history of coronary artery disease (CAD) than higher phase angle group (phase angle >4°) patients. Phase was significantly related with nutritional parameters. During a median follow up of 16.7 months, 14.1% (n=27) patients experienced a MACE, 11.0% (n=21) patients died. In multivariate Cox analyses, lower phase angle, higher CRP level and history of CAD were significantly related with all-cause mortality even after adjustment for covariates. However, phase angle was not significantly associated with MACE and sarcopenia.

Conclusion: In maintenance hemodialysis patients, phase angle was significantly related to mortality as well as nutritional status, but MACE and sarcopenia were not. Clinicians should be careful to find and treat correctable factors with low phase angle and high CRP level in maintenance hemodialysis patients.

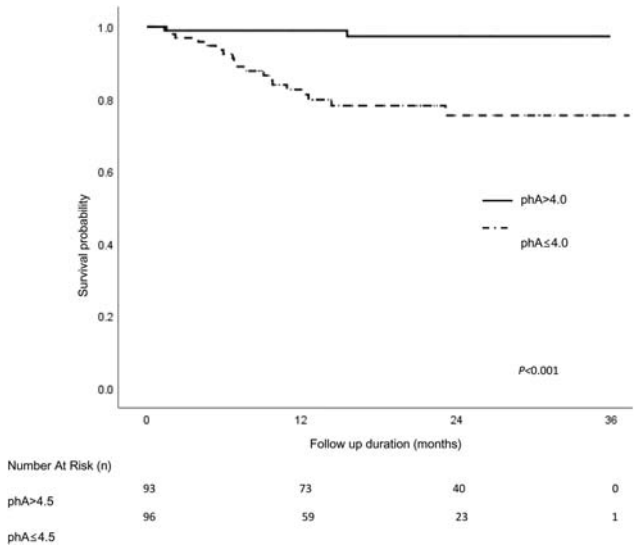


Figure:

P0949 EFFECT OF DIETARY PHOSPHORUS RESTRICTION ON FIBROBLAST GROWTH FACTOR,KLOTHO AND BODY COMPOSITION IN CHRONIC KIDNEY DISEASE PATIENTS

Trisha Sachan[1], Anita Saxena[1], Amit Gupta[1]

[1]*SGPGIMS, Nephrology, Lucknow, India*

Background and Aims: Changes in dietary phosphorus regulate serum FGF-23, parathyroid hormone, 1,25(OH)(2)D and Klotho concentrations . Cardiovascular disease (CVD) is the principal killer of patients with chronic kidney disease and hyperphosphetemia is a potent risk factor it. Of many causative factors for CVD in CKD, dietary interventions involving restriction of dietary phosphorous intake can help reduce onset of CVD at early stages of CKD with other corrective measures. Muscle wasting is a consequence of uremic syndrome which alters body composition. The aim of the study was to study effect of dietary phosphorous restriction on FGF-23, iPTH, Klotho, 1,25(OH)(2)D and body composition in chronic kidney disease patients.

Method: This is a longitudinal study with 12 months intervention, approved by Ethics Committee of the institute. A total 132 subjects were recruited (66 healthy controls, 66 CKD patient. of 66 patients 33 were in CKD stage 1 and 33 in stage 2. GFR was calculated with the help of MDRD formula. Biochemical parameters of subjects were evaluated at baseline, 6 and 12 months along with the anthropometric measurements (body weight, height, mid upper arm circumference (MUAC), and skin folds). Three days dietary recall was taken to evaluate energy, protein and phosphorous intake. CKD patients whose dietary phosphorous intake was more than 1000 mg/day, were given intense dietary counseling and prescribed dietary modifications by restricting dietary phosphorous between 800-1000 mg/day.

Results: The mean age of controls and patients was 37.01 ± 9.62 and 38.27 ± 12.06 and eGFR of 136.94 ± 11.77 and 83.69 ± 17.37 respectively. One way ANOVA showed significant difference among controls and the study groups in hemoglobin ($p<0.001$), s albumin ($p<0.001$), FGF-23 ($p<0.001$), klotho ($p<0.001$), urinary protein ($p<0.001$) and Nephron Index ($p<0.001$).The mean energy intake ($p = 0.001$) and dietary phosphorous intake ($p<0.001$) of the CKD patients decreased significantly with the decline in the renal function along with the anthropometric measures i.e. BMI ($p = 0.041$),WHR ($p = 0.015$) and all four skin folds ($p<0.001$). On applying Pearson's correlation, eGFR correlated negatively with urinary protein (-0.739, 0.000), FGF-23 (-0.679, 0.000) and serum phosphorous (-0.697, 0.000) and positively with klotho (0.872, 0.000). FGF-23 correlated negatively with klotho (-0.742, 0.000). Dietary phosphorous was found to be positively correlated with urinary protein (0.496, 0.000), serum phosphorous (0.680, 0.000) and FGF-23 (0.573, 0.000) and negatively with Klotho (-0.602, 0.000). Nephron index revealed a positive correlation with eGFR (0.529, 0.000). Urinary protein correlated negatively with klotho (-0.810, 0.000). A multiple linear regression was run to predict eGFR from anthropometric variables such as BMI, WHR, MUAC, skin folds thickness and handgrip strength. All anthropometric variables predicted decline in eGFR ($p<0.05$, $R^2 = 0.223$). At 6 and 12 months; repeated ANOVAs analysis showed a statistically significant difference in serum creatinine ($p=0.000$), serum phosphorous ($p=0.000$), FGF-23($p=0.000$) and klotho ($p=0.000$).

Conclusion: Elevated levels of FGF-23 and decreased Klotho levels, with the moderate decline in renal function improved with the restricted phosphorous diet at 6 and 12 months emphasizing the importance of phosphorus restriction at an early stage.

P0950

EFFECT OF THYROID HORMONE TREATMENT ON RENAL REABSORPTION OF GLUCOSE IN ALLOXAN-INDUCED DIABETIC RATS

Gireesh Dayma[1]

[1]*Manipal University Jaipur, Basic sciences, Jaipur,, India*

Background and Aims: The thyroid hormone (TH) plays an important role in glucose metabolism. Recently, we showed that the TH improves glycemia control by decreasing cytokines expression in the adipose tissue and skeletal muscle of alloxan-induced diabetic rats, which were also shown to present primary hypothyroidism. In this context, this study aims to investigate whether the chronic treatment of diabetic rats with T3 could affect other tissues that are involved in the control of glucose homeostasis, as the liver and kidney.

Method: Adult male Wistar rats were divided into nondiabetic, diabetic, and diabetic treated with T3 (1.5 ?g/100 g BW for 4 weeks). Diabetes was induced by alloxan monohydrate (150 mg/kg, BW, i.p.). Animals showing fasting blood glucose levels greater than 250 mg/dL were selected for the study.

Results: After treatment, we measured the blood glucose, serum T3, T4, TSH, and insulin concentration, hepatic glucose production by liver perfusion, liver PEPCK, GAPDH, and pAKT expression, as well as urine glucose concentration and renal expression of SGLT2 and GLUT2. T3 reduced blood glucose, hepatic glucose production, liver PEPCK, GAPDH, and pAKT content and the renal expression of SGLT2 and increased glycosuria.

Conclusion: Results suggest that the decreased hepatic glucose output and increased glucose excretion induced by T3 treatment are important mechanisms that contribute to reduce serum concentration of glucose, accounting for the improvement of glucose homeostasis control in diabetic rats.

P0951

THE DIETARY TREATMENT EFFECTIVENESS IN HEMODIALYSIS PATIENTS WITH DIABETES MELLITUS TYPE 2 AND FEATURES OF PROTEIN-ENERGY WASTING

Nataliia Mikhailova[1], Svetlana Tishkina[2], Valentin Ermolenko[3], Anna Pushkina[4], Andrey Kertsev[5]

[1]Russian Medical Academy of Continuous Professional Education, Nephrology, Moscow, Russia, [2]Moscow City Clinical Hospital №1 n.a. N.I.Pirogov, Hemodialysis, Moscow, Russia, [3]Russian Medical Academy of Continuous Professional Education, nephrology, Moscow, Russia, [4]OOO Fespharm Company, Hemodialysis, Moscow, Russia and [5]Moscow City Clinical Hospital № 1 n.a.N.I. Pirogov, Hemodialysis, Moscow, Russia

Background and Aims: The percentage of patients receiving RRT for ESRD secondary to diabetes mellitus (DM) is equal to 20-30% nowadays and is trending upward. Unfavourable changes in nutrition and body composition is highly prevalent in patients with chronic kidney disease (CKD) undergoing dialysis. DM type 2 (DM2) coupled with CKD is an additional factor for nutrition abnormalities in dialysis patients due to more prominent inflammatory status and insulin resistance. Resting energy expenditure is significantly higher in hemodialysis patients with DM2 than in those without it. Daily energy intake as usual is substantially less than required in the most dialysis patient, suggesting that patients could develop protein-calorie wasting and sarcopenia. The aims of our study were to compare of nutritional status in hemodialysis patients with and without DM2 and to treat revealed nutritional abnormalities by correction of the protein and energy intake.

Method: 79 hemodialysis patients (aged 50 to 70 years) were divided in two groups: 40 with DM2 and 39 without DM2. The groups didn't distinguish by age, gender, comorbidity, dialysis duration and adequacy. In the DM2 group there were no patients with severe diabetes complications or decompensation. All patients kept a 3-days food diary for assessment of protein and other nutrients and energy intake. The examination, which included anthropometry, measurement of body composition by bioimpedance analysis, biochemical parameters (serum albumin, transthyretin, C-reactive protein (CRP), interleukins 1 and 6 (IL1 and IL6), advanced glycation endproducts (AGE)), was performed at baseline, and then after 6 and 12 weeks of the dietary treatment. The pattern of the diet for every patient was based on the individual parameters of nutrient and energy intake obtained from the food diary. The aim of the diet was to make good the deficit of protein and energy intake.

Results: Baseline BMI and degree of abdominal obesity were significantly higher in DM2 group, but lean mass (LM), hand grip strength and gait velocity were significantly less. The significantly more decreased level of transthyretin was identified in DM2 group. Levels of AGE and CRP were not different between the groups, but were twice higher of normal range. IL6 was significantly higher in DM2 group. Protein and energy intake were under dietary recommendations for dialysis patients in DM2 group. We identified positive association between protein intake and levels of albumin and transthyretin and negative with IL1, IL6 and AGE in patients with DM2. In patients without DM2 we revealed negative correlation between LM and CRP. The dynamic of the main anthropometric and biochemical parameters are represented in the table.

	DM2 +			DM2 -		
	baseline	6 week	12 week	baseline	6 week	12 week
Mean protein intake (g/kg/d)	0,96	1,10	1,50*	1,32	1,51	1,20*
Mean energy intake (kkal/kg/d)	23,6	30,0	31,0*	36,1	34,6	37,0
Lean mass (%)	35	35,5	37	49	49	50
Transthyretin (mg/l)	170,85	189,05	193,04*	186,13	213,06	218,46*
IL-6 (pg/ml)	5,7	5,4	4,1*	3,5	3,6	3,7
CRP (mg/l)	10,3	10,0	5,4*	9,1	10,0	6,2*
AGE (pg/ml)	64.9	64,7	50,6*	71,7	64,3	64,2*

Conclusion: A degree of persistent inflammation and sarcopenia more prominent in hemodialysis patients with DM2. Absence of appetite due to inflammation is a probable cause of low protein and energy intake in those patients. Balanced diet based on individual nutritional requirements can effectively improve nutritional status of the dialysis patients with DM2 and decrease inflammation.

P0952 **NEUTROPHIL GELATINASE - ASSOCIATED LIPOCALIN LEVEL AS A MARKER OF MALNUTRITION IN HEMODIALYSIS PATIENTS**

Alaa Sabry[1,2], Rasha Mahmoud[3], Shimaa Alsaody[3]

[1]Faculty of Specific Education Mansoura - University, Egypt, [2]MANSOURA UNIVERSITY, FACULTY OF MEDICINE, Egypt and [3]MANSOURA UNIVERSITY, Egypt

Background and Aims: Among hemodialysis patients, malnutrition is a common health problem, it is a marker of poor prognosis in these patients, associated with increased risk of hospitalization and mortality. NGAL is an iron transporting factor which increases in the serum in acute and chronic kidney disease. The aim of our study is to assess the use of NGAL as a marker of malnutrition in patients with stage 5 CKD maintained on hemodialysis.

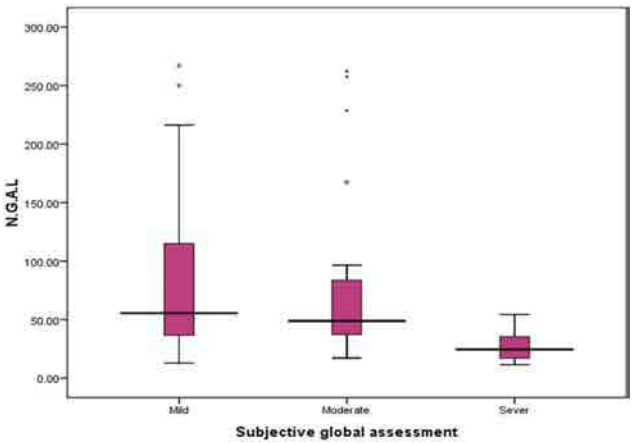
Method: This is a cross-sectional study of 80 regular hemodialysis (HD) patients (51 males and 29 females). All cases of this study were subjected to: Anthropometric measurements . Biochemical measurements: Neutrophil Gelatinase-associated Lipocalin Level in blood using commercially available ELIZA kits, Serum albumin, Blood urea, Complete blood count, Serum electrolytes .

Results: According to the result we found in our study 100% of CKD having malnutrition according to SGA, MIS and our data however most of our patients are mild malnutrition.

We found also a significant decrease in some anthropometric parameters including BMI, fat mass, TSF, MAC, MAMC and MAMA with advanced malnutrition in hemodialysis patients. In this study, we use Twenty-four hours dietary recall and we found most of patients were with low protein (96.2%) and calorie (68.8%) contents. Dialysis adequacy (Kt/V) can affect the nutritional status of patients Kt/V was adequate in all malnutrition groups. These findings are consistent with an earlier report in which HD patients with Kt/V>1.4 had a significantly higher rate of malnutrition than patients with Kt/V ≤1.4. in this study NGAL serum levels were significantly (P=0.018) reduced with the severity of malnutrition. In this study, Spearman correlation analysis revealed that NGAL serum levels were significantly correlated with SGA (r =o,247 P =0.027) and albumin serum levels (r =0.402, P <0.001).

NGAL serum levels were significantly (P=0.018) reduced with the severity of malnutrition. Using ROC curve analysis, NGAL serum levels had a good ability (AUC=0.845) to predict severe malnutrition with good sensitivity (83.3%) and specificity (78.4%).

Conclusion: NGAL is well correlated with other standard markers used routinely in assessment of nutritional status of hemodialysis patients. Patients with high NGAL levels were closely related to good nutritional status. Its serum levels had a good diagnostic power for severe-malnourished patients, as it helps us for early prediction to malnutrition.



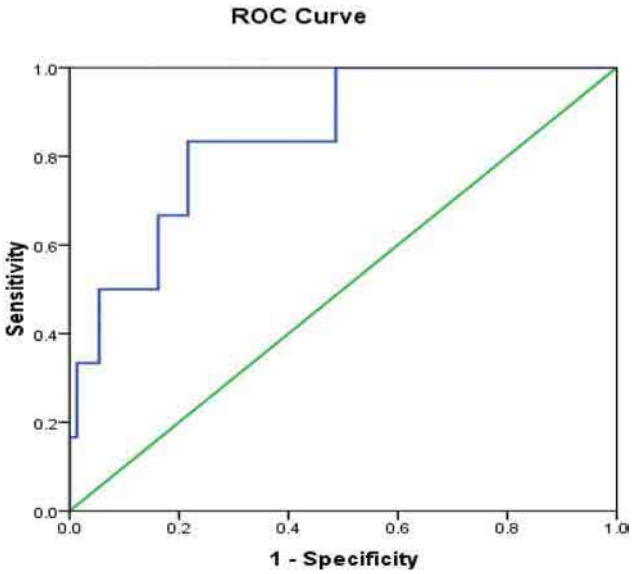


Figure 1: Scatter diagram for negative correlation between NGAL and Subjective global assessment

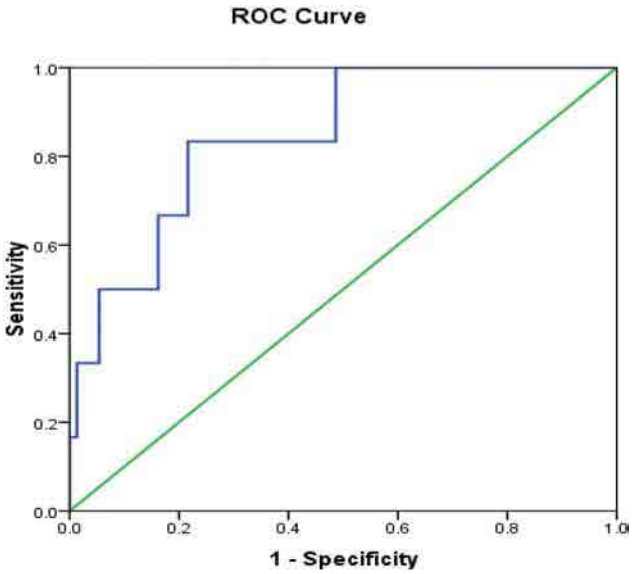


Figure 2: Scatter diagram for positive correlation between NGAL and albumin

Table (1): Relation between Subjective global assessment and N.G.A.L, Kt_V and URR.

Variables	Subjective global assessment			Test of significance	p-value
	Mild (n=53)	Moderate (n=21)	Sever (n=6)		
N.G.A.L Median (Min-Max)	55.45 (12.84-267.04) a	48.83 (17.09-262.28) b	24.42 (11.42-54.36) ab	KW=18.002	0.018*
Kt_V Mean ± SD	1.27±0.32a	1.38±0.25b	2.01±0.18ab	F=15.50	<0.001*
URR	65.63±11.25	68.25±6.25	70.83±19.1	F=0.876	0.420

K.W :Kruskal wallis test.F:ANOVA test, *significant p<0.05 ab:similar letters indicate significant difference between groups.

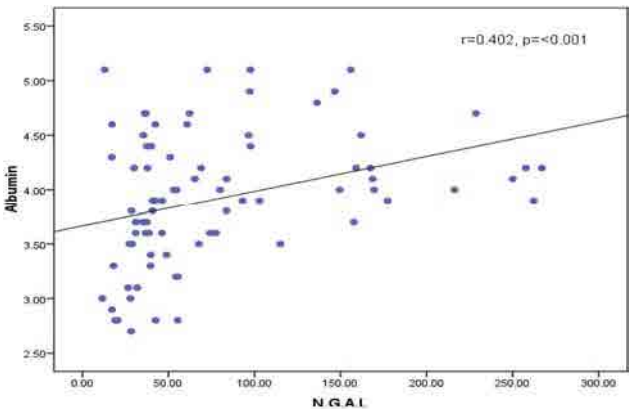


Figure 3: Scatter diagram for positive correlation between KT V and Subjective global assessment

P0953 NITRIC OXIDE AND LEFT VENTRICULAR HYPERTROPHY IN PATIENTS WITH CHRONIC RENAL FAILURE

Leila Azouaou[1], Khelfi Abderrezak[2], Bellouti Wafa[1], Medina Arab[2]

[1]university algiers, medecine, alger, Algeria and [2]university algiers, farmacy, algiers, Algeria

Background and Aims: Nitric oxide, nitric oxide, nitric oxide or NO is an endogenous molecule released by endothelial cells, macrophages, liver cells and neurons. There are three forms of nitric oxide synthase in the body. : the inducible form (iNO), the neuronal form and the endothelial form (eNO). In this work we are interested in (iNO) in patients with CKD and their impact on cardiac complications.

Method: A study of 202 patients with chronic renal failure at different stages (2.3.4.5 and 5D) was performed in our department. We investigated the correlation between mean (iNO) values in patients with CKD and its relationship with left ventricular hypertrophy.

Results: The mean age of the patients is 56.5 ± 17 years with a sex ratio of 1.43. The mean value of (iNO) is 65.82 ± 1.06 µmol / l. Its value increases significantly with the degradation of renal function ($p < 0.05$) (stage 2 (61.75 ± 2.34), stage 3 (63.91 ± 2.21).), stage 4 (64.08 ± 2.18), stage 5 (67 ± 2.7) and stage 5D (72.47 ± 2.18µmol / l). It is found that the mean value of nitric oxide NO is slightly higher in patients with HVG + (67.58 ± 1.48) versus HVG-patients (63.1 ± 1.39) ($p < 0.05$).Discussion: iNOS secreted nitric oxide (NO) initiates cardiac remodeling to lead to left ventricular hypertrophy and cardiac fibrosis

Conclusion: Cardiac complications are the leading cause of death in patients with chronic renal failure. oxidative stress is a risk factor for these cardiac complications, iNOS accelerates cardiac aging.

CKD. REHABILITATION

P0955

IS THERE AN ENDOCRINE CONTRIBUTION TO THE SEXUAL DYSFUNCTION SEEN IN END STAGE RENAL DISEASE PATIENTS?

Haitham Elbardisi[1], Ahmad Majzoub[1], Fadwa Al-Ali[2], Mohamed Elesnawi[2], Abdullah Hamad[2], Ibrahim Al Emadi[1], Mohamed Arafa[1]

[1]Hamad Medical Corporation, Urology, Doha, Qatar and [2]Hamad Medical Corporation, Nephrology, Doha, Qatar

Background and Aims: Male sexual dysfunction is commonly prevalent in patients with end stage renal disease (ESRD) and has been partly attributed to the concurrent state of hyperprolactinemia and hypogonadism, often observed in this patient population. The aim of this study was to evaluate the hormone profile and sexual function of ESRD patient, using validated questionnaires, in attempt to explore this association.

Method: This was a prospective study which included 98 patients with ESRD who followed in the outpatient department of a tertiary medical centre over a period of 1 year. Patients receiving treatment for hyperprolactinemia or those known to have an endocrine disorder were excluded in addition to patients receiving medical or surgical treatment for erectile dysfunction (ED) or premature ejaculation (PE). After filling the international index for erectile function-5 and the Arabic index for PE questionnaire, morning serum samples were taken from patients to measure testosterone and prolactin levels. Descriptive statistics was used to report frequency or means of variables. Chi-square test was used to examine associations between categorical variables. $P<0.05$ was considered statistically significant.

Results: Out of the 98 ESRD patients, 72 (73.6%) were treated with hemodialysis, 13 (13.2%) with peritoneal dialysis and 13 (13.2%) with medical treatment only. Diabetes mellitus was observed in all patients (type 1, 52%; and type 2, 48%), while hypertension, coronary heart disease and dyslipidemia were detected in 97.1%, 34.3% and 25.5%, respectively. The mean age, serum testosterone and prolactin levels were 52.4 ± 12.1 years, 12.95 ± 6.5 nmol/L and 514.2 ± 592.8mIU/L. Results of the PE index questionnaire revealed that 86 (87.7) patients had PE, 9 (9.1%) probable PE and 3 (3.1%) no PE. With IIEF-5, ED was detected in 96 patients; it was severe in 23 (23.5%), moderate- severe ED in 29 (29.4%), mild-moderate ED in 30 (30.4%) and mild in 14 (14.7%). 55 patients had high prolactin while 33 had low testosterone levels. Table 1 presents the IIEF-5 and PE questionnaire results in patients with low/normal testosterone and normal/high prolactin. No significant differences were observed in IIEF or PE levels between patients with low/normal testosterone and normal/high prolactin.

Conclusion: ESRD is commonly associated with sexual dysfunction that is more likely to be attributed to organic causes rather than solely to endocrine disturbances.

Table 1 results of the IIEF-5 and AIPE questionnaire in patients with low/normal testosterone and normal/high prolactin.

		Prolacin		Testosterone	
		normal (n=43)	high (n=55)	low (n=33)	normal (n=65)
IIEF_ levels	severe ED	5 (11.6%)	17 (30.9%)	9 (27.3%)	13 (20.0%)
	moderate-severe ED	16 (37.2%)	13 (23.6%)	8 (24.2%)	20 (30.7%)
	mild to moderate ED	16 (37.2%)	15 (27.3%)	9 (27.3%)	22 (33.8%)
	mild ED	6 (14%)	8 (14.5%)	7 (21.2%)	8 (12.3%)
	no ED	0 (0%)	2 (3.6%)	0 (0%)	2 (3.2%)
AIPE_ levels	no PE	2 (4.7%)	1 (1.8%)	0 (0%)	3 (4.6%)
	probable PE	2 (4.7%)	6 (10.9%)	1 (3.0%)	7 (10.7%)
	PE	39 (90.7%)	48 (87.3%)	32 (97%)	55 (84.6%)

IIEF: international index for erectile function, AIPE: Arabic index for premature ejaculation, ED: erectile dysfunction, PE: premature ejaculation
$p>0.05$ for all

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P0956 **HOW DO MARKERS OF FRAILTY VARY ACROSS KIDNEY DISEASE TRAJECTORY? A MULTICENTRE CROSS-SECTIONAL STUDY OF 4736 PATIENTS**

Courtney J Lightfoot[1], Thomas Wilkinson[1], Alice Smith[1]

[1]*University of Leicester, Department of Health Sciences, United Kingdom*

Background and Aims: Frailty is a complex health state of increased vulnerability to stressors and is common in those with chronic kidney disease (CKD). Frailty is strongly associated with progressive renal impairment and independently linked with adverse outcomes in all stages of CKD such as disability, falls, hospitalisation, and mortality. How frailty varies across the disease trajectory is not well-defined, particularly in those with early stages of disease. Identifying those with CKD who may be at risk of becoming frail could inform the early intervention and understanding how frailty changes across the disease spectrum may aid better future management of these patients.

Method: This is a secondary analysis of data of n=4736 CKD patients (42% female, mean age 59.7 (SD: 16.3) years) from a prospective observational study of physical activity behaviours. A modified assessment of frailty (based on the Fried phenotype model) was conducted across each of the CKD stages ((n=262 CKD stage 1/2, n=678 CKD stage 3, n=610 CKD stage 4/5, n=1094 haemodialysis (HD), n=177 peritoneal dialysis (PD), n=1915 transplant (TX)). Markers of frailty were defined as (1) poor endurance (defined as a VO2 peak of <20ml/kg/min estimated from the Duke Activity Index Scale); (2) low physical activity level (classified as 'insufficiently active' using General Practice Physical Activity Questionnaire); and (3) slowness (self-reported slow walking pace (less than 3mph)). Participants were classified as 'frail' if ≥2 markers were present. Frequency analysis and chi-squared tests were conducted to identify and compare patients with ≥2 markers of frailty across the disease trajectory. Binominal logistical regression was performed to determine which factors were associated with being frail.

Results: Across the total cohort, the majority (56%) of patients exhibited ≥2 markers of frailty. The presence of frailty increased concurrently with disease decline (39% CKD stage 1/2, 58% CKD stage 3, 74% CKD stage 4/5, 76% HD, 66% PD, 39% TX). The prevalence of frailty was significantly higher in patients in CKD stage 3, CKD stage 4/5, HD and PD patients when compared to CKD stage 1/2 and TX patients (p<.001). Frailty was significantly higher in patients in CKD stage 4/5 and on HD compared to those in CKD stage 3 (p<.001). Patients who were female (OR = 1.42 [1.23 to 1.65] p<.001), older (OR= 1.05 [1.05 to 1.06] p <.001), and of non-white ethnicity (OR = 2.41 [2.00 to 2.90] p<.001) had an increased likelihood of being frail. Increased number of comorbidities (OR = 1.26 [1.18 to 1.34] p<.001) were associated with an increased likelihood of being frail (Figure 1).

Conclusion: The proportion of patients with ≥2 markers of frailty increased with disease progression until it reached a peak in HD with almost 8 out of 10 HD patients exhibiting frailty. Frailty prevalence was reduced in those with a renal TX. Over half of those in CKD stage 3 and three-quarters with CKD stage 4/5 had ≥2 markers of frailty present. Worryingly, markers of frailty were present early in the disease process with over 1/3 of patients with CKD stage 1/2 classified as frail by this modified phenotype model. Age, sex, ethnicity, and number of comorbidities were associated with the likelihood of being frail. It is important that healthcare providers actively attempt to identify patients at risk of frailty to ensure appropriate interventions addressing risk factors that may exacerbate the progression of frailty can be implemented.

Figure 1. Factors associated with the likelihood of being frail

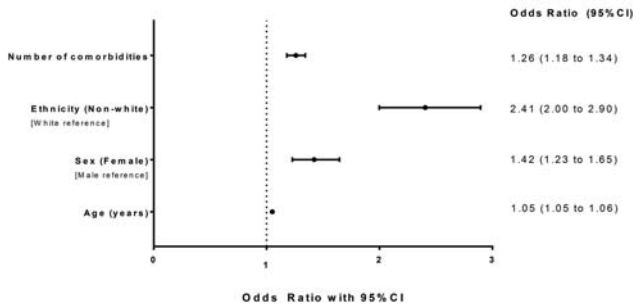


Figure:

P0957 DISABILITY OF DIALYSIS PATIENTS AND CONDITION OF THEIR BLOOD VESSELS

Tomasz Gołębiowski[1], Gawryś Ada[1], Letachowicz Krzysztof[1], Skolimowska Beata[2], Ostrowska Bożena[2], Konieczny Andrzej[1], Olczyk Piotr[1], Krajewska Magdalena[1], Kusztal Mariusz[1]

[1]Wroclaw Medical University, Department of Nephrology and Transplantation Medicine, Wrocław, Poland and [2]University School of Physical Education in Wrocław, Department of Occupational Therapy, Wrocław, Poland

Background and Aims: Epidemiological data indicate constant increase of mean age among hemodialysis patients. These population have high burden of comorbid conditions, including cardiovascular (CV) diseases, which lead to disability and the need for continuous care. The aim of the study was to analyze the problems of disability in hemodialysis patients in the context of cardiovascular complication and vascular condition.

Method: In this cross-sectional study 129 patients (mean age 64.5 y, 54 females, with mean dialysis vintage 61 months) were enrolled from 3 satellite dialysis centers (inclusion criteria: age ≥18 y, dialysis vintage≥3 months). Demographic and comorbidity data were collected from medical records and during interview. The degree of disability (Bartel scale), 10-year cardiovascular risk (QRISK®3 online calculator), degree of imbalance (questionnaire - Falls Efficacy Scale – International (FES-I)) were assessed.

In addition, ambulatory measurements of hemodynamic parameters with Mobil-O-Graph monitor (IEM, Stolberg,Germany), which records oscillometric arm blood pressure (SBP and DBP), central systolic (cSBP) and diastolic (cDBP), pulse pressure (pPP), ejection fraktion - (EF), cardiac output - (CO) and pulse waves. It calculates augmentation index (AIx@75) as measure of wave reflections, and pulse wave velocity (PWV) as measure of arterial stiffness.

Results: The most common causes of renal failure in the study group were ischemic - 35%, and diabetic nephropathy 26% (Fig. 1). Only 8 out of 129 pts. (6.2%) were professionally active, 40 (31%) received disability pension and 81 (62.8%) retirement. 25 (19%) used a wheelchair for transport and 21 (16%) used crutch. More than half (51%) were independent in everyday activities reaching 80-100 points on the Bartel scale, however only 14% were fully independent (100 points). Minimally dependent (60-79 points) constituted 27% (35 pts) of all patients, partially dependent (40-59 points) - 10% (13 pts), highly dependent (20-39 points) - 7% (9 pts) and fully dependent (<20 points) 5% (6 pts). The most common causes of disability were heart problems, including heart failure in 20.9%, lower limb ischemia, diabetic foot and amputation in 13.1% and cerebrovascular event in 10.8% followed by weakness associated with dialysis and degenerative joints disease (Fig. 2). Less disable group (80-100 points on the Bartel scale) showed significantly lower PWV, lower QRISK®3 and FES I index compared to the non self-reliant group (Fig 3). The degree of disability according to Bartel scale negatively correlated with age, PWV, QRISK®3 and FES I index (Fig 4).

Conclusion: Our results indicate that half of the population of hemodialysis patients show some degree of functional dependence. The group of patients with higher degree of disability are older and characterize of the more advanced changes in the arteries, higher risk of the CV incidents and increase risk of fall.

Cause of renal failure	No	%
Ischeamic nephropathy/hypertension	45	35
Diabetic nephropathy	34	26
Glomerulonephritis	24	19
Autosomal dominant polycystic kidney disease	8	6,2
Pyelonephritis (reflux, stones)	9	7
Urology nepolasm (kidney, prostate)	6	4,7
Unknown	2	1,6
Mieloma	1	0,8

Fig. 1 Causes of renal failure.

Disorders leading to diability	No	%
Heart failure/coronary heart disease	27	20,93
Lower limb ischemia, diabetic foot and amputation	17	13,18
Central nervous system disorder	14	10,85
Sarcopenia/weakness associated with dialysis	28	21,71
Degenerative joints disease	18	13,95
Vision and hearing loss	4	3,10
Respiratory tract disorders	3	2,33
Fully independent	18	13,95
Total	129	100,00

Fig. 2 Disorders leading to disability.

	self-reliant, No 67		not self-reliant, No 62		
Blood pressure	**Mean**	**±**	**Mean**	**±**	**p**
SBP (mmHg)	142,8	26,3	139,7	29,9	0,530
MBP (mmHg)	112,5	20,0	106,2	20,8	0,083
DBP (mmHg)	86,9	17,0	77,8	15,7	0,002
pPP (mmHg)	55,9	17,5	61,9	20,9	0,078
HR (1/min.)	73,5	14,3	72,1	11,6	0,541
cSBP (mmHg)	127,8	22,6	123,8	24,8	0,341
cDBP (mmHg)	89,0	17,5	79,6	16,0	0,002
cPP (mmHg)	38,7	12,7	44,2	15,2	0,027
AIx@75 (%)	21,6	14,2	22,9	12,9	0,602
Hemodynamic					
EF (ml)	72,9	14,9	73,3	14,4	0,898
CO (l/min.)	5,3	1,1	5,2	1,1	0,869
TVR (s*mmHg/ml)	1,3	0,3	1,3	0,4	0,251
Cardiac index (l/min.*1/m²)	2,9	0,7	2,9	0,8	0,677
Vascular stiffnes					
Augmentation pressure (mmHg)	10,0	8,4	12,6	9,6	0,102
Reflex (%)	60,6	10,8	63,0	9,9	0,197
PWV (m/s)	8,8	2,0	10,9	2,2	0,000
Body size					
BMI (m²/kg²)	26,4	5,3	26,5	5,2	0,862
Age (y.)	57,9	14,7	71,6	12,5	0,000
Weight (kg)	75,4	19,2	73,1	16,0	0,458
Cardiovascular & fall risk					
QRISK3	22,6	13,0	32,9	11,8	0,000
FES-I	23,4	10,1	43,3	14,8	0,000

Fig. 3 Characteristics of the groups; self-reliant (80-100 points on the Bartel scale) and non self-reliant patients(<80 points on the Bartel scale).

Variable	r
SBP (mmHg)	0,05
MBP (mmHg)	0,12
DBP (mmHg)	0,21
pPP (mmHg)	-0,12
HR (mmHg)	0,04
cSBP (mmHg)	0,06
cDBP(mmHg)	0,20
cPP (mmHg)	-0,14
Aix @75 (%)	0,01
EF (ml)	0,00
CO (l/min)	0,01
PWV (m/s)	-0,41
BMI (kg/m²)	-0,05
QRISK3 (%)	-0,34
FES I (points)	-0,57
Age (y.)	-0,41
HD vintage (m.)	-0,11

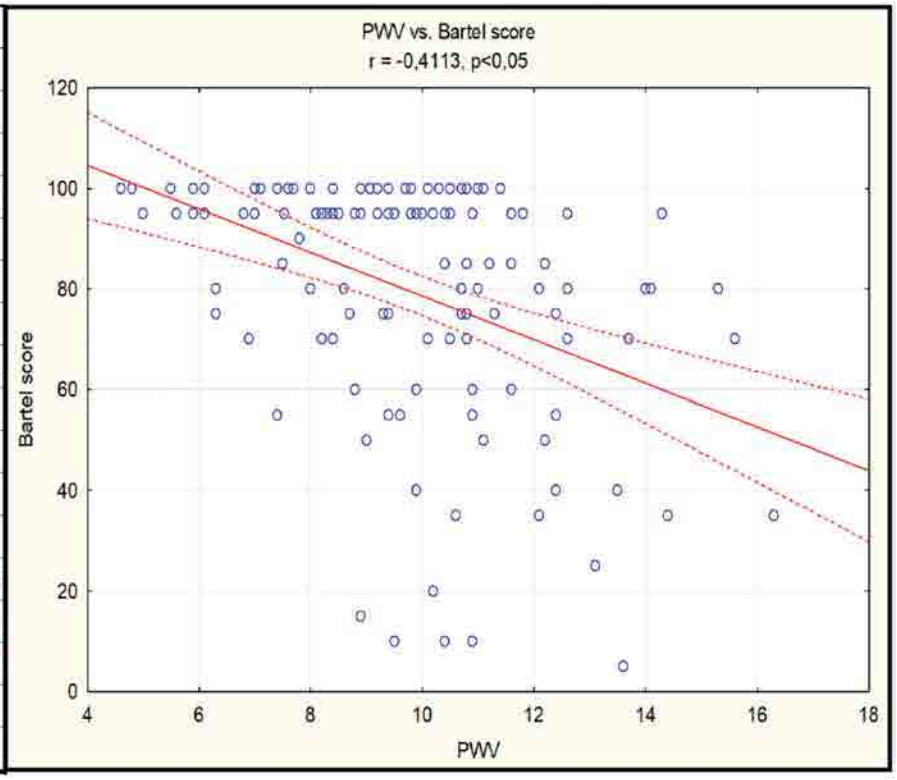


Fig. 4 Correlations (r) between the Bartel score and other variables. Results in red with $p<0.05$.

P0958

THE EX-FRAIL CKD TRIAL: A PILOT RANDOMISED CONTROLLED TRIAL OF A HOME-BASED EXERCISE PROGRAMME FOR PRE-FRAIL AND FRAIL, OLDER ADULTS WITH CHRONIC KIDNEY DISEASE

Andrew Nixon[1,2], Theodoros Bampouras[3,4], Helen Gooch[5], Hannah Young[6], Kenneth Finlayson[7], Neil Pendleton[8], Sandip Mitra[9,10], Mark Brady[1], Ajay Dhaygude[1]

[1]Lancashire Teaching Hospitals NHS Foundation Trust, Department of Renal Medicine, Preston, United Kingdom, [2]The University of Manchester, Division of Cardiovascular Sciences, Manchester, United Kingdom, [3]Lancaster University, Lancaster Medical School, Lancaster, United Kingdom, [4]Lancaster University, Centre for Ageing Research, Lancaster, United Kingdom, [5]Lancashire Teaching Hospitals NHS Foundation Trust, Core Therapies Department, Preston, United Kingdom, [6]University of Leicester, Department of Respiratory Sciences, Leicester, United Kingdom, [7]University of Central Lancashire, Research in Childbirth and Health Unit, Preston, United Kingdom, [8]The University of Manchester, Division of Neuroscience and Experimental Psychology, Manchester, United Kingdom, [9]The University of Manchester, Manchester Academy of Health Sciences Centre, Manchester, United Kingdom and [10]NIHR Devices for Dignity MedTech & In-vitro Diagnostics Co-operative, United Kingdom

Background and Aims: Frailty is highly prevalent in adults with chronic kidney disease (CKD) and is associated with adverse health outcomes. However, exercise training may improve physical function leading to associated improvements in outcomes. The EX-FRAIL CKD trial (ISRCTN87708989) aimed to inform the design of a randomised controlled trial (RCT) that investigates the efficacy of a progressive home-based exercise programme in pre-frail and frail older adults with CKD.

Methods: Patients aged $\geq$65 years with CKD G3b-5 and a Clinical Frailty Scale score $\geq$4 were eligible for participation. Participants categorised as pre-frail or frail, following Frailty Phenotype (FP) assessment, were randomised to receive a tailored 12-week home-based exercise programme or usual care (UC). Primary outcome measures included recruitment, intervention adherence, outcome measure completion and participant attrition rate. Secondary outcome measures included frailty status (FP), physical function (walking speed, handgrip strength and Short Physical Performance Battery [SPPB]), fall concern (Falls Efficacy Scale-International tool [FESI]), symptom-burden (Palliative Care Outcome Scale-Symptoms RENAL [POS-S RENAL]) and health-related quality of life (Short Form-12v2 [SF-12]). Outcome measures are reported descriptively with 95% confidence intervals (CI) as recommended for pilot trials. Progression criteria to RCT stage were defined as: (1) eligibility: STOP <5%, GO >10%; (2) recruitment: STOP <10%, GO >30%; (3) exercise adherence: STOP: <30%, GO >70%; (4) outcome measure completion: STOP <70%, GO >80%; and (5) loss to follow-up: STOP >50%, GO <25%.

Results: Six hundred and sixty-five participants had an eligibility assessment with 201 (30% [95% CI 27-34]) patients eligible for enrolment. Thirty-five (17% [95% CI 12-23]) participants were recruited. Six participants were categorised as robust and therefore withdrawn prior to randomisation. Fifteen participants were randomised to exercise (mean age 77.0$\pm$8.3 years; mean eGFR 18.9$\pm$7.0 ml/min/1.73m^2) and 14 to UC (mean age 78.8$\pm$7.0 years; mean eGFR 20.4$\pm$7.2 ml/min/1.73m^2). Eleven (73% [95% CI 45-92]) exercise group participants completed an average of $\geq$2 exercise sessions/week. Eight (28% [95% CI 13-47]) participants were lost to follow-up. Retained participants (n=21, 100% [95% CI 84-100]) completed all outcome measures. There were 32 adverse events in the exercise group and 22 in the UC group. Within the exercise group, there were 2 hospitalisations (considered unrelated to exercise) and 12 adverse reactions: musculoskeletal pain (9), fall (1), nocturnal leg cramps (1) and postural dizziness (1). The odds ratio for improvement in frailty status with exercise was 5.50 (95% CI 0.46-65.16) and odds ratio for deterioration in frailty status was 0.63 (95% CI 0.05-8.20). The adjusted mean group difference in walking speed, grip strength and SPPB between exercise and UC groups were: 0.01 metres/second (95% CI -0.07-0.10), 3.6 kg (95% CI -0.6-7.9) and 0.5 (95% CI -0.9-1.8), respectively. The adjusted mean group difference in POS-S RENAL, FESI, SF-12 Physical Component Summary and SF-12 Mental Component Summary scores were: -1.4 (95% CI -6.6-3.7), 3.4 (95% CI -3.5-10.3), -3.9 (95% CI -9.3-1.5) and 0.2 (95% CI -6.2-6.6), respectively.

Conclusion: Eligibility, adherence and outcome measure progression criteria thresholds were exceeded; however, recruitment and loss to follow-up progression criteria thresholds were not achieved. Analysis of a nested qualitative study will explore perceived barriers to participation and retention. The EX-FRAIL CKD trial demonstrates that it is possible to progress to a definitive RCT with adaptations that address the barriers described. It has also provided preliminary evidence that frailty status and physical function may be improved with a home-based exercise programme in patients living with frailty and CKD.

P0959

EFFECT ON THE DIALYSIS DOSE OF THE EXERCISE WITH VIRTUAL REALITY DURING THE FIRST VERSUS SECOND PART OF THE DIALYSIS SESSION

Alicia Garcia-Testal[1], Rafael Garcia-Maset[1], José Antonio Gil-Gómez[2], Francisco José Martínez-Olmos[3], Noemi Valtueña-Gimeno[3], Lucia Ortega-Perez de Villar[4], Ana Ferrer-Salva[3], Jocelyne Piñón-Ruiz[3], Maari Elvi Amanda Lehtoviita[3], KATARZYNA KARANDYSZ[3], Hector Lavirgen Heras[5], Delia Pans Alcaina[5], Víctor López Tercero[5], Inmaculada Rico-Salvador[1], Pilar Royo-Maicas[1], Eva Segura-Ortí[3]

[1]Hospital de Manises, Nephrology, Manises, Valencia, Spain, [2]Universitat Politècnica de València, University Institute of Automation and Industrial Computer Science, Valencia, Spain, [3]Universidad Cardenal Herrera-CEU, CEU Universities, Physiotherapy, Alfara del Patriarca, Valencia, Spain, [4]Universidad Europea de Valencia, Physiotherapy, Valencia, Spain and [5]Hospital de Manises, Nephrology, Hemodialysis Unit, Manises, Valencia, Spain

Background and Aims: Exercise using non-immersive virtual reality (VR) is a novel rehabilitation method for patients undergoing hemodialysis treatment. This method has shown in a pilot study improved physical function and health-related quality of life.

There is controversy about the effect of intradialysis exercise on the dialysis dose. Furthermore, theoretical models also indicate that intradialytic exercise at the end of session may be beneficial in postdialysis rebound.

Objective: to determine effect of exercise with virtual reality during the first two hours and the last two hours of dialysis session on postdialysis rebound and dialysis dose.

Method: The design was a randomized clinical trial. Patients were randomized to exercise in the first (Start group) or last two hours (End group) of dialysis session. Dialysis dose was measured through the monocompartimental Kt/V, and the potassium, urea, phosphorus and creatinine rebound was calculated after both baseline and exercise sessions at 17 weeks. Intradialysis exercise consisted of a video game adapted to dialysis: Treasure hunting. It is a non-immersive VR game in which the patient must catch some objectives avoiding obstacles by moving the lower limbs. The exercise session lasted from 20 to 40 minutes. Intensity was checked through the rate of perceived exertion. An mixed ANOVA of repeated measures was used to assess the effect of the intervention. Patients exercised for 17 weeks.

Results: 43 patients participated, 11 dropouts, 17 in Start group and 15 in End group. Mean age 73 years, males 28. There were no significant differences in rebound urea, creatinine, potassium and phosphorus 30 minutes after finishing dialysis. The mean baseline Kt/V was 1.65 (SD 0.21) and with exercise 1.75 (SD 0.25). The mixed ANOVA analysis showed a significant time effect with an increase in Kt/V (mean 0.10, 95% CI 0.02-0.19, p 0.018) from exercise session vs baseline. No group per time significant interaction was found, so that there was no difference in the dialysis dose between Start and End group.

Conclusion: Intra-dialysis exercise with virtual reality can improve the dose of dialysis, no matter the timing of the exercise is performed.

P0960

HOME BASED RESISTANCE EXERCISE PROGRAM AND SARCOPENIA IN HEMODIALYSIS PATIENTS: IT IS A USEFUL INTERVENTION?

Vicent Esteve Simó[1], Anna Junqué Jiménez[1], Verónica Duarte Gallego[1], Irati Tapia González[1], Fátima Moreno Guzmán[1], Miquel Fulquet Nicolás[1], Mónica Pou Potau[1], Anna Saurina Solé[1], Manel Ramírez de Arellano Serna[1]

[1]*Consorci Sanitari Terrassa, Nephrology, Terrassa, Spain*

Background and Aims: Sarcopenia is a skeletal muscle disorder associated with adverse outcomes including falls, physical disability and mortality particularly in hemodialysis (HD) patients. Currently, progressive resistance training exercise has been shown a proven method to treat and prevent sarcopenia. Nevertheless, these findings are poorly investigated in HD patients since exercise programs are not widespread.

The aim of our study was to assess the effect of a home-based resistance exercise program (HBREP) on muscular strength, functional capacity and body composition in our hemodialysis patients with sarcopenia according to the European Working Group on Sarcopenia in Older People criteria (EWGSOP2).

Method: A 12 weeks single-center prospective study. HD patients from our institution with EWGSOP2 sarcopenia diagnosis were enrolled in a HBREP. Demographical an anthropometrical data, main biochemical and nutritional parameters, hand grip (HG) muscular strength, functional capacity tests: Sit to stand to seat 5 (STS5); Short Physical Performance Battery (SPPB), gait speed (GS), as well as body composition determined by electrical bioimpedance (BIA) and sarcopenia severity were analized.

Results: 18 HD patients with sarcopenia (71.4% severe) were included (4 drop out).78.6% men. Mean age 74.7 years and 53.3 months on HD. The main etiologies of ESRD were the HBP (21.4%) and DM (14.3%). Globally, a significant improvement was observed at the end of the study in relation to muscular strength (HG 19.9±6.1 vs 22.2±7.1 kg, p 0.001) and functional capacity tests (STS5 21.9±10.3 vs 17.2±9.9 sec, p 0.001; SPPB (6.9±2.3 vs 9.1±2.5 score, p 0.001 and GS 0.8±0.1 vs 0.9±0.2 m/s, p 0.015). Likewise, higher total skeletal muscle mass (SMM, 14.3±2.8 vs 14.5±2.9 kg) and SMM index (SMM/height^2, 5.5±0.7 vs 5.7±0.9 Kg/m^2) were found at the end of the study, although these differences were not significant. Finally, 2 patients (14.8%) reverse the EWGSOP2 sarcopenia criteria and 3 (21.4%) enhanced their severe sarcopenia. No relevant changes regarding anthropometrical data, main biochemical and nutritional parameters or dialysis adequacy were observed at the end of the study.

Conclusion: A home-based resistance exercise program improves muscular strength, functional capacity and body composition in our sarcopenic hemodialysis patients. With our results, home-based resistance exercise programs should be considered a key point in the prevention and treatment of skeletal muscle mass reduction due to sarcopenia in these patients. Further studies are mandatory to confirm our encouraging results.

P0961 PHYSICAL REHABILITATION OF PATIENTS WITH CHRONIC KIDNEY DISEASE OF PRE -DIALYSIS STAGES.

Durdona Saipova[1]

[1]*Tashkent Medical Pediatric Institute, Internal disease, Tashkent, Uzbekistan*

Background and Aims: Chronic kidney disease is a global public health problem. Poor physical condition and skeletal muscle depletion are associated with the combined effects of uremic acidosis, protein-energy deficiency and inflammatory depletion, which leads to further exacerbation of a sedentary lifestyle. The aim of the determination of physical performance and the effectiveness of physical training during the 12-week program in patients with CKD of pre-dialysis stages.

Method: We examined 130 patients with CKD 2-4 stages. Clinical parameters (BP, BMI, mid-thigh circumference, mid-shoulder circumference, mid-calf circumference), laboratory data (serum creatinine, serum cholesterol, serum albumin, serum phosphorus, serum calcium) were evaluated in all patients according to the formula CKD-EPI 2011. Physical performance was determined by the results of cardiopulmonary stress test. In accordance with the initial data of the patients, a 12-week physical rehabilitation program was individually selected, which included morning exercises, physiotherapy exercises and dosed walking . The data obtained were subjected to statistical processing.

Results: The average age of patients was 54.8 years. Of these, 52 women (40%) and 78 (60%) men. The estimated glomerular filtration rate varied from 30 to 60 ml / min / 1.73 m2, which corresponded to the indicators of the pre-dialysis stages of CKD. After a 12-week rehabilitation program, the maximal oxygen consumption (V O_2peak) increased in 70% of regularly engaged patients by 1.2 times (22.31 ml / min / kg and 27.05 ml / min / kg, respectively), and in 30% of those who did not pass the course Exercise therapy, the indicator of maximum oxygen consumption after 12 weeks was 21.7 ml / min / kg (with an initial 23.7 ml / min / kg) The average blood pressure decreased slightly (from 111 $\pm$ 5 initially to 106 $\pm$ 5 mm Hg after 12 weeks, $p<0.05$) When measuring anthropometric parameters, it was found that the circle the mid-thigh increased from 46.5 $\pm$ 6.0 cm to 0.6 cm, the circumference of the middle of the shoulder increased from 31.1 $\pm$ 4.0 cm to 0.4 cm. The circumference of the middle part of the lower leg was initially 356.7 $\pm$ 3.8 cm, and after 12 weeks of training it increased 0.3 cm. In 9 patients, these parameters did not change after a 12-week program.

Conclusion: Regular physical training led to an increase in the maximum oxygen consumption by 1.2 times. It was noted that regular training contributes to a slight increase in muscle mass in patients with CKD. The importance of regularity of physical therapy classes was also revealed.

P0962 CHRONIC KIDNEY DESEASE AND URINARY TRACT INFECTION IN PREGNANTS

Olga Vetchinnikova[1], Irina Nikolskaya[2]

[1]M.F. Vladimirsky Moscow Regional Research and Clinical Institute, Department of Transplantology Nephrology and Artificial Organs Faculty of Postgraduate Education, Moscow, Russia and [2]Moscow Regional Research Institute of Obstetrics and Gynecology, Observational Obstetric Department

Background and Aims: Pregnant women with chronic kidney disease (CKD) are at risk of developing/exacerbating urinary tract infection (UTI) due to the presence of additional ("specific") risk factors. The aim of our study was estimation the features of UTI in women with CKD during pregnancy.

Method: The study included 139 women with CKD G1-G3 who had UTI during pregnancy. Most women (63) had chronic glomerulonephritis, 47 had with chronic pyelonephritis, and the rest had diabetic nephropathy (11), chronic tubulointerstitial nephritis (9), renal transplant (7) and lupus nephritis (2). An analysis of the bacteriological examination of urine, the sensitivity of pathogens to antibiotics, clinical manifestations and perinatal complications was performed.

Results: The following forms UTI are diagnosed: asymptomatic bacteriuria (50.4%), exacerbation of chronic pyelonephritis, including renal transplant (33.1%), acute pyelonephritis (16.5%). The true bacteriuria is determined identically at all stages of CKD, in those with chronic pyelonephritis in 70%, chronic glomerulonephritis in 45% of cases ($p = 0.02$). Gram-negative microorganisms become apparent in 73.6% of pregnant women with CKD, less often in patients with glomerular pathology than with chronic pyelonephritis (66% versus 81%). Escherichia coli among gram-negative microorganisms was 74.4%, a high frequency of detection of strains with the production of extended-spectrum β-lactamases was established. The course of asymptomatic bacteriuria in pregnant women with non-diabetic glomerulopathy was characterized by a moderate tendency to relapse and moderate release of resistant pathogens. The course of asymptomatic bacteriuria in patients with diabetic nephropathy and after kidney transplantation, on the contrary, had a pronounced tendency to relapse and the frequent release of resistant pathogens. Exacerbation of chronic pyelonephritis proceeded with minimal clinical manifestations, a vivid clinical picture of exacerbation of the disease was determined in one third of pregnant women. It was characterized by a high tendency to relapse and the development of systemic infection, a high frequency of release of resistant pathogens. Pregnant women with CKD who underwent UTI had a high risk of giving birth to premature babies (23% versus 11% $p=0.01$) who were required to carry out artificial lung ventilation and transfer to stage nursing (34% versus 16%, $p=0.01$).

Conclusion: The course of UTI in pregnant women with CKD is characterized by a high prevalence, dependence on primary renal disease, the release of resistant pathogens, and a high probability of an atypical clinical picture.

P0963 MANAGEMENT OF SLEEP DISORDERS IN END-STAGE RENAL DISEASE, IS IT REALLY IMPORTANT?

Liliana-Ana Tuta[1,2], Tofolean Doina-Ecaterina[1,2], Tudor Alexandra[1,2], Campineanu Bogdan[1,2]

[1]Ovidius University of Constanta, Faculty of Medicine, Internal Medicine, Constanta, Romania and [2]County Clinical Emergency Hospital of Constanta, Internal Medicine, Constanta, Romania

Background and Aims: Sleep apnoea (SA), either obstructive and central (OSA and CSA, respectively) associated with and excessive daytime sleepiness (EDS) are common sleep disorders among patients with end-stage renal disease (ESRD). Fluid overload characterizes end-stage kidney disease and plays an important role in the pathogenesis of OSA, CSA and EDS. In our study we assessed the prevalence of sleep apnoea and excessive daytime sleepiness in patients from a nephrology and dialysis unit from south-eastern Romania.

Method: 86 patients with ESRD pre-dialysis (eGFR $<$ 15 ml/min/1,73 ṁ) or on maintenance haemodialysis were monitored for an interval of 2 years. We used questionnaires to assess the prevalence of SA and EDS. All subjects underwent overnight polysomnography (PSG). Extracellular fluid volume of the total body, neck, thorax and right leg were measured using bioelectrical impedance. We also examined the association between sleep apnoea, EDS, the underlying causes of ESRD, co-morbidities, medication used, and other demographic data.

Results: The mean patients age was 57.5 years $\pm$ 14.9 years; 65.1% were male, and 34.9% were female. The prevalence of SA as defined by the Berlin questionnaire (BQ) was 49.5% in males and 34.8% in females, which was not a statistically significant difference (P = 0.029). Sleep apnoea was significantly associated with age, obesity, diabetes, hypertension, fluid overload and 2nd or 3rd haemodialysis shift (P-values, 0.001, $<$ 0.0001, $<$ 0.002, $<$ 0.008, $<$0.0001, and $<$ 0.005. Sleep apnoea was also significantly associated with other sleep disorders such as restless leg syndrome, insomnia, habitual snoring, and EDS (P-values, $<$ 0.001, $<$ 0.001, $<$ 0.001, and $<$ 0.001, respectively). The prevalence of EDS was 35,5%, and EDS was significantly associated with age (over 60 years old), diabetes mellitus, hypertension and obesity. 18 patients (20.9%) had refractory hypertension, that improved after CPAP administration, and 10 of these patients (over 50% with refractory HT), that refused the application of appropriate therapy of sleep disorders, suffered a major cardiovascular event during our study.

Conclusion: Sleep apnoea, excessive daytime sleepiness and other sleep disorders are relatively common in pre-dialysis and haemodialysis patients and are significantly associated with refractory hypertension and severe cardio-vascular events. That is why a greater attention should be given to the diagnosis and management of sleep disorders, as one of the important steps in nursing and our patients' rehabilitation.

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DIABETES. BASIC RESEARCH

P0970

EXOSOMAL MIR-92A-1-5P DERIVED FROM PROXIMAL TUBULAR EPITHELIAL CELLS INDUCES EPITHELIAL-MESENCHYMAL TRANSITION IN MESANGIAL CELLS IN DIABETIC NEPHROPATHY

Yi-Chun Tsai[1], Mei-Chuan Kuo[2], Ya-Ling Hsu[3]

[1]Kaohsiung medical university hospital, Kaohsiung medical university, Nephrology, Taiwan, R.O.C., [2]Kaohsiung medical university hospital, Kaohsiung Medical University, Nephrology, Taiwan, R.O.C. and [3]Kaohsiung medical university, Graduate institute of medicine, Taiwan, R.O.C.

Background and Aims: Diabetic nephropathy (DN) has been the leading cause of end-stage renal disease in the world-wide. Exosomes play a key role in signal transduction between cell-cell communication in kidney pathophysiology. The aim of this study is to investigate that HK-2 cells-derived exosomal miR-92a-1-5p causes epithelial-mesenchymal transition (EMT) in mesangial cells (MCs), further leading to DN progression.

Method: The function of HK-2 cells-derived exosomes under normal glucose (NG) and high glucose (HG) was analyzed in mouse MCs model. Total RNAs were extracted from renal proximal tubular epithelial cells (RPTECs) of normal individual and type 2 diabetes for small RNA expression profiling using next-generation sequencing (NGS), then analyzed using systematic bioinformatics analyses. The expression of miR-92a-1-5p was examined in HK-2 cells-derived exosomes and MCs treated with HK-2 cells-derived exosomes under HG. The role of miR-92a-1-5p in EMT was evaluated using MCs model under NG and HG conditions. Urinary exosomal miR-92a-1-5p levels were measured in 50 type 2 diabetic patients and 34 healthy volunteers who were enrolled to determine the relationship between urinary exosomal miR-92a-1-5p and kidney function.

Results: Decreased E-cadherin, and increased N-cadherin and Vimentin expression were found in mouse MCs treated with HK-2 cells-derived exosomes under HG. Transcriptome analysis of RPTECs of normal individual and type 2 diabetic patient indicated that miR-92a-1-5p contributes to HG-induced renal proliferation. HG elevated miR-92a-1-5p expression in HK-2 cells and exosomes derived from-HK-2 cells, at meanwhile exosomal miR-92a-1-5p derived from-HK-2 cells under HG leads to EMT in mouse MCs. miR-92a-1-5p mimic increased EMT in mouse MCs under NG, and miR-92a-1-5p inhibitor reversed EMT in mouse MCs induced by exosomes derived from HK-2 cells under HG. EMT of mouse MCs was enhanced in the presence of exosomes isolated from the urine of type 2 diabetic patients with high levels of exosomal miR-92a-1-5p. Type 2 diabetic patients had higher urinary exosomal miR-92a-1-5p levels than normal individuals. Higher urinary exosomal miR-92a-1-5p levels were significantly correlated with lower renal function and higher albuminuria in human model.

Conclusion: Exosomal miR-92a-1-5p derived from HK-2 cells under HG induces EMT in mesangial cells. Blocking miR-92a-1-5p epigenetic regulatory network might be a potential therapeutic strategy to prevent EMT in DN.

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P0971

IDENTIFICATION OF HUB GENES ASSOCIATED WITH THE DEPOSITION OF EXTRACELLULAR MATRIX AND SPECIFIC FOR DIABETIC NEPHROPATHY BY WEIGHTED GENE CO-EXPRESSION NETWORK ANALYSIS

Songtao Feng[1], Linli Lv[1], Gao Yueming[1], Cao Jingyuan[1], Di Yin[1], Bicheng Liu[1]

[1]*Zhong Da Hospital, Southeast University School of Medicine, Nephrology, Nanjing, P.R. China*

Background and Aims: Diabetic nephropathy (DN) and its most severe manifestation, end-stage renal disease (ESRD), remains one of the leading causes of reduced lifespan in people with diabetes. Identifying novel molecules that are involved in the pathogenesis of DN has both diagnostic and therapeutic implications. The gene co-expression network analysis (WGCNA) algorithm represents a novel systems biology approach that provide the approach of association between gene modules and clinical traits to find the module involvement into the certain phenotypic trait. The goal of this study was to identify hub genes and their roles in DN from the aspect of whole gene transcripts analysis.

Method: Various types of chronic kidney diseases (CKD), including DN, microarray-based mRNA gene expression data, listed in the Gene Expression Omnibus (GEO) database, were analyzed. Next, we constructed a weighted gene co-expression network and identified modules distinguishing DN from normal or other types of CKD by WGCNA. Functional annotations of the genes in modules specialized for DN were analyzed by Gene Ontology (GO) enrichment analysis. Through protein-protein interaction (PPI) analysis and hub gene screening, the hub genes specific for DN were obtained. Furthermore, we drew ROC curves to determine the diagnosis and differential diagnosis value to DN of hub genes. Finally, another study of microarray in the GEO database was selected to verify the expression level of hub genes and in the "Nephroseq" database, the correlation between the gene expression level and eGFR was analyzed.

Results: "GSE99339", glomerular tissue microarray in 187 patients with a total of 10947 genes, was selected for analysis. After excluding the inappropriate cases, a total of 179 specimens were analyzed, including 14 cases of DN, 22 cases of focal segmental glomerulosclerosis (FSGS), 15 cases of hypertensive nephropathy (HT), 26 cases of IgA nephropathy (IgAN), 13 cases of minimal change disease (MCD), 21 cases of membranous nephropathy (MGN), 23 cases of rapidly progressive glomerulonephritis (RPGN), 30 cases of lupus nephritis (LN) and 14 cases of kidney tissue adjacent to tumor. Co-expression network analysis by WGCNA identified 23 distinct gene modules of the total 10947 genes and revealed "MEsaddlegreen" module was strongly correlated with DN (r=0,54), but not with other groups. GO functional annotation showed that these 64 genes in the "MEsaddlegreen" module mainly enriched in the deposition of extracellular matrix, which represents the specific and diagnostic pathophysiological process of DN. Further PPI and hub gene screening analysis revealed that LUM, ELN, FBLN1, MMP2, FBLN5 and FMOD can be served as hub genes, which had been proved to play an important role in the deposition of extracellular matrix. Furthermore, we found that the expression of hub genes was the highest in DN group and for the diagnosis value of DN by each gene, the area under the ROC curve is about 0.75~0.95. The external verification of another study showed that compared with the normal control group, the expression of these hub genes was the highest in the DN group, and their expression level was negatively correlated with eGFR.

Conclusion: Using WGCNA and further bioinformatics approach, we identified six hub genes that appear to be identical to DN development. As such, they may represent potential diagnostic biomarkers as well as therapeutic targets with clinical utility.

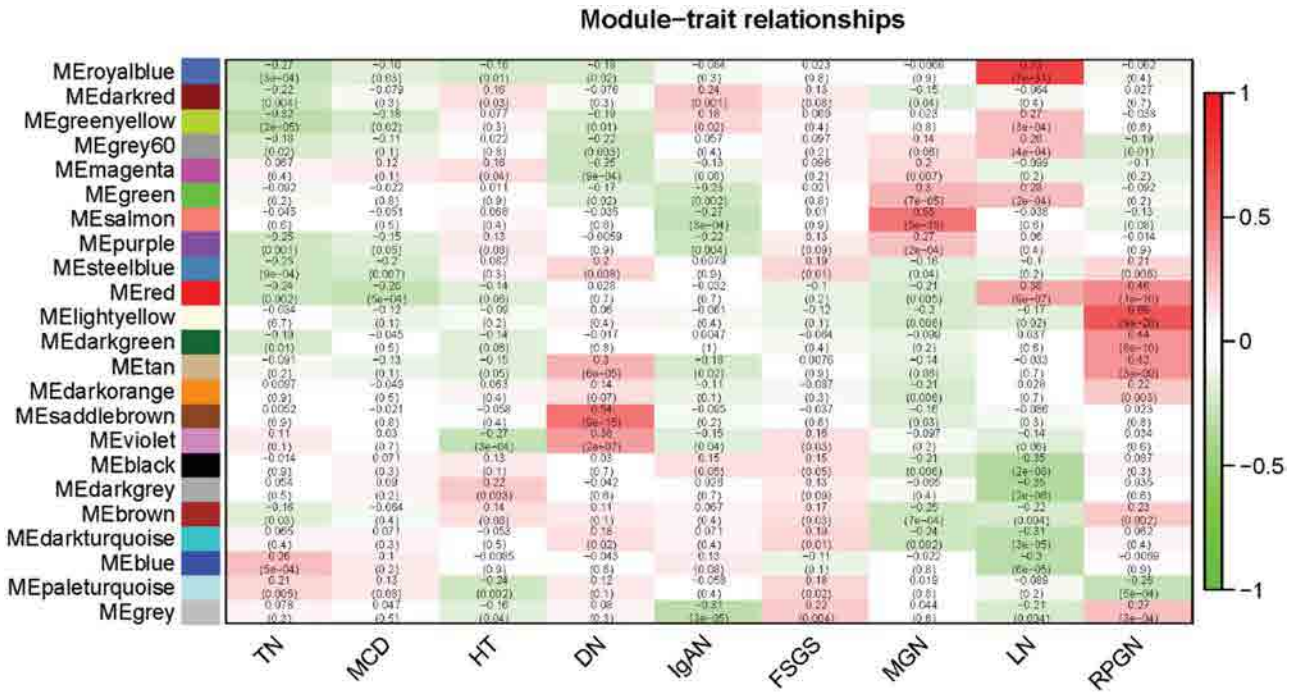


Figure:

P0972

INHIBITION OF LYSINE63 UBIQUITINATION PREVENTS THE PROGRESSION OF RENAL FIBROSIS IN DIABETIC NEPHROPATHY IN VITRO AND IN VIVO

Francesca Conserva[1], Paola Pontrelli[1], Rossella Menghini[2], Michele Rossini[1], Alessandra Stasi[1], Chiara Divella[1], Claudia Cinefra[1], Simona Simone[1], Giovanni Battista Pertosa[1], Anna Gallone[3], Massimo Federici[2], Loreto Gesualdo[1]

[1]University of Bari, Dept. of Emergency and Organ Transplantation, Italy, [2]Dept. of Systems Medicine, University of Rome Tor Vergata, Italy and [3]Dept. of Basic Medical Sciences, Neurosciences and Sense Organs, University of Bari, Italy

Background and Aims: Diabetic Nephropathy (DN) is the primary cause of end stage renal disease (ESRD). Our group demonstrated that in DN an accumulation of lysine63 (K63)-ubiquitinated proteins at tubular level is involved in the progression of renal damage, in particular renal fibrosis. Current treatments do not provide complete renoprotection and targeted therapies that prevent fibrosis or delay its progression are still lacking.

Aim of the present study was to evaluate the renoprotective effect of specific drug and their combinations, including an inhibitor of K63 ubiquitination (K63Ub) and/or an anti-hypertensive agent, in vitro and in vivo in a murine model of DN.

Method: Renal Proximal Tubule Epithelial Cells (HK2) were pre-incubated with a specific inhibitor of K63Ub and/or with the ACE-inhibitor Ramipril. Accumulation of K63 ubiquitinated proteins along with α-sma expression, indicator of epithelial-to-mesenchymal transition (EMT), were analyzed through immunofluorescence and western blotting. The same drug combination was also tested in streptozotocin (STZ)-treated DBA/2J mice, a model of human DN. In mice, K63Ub was evaluated by IHC, while renal fibrosis was evaluated by Sirius red and Collagen III expression. Urinary albuminuria was measured by ELISA.

Results: We observed that the association of the specific K63Ub inhibitor with Ramipril was able to block hyperglycemia-induced EMT in HK2 cells by significantly reducing α-sma expression, when compared to single drugs alone ($p<0.05$).To demonstrate the efficacy of these drug combinations in reducing the progression of renal damage in DN we firstly confirmed the increased accumulation of K63 Ub proteins in DBA/2J STZ-treated mice ($p=0.01$). Interestingly, increased K63Ub in diabetic mice was also associated to increased tubular-interstitial fibrosis ($p<0.05$). Treatment of STZ-mice with the specific K63Ub inhibitor was able to reduce both K63Ub proteins accumulation and renal fibrosis, evaluated on kidney samples by IHC against Collagen III ($p\leq0.05$) and by Sirius Red staining ($p\leq0.05$) when compared to both untreated mice and mice treated with ramipril. Importantly, treatment with the K63Ub inhibitor alone did not reduce albuminuria (STZ-mice: 561.29 ± 390.56; STZ+K63Ubinhibitor: 724.25 ± 690.89; p=n.s.), while the drug combination including the specific K63Ub inhibitor and Ramipril, significantly reduced both K63Ub-related fibrosis and albuminuria ($p=0.01$), demonstrating an addictive and synergic effect of these molecules when used in combination.

Conclusion: Our data demonstrated and confirmed the importance of K63Ub in the progression of renal fibrosis *in vitro* and *in vivo*. We proposed and patented a novel combination of drugs that ameliorates both fibrosis and proteinuria in DN. Novel treatment regimens could represent an important goal for reducing the incidence of ESRD related to diabetes complication.

P0973

ALLOSTERIC C-C CHEMOKINE RECEPTOR TYPE 2 (CCR2) INHIBITION IMPROVES RENAL FUNCTION IN A MURINE MODEL OF DIABETIC NEPHROPATHY

Zhenhua Miao[1], Linda S. Ertl[1], Bin Zhao[1], Yu Wang[1], Dale Newland[1], Yibin Zeng[1], Jeffrey McMahon[1], Xiaoli Liu[1], Ton Dang[1], Shichang Miao[1], Penglie Zhang[1], Chris Li[1], James Campbell[1], Rajinder Singh[1], Israel F. Charo[1], Thomas J. Schall[1]

[1]*ChemoCentryx, Inc, Mountain View, United States of America*

Background and Aims: Diabetic nephropathy (DN) is a syndrome characterized by pathological levels of proteinuria, glomerular lesions and reduction in the glomerular filtration rate (GFR) in diabetic patients. Several lines of evidence support a role of CCR2 in the pathogenesis of DN. Recent studies have demonstrated that existing small molecule CCR2 antagonists can be placed in two classes, distinguished by their interaction with one of two distinct binding sites on CCR2: an extracellular site for which antagonists compete directly with native ligands (the orthosteric site), or an intracellular allosteric binding site. To better understand the functional differences between these antagonists we compared an example of each class in a murine model of DN. Our results revealed that the allosteric, but not the orthosteric CCR2 inhibitors ameliorated the proteinuria and improved glomerular histopathology in this model of DN.

Method: We used db/db mice to model DN. Several structurally distinct CCR2 inhibitors with that bind to either the allosteric (CCR2-RA-[R] and CCX872) or orthosteric (MK-0812 and CCX598) sites were compared. Pharmacokinetic (PK) properties and renal functional parameters were assessed, including trough drug levels and proteinuria (urinary albumin excretion rate UAER; urine albumin creatinine ratio UACR). Histopathology and electron microscopy (EM) were performed to assess any potential tissue-protective effects of the antagonists.

Results: Both the allosteric inhibitors (CCR2-RA-[R] and CCX872) and the orthosteric inhibitors (MK-0812 and CCX598) were potent CCR2 antagonists with desirable PK in mouse in so far as both classes effectively blocked CCR2-mediated monocyte migration into the peritoneal cavity in the thioglycollate-induced peritonitis model. At comparable drug coverage levels, CCR2-RA-[R] and CCX872 rapidly and significantly reduced UAER/UACR (CCX872: 70 % at day 7 vs vehicle, $p<0.0001$; and 60 % at day 14 vs vehicle, $p=0.001$; CCR2-RA-[R]: 60 % at day 7 vs vehicle, $p=0.0001$; and 58 % at day 14 vs vehicle, $p=0.005$), but MK-0812 and CCX598 did not exhibit proteinuria lowering effect. Histological parameters including glomerular injury and glomerular basement membrane (GBM) thickness were also improved after CCX872 treatment in db/db mice.

Conclusion: Allosteric antagonists of CCR2 provide significant and rapid renal protection in the db/db murine model of DN, as evidenced by improvements in renal function and histological parameters, while potent orthosteric CCR2 antagonists were not effective in the model. Our data suggest that targeting the effectiveness of CCR2 antagonists in DN are directly dependent on binding to the allosteric site of CCR2.

P0974 **ADIPORON AMELIORATES DIABETIC CARDIOMYOPATHY IN DBDB MICE THROUGH IMPROVING CERAMIDE-DEPENDENT LIPOTOXICITY**

Yaeni Kim[1], Ji Hee Lim[1], Eun Nim Kim[1], YONGJIE JIN[1], Hyung Duk Kim[1], Tae Hyun Ban[1], Bum Soon Choi[1], Cheol Whee Park[1]

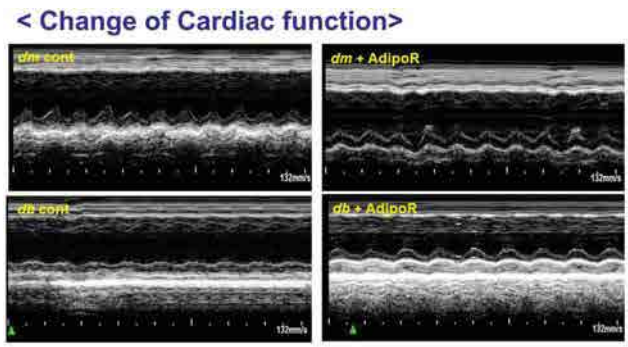
[1]*Division of Nephrology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South*

Background and Aims: The accumulation of lipid and its metabolites in tissues, including the heart, causes lipotoxicity. Sphingolipids such as ceramides are particularly deleterious. Lowering the accumulation of ceramide can improve metabolic damage of various tissues. Recent reports showed that adiponectin receptors (AdipoRs) have sequence homology with ceramidase enzymes, and an increase of ceramidase activity with overexpression of adiponectin in mice improves ceramide-dependent lipotoxicity. Therefore, we investigated the possible roles of Adiporon, which mimics the effects of adiponectin, in the view of prevention and development of diabetic cardiomyopathy in diabetic mouse model.

Method: Male *db/db* mice and *db/m* controls were fed either a regular diet chow or a diet containing adiporon (30 mg/kg/day p.o. for 4 weeks from 17 to 20 weeks of age) and biochemical and morphological parameters were examined at 20 weeks of age.

Results: In *db/db* mice, left ventricular developed pressure (LVDP), heart rate (HR) and coronary flow rate (CFR) were decreased compared to *db/m* control mice, indicating cardiovascular dysfunction in diabetic heart. The treatment with AdipoRon remarkably improved the diabetes-induced contractile impairment, without any influence on HR. Adioporon also decreased fibrosis, inflammation cell infiltration and accumulations of free fatty acid, triglycerides and ceramide in the heart. In the molecular level, increased expressions of AdipoR1 and AdipoR2 and acid ceramidase activity in the heart were observed in *db/db* mice with Adiporon administration. Consistent up-regulations of phosphorylated AMPK and PPAR-α level were associated within the same group. Subsequent improvement of enhanced lipid metabolism and decrement of cellular apoptosis with adiporon treatment were also noted.

Conclusion: Adiporon may control oxidative stress in heart through AMPK and PPAR-α activated pathway and further contribute to prevent deterioration of cardiac function. The protective role of adiporon against the development of diabetic cardiomyopathy seems to occur through a direct action on the heart independently of systemic effects of adiponectin. Our results suggest adiporon as a promising therapeutic agent of diabetic cardiomyopathy through ameliorating ceramide-dependent lipotoxicity.



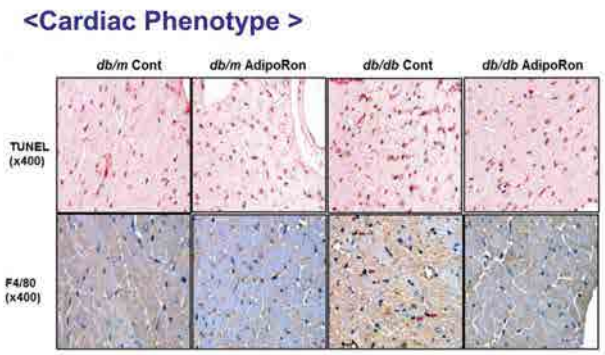


Figure:

P0975

EFFECT OF REGULATED INTRAMEMBRANE PROTEOLYSIS ON MEGALIN EXPRESSION DURING OXIDATIVE STRESS EXPOSURE.

Yoshifumi Kurosaki[1], Futoshi Ikarashi[1], Akemi Imoto[1], Fumitaka Kawakami[1], Masanori Yokoba[2], Tsuneo Takenaka[3], Masato Katagiri[2], Takafumi Ichikawa[1], Rikke Nielsen[4], Naohito Ishii[1]

[1]Kitasato University Graduate School of Medical Sciences, Department of Molecular Medical Biology, Sagamihara, Japan, [2]Kitasato University Graduate School of Medical Sciences, Department of Clinical Medicine, Sagamihara, Japan, [3]International University of Health and Welfare, Department of Medicine, Japan and [4]Aarhus University, Department of Biomedicine, Aarhus, Denmark

Background and Aims: Megalin, an endocytic receptor in proximal tubular cells, plays a critical role in renal tubular protein reabsorption. We previously reported that oxidative stress induced the temporally increase in renal megalin expression through the PI3K/AKT signaling pathway, but that megalin elevation is normalized or decreased during long term exposure to oxidative stress (hydrogen peroxide). However, the underlying mechanisms are unclear. Studies have addressed that megalin is subjected to regulated intramembrane proteolysis (RIP). Intracellular megalin COOH-terminal fragment (MCTF) is produced by protein kinase C-regulated, metalloprotease-mediated ectodomain shedding and further cleavage by gamma-secretase to produce the soluble megalin intracellular domain (MICD). The MICD in turn translocates to the nucleus where it decreases expression of the *Lrp2* gene encoding megalin. In the present study, we evaluated the effect of megalin RIP on the oxidative stress-regulated megalin expression.

Method: HK-2 cells were cultured with hydrogen peroxide (0.4 mmol/l) for 4.5 or 24 h, followed by treatment with gamma-secretase inhibitor, Compound E (5 mmol/L) or PKC activator, Phorbol 12-myristate 13-acetate (PMA, 0.5 mmol/L). Megalin expression was determined by performing western blotting or real-time PCR. The MCTF in medium was detected by western blotting. In animal experiments, Sprague-Dawley rats were randomly divided into two groups (n = 5): (i) STZ group (diabetic phenotype induced by streptozotocin administration) and (ii) sham group (vehicle). Urine was collected at two weeks after STZ administration, and the excretion of MCTF in urine was analyzed.

Results: Treatment of HK-2 cells with hydrogen peroxide (0.4 mmol/L) significantly increased megalin protein and mRNA levels at 4.5 h. Pretreatment of Compound E showed further increase in megalin expression in hydrogen peroxide-exposed cells. It was also found that presenilin-1 and -2, which are components of gamma-secretase, double knockdown with siRNA increased megalin expression in hydrogen peroxide treated-cells. On the other hand, PMA treatment inhibited the increase in both megalin protein and mRNA levels. In the cells treated with hydrogen peroxide for 24 h, megalin mRNA levels were normalized, but pretreatment of Compound E kept the elevation in megalin mRNA levels at 24 h after the treatment with hydrogen peroxide. Interestingly, megalin MCTF in the medium was increased by hydrogen peroxide treatment in a dose-dependent manner. Furthermore, megalin MCTF excretion in the urine of STZ-induced diabetes was significantly increased compared to sham rats.

Conclusion: These results suggested that oxidative stress-induced megalin upregulation was inhibited by RIP activation of megalin, suggesting that megalin RIP plays a role as a negative feedback system to oxidative stress-induced megalin upregulation. Furthermore, our data indicate that oxidative stress induces urinary excretions of MCTF in diabetic rats during the normoalbuminuric stage and potentially act as a marker of diabetic kidney disease.

P0976

ALTERED EXPRESSION OF LONG NON-CODING AND MESSENGER RNAS IN DIABETIC NEPHROPATHY FOLLOWING TREATMENT WITH ROSIGLITAZONE

Liwen Zhang[1], Ying Zhou[1,2], Fangfang Zhou[1,2], Xialian Yu[1,2], Jian Liu[1,2], Yunzi Liu[1,2], Weiming Wang[1,2]

[1]Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Department of Nephrology, Shanghai, P.R. China and [2]Institute of Nephrology, Shanghai Jiao Tong University School of Medicine, Shanghai, P.R. China

Background and Aims: The value of rosiglitazone (RSG) in the protection of kidneys from diabetic injury was recognized, however, the adverse systemic side effects limit its clinical application. Long noncoding RNAs (lncRNAs) are primarily described as signal molecules since they interact with cellular components, and have been shown to exhibit strong tissue and cell specificity. The aim of this study is to elucidate the novel renoprotective molecular mechanism of RSG and to propose lncRNA targets for diabetic nephropathy treatment, which may provide a new approach to avoid systemic side effects of RSG.

Method: Db/db mice were treated with RSG as dbR group or vehicle as dbdb group, and db/m mice as control group. Plasma, urine and kidney cortex were collected, and unbiased RNA sequencing of three renal cortical samples from each group was performed.

Results: Db/db mice developed hyperglycemia, impaired intra-peritoneal glucose tolerance, proteinuria, decreased mitochondrial SOD activity, podocyte impairment, epithelial-mesenchymal transition, glomerulosclerosis and tubulointerstitial fibrosis, however, RSG treatment improved these changes. RNA-seq profiling revealed that the development of DN caused an up-regulation in the expression of 1176 mRNAs and a down-regulation in the expression of 1010 mRNAs ($p<0.05$) compared to controls, with the expression of 251 mRNAs being returned to normal following treatment with RSG. Further, 88 up-regulated and 68 down-regulated lncRNAs ($p<0.05$) were identified in db/db mice compared to controls, 10 of which had their normal expression restored following treatment with RSG. Bioinformatic analysis revealed that the primary pathways involved in the pathogenesis of DN, and subsequently in the therapeutic effects of PPARγ, are related to inflammatory and metabolic processes. Six lncRNAs that exhibited opposite expression patterns in dbdb vs. control and dbR vs. dbdb analyses were randomly chosen and qualified by qRT-PCR, including a novel lncRNA and lncRNA-AI838599. From GSEA analysis, three co-expressed mRNAs of lncRNA-AI838599 (Gadd45b, Per1 and Sphk1) were cores enriched in the Hallmark TNFα signaling via NFκb Gene Set (MSigDB).

Conclusion: RSG treatment can attenuate DN in experimental models through regulation of metabolism and inflammation, and lncRNA-AI838599 emerges as a key rosiglitazone-regulated gene in DN treatment through TNFα-NFκb pathway.

P0977

LOW EXPRESSION OF AUTOPHAGY-RELATED PROTEIN 5 (ATG5) LEADS TO SUPPRESSION OF AUTOPHAGY IN PATIENTS WITH DIABETIC NEPROPATHY AND RETINOPATHY

Nakhoul Nakhoul[1], Rula Nakhoul[2], Remah Abass[2], Evgeny Farber[3], Hagar Tadmor[4], Farid Nakhoul[3,5]

[1]Baruch padeh Poria Medical Center, Azrieli Faculty of Medicine Ramat Gan University, Ophtalmology, Lower Galilee, Israel, [2]Baruch padeh Poria Medical Center, Diabetes and Metabolism Lab, Lower Galilee, Israel, [3]Baruch padeh Poria Medical Center, Azrieli Faculty of Medicine Ramat Gan University, Nephrology and Hypertension, Lower Galilee, Israel, [4]Baruch padeh Poria Medical Center, Azrieli Faculty of Medicine Ramat Gan University, Diabetes and Metabolism Lab, Lower Galilee, Israel and [5]Azrieli Faculty of MedicineBar-Ilan University, Diabetes and Metabolism Lab & Nephrology and Hypertension, Ramat Gan, Israel

Background and Aims: Autophagy is a catabolic mechanism that involves lysosomal-dependent degradation of unnecessary or dysfunctional intracellular components. Autophagy plays role in many biological processes, including diabetic nephropathy (DN) and diabetic retinopathy (DR). Autophagy-related gene 5 (ATG5) is one of the most important participants in the autophagy mechanism. Deficiencies in ATG5 protein levels are associated with several diseases by influencing the level of autophagy pathway. Our study's aim was to investigate if aberrant expression of ATG5 protein or *Atg5* gene is associated with DN or DR.

Method: The study included 120 human participants in 4 groups – Healthy, diabetic (DM), DN and DR; and 10 mice in 2 groups – healthy and DN. Western blot analyses of ATG5 and its downstream collaborator LC3B were performed on human white blood cell (WBC) lysates and murine renal lysates. Immunohistochemical analysis was performed on mice renal tissues. Quantitative real-time PCR analysis of ATG5 was performed on total mRNA isolated from human WBC.

Results:

1. ATG5 protein expression by western blot analysis was significantly decreased in DM patients, with and without complications [0.66 ± 0.06 A.U in DM patients (n=30 p <0.01), 0.62 ± 0.06 A.U in DN, (n=30 p<0.001) and 0.67± 0.05 A.U in DR patients (n=30 p<0.01)], compared with the healthy control subjects [0.97 ± 0.04 A.U (n=30)].
2. There was nearly a 2.5-fold decrease in the percentage of ATG5-stained areas in the tubules of DN mice (4.42 ± 1.08%) compared with W.T mice (10.87 ± 1.01%).
3. The expression of *Atg5* gene between the various study groups by qRT-PCR analyses (fig.1), the *Atg5* gene in DN (0.0069 ± 0.0005) and DR patients (0.0069 ± 0.0004) was down regulated at the mRNA levels, compared with healthy controls (0.0083 ± 0.0008).
4. substantial reduction of LC3-II levels (autophagy marker) in DM patients (0.50 ± 0.04 A.U, n=18 p < 0.001) DN patients (0.44 ± 0.05 A.U, n=19 p < 0.001) and DR patients (0.43 ± 0.05 A.U, n=18 p < 0.001) compared with the healthy control individuals (0.81 ± 0.05 A.U n=19).
5. The renal LC3-II protein expression was found to be greatly decreased in the tubules of DN mice when compared with W.T mice

Conclusion:

1. Our findings indicate that ATG5, as well as its downstream collaborator LC3-II, are often down-regulated in diabetic patients, which contributes to deficiencies in autophagy process. Impairment of this process can lead to accumulation of abnormal proteins and damage molecules that can lead to the development and progression of DN &DR.
2. Therapeutic potential of ATG5 modulations as a novel treatment strategy for DN or DR patients through the autophagy mechanism, as well as ATG5 may serve as a goal in the development of drugs for diabetic and its complications.

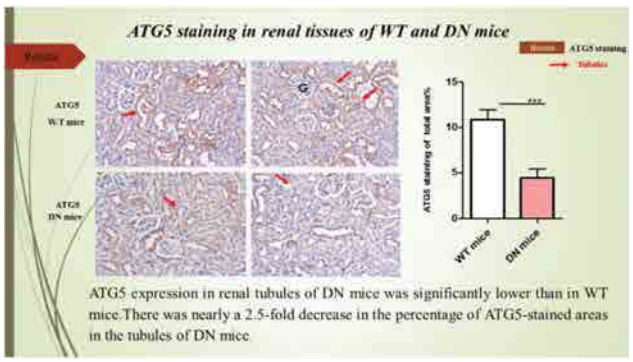


Figure. 1

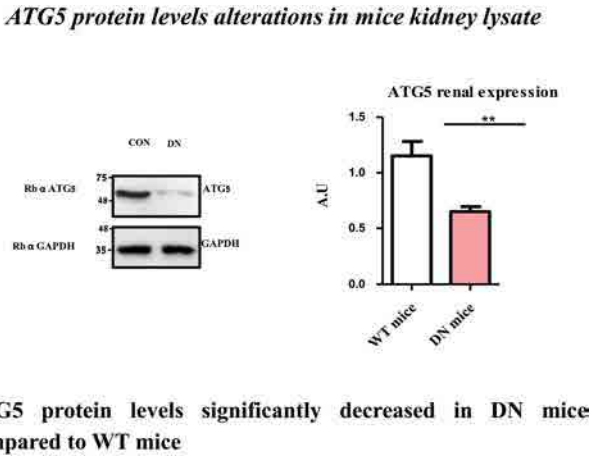


Figure. 2

P0978

THE EFFECTS OF CHRONIC DAPAGLIFLOZIN TREATMENT ON THE RENAL MICROVASCULATURE IN A RAT MODEL OF TYPE 2 DIABETES

Connie Ow[1], Vijayakumar Sukumaran[1], Jennifer Ngo[1], Cheng Kun Du[1], Akihiro Fujiwara[2], Hirotsugu Tsuchimochi[1], Hiroshi Hosoda[3], Roger Evans[4], James Pearson[1,4]

[1]National Cerebral and Cardiovascular Research Centre, Cardiac Physiology, Osaka, Japan, [2]National Cerebral and Cardiovascular Research Centre, Clinical Laboratory, Osaka, Japan, [3]National Cerebral and Cardiovascular Research Centre, Regenerative Medicine and Tissue Engineering, Osaka, Japan and [4]Monash University, Department of Physiology, Melbourne, Australia

Background and Aims: Chronic kidney disease (CKD) is an ever-growing concern and CKD associated with diabetes accounted for ∼ 35% of new cases of end-stage renal failure. Clinical trials with insulin-independent sodium-glucose co-transporter 2 (SGLT2) inhibitors not only showed significant improvements in hyperglycemia and thus renal damage, but also reduced the risk of adverse cardiovascular events. Microvessels supply local tissue oxygen demands and are important controllers of regional perfusion. Endothelial dysfunction has been posited to be an important factor driving the pathogenesis of diabetic nephropathy, largely through impaired eNOS activity and thus reduced nitric oxide bioavailability. Thus, we aim to determine the effects of SGLT2 inhibition on vasodilator function in the renal vasculature. We hypothesize that rats chronically treated with dapagliflozin, a SGLT2 inhibitor, improves renal endothelial function and the microvessels are better able to maintain perfusion in response to the inhibition of nitric oxide synthase and prostaglandin blockade.

Method: Male Zucker fatty diabetic rats (8 wk old), a model of type 2 diabetes, were given daily oral gavage of 1 mg/kg dapagliflozin or its vehicle for up to 22 wks of age (n=6/group). Renal excretory function, glomerular filtration rate (GFR) and indices of renal injury was assessed before treatment and after every 4 wks up until 22 wks of age. GFR was assessed via transcutaneous clearance of FITC-sinistrin. Vasodilator function of the renal microvasculature was assessed via X-ray microangiography. We conducted successive imaging of the microvessels before and during infusion of acetylcholine (ACh) and sodium nitroprusside (SNP) which facilitated the assessment of endothelium dependent and independent dilation respectively. After which, rats were given successive boluses of L-NAME and indomethacin to assess the vasodilatory function of the microvasculature independent of nitric oxide and prostaglandins respectively. These inhibitors were given under the conditions of SNP clamp which allowed for us to titrate the blood pressure to baseline levels. Lastly, we assessed the ability of endothelium hyperpolarizing factors (EDHFs) to maintain microvascular perfusion when SNP infusion ceased and an infusion of ACh commenced while still under the effects of L-NAME and indomethacin.

Results: As expected, dapagliflozin alleviated hyperglycemia across the treatment period. There was a tendency for dapagliflozin to ameliorate the decline of GFR, although this apparent effect was not statistically significant. Dapagliflozin did not appear to improve indices of renal injury. Treatment with dapagliflozin alleviated polyuria but did not appear to have an impact on urine osmolarity or sodium excretion. The responses (vessel diameter) of renal microvessels to ACh and SNP was greater in dapagliflozin than in vehicle fed rats. The microvessels of vehicle fed rats appeared to undergo relative constriction in response to L-NAME and indomethacin even under the effects of SNP clamp. In contrast, microvessels of dapagliflozin fed rats appeared to be relatively well-perfused after NOS and COX blockade. This suggests that dapagliflozin may improve endothelial dysfunction commonly associated with diabetic nephropathy. Following NOS and COX blockade, ACh was infused in rats to determine the status of vasodilatory function mediated by EDHFs. The microvessels in diabetic rats did not appear to be dilated after infusion of ACh, suggesting that vasodilatory effects of EDHFs on the vasculature is diminished in diabetic rats. Dapagliflozin appeared to improve this effect in that the renal microvessels were dilated even when NOS and COX production was blocked/inhibited.

Conclusion: Chronic treatment of dapagliflozin may improve endothelial dysfunction and thus retard the progression of diabetic nephropathy in a rat model of type 2 diabetes.

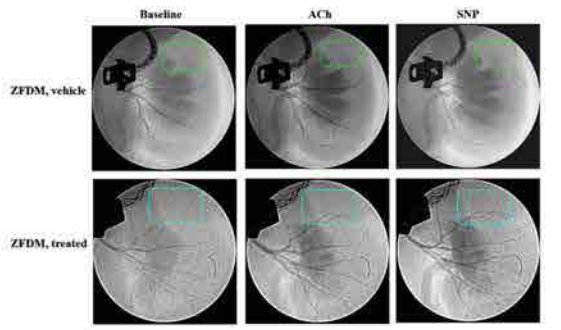


Fig 1: Renal microangiography. X-ray images of the rat microvasculature was taken during the baseline period and after successive intravenous infusions of acetylcholine (ACh) and sodium nitroprusside (SNP). Note the relative improved response to both vasodilators in dapagaliflozin fed rats.

P0979

BENEFICIAL EFFECT OF CHLOROQUINE AND AMODIAQUINE ON DIABETIC TUBULOPATHY BY ATTENUATING MITOCHONDRIAL NOX4 AND ENDOPLASMIC RETICULUM STRESS

So-Young Lee[1], Dong Ho Yang[1], Yu Ho Lee[1], Mi Jung Lee[1], Hyung-Jong Kim[1], MinJi Sung[1], Hyun-Ju An[1], Sang-Ho Lee[2]

[1]CHA Bundang Medical Center, CHA University, Internal Medicine, Seongnam, Korea, Rep. of South and [2]Kyung Hee Univ. Hospital at Gangdong, Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: Oxidative stress induced by chronic hyperglycemia is recognized as a significant mechanistic contributor to the development of diabetic kidney disease (DKD). Nonphagocytic nicotinamide adenine dinucleotide phosphate oxidase 4 (Nox4) is a major source of reactive oxygen species (ROS) in many cell types and in the kidney tissue of diabetic animals. We designed this study to explore the therapeutic potential of chloroquine and amodiaquine for inhibiting mitochondrial Nox4 and diabetic tubular injury.

Method: Human renal proximal tubular epithelial cells (hRPTCs) were cultured in high-glucose media (30 mM D-glucose), and diabetes was induced with streptozotocin (STZ, 50 mg/kg i.p. for 5 days) in male C57/BL6J mice. Chloroquine and amodiaquine were administered to the mice via intraperitoneal injection for 14 weeks.

Results: Chloroquine and amodiaquine inhibited mitochondrial Nox4 and increased mitochondrial mass in hRPTCs under high-glucose conditions. Reduced mitochondrial ROS production after treatment with the drugs resulted in decreased endoplasmic reticulum (ER) stress, suppressed inflammatory protein expression and reduced cell apoptosis in hRPTCs under high-glucose conditions. Notably, chloroquine and amodiaquine treatment diminished Nox4 activation and ER stress in the kidneys of STZ-induced diabetic mice. In addition, we observed attenuated inflammatory protein expression and albuminuria in STZ-induced diabetic mice after chloroquine and amodiaquine treatment.

Conclusion: We substantiated the protective actions of chloroquine and amodiaquine in diabetic tubulopathy associated with reduced mitochondrial Nox4 activation and ER stress alleviation. Further studies exploring the roles of mitochondrial Nox4 in the pathogenesis of DKD could suggest new therapeutic targets for patients with DKD.

Figure: None

P0980

IMPLICATIONS OF ADIPOSE EARLY DOWNREGULATION OF INTEGRIN-LINKED KINASE (ILK) IN THE DEVELOPMENT OF METABOLIC SYNDROME IN MICE

Mercedes Griera-Merino[1,2], Diego García-Ayuso[1,2], Lourdes Bohorquez Magro[1,2], Sofía Campillo de Blas[1,3], Marta Barrionuevo-González[4], Elena Gutiérrez-Calabrés[1,2,4], Laura Calleros[1,2], Diego Rodríguez-Puyol[1,3,4], Manuel Rodríguez-Puyol[1,2], Sergio De Frutos García[1,2,4]

[1]Instituto Ramon y Cajal de Investigación Sanitária (IRYCIS), Fundación Renal Iñigo Álvarez de Toledo (FRIAT), REDinREN from Instituto de Salud Carlos III and NOVELREN from Comunidad de Madrid, Madrid, Alcalá de Henares, , [2]Universidad de Alcalá, Systems Biology, Physiology Unit,, Alcalá de Henares, Spain, [3]Hospital Príncipe de Asturias, Nephrology Unit and Department of Medicine from Universidad de Alcalá, Alcalá de Henares, Spain and [4]Hospital Príncipe de Asturias, Biomedical Research Foundation, Alcalá de Henares, Spain

Background and Aims: Insulin resistance (IR)-related metabolic disorders, such as diabetes type 2 and obesity, are linked to renal and cardiovascular risk. Unfortunately, they lack a better prognosis before their full establishment. An important mechanism associated to the IR development is the dysregulation of lipolysis in white adipose tissue (WAT), which is driven by the excessive lipid accumulation, together with inflammation and the excessive deposition of ECM components such as collagens and fibronectin, known as fibrosis. The intracellular lipid adjustment is affected by changes in the expression and activity of the hormone-sensitive lipase (HSL) and the intracellular and circulating balance of the lipolysis products glycerol and free fatty acids.

We published that transgenic depletion of the scaffold intracellular protein Integrin-linked kinase (ILK), one of the adhesome translators of the ECM signals, modulates IR in WAT [Hatem-Vaquero et al. J Endocrinol. 2017]. We also published that ILK downregulation in WAT is an early event in a short-term high fat diet (HFD) mice model that correlates with a faster insulin sensitivity loss, accompanied with an early increase of body weight and the erratic expression of WAT adipokines and metabolites transporters. [Hatem-Vaquero et al. Cell Physiol Biochem 2020]. Here we used in vivo and in vitro approaches to decode the role of ILK downregulation during WAT expansion and altered lipolysis.

Method: Adult mice with global transgenic downregulation of ILK expression (cKD-ILK) and littermates without that depletion (CT) were fed with either standard (STD) or high fat (HFD) diets during 2 and 6 weeks. We determined the weight changes on body and WAT depots, epididymal (eWAT) and subcutaneous (scWAT), and the circulating lypolisis product glycerol. The expression of ECM component fibronectin (FN), fibrosis marker TGF-beta and the glycerol transporter AQP3 were determined in eWAT by RT-qPCR or Western blot. Comparative studies were performed in cultured C3H10t1/2-based adipocytes where ILK expression was deliberately downregulated by the transfection of siRNAs against ILK or in control adipocytes (scramble siRNAs). We determined the expression of ILK, total and active HSL isoforms (HSL, p-HSL s660) by RT-qPCR or Western blot and the intracellular fat droplet content (by adipo-red dye)

Results: HFD increased progressively CT eWAT, scWAT and whole body weight gains. HFD-fed cKD-ILK have an earlier increase of body and eWAT weights. However, the scWAT weight ratio against eWAT was inverted in the same cKD-ILK animals. This early depot-specific response to HFD coincide with increase in IR [Wajchenberg BL. Endocr Rev 2000]. HFD-fed cKD-ILK WAT early expressed altered levels of fibrotic markers (TGF-beta and Fibronectin). HFD-fed cKD-ILK shown a temporary increase of circulating glycerol and its WAT transporter AQP3. In cultured adipocytes with downregulated expression of ILK, the intracellular fat droplet was increased and the HSL contain and its lipolysis activity (measured as levels of p-HSL isoform) were reduced.

Conclusion: We suggest ILK as a modulator during the obesity establishment. Considering the observed relation between ILK expression with the altered lipolysis and fibrosis patterns observed in visceral WAT, ILK downregulation may be a predictive value and probably its pharmacological upregulation may be a novel therapeutic strategy against obesity and IR.

P0981 **ANTIDIABETIC AND RENOPROTECTIVE ROLE OF METFORMIN ON METABOLIC PARAMETERS IN KIDNEY OF DIABETIC AGING RATS**

Pardeep Kumar[1], Najma Baquer[1]

[1]*Jawaharlal Nehru University, School of Life Sciences, New Delhi, India*

Background and Aims: The objective of this study was to investigate renoprotective effects of metformin on renal function, mitochondrial and antioxidant enzymes, oxidative stress biomarker, DNA degradation and expression of glucose transporters in of diabetic aging female rats.

Method: Young (3 months) adult (12 months) and aged (24 months) rats will be diabetic by using alloxan monohydrate. Metformin was administered i.p. at a dose of 200 mg/kg/day for 30 days to both control and diabetic aging rats. A detailed study was carried on membrane fluidity, lipofuscin, antioxidant enzymes and DNA degradation to identify the antidiabetic and antiaging role of metformin using biochemical ,molecular and histiochemical study. Renal function was assessed by measuring proteinuria, enzymuria, expression of glucose transporters, renin-angiotensin system, and activities of polyol pathway enzymes.

Results: Present study shows that there was a similar pattern of increased lipid peroxidation, lipofuscin, DNA degradation and glucose transporters expression with upregulation of renal angiotensin-converting enzyme and a decrease in membrane fluidity, glutamate dehydrogenase, Na+ K+ ATPse, antixodant enzymes activities in both aging and diabetes. Metformin treatment helped to reverse the age related changes studied, to normal levels, elucidating an anti-aging, antidiabetic and renoprotective action. Metformin effectively countered the diabetes-induced structural abnormalities of renal tissue of aging rats.

Conclusion: Metformin was found to be an effective treatment in stabilizing and normalizing the renal functions; therefore this therapy can be considered an alternative to be explored further as a means of diabetic and aged related disorders control. The results of this study will be useful for pharmacological modification of the aging process and applying new strategies for control of age related disorders including metabolic syndrome.

P0982

PTEN-INDUCED KINASE 1 (PINK1) DEPLETION ALTERS MITOCHONDRIAL EFFICIENCY AND GLYCOLYSIS IN HUMAN PODOCYTES

Irena Audzeyenka[1,2], Dorota Rogacka[1,2], Agnieszka Piwkowska[1,2]

[1]Mossakowski Medical Research Centre Polish Academy of Sciences, Warszawa, Poland and [2]University of Gdańsk, Faculty of Chemistry, Gdańsk, Poland

Background and Aims: Podocytes are terminally differentiated cells, which constitute an inner layer of the renal filtration barrier. Podocytes are characterized by high metabolic activity, and their elevated energy requirements are met by maintaining the appropriate mitochondrial number and quality, which depend on mitochondrial biogenesis and mitophagy. Alteration of mitochondrial dynamics is linked to the development of insulin resistance and diabetes. The main goal of the research was to determine the role of mitophagy in podocytes bioenergetics and to elucidate the effects of hyperglycemia on mitochondrial dynamics.

Method: In order to inhibit mitophagy, we generated a human podocyte cell line stably expressing PINK1 shRNA through lentiviral transduction. Biochemical analyses were performed to assess the oxidative phosphorylation efficiency (by measurement of oxygen consumption rate; OCR) and glycolysis contribution to the total cell energy production (by measurement of extracellular acidification rate; ECAR) in the differentiated shPINK1 podocytes. The expression levels of mRNAs and proteins were evaluated in podocytes cultured in standard glucose (11 mM) and high glucose (30 mM) concentrations using real-time PCR and western blot. Intracellular mitochondrial network was visualized by MitoTrackert^{TM} staining. The co-localization of proteins in podocytes was analysed by double immunofluorescence labelling and confocal microscopy.

Results: PINK1-deficiency resulted in the significant decrease of maximal respiration and spare respiratory capacity in podocytes (by 40% and 70%, respectively). Non-mitochondrial respiration was also decreased by 45% in shPINK1 cells. Interestingly, basal respiration and ATP production appeared similar in shPINK1 and control podocytes. PINK1 depletion increased glycolytic flux by 70%, in addition, the accompanying decline in glycolytic capacity and glycolytic reserve was observed (by 38% and 63%, respectively). Moreover, we observed accumulation of small and ring-shaped mitochondria in PINK1-deficient podocytes compared with the control cells.

We showed a decreased expression of PINK1 and Parkin (mRNA and protein) in normal human podocytes cultured in hyperglycemic medium, which was associated with an elevated levels of mitochondrial fission markers (DRP1, FIS1) and with a decreased levels of PGC1α and TFAM, which play a role in mitochondrial biogenesis and mtDNA replication.

Conclusion: In this research, we demonstrated a novel role of mitophagy in podocyte bioenergetics. Moreover, we showed that high glucose inhibits mitophagy and promotes mitochondrial fission leading to the accumulation of damaged mitochondria and podocyte injury, which underlies the pathogenesis of diabetic nephropathy.

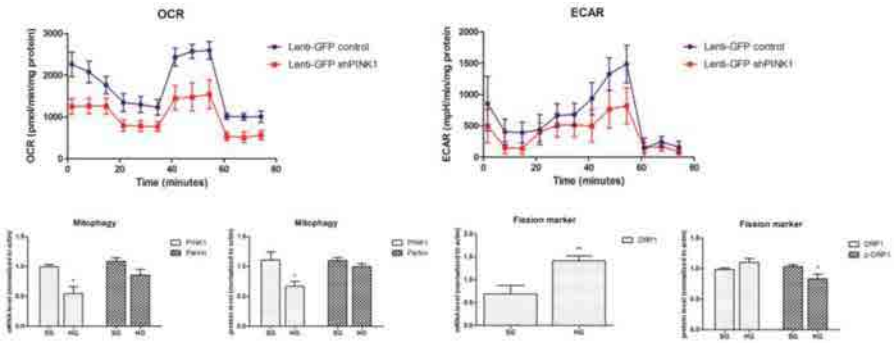


Figure:

P0983 INHIBITION OF ATF3 BY RAF INHIBITOR GW5074 ON DIABETIC NEPHROPATHY

Jee Young Han[1], Jin Joo Cha[2], Young Sun Kang[2], Jung Yeon Ghee[2], Ji Ae Yoo[2], Dae Cha[2]

[1]Inha University, Pathology, Incheon, Korea, Rep. of South and [2]Korea University, Ansan Hospital, Internal Medicine, Ansan, Korea, Rep. of South

Background and Aims: Activating Transcription Factor 3 (ATF3) is a stress-adaptive transcription factor, which has been suggested to be involved in maintaining glucose homeostasis. ATF3 respond rapidly to various stimuli like high glucose, fatty acids and oxidative stress, and is observed to either protective or detrimental effects in diabetic condition. Therefore to elucidate the exact role in diabetic nephropathy of ATF3, we investigated the role of ATF3 by inhibition with Raf-inhibitor GW5047 on diabetic mice model.

Method: ATF3 level was examined in the mouse podocytes and NRK cells with either overexpression or downregulation with ATF3. 8 week db/m and db/db mice as the model of diabetic mice were examined for the expression of ATF3 and were treated with GW5074, a Raf1 kinase inhibitor targeting the ATF3 intraperitoneally with a dose of 0.5mg/kg for 12 weeks.

Results: In cultured mouse podocytes and NRK cells, high glucose and angiotensin II markedly increased ATF3 expression. Gene Expressions of NOX4, MCP-1 and NF-kB were augmented by ATF3, and were attenuated by ATF3 siRNA. In db/db mice, plasma ATF3 level was not different from control db/m, however the urinary ATF3 excretion was significantly higher. Treatment of GW5074 decreased urinary ATF3 excretion. After 12 week treatment, serum creatinine level was significantly lower in the treatment db/db group, with less systemic oxidative stress. There were no significant differences in body weight, whereas the food intake was decreased in GW5047 group. Overall lipid profile or HOMA-IR, HbA1c level was not different from each group. Serum adiponectin were otherwise increased in GW5074 group. Urinary excretion of albumin at 2 month of treatment decreased with urinary nephrin excretion. Trend of increased gene expression of JNK, p-38, smad2, ERK which was downregulated by GW5074 was noted.

Conclusion: These findings suggest that in diabetic condition, the activation of ATF3 is associated pathogenesis of diabetic nephropathy and targeting ATF3 may have a protective role in the disease progression.

P0984 SGLT2 INHIBITION PREVENTS RENAL FIBROSIS IN CYCLOSPORINE NEPHROPATHY

Giovanna Castoldi[1], Raffaella Carletti[2], Silvia Ippolito[3], Massimiliano Colzani[1], Francesca Barzaghi[1], Andrea Stella[1], Gianpaolo Zerbini[4], Gianluca Perseghin[1,5], Giovanni Zatti[1,6], Cira Di Gioia[2]

[1]Dipartimento di Medicina e Chirurgia, Universita' degli Studi di Milano-Bicocca, Monza, Italy, [2]Dip. Scienze Radiol., Oncol., Anatomopatologiche. Istituto Anatomia Patologica, Sapienza Universita' di Roma, Rome, Italy, [3]Laboratorio Analisi Chimico Cliniche, Ospedale San Gerardo. ASST Monza, Monza, Italy, [4]Unita' Complicanze del Diabete., IRCCS Istituto Scientifico San Raffaele, Milano, Italy, [5]Dip. Medicina Interna e Riabilitazione, Policlinico di Monza, Monza, Italy and [6]Clinica Ortopedica, Ospedale San Gerardo. ASST Monza., Monza, Italy

Background and Aims: Sodium glucose cotransporter 2 (SGLT2) inhibitors, a new class of antidiabetic drugs, showed nephroprotection in type 2 diabetic patients. The mechanisms underlying nephroprotection are not completely known and it is unclear whether the nephroprotective effects are present also in non-diabetic nephropathy. The aim of this study was to evaluate the effects of empagliflozin, a SGLT-2 inhibitor, in cyclosporine nephropathy in the absence of diabetes.

Method: Ten days before the beginning and then during the entire experimental periods, low-salt diet (Teklad 7034) was administered to Sprague Dawley rats. Cyclosporine-A (CsA, 15 mg/kg/day, intraperitoneal injection; n=6) and CsA plus empagliflozin (Empa, 10 mg/kg /day, per os; n=6) were administered for 4 weeks. Control group was treated with placebo (n=6). Blood pressure was measured by plethysmographic method at the beginning and at the end of the experimental period. At the end of the protocol, the kidneys were excised for histomorphometric analysis of renal fibrosis and for immunohistochemical evaluation of inflammatory infiltrates and tyrosine hydroxylase expression, used as marker of symphatetic nerve activity.

Results: The rats treated with CsA showed a significant increase ($p < 0.01$) in blood pressure, which was slightly reduced by administration of empagliflozin. CsA administration caused an increase in glomerular and tubulo-interstitial fibrosis ($p < 0.05$), renal inflammatory infiltrates ($p < 0.05$) and tyrosine hydroxylase expression ($p < 0.01$) as compared to the control rats. Treatment with empagliflozin reduced glomerular and tubulo-interstitial fibrosis ($p < 0.05$), inflammatory cell infiltration ($p < 0.01$) and tyrosine hydroxylase expression ($p < 0.01$), as compared to CsA-treated rats.

Conclusion: Empagliflozin administration showed protective effects on cyclosporine nephropathy, decreasing renal fibrosis, macrophage infiltration and tyrosine hydroxylase expression. These data suggest that the nephroprotective role of empagliflozin could not be restricted only to diabetic nephropathy.

P0985 EFFECTS OF SILVER NANOPARTICLES ON RENAL FUNCTION IN FAT-FED AND STREPTOZOTOCIN-TREATED RATS

Pardeep Kumar[1]

[1]*Jawaharlal Nehru University, School of Life Sciences, New Delhi, India*

Background and Aims: The present study investigated the effects of silver nanoparticles on serum parameters of renal function, on oxidative stress markers (malondialdehyde [MDA] and 8-isoprostane), and on expression level of insulin receptor, glucose transporter 2 (GLUT2), glucokinase genes and heat-shock proteins (HSPs) in rats.

Method: Male Wistar rats (n=64, 10 weeks old) were divided into four groups. Group 1 received a standard diet (12% of calories as fat). Group 2 received a standard diet, plus silver nanoparticles (SNPs); received a single daily oral dose of SNP of 100 mg/kg in suspension. Group 3 received a high-fat diet (40% of calories as fat) for 2 weeks, and was then injected with streptozotocin (STZ) on day 14 (STZ, 40 mg/kg intraperitoneally). Group 4 was treated in the same way as group 3 (HFD/STZ), but was supplemented with SNP 100mg /kg/body weight/day. Oxidative stress in the kidneys of diabetic rats was evidenced by an elevation in levels of MDA and 8-isoprostane. Protein concentrations of insulin receptor, GLUT2, glucokinase genes and heat-shock (HSP60 and HSP70) in renal tissue were determined by Western blot analyses.

Results: SNP supplementation lowered kidney concentrations of MDA, 8-isoprostane levels, serum urea-N, and creatinine, and reduced the severity of renal damage in the STZ-treated group (i.e., the diabetes-induced group). The expression of insulin receptor, GLUT-2, glucokinase genes and HSPs was lower in the STZ group that received SNP than in the group that did not. No significant effect of SNP supplementation was detected in regard to the overall measured parameters in the control group.

Conclusion: This study supported the efficacy of SNP in reducing renal risk factors and impairment because of diabetes and act as potent antidiabetic agent.

P0986

NO/CGMP PATHWAY MODULATES GLUCOSE UPTAKE VIA REGULATION OF SIRT1 DEACETYLASE EXPRESSION AND ACTIVITY IN PODOCYTES EXPOSED TO HIGH GLUCOSE CONCENTRATIONS

Dorota Rogacka[1,2], Irena Audzeyenka[3,4], Agnieszka Piwkowska[3,4]

[1]Mossakowski Medical Research Centre, Polish Academy of Sciences, Laboratory of Molecular and Cellular Nephrology, Warsaw, Poland, [2]Faculty of Chemistry, University of Gdansk, Department of Molecular Biotechnology, Gdańsk, Poland, [3]Mossakowski Medical Research Centre, Polish Academy of Sciences, Laboratory of Molecular and Cellular Nephrology, Warsaw, Poland and [4]Faculty of Chemistry, University of Gdansk, Department of Molecular Biotechnology, Gdańsk, Poland

Background and Aims: Glomerular podocytes have become the aim of the extensive research in diabetes because of their importance in the development of diabetic nephropathy. High glucose concentration affects podocyte metabolism and function leading to the development of insulin resistance. Moreover, it decreases deacetylase SIRT1 protein amount and activity, leading to abolition of insulin effect on glucose uptake into the cells. The aim of our study was to examine the involvement of NO/cGMP pathway in the regulation of sirtuin 1 (SIRT1) protein expression and activity in podocytes, in the context of high-glucose induced insulin resistance. This work was supported by grant from the National Science Centre (2016/23/B/NZ4/03448).

Method: Experiments were performed in primary rat podocytes cultured with normal (NG, 11.1 mM) or high (HG, 30 mM) glucose concentrations for 5 days. RT-PCR and immunodetection methods were used to detect mRNA and protein expressions. Glucose uptake was measured by the addition of 1 µCi/well of 2-deoxy-(1,2-^{3}H)-D-glucose uptake diluted in non-radioactive ɒglucose (50 µM final concentration) with or without 300 nM insulin. SIRT1 activity was determined with a SIRT1 Fluorometric Kit according to the manufacturer's instructions. SIRT1 expression was modified by transfection with SIRT1 siRNA. To examine the effect of NO/cGMP pathway activity on SIRT1, cells were incubated in the presence of SNAP, a mimetic of nitric oxide synthase activity (NOS), and 8-Br-cGMP, protein kinase G (PKG) activator. We also used L-NAME – NOS inhibitor, and Rp-8-Br-cGMPs, PKG inhibitor.

Results: SIRT1 protein expression and activity were decreased in podocytes exposed to high glucose concentrations. We showed that in the presence of SNAP and 8-Br-cGMP, SIRT1 protein amount and activity were increased, leading also to enhancement of basal and insulin-dependent glucose uptake. In podocytes, transfected with SIRT1 siRNA, treatment with NO/cGMP pathway activators SNAP or 8-Br-cGMP increased glucose uptake. NO/cGMP pathway inhibitors exerted opposite effects on SIRT1 protein level and activity as well as on glucose uptake. Insulin action on glucose uptake into podocytes cultivated in the presence of normal glucose concentrations was abolished after NO/cGMP pathway inhibition.

Conclusion: We found that impairment of insulin effect on glucose uptake in HG-exposed podocytes, which was associated with SIRT1 downregulation, may be prevented by NO-dependent signaling modulation.

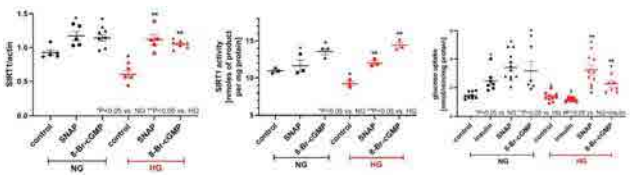


Figure:

P0987 **MIR-181A IMPROVED RENAL INFLAMMATION VIA TARGETING TNF-A IN DIABETIC NEPHROPATHY**

Dan Liu[1], Bicheng Liu[1]

[1]*Institute of Nephrology, Zhong Da Hospital, Southeast University, Nanjing, P.R. China*

Background and Aims: Recent studies have revealed that miR-181a is involved in various inflammation associated diseases, however, its participation in pathogenesis of diabetic nephropathy (DN) remains unclear. Hence, we investigated the involvement of miR-181a in the pathogenesis of DN patients and in animal model.

Method: miR-181a level was measured in the kidney of DN patients and DN mice model (db/db mice) by RT-PCR. To investigate the interaction of miR-181 a with the 3'-UTR of potential target transcripts, Luciferase reporter assays were performed. miR-181a-GFP-AAV and miR-181a inhibitor was generated to over-express or downregulate miR-181a in the kidney of db/db mice respectively. The expression of target gene and inflammatory proteins were measured in the kidney of our animal model.

Results: In DN patients and DN mice, a significant decrease in miR-181a levels in kidney were revealed by Expression analyses performed. Overexpression of miR-181a reduced proinflammatory genes (TNF-α, IL-1β, and IL-18) expression, whereas suppression of miR-181a worsened these changes. Furthermore, there was a negative linear correlation between miR-181a and TNF-α, IL-1β, and IL-18 expression levels in the kidney from DN patients. Luciferase assays revealed TNF-α as a direct target of miR-181a.

Conclusion: Our data emphasized on the anti-inflammatory actions of miR-181a via targeting TNF-α in the context of renal inflammation in DN. Hence, miR-181a could be served as a potential therapeutic options for controlling renal inflammation in DN.

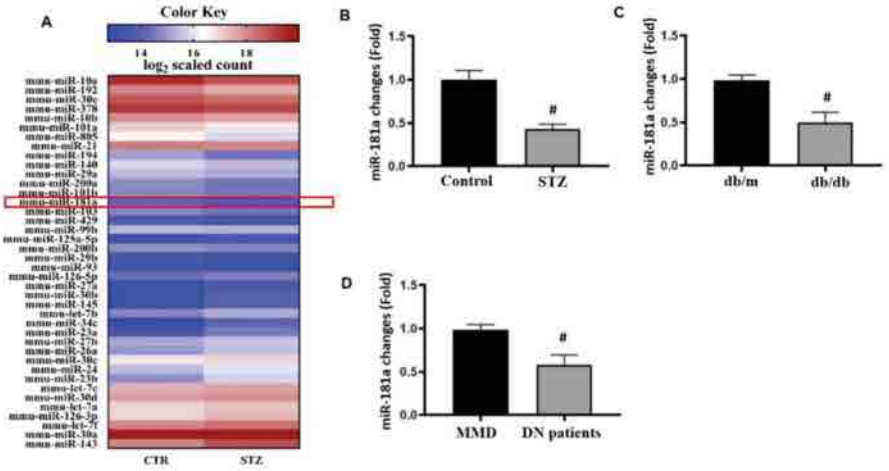


Figure:

P0988

THE PROTECTIVE EFFECT OF RED ORANGE AND LEMON EXTRACT (RLE) IN DIABETIC OBESE ZUCKER RATS IS RELATED TO ITS ACTION ON THE NADPH OXIDASE SUBUNIT.

Sara Damiano[1], Consiglia Longobardi[2], Chiara Lauritano[3], Emanuela Andretta[1], Giovambattista Capasso[2], Salvatore Florio[1], Roberto Ciarcia[1]

[1]University of Naples "Federico II", Department of Veterinary Medicine and Animal Productions, Naples, Italy, [2]University of Campania "Luigi Vanvitelli", Department of Translational Medical Sciences - Nephrology, Naples, Italy and [3]Anton Dohrn Zoological Station, Marine Biotechnology Department, Naples, Italy

Background and Aims: Type 2 diabetes mellitus is a pathological and chronical condition that induce a rearrangement in carbohydrate metabolism (Kaneto H et al. Antioxid Redox Signal. 2007). Even if the pathological mechanism of DN is not yet clear, NADPH oxidase (NOX) has been demonstrated to be involved in kidney ROS (Reactive Oxygen Species) generation during diabetic state (Palicz A. et al. J Biol Chem. 2001). Therefore, NOX-4, whose p22-phox subunit have shown a pivotal role in diabetes development, has been considered a potential pharmacological target in DN (Gill PS and Wilcox CS. Antioxid Redox Signal. 2006). In previous experiments performed on diabetic rat animal model with DN, we have found a beneficial effect of an extract rich in anthocyanins (ANT), members of flavonoids group (Shih PH. J Agric Food Chem. 2007). The aim of the present work was to investigate the molecular mechanisms involved in the DN and the protective effects of the new extract particularly abundant in ANT, the Red orange and Lemon Extract (RLE).

Method: Zucker diabetic fatty rats were divided into three groups and treated by gavage daily until 30 weeks of age, as follows: control group (ZF rats) received 1 mL of normal saline; ZDF Group (ZDF rats) received 1mL of normal saline; ZDF + RLE group (ZDF rats) treated with 90 mg/ kg of RLE dissolved in 1mL of normal saline. We examined the gene and protein expression of NOX4 catalytic subunit and its regulatory subunit p22-phox through Real Time PCR and western blot analysis.

Results: The expression gene levels of NOX4 significantly increased in diabetic rats ZDF, compared to control ZF (***$p<0.001$). Exposure of ZDF rats with RLE induces a decreased expression of NOX4 (Figure 1) compared to ZDF. On the contrary, there were not significant expression levels variations for regulatory subunit p22-phox. Western blot results are in agreement with Real Time PCR data, in fact an increase in NOX4 protein levels (*$p<0.05$) is evident, but no significant increase in p22-phox subunit was observed.

Conclusion: In conclusion, we hypothesize that the protective effect of RLE on the development of DN is related to its ability to inhibit NADPH oxidase activity and opens new perspectives for the treatment of DN.

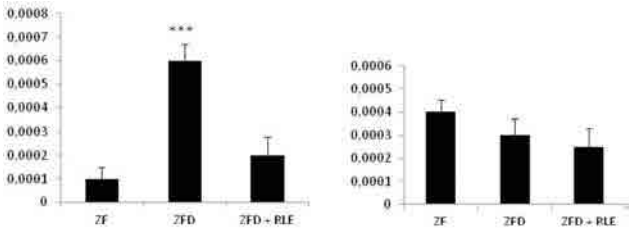


Figure 1: Figure represents mRNA levels (measured as mean normalized expression, MNE) of NOX4 (fig. a) and p22 (fig. b), in diabetic rats (ZDF) and diabetic rats treated with RLE (ZDF + RLE) compared to the control rats (ZD) (***$p < 0.001$).

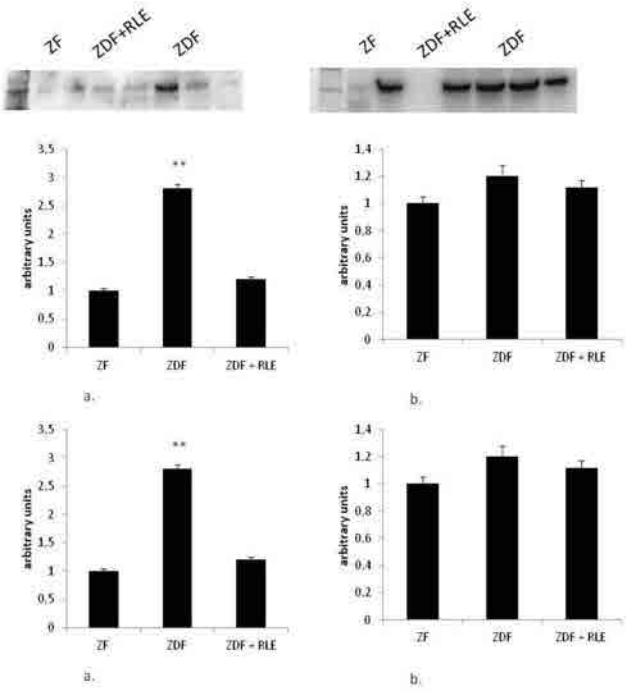


Figure 2: Figure represents proteins expression of NOX4 (fig. a) and p22 (fig. b), in diabetic rats (ZDF) and diabetic rats treated with RLE (ZDF + RLE) compared to the control rats (ZD) and normalized towards beta-tubulin (**$p < 0.01$).

P0989 VDR/ATG3 AXIS REGULATES SLIT DIAGRAM TO TIGHT JUNCTION TRANSITION VIA P62-MEDIATED AUTOPHAGY PATHWAY IN DIABETIC NEPHROPATHY

Jingyi Qian[1], Bin Wang[1], Bicheng Liu[1]

[1]*Institute of Nephrology, Zhong Da Hospital, Southeast University, School of medicine, NanJing, P.R. China*

Background and Aims: Vitamin D receptor (VDR) loss, slit diagram (SD) to tight junction (TJ) transition and impaired autophagic flux contribute to podocyte injury in diabetic nephrology. This study aims to examine the effect and mechanism of VDR on autophagic flux and SD-TJ transition in diabetic nephropathy.

Method: Renal biopsy tissues from DN patients at stage IIa, IIb, III, IV and patients with minimal lesions were used to evaluate the expression of VDR, autophagic flux and SD-TJ transition glomeruli. In vitro, cultured podocytes were treated with serum starvation (SS), autophagic inhibitors (3-methyladenine 3-MA or chloroquine CQ) to determine the degradation pathway of TJ marker ZO-1. Meanwhile, db/db mice and STZ-induced rats were used to explore the therapeutic effect and mechanism of VDR agonist in diabetic nephropathy.

Results: SD-TJ transition between foot processes could be observed under electron microscopy in DN patients at all stages, whereas foot processes were separated by the filtration slit and appeared to be single cross-strands in the normal glomeruli. There was a trend of increasing expression of autophagic marker p62 and ZO-1 and the expression of p62 is positively correlated with the changes of ZO-1 in the glomeruli of DN patients. In vitro, inhibiting autophagy with 3-MA and CQ resulted in the accumulation of ZO-1 in cultured podocytes. In addition, Co-IP experiments further convinced the interaction between p62 and ZO-1, which was enhanced by the activation of autophagy. Podocytes apoptosis and the activity of caspase 3 and caspase 8 were significantly increased in the presence of 3-MA or CQ, while these effects were rescued by silencing p62. According to VDR gene expression data in GEO database, VDR expression was decreased in diabetic nephropathy patients compared with normal people. Knocking down VDR lowered the expression of atg3 and leaded to the blockage of autophagy, which could be reversed by over-expressing Atg3. Podocytes treated with high glucose resulted in the decrease of VDR and Atg3, impaired autophagic flux and aggravated podocytes injury. However, VDR agonist treatment partially reversed all the changes. In vivo, db/db mice and STZ-induced rats (DN animal models) exhibited SD-TJ transition, massive proteinuria, decreased expression of VDR and podocin and the increased accumulation of p62 and ZO-1, all of which could be partially reversed by VDR agonist.

Conclusion: VDR loss contributed to the impairment of autophagic flux and SD-TJ transition via down-regulation Atg3 in diabetic nephropathy. Here, we identified a new mechanism and evidence for VDR agonist to treat diabetic nephropathy.

P0990

RENINAAV DOSE-DEPENDENTLY EXACERBATE ALBUMINURIA AND GLOMERULOSCLEROSIS, AND REDUCE GFR IN FEMALE UNINEPHRECTOMIZED DB/DB MICE

Mette Viberg Østergaard[1], Rune Ida[1], Annemarie Aarup Pedersen[1], Thomas Secher[1], Frederikke Emilie Sembach[1], Sebastian Tølbøl Thrane[1], Urmas Roostalu[1], Keld Fosgerau[1], Lisbeth N Fink[1], Niels Vrang[1]

[1]*Gubra, Hørsholm, Denmark*

Background and Aims: Diabetic nephropathy (DN) is a long-term complication that occurs in ∼40% of diabetes patients and is a leading cause of end-stage renal disease. Despite recent emergence of SGLT2 inhibitors and GLP-1 receptor agonists for nephroprotection in diabetes patients, drug discovery has been halted by the lack of reliable rodent models exhibiting features of human DN. In a newly established mouse model of progressive DN, we investigate the effects of hypertension on kidney injury.

Method: Female db/db mice were uninephrectomized (UNx) at 8 weeks of age and injected i.v. with a Renin adeno-associated virus (AAV) construct at different doses to induce hypertension, while a LacZAAV construct was used as negative control. db/+ mice served as healthy controls. Hypertension was measured by tail cuff and glomerular filtration rate (GFR) transcutaneous recoding of FITC-sinistrin after i.v. bolus injection at 22 weeks of age. Urine ACR measured in spot urine samples collected before termination 24 weeks of age. Terminal kidney samples were collected for 3D image analyses, histopathological evaluation, and next generation sequencing for gene expression analyses.

Results: GFR measurements indicated hyperfiltration in all AAV-injected UNx db/db mice compared to db/+ mice, while ReninAAV tended to dose-dependently decrease GFR compared to LacZAAV in UNx db/db mice. Urine ACR was worsened by ReninAAV-induced hypertension compared to LacZAAV controls. Automized AI-based glomerulosclerosis scoring showed ReninAAV dose-dependent increases in glomerulosclerosis compared to LacZAAV controls. 3D kidney imaging demonstrated increased glomerular volume in LacZAAV UNx db/db mice compared to db/+ mice with no further effect in ReninAAV groups. RNA sequencing revealed upregulated gene expression markers of fibrogenesis (incl. *Col1a1*, *Col3*, *Col4*, *Fn1*, *Lamc2* and *Vim*) and tubular injury markers (*Ngal* and *Kim-1*), as well as downregulation of proximal tubular markers (*Megalin* and *Aqp1*) in ReninAAV UNx db/db mice compare to LacZAAV controls.

Conclusion: ReninAAV-induced hypertension in female UNx db/db mice accelerates kidney injury in uninephrectomized db/db mice and aggravates GFR, albuminuria and glomerulosclerosis in parallel with increased expression of genes associated with tubular injury renal fibrosis. Together, these data confirm that ReninAAV UNx db/db mice is a reliable model of DN with features of late stage human disease.

P0991

EFFECTS OF TRIGONELLA FOENUM GRAECUM AND SODIUM ORTHOVANADATE ON ALTERED RENAL MEMBRANE FUNCTIONS IN ALLOXAN DIABETIC RATS

Pardeep Kumar[1], Najma Baquer[1]

[1]*Jawaharlal Nehru University, School of Life Sciences, New Delhi, India*

Background and Aims: The present study was carried out to observe, the antihyperglycemic and renoprotective effect of sodium orthovanadate (SOV) and *Trigonella foenum graecum* seed powder (TSP) administration on blood glucose, renal functions, expression of glucose transporter, DNA fragmentation, inflammatory cytokines and oxidative stress markers in kidney tissues and to see whether the treatment with SOV and TSP was capable of reversing the diabetic effects.

Method: Diabetes was induced by administration of alloxan monohydrate (15 mg/100 g body weight.) and rats were treated with 2 IU insulin, 0.6mg/ml SOV, 5% TSP in the diet and a combination of 0.2 mg/ml SOV and 5% TSP separately for three weeks. Renal damage was assessed by measuring proteinuria, enzymuria, expression of glucose transporters, renin-angiotensin system, and activities of polyol pathway enzymes.

Results: Diabetic rats showed hyperglycemia with almost four fold high blood glucose levels. Activity of Na^+K^+ATPase decreased in diabetic kidney. Diabetic rats exhibited an increased level of lipid peroxidation, intracellular Ca^{2+} levels, and decreased membrane fluidity. Combined therapy of lower dose of SOV with TSP significantly reduced metabolites of polyol pathway, oxidative stress, nitric oxide, and N-acetyl-β-d-glucosaminidase activity with glucose transporter in kidney of alloxan diabetic rats. Markers of podocyte damage in kidney (nephrin, podocin, and podocalyxin) and their urinary excretion were normalized along with downregulation of the expression of kidney injury molecule-1 by SOV and TSP treatment. TSP treatment alone is partially effective in restoring the above diabetes induced alterations. Dietary combined SOV and TSP effectively countered the diabetes-induced structural abnormalities of renal tissue.

Conclusion: Our results showed that lower doses of SOV (0.2mg/ml) could be used in combination with TSP to effectively in normalization of altered metabolic parameters and membrane linked enzymes without any harmful side effect and renoprotective actions.

P0992

PHARMACOLOGICAL UPREGULATION OF INTEGRIN-LINKED KINASE (ILK) REDUCES VISCERAL ADIPOSITY IN A METABOLIC SYNDROME MICE MODEL

Mercedes Griera-Merino[1,2], Diego García-Ayuso[1,2], Elena Gutiérrez-Calabrés[1,2,3], Lourdes Bohorquez Magro[1,2], Sofía Campillo de Blas[1,2], David Vaillo[1,3], Laura Calleros[1,2], Diego Rodríguez-Puyol[1,3,4], Manuel Rodríguez-Puyol[1,2], Sergio De Frutos García[1,2,3]

[1]Instituto Ramon y Cajal de Investigación Sanitária (IRYCIS), Fundación Renal Iñigo Álvarez de Toledo (FRIAT), REDinREN from Instituto de Salud Carlos III and NOVELREN from Comunidad de Madrid, Madrid, Systems Biology, Physiology Unit,, Alcalá de Henares, Spain, [2]Universidad de Alcalá,, Department of Systems Biology, Physiology Unit, Alcalá de Henares, Spain, [3]Hospital Príncipe de Asturias, Biomedical research foundation, Alcalá de Henares, Spain and [4]Hospital Príncipe de Asturias, Nephrology Unit and Department of Medicine from Universidad de Alcalá, Alcalá de Henares, Spain

Background and Aims: Important mechanism associated to the development of Insulin resistance (IR) are dysregulation of lipid adjustment and excessive deposition of extracellular matrix (ECM) in the visceral white adipose tissue (WAT). The transgenic depletion of the ECM-to-cell scaffold intracellular protein Integrin-linked kinase (ILK) modulates IR in WAT [Hatem-Vaquero et al. J Endocrinol. 2017] and body weight gain and adipose malfunction correlates with early downregulation of ILK expression in WAT during a short-term high fat diet (HFD) mice model [Hatem-Vaquero et al. Cell Physiol Biochem 2020]. Thus, we demonstrated that transcriptional regulation of ILK might govern the expansion of adipocytes. Between several transcriptional factors implicated in lipid metabolism, the activation of the transcription factor peroxisome proliferator activated receptor (PPAR) family member PPARβ/δ ameliorates IR. Taking in consideration that it modulates the expression of ILK in other contexts aside metabolism [Di-Poï N et al. J Steroid Biochem Mol Biol. 2003, Zhu B et al. Oncogene. 2014], here we activated PPARβ/δ in vivo and in vitro to upregulate adipose ILK expression and prevent WAT expansion.

Method: Adult mice were fed with either standard (STD) or HFD diets during 4 weeks and divided into groups treated with PPARβ/δ activator L-165041 (i.p. 2 mg/kg b.w per day) or vehicle for 2 additional weeks with maintained diet challenges [Lim HJ et al. Eur J Pharmacol. 2009]. Body and epididymal WAT depot (eWAT) weights changes were compared and ILK expression was determined by RT-qPCR. Comparative studies were performed in cultured C3H10t1/2-based adipocytes where ILK expression was deliberately downregulated by the transfection of siRNAs against ILK or in control adipocytes (scramble siRNAs). After cells were treated with L-165041 (1 microM, 24h), we determined the intracellular triglyceride content (by adipo-red dye), the expression of ILK and its downstream substrate AKT (total and active p-AKT in ser473) by RT-qPCR or Western blot.

Results: HFD increased progressively eWAT and whole body weight gains, which coincide with increase in IR. PPARβ/δ-activated mice under STD or HFD have preventive reduction of weight gains and increased expression of ILK in eWAT.

Downregulated ILK expression in culture adipocytes coincide with increased triglyceride content, whereas the activation of PPARβ/δ reduced it at the same time that increased ILK expression and activity.

Conclusion: We suggest ILK modulation as a novel therapeutic strategy during the obesity establishment. The pharmacological activation of PPARβ/δ increases ILK expression and activity, which correlates with a weight loss in IR-based models in vivo. Although the increased presence of ILK induces the phosphorylation of AKT, in turn one of the main mediators during insulin signalling, we cannot conclude the role of ILK-mediated AKT modulation during the reduction of the adipocyte expansion observed

P0993 GYMNEMA SYLVESTRE EXTRACT ATTENUATE THE PATHOLOGICAL PROGESSION OF DIABETIC NEPHROPATHY IN RATS

Sumit Rajput[1]

[1]*Bharati Vidyapeeth Deemed University, Physiology, Pune, India*

Background and Aims: Diabetic nephropathy is not only a common and severe microvascular complication of diabetes mellitus but also the leading cause of renal failure. Aqueous extract of leaves of Gymnema sylvestre (ALGS) has been reported to cause reversible increases in intracellular calcium, hypolipidemic activity and insulin secretion in mouse and human β cells with type 2 diabetes.

The present study aimed to investigate the antidiabetic and renoprotective effects of ALGS in a rat model of type 2 diabetic mellitus.

Method: Male Sprague-Dawley rats with type 2 diabetes induced by a high-fat diet (HFD)/streptozotocin (STZ) were treated with ALGS at dosages of 0.5% and 1% (w/w) daily for 4 weeks. At the end of the experimental period, body weight, serum glucose levels, insulin levels, and kidney function were assessed. Furthermore, antioxidant enzyme and lipid peroxide levels were determined in the kidney with histopathological examination Molecular mechanism underlying the functioning of ALGS, mouse glomerular mesangial cells (MES-13) treated with high glucose (HG, 25 mM glucose) were chosen as a model for an examination of the signal transduction pathway of ALGS.

Results: The results revealed that ALGS improved diabetic kidney injury by reducing blood glucose, serum creatinine, and blood urea nitrogen levels and enhanced antioxidant enzyme activities in kidney tissue. Treatment with ALGS significantly reduced the malondialdehyde and 8-hydroxy-2-deoxyguanosine levels and increased serum insulin levels; expression of renal superoxide dismutase, catalase, and glutathione peroxidase activities; and glutathione content. Histological studies have also demonstrated that ALGS treatment inhibited the dilation of Bowman's capsule, which confirmed its renoprotective action in diabetes. In addition, treatment with ALGS attenuated 25 mM HG-induced suppressed nuclear factor erythroid 2-related factor 2 and antioxidant enzyme expression in MES-13 cells.

Conclusion: The results of present study reveal that **ALGS** extract could be useful intervention in the treatment of diabetes mellitus and, through antioxidative pathways.

P0994

PROTECTIVE EFFECTS OF CATECHIN ON GENE EXPRESSION OF GLUCOSE METABOLISM IN STREPTOZOTOCIN-INDUCED DAIBETIC NEPHROPATHY IN RATS

BYUNG CHUL SHIN[1], JONG HOON CHUNG[1], Hyun Lee Kim[1]

[1]*Chosun University Hospital, Internal Medicine, Divison of Nephrology, Gwangju, Korea, Rep. of South*

Background and Aims: Diabetes patients continue to increase worldwide, and persistent hyperglycemia could induce diverse complications, such as diabetic nephropathy. The purpose of this study was to investigate the transcriptoms of liver, muscle and adipose tissue to observe the effects of catechin on glucose metabolism in diabetic nephropathy rats.

Method: The experimental group was divided into control group, diabetic nephropathy (DN) group and DN + catechin group. The control and diabetic groups received tap water as drinking water and the DN + catechin group received tap water containing 0.1% catechin as drinking water for 12 weeks. After 12 weeks, blood glucose, BUN and creatinine levels were measured in the blood and transcriptomes were examined in liver, soleus muscle and visceral fat. The gene expression levels of glucose metabolism-related enzymes, lipid metabolism-related enzymes and insulin signaling pathway-related proteins were compared between each experimental group.

Results: Fasting blood glucose in the diabetic + catechin group was decreased by 8%, 13%, 15% and 18% at 2, 4, 8 and 12 weeks, respectively, compared to the diabetic group. After 12 weeks, serum BUN levels in the DN + catechin group decreased by 35% and serum creatinine levels by 33%, respectively, compared to the DN group. Glucose metabolism-related genes in the DN group were decreased in liver Gck, Pdp2 and Phkb mRNA levels, and Aldob mRNA levels in soleus muscle were decreased. In DN group, expression of Pfkm, Eno3 and Pgam2 in visceral fat were increased and Aldob and Pklr expression was decreased. Hepatic Gck, Pdk4 and Phkb mRNA levels were increased in the DN + catechin group compared to the DN group.

Conclusion: Catechin has the effect of improving diabetic nephropathy, which is thought to be the result of increased expression of liver glucose metabolism related enzymes and proteins related to insulin signal transduction pathways. Further study is needed to elucidate the mechanism of action on catechin gene expression and its usefulness as a functional substance.

P0995

EVALUATION OF ANTIDIABETIC, ANTIOXIDANT AND NEPHROPROTECTIVE ACTIVITY OF FLAVONOID RICH FRACTION OF HYBANTHUS ENNEASPERMUS IN DIABETIC RATS: IN-SILICO MOLECULAR DOCKING STUDIES FOR SOD, CATALASE, GPX, XANTHINE OXIDASE AND NF-KB.

Dinesh Kumar Patel[1]

[1]*Sam Higginbottom University of Agriculture, Technology and Sciences, Uttar Pradesh, Department of Department of Pharmaceutical Sciences, Allahabad, India*

Background and Aims: Diabetes mellitus is a chronic metabolic disease affected a wide range of population all over the world and leads to development of secondary complications. Enzymes play key role in the development of secondary complication.

Method: The flavonoid rich fraction was prepared using ethyl acetate. Oral glucose tolerance test normoglycemic effect of flavonoid rich fraction of *Hybanthus enneaspermus* (EHE) was evaluated at a dose of 45 and 90 mg/kg, p.o. Further effect of EHE on blood glucose, body weight, enzymes such as super oxide dismutase (SOD), catalase and thiobarbituric acid reactive substances (TBARS) and lipid parameters were estimated out at 45 and 90 mg/kg p.o. per day for 21 days in streptozotocin-induced type-2 diabetic rats. Molecular docking technique was also performed against Super Oxide Dismutase (SOD), Catalase, Glutathione Peroxidase (Gpx), xanthine oxidase and nuclear factor kappa B (NF-κB) for selected phytoconstituents.

Results: EHE contain significant amount of phenolic, tannin, flavonoid and saponin. EHE significantly decreased blood glucose level in diabetic rats. All the tested lipid parameters and enzyme level of SOD, Catalase and Gpx were significantly restored to the normal level in the EHE treated rats. Moreover, there was a significant increase in the body weight in the EHE treated rats. Docking study showed the best binding affinity and interaction of phytoconstituents with xanthine oxidase and NF-κB signified their role in kidney disorders.

Conclusion: EHE has very impressive profile as an antidiabetic, antioxidant and nephroprotective activity via enzymes modulation and it may prove to be effective treatment for kidney disorders in hyperglycemia.

P0996

THE INVOLVEMENT OF PRO-INFLAMMATORY IL-1 CYTOKINES IN TUBULAR INJURY IN DIABETIC KIDNEY DISEASE

Vladislav Slobodsky[1,2], Adi Litmanovich[1,2], Kamal Hassan[1,3], Khaled Khazim[1,3]

[1]Azrieli Faculty of Medicine, Bar Ilan University, Safed, Israel, Israel, [2]The Institute for Medical Research, Galilee Medical Center, Nahariya, Israel, Israel and [3]Galilee Medical Center, Nahariya, Israel, Nephrology, Israel

Background and Aims: Pro-inflammatory cytokines are one of several factors which contribute to the progression of diabetic kidney disease (DKD), a condition characterized by chronic kidney inflammation which results in the tubulointerstitial fibrosis which contributes to the progression of DKD. Interleukin 1 (IL-1) two main agonists IL-1α and IL-1β activate a pro-inflammatory cascade in response to different inflammatory stimuli, including hyperglycemia. It was previously shown that a deficiency of NLRP3 which is required for the conversion of IL-1 to its active state, protects mice from the development and progression of DKD. We hypothesize that the chronic hyperglycemia in diabetic patients triggers the activation and release of IL1α and/or IL-1β from renal tubular cells and that this activation leads to the tissue fibrosis. We aim to assess Il-1 and fibronectin expression in an immortalized proximal tubule epithelial cell line from normal adult human kidney (HK-2). In addition, we evaluate the influence of Anakinra™, a pharmaceutical inhibitor of the Il-1 receptor, currently indicated mainly for rheumatoid diseases, on the levels of fibronectin expression in this model.

Methods: HK-2 cells were cultured and treated with either physiological glucose concentration (5.5mM), high glucose (30mM) or 30mM mannitol as osmotic control for 24 hours to evaluate their effects on Il-1 expression and fibronectin expression. mRNA levels of IL-1α, IL-1β and fibronectin were assessed in q-PCR, and protein expression levels were quantified by western blotting. Immunofluorescence was used to visually demonstrate the presence of IL-1α and IL-1β upon stimulation. Finally, Anakinra™ was added to the tissue cultures in a range of physiologic prescribed concentrations and its effect on cell fibrosis was assessed by the measurement of fibronectin expression 24 hours later by western blotting.

Results: mRNA and protein expression of IL-1α but mostly IL-1β was elevated in HK-2 cells under hyperglycemic conditions but not in physiological glucose environment or under high osmotic conditions. Fibronectin levels were elevated in the high glucose treated cells compared with control. Finally, Anakinra™ was found to attenuate fibronectin expression under high glucose conditions, compared with the untreated cells.

Conclusion: Proinflammatory IL-1α and IL-1β cytokines are expressed by HK-2 cells upon stimulation with glucose and result in the fibrosis on the cells measured by the production of fibronectin. The addition of Anakinra™, an IL-1 receptor blocker, to the cell culture attenuate the expression of fibronectin by the tubular cells. Our research is the first to describe a causation between hyperglycemia, IL-1 elevated levels and fibrosis in HK-2 cells, as demonstrated by the beneficial effect of Anakinra™ on lowering fibronectin expression.

P0997

BLUEBERRY JUICE IMPROVED THE METABOLIC PROFILE IN A PREDIABETIC RAT MODEL INDUCED BY A HYPERCALORIC DIET WITHOUT RENOPROTECTION

André Alves[1,2], Inês Preguiça[1,2], Adelaide Barbosa[1], Pedro Vieira[1,3], Diana Martins[3,4], Sara Nunes[1,2], Sofia D. Viana[1,2,3], Flávio Reis[1,2]

[1] Faculty of Medicine, University of Coimbra, Portugal, Institute of Pharmacology & Experimental Therapeutics & Coimbra Institute for Clinical and Biomedical Research (iCBR),, Coimbra, Portugal, [2]Center for Innovative Biomedicine and Biotechnology (CIBB), University of Coimbra, Coimbra, Portugal, [3]Polytechnic Institute of Coimbra, ESTESC-Coimbra Health School, Pharmacy/Biomedical laboratory sciences, Coimbra, Portugal and [4]Institute for Research and Innovation in Health, University of Porto, Porto, Portugal

Background and Aims: Blueberries (BB), due to their enriched content in polyphenolics and in other compounds with potential cytoprotective properties, have been associated with beneficial effects in distinct cardiometabolic conditions. The goal of this study was to evaluate the metabolic and renal effects of long-term blueberry juice (BJ) treatment in a rat model of prediabetes induced by a hypercaloric diet.

Method: Prediabetes was developed in adult male Wistar rats through the ingestion of high-sucrose (35% HSu) and high-fat (60% HF) diets during 23 wks (HSuHF animals, n=16). After 9 weeks, half of the former rats received BJ orally (25g/kg BW, HSuHF+BJ group). Control animals (n=8) received standard diet during the entire protocol. Glycemic, lipidic and insulinemic profiles were evaluated throughout the protocol, as well as gut microbiota composition, gut barrier permeability, endotoxemia (LPS) and inflammation (hs-CRP). Renal function was assessed by using serum and urinary measures of creatinine, uric acid and blood urea nitrogen and calculating the glomerular filtration rate (GFR). Histological characterization of the kidney was performed by H&E and lipid deposition by Oil Red O staining and quantification of triglycerides. Serum and renal tissue inflammatory markers were evaluated by Elisa (hs-CRP) and by RT-qPCR and/or WB (IL-6, TNF-α, iNOS, MMP2, TLR-4 and RAGE). The study was approved by the local animal welfare body (Ref: 9-2018). Values are presented as means ± S.E.M. and possible differences evaluated by ANOVA/post-hoc tests.

Results: While no major changes between groups were found for gut microbiota, gut barrier and endotoxemia/inflammation, BJ treatment was able to ameliorate hypercaloric diet-induced glucose intolerance, insulin insensitivity and plasma hypertriglyceridemia. In addition, in the HSuHF+BJ rats there was a trend to alleviate the reduction of GFR found in the HSuHF animals, as well as some early glomerular lesions, including mesangial expansion and basal membrane thickening. However, this nutraceutical intervention was unable to halt or slow down glomerular crescent-like lesions, renal lipidosis and the overexpression of renal IL-6 found in the HSuHF-treated animals.

Conclusion: Despite the metabolic improvement viewed by the amelioration of glucose intolerance, insulin insensitivity and hypertriglyceridemia, in this rat model of prediabetes a nutraceutical intervention with BJ presented very modest renoprotective effects.

Acknowledgements: FEDER, COMPETE and FCT (CENTRO-01-0145-FEDER-000012-HealthyAging2020, UID/NEU/04539/2013, UID/NEU/04539/2019, POCI-01-0145-FEDER-007440, POCI-01-0145-FEDER-031712, PTDC/SAU-NUT/31712/2017 and SFRH/BD/109017/2015), as well as COAPE and MIRTILUSA.

P0998

IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES AND SIGNALING PATHWAYS IN DIABETIC NEPHROPATHY BY BIOINFORMATICS ANALYSIS

Shumei Tang[1], Xiangcheng Xiao[1]

[1]*Central South University XiangYa Hospital, Department of Nephrology, Changsha, P.R. China*

Background and Aims: Diabetes has considerable negative impact on morbidity and mortality and causes huge social and economic burden. As one of the most serious microvascular complication of diabetes, diabetic nephropathy (DN) leads to a large population of end-stage renal disease in many countries. The pathogenesis of DN is always a hot topic and the underlying molecular events are not completely clear. Tubular injury plays an important role and may be the initial event. Although few therapeutic treatments could postpone the onset and development, the morbidity of DN remains high. More available therapeutic treatments are urgently needed as well as early stage diagnostic markers and more credible prognostic molecular markers. As a wide range application of high-throughput omics technology, various public network database platforms have included extensive transcriptomics data for deeper bioinformatics analysis. Integrating these data provides better understandings of molecular functions and biological processes. We performed integrated bioinformatics to recognize differentially expressed genes and discussed potential molecular mechanisms in DN.

Method: The expression profiles of GSE30529, GSE47184, GSE99325 and GSE104954 were downloaded from the Gene Expression Omnibus database. The four microarray datasets were centralized, integrated and performed a difference analysis. Next, differentially expressed genes (DEGs) were deeply analyzed by gene ontology annotation and enrichment analysis. STRING database was used to conducted a PPI network and Molecular Complex Detection (MCODE) software was used to identify central genes.

Results: The four files contain 63 tubular biopsy samples from patients with DN and 41 control tubule samples. We identified 18 target DEGs, C3, PROM1, LUM, CPA3, SERPINA3, ANXA1, CX3CR1, AGR2, CD48, REG1A, RARRES1, CYP24A1, C1R, CFB, CDH6, PVALB, GADD45B and KLK1. GO analysis indicated that biological processes of DEGs concentrate on proteolysis, inflammatory response, complement activation and regulation of complement activation. Main cellular components include extracellular exosome, extracellular region, extracellular space, blood microparticle, protein complex and plasma membrane. Molecular functions include calcium ion binding and serine-type endopeptidase activity. DEGs were found that maybe mainly involved in staphylococcus aureus infection, renin-angiotensin system, and complement and coagulation cascades by KEGG pathway analysis. The PPI network of DEGs were established by STRING database and one significant modules were identified by MCODE software. In addition, 3 hub genes, C3, CX3CR1 and ANXA1, were discerned from the PPI network.

Conclusion: To better clarify the underlying molecular mechanisms and provide more effective targets, this study screened DEGs and pathways in DN using bioinformatics analyses.

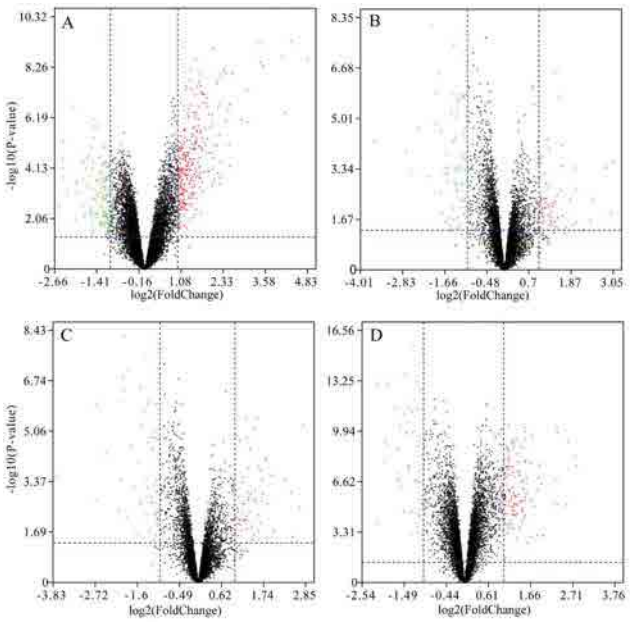


Figure:

P0999

URINARY EXCRETION OF ADENYLATE AND URIDYLATE NUCLEOTIDES IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

Kornelia Sałaga-Zaleska[1], Piotr Pikuł[2], Ewelina Kreft[1], Gabriela Chyła[1], Agnieszka Kuchta[1], Maciej Jankowski[1]

[1]Medcial University of Gdansk, Department of Clinical Chemistry, Gdansk, Poland and [2]Laboratory Medicine Center of Medical University of Gdańsk, Gdansk, Poland

Background and Aims: Extracellular nucleotides (ATP, ADP, UTP, UDP) acting through P2-receptors regulate renal vascular tone and glomerular permeability tor albumin. Both phenomenons are dysregulated in diabetes and are conducive to development of diabetic nephropathy. The aim of study was to investigate the urinary excretion of adenylate and uridynate nucleotides and the effects of suramin, P2-receptors antagonist and non-competitive inhibitor of ectoATPase, on those parameters in streptozotocin-induced diabetic rats.

Method: Diabetes in Wistar rats was induced by streptozotocin injection (65 mg/kg, i.p, day 0) and suramin was injected (10 mg/kg, i.p) on day 7 and 14. Nucleotides concentration in urine collected in metabolic cages on day 21 (3-weeks diabetes) were measured using HPLC method wit UV detector. All values are expressed as mean ± SEM.

Results: The excretion of ATP, UTP, ADP and UDP in diabetes were increased i.e. ATP: 34.99±1.73 vs 18.56±1.59 µmol/24h ($p<0.001$); UTP: 0,72±0.06 vs 0.47±0,08 vs µmol/24h ($p=0.03$); ADP: 0,70±0.56 vs 0.28±0,04 vs µmol/24h ($p=0.001$); UDP: 9.08±1.28 vs 5.06±0,83 vs µmol/24h ($p=0.02$). UMP excretion was decreased 7.04±0.89 vs 11.36±0,621 µmol/24h ($p=0.002$) but AMP excretion was not affected by diabetes i.e. 0.86±0.09 vs 0.89±0.12 µmol/24h ($p=0.08$). Suramin administration did not affect urinary excretion of investigated nucleotides.

Conclusion: diabetes increases the urinary excretion of ATP, ADP, UTP and UDP and this effect is not modified by suramin. The changes in extracellular metabolism of nucleotides may affect the renal function during diabetes. This work was supported by National Science Centre Poland Grant (2016/23/B/NZ5/02632) to MJ.

DIABETES. CLINICAL STUDIES

P1001 RENAL DAMAGE ASSOCIATED WITH INTRAVITREAL ADMINISTRATION OF ANTI-VEGF DRUGS.

Maria Fernandez-Vidal[1], Candela Moliz[1], Beatriz Redondo[1], Teresa Bada Bosch[1], Lucia Aubert[1], Justo Sandino[1], Manuel Praga[1], Florencio Garcia[1], Enrique Morales[1]

[1]*Spain*

Background and Aims: Vascular endothelial growth factor inhibitors (anti-VEGF) have been shown to be effective in the treatment of macular degeneration and diabetic macular edema. It is known that systemic administration of these drugs can produce adverse renal effects, such as decreased glomerular filtration rate (eFGR), proteinuria, hypertension or thrombotic microangiopathy. However, there is little information about it when the administration is intravitreal. The aim of this study was analyzed the effect of anti-VEGF drugs on renal function and proteinuria.

Method: Observational and prospective study on diabetic patients, which were divided into two groups: non-cronic kidney disease (CKD) (group 1) and CKD (group 2). We analyzed clinical and analytical variables during follow-up.

Results: We included 45 diabetic patients (55.6% males) with a median age of 75 (50-91) years. Forty one patients (91.1%) were hypertensive and thirty three (73.3%) were CKD patients. Twenty six (57.8%) received bevazicumab, while the rest (42.2%) received ranibizumab, with a median dose of 6 (1-22). The median follow-up was 25 (9-94) months.

The evolution of eFGR and albuminuria are described in Figure 1, where it stands out the increase in albuminuria in group 2. Regarding the drug type, there were no differences. Within the CKD group, one patient presented two episodes of decompensation of heart failure after the administration of an anti-VEGF drug, and two required the initiation of renal replacement therapy.

Conclusion: Based on the results of our cohort, we believe that it would be advisable to establish a closer monitoring in diabetic patients who are administered an intravitreal anti-VEGF drug, with determination of renal function as well as albuminuria to establish an early diagnosis of possible complications.

	Group 1 - No CKD (n = 12)	Group 2 - CKD (n = 33)	Statistical significance (p)
Baseline eFGR *(ml/min)*	77 (69-86)	33 (24-49)	0.1
Baseline albuminuria *(mg/g)*	33 (10-65)	524 (100-1217)	**0.001**
End of follow-up eFGR *(ml/min)*	70 (54-81)	30(20-44)	0.15
eFGR slope (%)	8.3 (0-13)	16.5 (1-28)	0.073
End of follow-up albuminuria *(mg/g)*	26 (7-62)	601 (205-1733)	**0.001**

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P1002 **EFFECT OF VITAMIN D ON URINARY ANGIOTENSIOGEN LEVEL IN EARLY DIABETIC NEPHROPATHY**

Himansu Mahapatra[1], Adarsh Kumar[2], Bindu Kulshreshtha[3], Anubhuti Chirkara[4]

[1]Dr. R.M.L. Hospital, Nephrology, New Delhi, India, [2]Dr. Ram Manohar Lohia Hospital, Nephrolog, New Delhi, India, [3]Rml Hospital, Endocrinology, New Delhi, India and [4]Dr. Ram Manohar Lohia Hospital, Biochemistry, New Delhi, India

Background and Aims: UrinaryAngiotensinogen (UAGT) is supposed to be a marker of activation of intrarenalreninangiotensin system (RAS) system in early Diabetic Nephropathy (DN). Vitamin D has been studied as a negative regulator of the circulating and tissue RAS activity; so its supplementation may prevent progression of DN. This study was planned to assess the RAS activation and effect of vitamin D supplementation in early diabetic nephropathy progression by estimatingUAGT level.

Method: A total of 730 Diabetic subjects were screened for early DN based on Inclusion criteria(eGFR $\geq$ 120ml/min/1.73m^2 with unrestricted ACR value eGFR of 60- 120 mL/min/1.73m2 and ACR 30-300mg) and Exclusion criteria(on ACE I or ARB, eGFR<60ml/min/1.73m^2, Hypercalcemia (>11.5mg%), UTI, Pregnancy, Hypertension, HbA1c (>8.0 %), vitamin D supplementation during the last 6 month).Of them 103 included subjects were underwent randomization to receive either Cholecalciferol(54) or matching Placebo(49) in a double blind method. All were subjected to routine investigations, urinary albumin: creatinine (UACR), UAGT, serum 25(OH)vitamin D, and intact parathyroid hormone (iPTH) at the zero and six months. A total 40 healthy controls without any comorbidity were also includedfor assessment of same investigations at zero month. Comparative results at zero months of all three groups were analyzed.

Results: The change in levels of UACR (mg/g), UAGT (ng/ml), vitamin D (ng/ml) and iPTH(pg/ml)in Cholecalciferol group from zero to six month were [Median (IQR)] : 12.50 (-24.82 to -5.95); p<0.001, -6.60 (-20.91 to -2.63);p<0.001, 5.75 (2.07-9.70); p<0.001, -5.35 (-11.55 to -3.67) ;p<0.001, respectively. After six months, median (IQR) of UAGT and UACR levels were significantly lower in the Cholecalciferol group as compared to Placebo group (p<0.001 and p= 0.04 respectively).Significant reduction of UACR (mg/g) and UAGT (ng/ml) level corroborating with increase in 25(OH) vitamin D(ng/ml) levelfrom zero to six months (all three p<0.001). There was significant correlation of vitamin D3 level with UAGT (r value: -0.255 & p value: 0.009) and UACR level (r value: -0.28& p value: <0.01). The median UAGT level was significantly higher in patients with early DN (Cholecalciferol&Placebo Group) than Control Group at zero month (p =0.001).

Conclusion: Significantly higher UAGT levels in early DN supports role of intrarenal RAS activation. Significant decrease in UAGT level in cholecalciferol group supports beneficial role of vitamin D supplementation in progression of early DN.

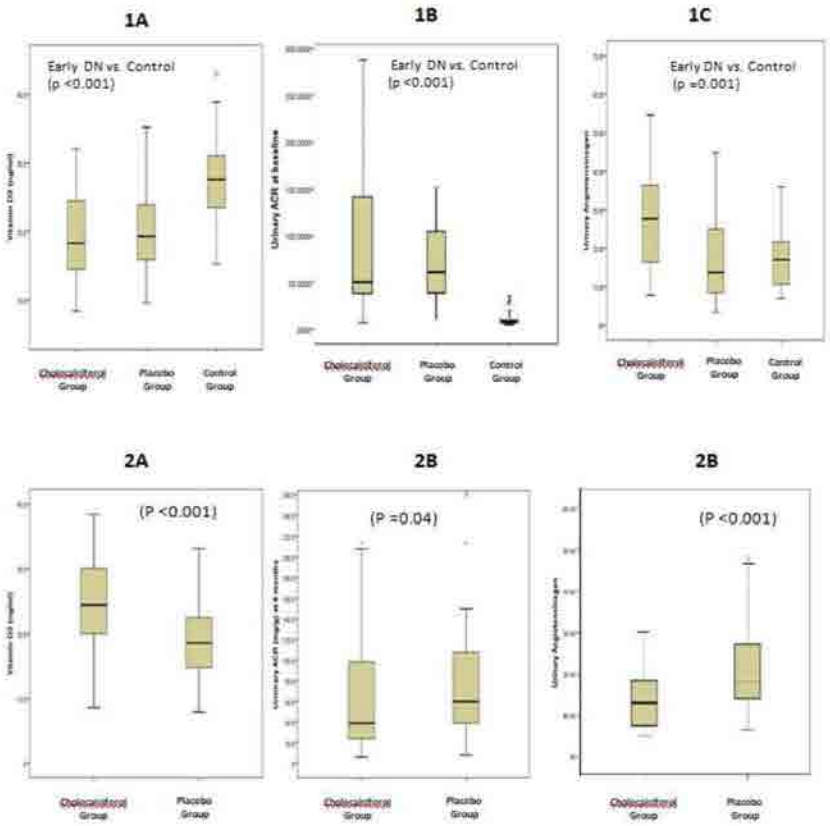


Figure 1: - 1A, 2B, 2C- Box plot showing relationship of cholecalciferol, placebo and control group serum 25(OH) vitamin D **(1A),** UACR **(1B)** and Urinary angiotensinogen **(1C)** levels at **baseline**
2A, 2B, 2C- Box plot showing relationship of cholecalciferol, placebo and control group Serum 25(OH) vitamin D **(2A),** UACR **(2B)** and Urinary angiotensinogen **(2C)** levels at **6th month** in cholecalciferol and placebo group.

P1003

STUDY DESIGN OF THE ROTATION FOR OPTIMAL TARGETING OF ALBUMINURIA AND TREATMENT EVALUATION (ROTATE-3): A ROTATION STUDY OF DIFFERENT ALBUMINURIA LOWERING DRUGS CLASSES TO STUDY INDIVIDUAL DRUG RESPONSE IN DIABETIC AND NON-DIABETIC CKD

Michele Provenzano[1], Maria Jesã°s Puchades Montesa[2], Luca De Nicola[3], Luis D'Marco[2], Carlo Garofalo[3], Ferdinando Carlo Sasso[3], Carlo Acierno[3], Nayara Panizo Gonzalez[2], Maria Romero-Parra[4], Taha Sen[5], Ida Gagliardi[1], Rafael Hoyo-Garcia[6], Michele Andreucci[1], Hiddo Lambers Heerspink[5], Jose Luis Gorriz[2]

[1]Università della Magna Grecia, Catanzaro, Nephrology, Catanzaro, Italy, [2]University Hospital Clinico. INCLIVA. Universidad de Valencia. GEENDIAB. Valencia. Spain., Nephrology, València, Spain, [3]Università Vanvitelli Napoli, Advanced Medical and Surgical Sciences, Caserta, Italy, [4]INCLIVA Institut d'Investigació Sanitària, Cardiovasculo-renal investigation Group, Valencia, Spain, [5]University Medical Center Groningen, Clinical Pharmacy and Pharmacology, Groningen, Netherlands and [6]CEU Cardinal Herrera University, Clincal Trials Master, Alfara del Patriarca, Spain

Background and Aims: Patients with diabetic kidney disease show a wide variability in their response to established and new treatments. SGLT2 inhibitors have also shown to slow the progression of kidney disease. Some studies have also shown kidney benefits for Mineralocorticoid Receptor Antagonists (MRA). A large outcome trial with the MRA finerenone is currently ongoing to assess effects of this MRA on major kidney outcomes. The individual trials will solve the issue whether a patient may have benefit from an SGLT2 inhibitor or MRA, but they do not address the key question which of the two or their combination is better to reduce albuminuria for each individual patient. Therefore, we designed the ROTATE-3 trial is designed to investigate the individual albuminuria response to MRA (eplerenone), SGLT2 inhibitor (dapagliflozin) or the combination.

Method: ROTATE-3 is a randomized, prospective, open label, multicentre, crossover trial with a total duration of 28 (to 42) weeks [EudraCT number: 2017-004641-25]. Patients with or without type 2 diabetes, $\geq$18 years and elevated albuminuria (100-3500 mg/24 hour) already receiving a stable (same dose at least 4 weeks) maximum tolerated dose of an ACE-inhibitor or Angiotensin Receptor Blocker will be enrolled.Patients receive in random order 4 weeks of treatment with the eplerenone 50 mg/day, dapagliflozin 10 mg/day or combination of both drugs with a 4-weeks wash-out period in between. After the last treatment period patients will proceed to a 4-weeks wash-out period. The primary study outcome is the correlation in albuminuria response to eplerenone and dapagliflozin for which 46 patients provides 80% power to detect a Pearson correlation coefficient of 0.4 between the log transformed albuminuria response to eplerenone and dapagliflozin. Blood is collected for clinical chemistry every two weeks during each treatment period. Patients are requested to collect one 24-hour urine sample at start and at end of each treatment period. Home blood pressure is monitored every 2 days.

Results: As of January 1st 2020 the study has enrolled 13 patients. It is anticipated that recruitment will be completed by December 2020 with study completion in August 2021.

Conclusion: The results of the ROTATE-3 study will provide more insight in the individual albuminuria lowering response to potentially two new treatment options for patients with CKD and may help to implement personalized medicine in diabetic kidney disease.Study sponsored by University Medical Center Groningen. The Netherlands.

P1004 **REDUCED ERYTHROCYTE LIFE SPAN IN PATIENTS WITH TYPE 2 DIABETES UNDERGOING LONG-TERM HAEMODIALYSIS**

Tobias Bomholt[1], Peter Oturai[1], Marianne Rix[1], Bo Feldt-Rasmussen[1], Mads Hornum[1]

[1]*Rigshospitalet, København, Denmark*

Background and Aims: Anaemia in long-term haemodialysis (HD) is caused by reduced erythropoietin levels but shortened erythrocyte life span is thought to contribute. However, reduced erythrocyte life span has never been documented in patients with type 2 diabetes (T2D) undergoing long-term HD. The aim of the study was to establish if the erythrocyte life span is decreased in in patients with type 2 diabetes (T2D) undergoing long-term HD and to investigate predictors of reduced erythrocyte life span.

Method: Patients with T2D undergoing long-term HD and patients with T2D without nephropathy (control group) (eGFR above 60ml/min) were included. Erythrocyte life span was measured using Chromium-51 (^{51}Cr) labelled erythrocytes. Blood radiotracer activity was measured 6-8 times over 3-5 weeks to calculate the erythrocyte half-life for each patient. Markers for haemolysis, blood pressure and time spend in dialysis were obtained 5 times over 16 weeks and correlated to the erythrocyte half-life.

Results: For patients with T2D undergoing HD (n=13), the median half-life was 34.5 days (30.6 - 40.7) compared with 44.6 days (43.5 - 58.0) in the control group (n=10) corresponding to a 23 % difference (p=0.0003). From the half-life, the median erythrocyte life span was estimated to 49.7 days (44.1-58.6) and 64.2 days (62.6-83.5), respectively. For patients with T2D undergoing HD no correlation was found between the erythrocyte half-life and markers of haemolysis, blood pressure or time spend in dialysis.

Conclusion: The half-life of erythrocytes was reduced by 23 % in patients with T2D undergoing long-term HD compared with a control group. This reflects that erythrocyte life span is reduced in these patients. No specific markers of haemolysis could be correlated to the findings.

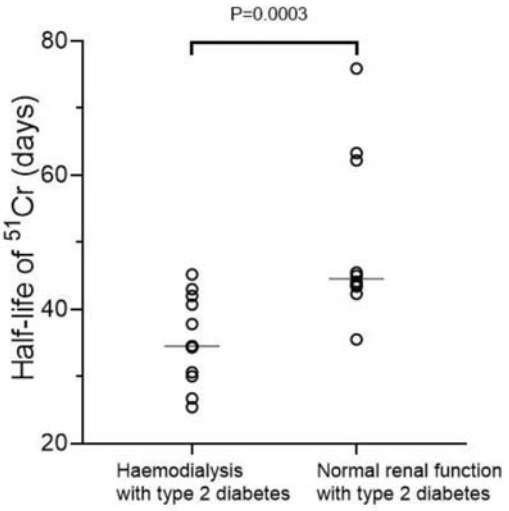


Figure 1 - Chromium-51 (^{51}Cr) half life for each patients with type 2 diabetes undergoing haemodialysis and patients with type 2 diabetes and normal renal function(eGFR above 60ml/min). A reduced half- life of ^{51}Cr reflects an increase loss of erythrocytes and a secondary loss of ^{51}Cr. Group median is illustrated as a horizontal line and a Mann-Whitney U test is used to compare groups.

Figure:

P1005

LONG NONCODING RNAS MAY INTERVENE IN PODOCYTE INJURY AND PROXIMAL TUBULE DYSFUNCTION THROUGH MODULATING MIRNAS EXPRESSION IN EARLY DIABETIC KIDNEY DISEASE OF TYPE 2 DIABETES MELLITUS PATIENTS

Ligia Petrica[1,2,3], FLORICA GADALEAN[4], ADRIAN VLAD[5], Mihaela Vlad[6], VICTOR DUMITRASCU[7], SILVIA VELCIOV[8], Cristina Anca Gluhovschi[8], Flaviu Bob[8], SORIN URSONIU[9], CATALIN JIANU[10], PETRU MATUSZ[11], Agneta Pusztai[11], OCTAVIAN CRETU[12], MILAS OANA[8], ALINA GOLEA-SECARA[8], ANCA SIMULESCU[8], MARIA MOGOS-STEFAN[8], MIHAELA PATRUICA[8], ROXANA POPESCU[13], Daliborca Vlad[14]

[1]"Victor Babes" University of Medicine and Pharmacy, Nephrology, Timisoara, Romania, [2], [3]Timişoara, Nephrology, Timişoara, Romania, [4]"Victor Babes" University of Medicine and Pharmacy Timisoara, Nephrology, Timisoara, Romania, [5]"Victor Babes" University of Medicine and Pharmacy Timisoara, Diabetes and Metabolic Diseases, Timişoara, Romania, [6]"Victor Babes" University of Medicine and Pharmacy Timisoara, Endocrinology, Timişoara, Romania, [7]"Victor Babes" University of Medicine and Pharmacy Timisoara, Pharmacology, Timişoara, Romania, [8]"Victor Babes" University of Medicine and Pharmacy Timisoara, Nephrology, Timişoara, Romania, [9]"Victor Babes" University of Medicine and Pharmacy Timisoara, Public Health Medicine, Timişoara, Romania, [10]"Victor Babes" University of Medicine and Pharmacy Timisoara, Neurology, Timişoara, Romania, [11]"Victor Babes" University of Medicine and Pharmacy Timisoara, Anatomy and Embryology, Timişoara, Romania, [12]"Victor Babes" University of Medicine and Pharmacy Timisoara, Surgery I, Timişoara, Romania and [13]"Victor Babes" University of Medicine and Pharmacy Timisoara, Cellular and Molecular Biology, Timişoara, Romania

Background and Aims: Interactions among multiple molecules and signalling pathways contribute to the pathogenesis and progression of diabetic kidney disease (DKD). Long noncoding RNAs (lncRNAs) play key roles in the pathophysiology of DKD involving actions of microRNAs (miRNAs). The aim of the study was to establish the involvement of selected lncRNAs in the epigenetic mechanisms of podocyte damage and tubular injury in DKD of type 2 diabetes mellitus (DM) patients. The molecular mechanisms of lncRNAs intervention were evaluated in relation to a particular miRNA profile.

Method: A total of 136 patients with type 2 DM and 25 healthy subjects were enrolled in a cross-sectional case series study and assessed concerning urinary albumin: creatinine ratio (UACR), eGFR, biomarkers of podocyte damage (synaptopodin, podocalyxin) and proximal tubule (PT) dysfunction (Kidney injury molecule-1-KIM-1, N-acetyl-D-glucosaminidase-NAG), urinary lncRNA metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), nuclear-enriched abundant transcript 1 (NEAT1), myocardial infarction-associated transcript (MIAT), taurine-upregulated gene 1 (TUG1), and urinary miRNA21, 124, 93, 29a (quantified by a real-time PCR System).

Results: Multivariable regression analysis yielded models in which urinary lncRNA MALAT1 correlated directly with urinary synaptopodin, podocalyxin, KIM-1, NAG, miRNA21, 124, UACR, and negatively with eGFR, miRNA93 and 29a ($p<0.0001$; $R^2=0.727$); urinary lncRNA NEAT1 correlated directly with synaptopodin, KIM-1, NAG, miRNA21, 124, and negatively with eGFR, miRNA93, and 29a ($p<0.0001$; $R^2=0.702$); urinary lncRNA MIAT correlated directly with miRNA93 and 29a, and eGFR ($p<0.0001$; $R^2=0.671$) and negatively with synaptopodin, KIM-1, NAG, UACR, miRNA21, and 124 ($p<0.0001$; $R^2=0.654$); urinary lncRNA TUG1 correlated directly with eGFR, miRNA93 and 29a, and negatively with synaptopodin, podocalyxin, NAG, miRNA21, and 124 ($p<0.0001$; $R^2=0.748$). The results provided document upregulated lncRNA MALAT1 and NEAT1, as well as miRNA21 and 124. By contrast, lncRNA MIAT and TUG1, and miRNA93 and 29a were downregulated.

Conclusion: In patients with type 2 DM lncRNAs exert distinct functions in different cell types, either deleterious or protective, at both glomerular and tubular level. LncRNAs may contribute to DKD through modulating miRNAs expression and activities. This observation holds true independently of albuminuria and DKD stage.

P1006

IMPACT OF GLUCOSE-LOWERING AND ANTIHYPERTENSIVE MEDICATIONS ON DEVELOPMENT OF MICROALBUMINURIA IN SUBJECTS WITH TYPE 2 DIATETES AND NORMOALBUMINURIA IN THE PRIORITY STUDY

Nete Tofte[1], Morten Lindhardt[1], Gemma Currie[2], Marie Frimodt-Moeller[1], Heiko Von der Leyen[3], Christian Delles[2], Harald Mischak[4], Peter Rossing[1,5], For the PRIORITY Investigators[6]

[1]Steno Diabetes Center, Copenhagen, Gentofte, Denmark, [2]University of Glasgow, Institute of Cardiovascular and Medical Sciences, United Kingdom, [3]Hannover Clinical Trial Center GmbH, Hannover, Germany, [4]Mosaiques Diagnostics, Hannover, Germany, [5]Copenhagen University, København, Denmark and [6]European Union Seventh Framework Programme

Background and Aims: In the PRIORITY study, it was recently demonstrated that the urinary peptidome-based classifier CKD273 was associated with increased risk for progression to microalbuminuria. In this sub-study, we aim to evaluate whether glucose-lowering and antihypertensive medications, many of which have been demonstrated to have albuminuria-lowering effects, may interfere with the predictive value of CKD273.

Method: A *post hoc* analysis of a prospective observational study with embedded randomised placebo-controlled trial.

Setting: 1775 subjects from 15 European sites with a mean follow-up time of 2.6 years (minimum of 7 days and a maximum of 4.3 years).

Patients: Subjects with T2D, normoalbuminuria and estimated glomerular filtration rate (eGFR) $\geq$ 45 ml/min/1.73m^2. Participants were stratified into high- or low-risk groups based on their CKD273 score in a urine sample at screening (high-risk defined as score $>$ 0.154).

Main outcome measures: Baseline medication or initiation during the study was assessed for the following medications: glitazones, glucagon-like peptide-1 receptor agonists (GLP1-RA), sodium-glucose cotransporter-2 inhibitors (SGLT2i), dipeptidyl peptidase-4 inhibitors (DPP4i), angiotensin-converting-enzyme inhibitors (ACEi), angiotensin-II-receptor blockers (ARB), calcium channel blockers (CCB) and beta blockers (BB). The main outcome was development of confirmed microalbuminuria (urinary albumin to creatinine ratio (UACR) $>$30 mg/g and with $\geq$30% increase from baseline) in 2 of 3 consecutive samples.

Results: The hazard ratio (HR (95% CI)) for development of microalbuminuria (high vs. low-risk) was 3.9 (2.9-5.3) in a crude Cox-model; and 2.4 (1.8-3.4; p$<$0.0001) when adjusted for age, sex, HbA1c, systolic blood pressure, retinopathy, eGFR and UACR. Adding baseline medications to the model did not significantly alter the results. When evaluating medications initiated during the study, more high- than low-risk subjects were started on glitazones, GLP1-RA, SGLT2i, CCB and BB (p$<$0.03), however, only initiation of DPP4i was associated with the outcome. Adjustment for DPP4i initiated during the study did not significantly change the HR for development of confirmed microalbuminuria (HR 2.5 (1.8 to 3.4); p$<$0.0001) in a model including eGFR and UACR. The HR for development of persistent microalbuminuria (spironolactone vs. placebo) was 0.81 (0.49-1.34; p=0.41), however, adjusting for DPP4i did not significantly alter this result.

Conclusion: Although several glucose-lowering and antihypertensive medications were more frequently prescribed in high-risk subjects, the CKD273 classifier prospectively predicted confirmed microalbuminuria, independent of baseline co-medications and medication initiated during the study. Moreover, initiated medications during the study could not explain the inability of spironolactone to delay progression to microalbuminuria.

P1007

CHANGES IN METABOLIC SYNDROME COMPONENTS AND RISK OF END STAGE RENAL DISEASE: A NATIONWIDE COHORT STUDY

Eun Sil Koh[1], Yura Chae[1], Sungjin Chung[1], Hyuk Sang Kwon[1]

[1]*The Catholic University of Korea Yeouido St. Mary's Hospital, Korea, Rep. of South*

Background and Aims: Few studies have investigated the impact of a change in metabolic syndrome (MetS) components on clinical renal outcomes in the general population.

Method: Using nationally representative data from the Korean National Health Insurance System, 13,310,924 subjects who underwent two health examinations over 2 years and were free from end-stage renal disease (ESRD) from 2009 to 2012 were followed to the end of 2016. The subjects were divided into four groups according to the change in MetS components between the two visits over 2 years: no MetS (–/–), post-MetS (–/+), pre-MetS (+/–), and both MetS (+/+).

Results: After a median follow up of 5.11 years, 18,582 incident ESRD cases were identified. In the multivariate adjusted model, the hazard ratio (HR) and 95% confidence interval (CI) for the development of ESRD in the both-MetS (+/+) group compared with the no-MetS (–/–) group was 5.65 (95% CI, 5.42–5.89), which was independent of age, sex, and baseline estimated glomerular filtration rate. Additionally, the HR for the pre-MetS (+/-) group versus the no-MetS (–/–) group was 2.28 (2.15–2.42). In subgroup analysis according to renal function, the impact of a change in MetS on the incidence of ESRD was more pronounced in individuals with advanced renal dysfunction. Subjects with resolved MetS components had a decreased risk of ESRD, but not as low as those that never had MetS components.

Conclusion: This provides evidence supporting the strategy of modulating MetS in the general population to prevent the development of ESRD.

P1008 **THERAPY WITH SODIUM-GLUCOSE COTRANSPORTER TYPE 2 INHIBITORS INCREASES KLOTHO IN TYPE 2 DIABETIC PATIENTS**

Juan Navarro-González[1], Carla Ferri[1], Ernesto Martín-Núñez[2], Javier Donate-Correa[2], Nayra Pérez-Delgado[3], Carolina Hernández-Carballo[4], Fátima Sánchez-Quintana[2], Víctor G. Tagua[2], Carol Prieto-Morín[3], Carmen Mora-Fernández[2]

[1]University Hospital Nuestra Señora de Candelaria, Research Division and Nephrology Service, Santa Cruz de Tenerife, Spain, [2]University Hospital Nuestra Señora de Candelaria, Research Division, Santa Cruz de Tenerife, Spain, [3]University Hospital Nuestra Señora de Candelaria, Clinical Analysis Service, Santa Cruz de Tenerife, and [4]University Hospital Nuestra Señora de Candelaria, Internal Medicine Service, Santa Cruz de Tenerife,

Background and Aims: Klotho (KL) is a transmembrane protein that is expressed the highest in the tubular cells of the kidneys. In addition to membrane KL, a secreted form of this protein that is present in blood and urine is generated by ectodomain shedding of membrane KL from the cell surface or from the KL gene through alternative splicing. Preserved KL expression has been related to physiological protection in the human kidneys. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are a new class of antidiabetic drugs with important renal benefits. The aim of the present proof-of-concept study was to analyze if treatment with SGLT2i is associated with changes in soluble KL concentrations as well as with modifications in mRNA expression levels of the *KL* gene in renal tubular cells.

Method: Thirty-four patients (18 males and 16 males; mean age *61±5 years)* with type 2 diabetes (mean diabetes time higher than 10 years) and CKD G2-A2, all treated with metformin and blockers of the renin-angiotensin system during more than one year, were included in the study. Twenty-four of them received SGLT2i during 6 months (8 empagliflozin, 8 canagliflozin, 8 dapagliflozin), and their data and evolution were compared with a group of 10 patients matched by age, sex and stage of CKD who received sulfonylureas or DPP4 inhibitors. Serum and urine levels of soluble KL and tumor necrosis factor-alpha (TNFa) were determined by ELISA. In addition, the effect of SGLT2i on mRNA expression levels of *KL* was assessed in vitro in renal tubular cells cultures.

Results: Baseline median values of serum and urinary KL and TNFa were similar in both groups. Urinary KL was inversely correlated with albuminuria and TNFa excretion ($r = -0.39$ and $r = -0.37$, respectively, $P<0.05$). There were no relationship between the serum and urinary levels of these molecules, suggesting their renal origin. At the end of the study, there was a similar improvement in metabolic control, with a reduction in blood pressure significantly higher in patients treated with SGLT2i. Estimated glomerular filtration rate and albuminuria decreased by 5.8% and 17%, respectively, in subjects receiving SGLT2i ($P<0.0001$), without changes in the control group. In patients under SGLT2i therapy there was a 21% significant reduction in urinary TNFa with a concomitant 41% increase in urinary KL ($P<0.001$); there was also a small but significant rise in serum KL ($P<0.01$ vs baseline). Partial correlation analysis showed that the changes in the urinary excretion of albumin and TNFa were associated with the variation in urinary KL after controlling for other variables ($r = -0.50$, $P<0.01$, and $r = -0.41$, $P<0.05$, respectively). Finally, renal tubular cells cultured with dapagliflozin showed a significant and dose-dependent increase of mRNA expression levels of *KL*.

Conclusion: Treatment with SGLT2i induces a reduction in albuminuria and modulates inflammation (as reflected by a decrease in the urinary excretion of TNFa), which is associated with a significant increase in soluble KL concentrations as well as mRNA expression levels of the *KL* gene. The preservation of KL by SGLT2i may be an important mechanism of renal protection in type 2 diabetes.

P1009

RENAL OUTCOMES IN DIABETIC KIDNEY PATIENTS TREATED WITH GLP1 AGONIST RECEPTORS VS SGLT2 INHIBITORS

Alba Maroto[1], Maria Marques Vidas[1], Ignacio Sanz[1], Paula López[1], Jose' M. Portoles[1]

[1]*Hospital Universitario Puerta de Hierro Majadahonda Madrid, Nephrology, Majadahonda, Spain*

Background and Aims: End stage renal disease of diabetic cause is an increasing issue worldwide. Both GLP1 antagonist receptors (GLP1ar) and the sodium-glucose co-transporter 2 inhibitors (SGLT2i) have shown promising results in preventing or ameliorating the progression of renal disease, however there is no data comparing the effect of both drugs on renal outcomes.

Method: Here we present the result of a retrospective study analyzing the main renal outcomes of 98 T2DM patients treated with GLP1ar (25% dulaglutide, 25% liraglutide, 50% semaglutide) or SLGT2 (46.9% dapagliflozin, 21% empagliflozin, 32.1% canagliflozin). All participants were on ACEi/ARB on maximally tolerated dose and patients that have been on both treatments at any time during observation period were excluded. Mean follow-up was 1,9 years, (SD 1,1).

Results: Main descriptive data are shown on the table: in summary, patients on SGLT2i had higher eGFR (64,7 SD 22,7 vs 43,7 SD 13,5) ml/min/1,73m^2 (p<0.001), lower BMI (30,2 SD 4,8 vs 35,0 SD 4,0 p<0,001) and were more frequently free from previous cardiovascular events (60% vs 29,4%, p 0,02)Incident kidney disease defined as drop of eGFR below 60 ml/min/1,73m^2 and/or new onset albuminuria occurred on 18 (39,1%) and 7 (87,5%) of patients on SGLT2i and GLP1ar respectively (p 0,01), however, nor SGLT2i or GLP1ar treated patients suffered significant decrease on eGFR along the study period (2.5% change in eGFR-SGLT2i and 5% in GLP1ar). We found no significant differences on arterial blood pressure or glycemic control along the study period and BMI decrease was only significative on GLP1ar patients (-7,7%, p<0.001)6,7% and 15,8% of patients treated with GLP1ar and SGLT2i respectively suffered one CV event along the follow-up period (p ns) with 6,7% deaths on both groups (0.03 death/patient-year). Adverse events were similar on both groups though discontinuation rate was higher on SGLT2i (16,7% gastrointestinal intolerance, 58% "others")**Conclusion:** We conclude that both GLP1ar and SGLT2i prevent progression of kidney disease in T2DM patients. Though GLP1ar patients showed higher rates of incident kidney disease, when initiated on already decreased GFR this treatment achieved similar results to SGLT2i in preventing progression of kidney disease even in high cardiovascular risk patients.

Table:

	SGLT2i (n 81)		GLP1ar (n 17)		
	mean	**SD**	**mean**	**SD**	**p**
Age (y)	68.4	2.6	71.2	7.6	0.4
Female (%)	27.7		11.8		0.2
No previous CV events (%)	60,2		29.4		0.02
New CV events (%)	15.8				0.4
Stroke	2,7				
Periferal arterial limb disease	1,4				
HF	4,1				
Death (any cause)	6,8		6,7		
basal eGFR CKD- EPI (ml/min)	61,14	21,32	41,26	14,41	P<0.001
3m	58.0	19.97	38,72	11,48	
6m	59,08	22,60	41,46	15,98	
12m	59,19	20,13	38,8	16,20	
24m	62,12	21,61	-	-	
basal UAC r (mg/g)	357,81	439,34	346,36	643,55	0,05
3m	232,63	328,48	231,67	247,46	NS
6m	388,09	618,56	289,88	550,95	
12m	353,10	429,58	358,6	711,60	

P1010 **EFFECTS OF SGLT2 INHIBITORS ON DIABETIC NEPHROPATHY: PODOCYTURIA ON FOCUS**

Serbay Ozkan[1], Halil İbrahim Saygi[1], Ozge Polat Korkmaz[2], Emre Durcan[2], Ahmet Murt[3], Serdar Sahin[2], Mevlut Tamer Dincer[3], Alev Bakir[4], Hande mefküre Özkaya[2], Sinan Trabulus[3], Nurhan Seyahi[3], Elif Güzel[1], Mustafa Sait Gönen[2]

[1]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Histology and Embryology, Fatih, Turkey, [2]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Division of Endocrinology and Metabolism, Department of Internal Medicine, Fatih, Turkey, [3]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Division of Nefrology, Department of Internal Medicine, Fatih, Turkey and [4]Halic University, Department of Biostatistics and Medical Informatics, Beyoğlu, Turkey

Background and Aims: Sodium-glucose co-transporter 2 (SGLT2) inhibitors which are a class of oral anti-diabetic drugs are being used in the treatment of type 2 diabetes (T2D). Basically these drugs reduce blood glucose by blocking glucose reabsorption of primary sodium-coupled glucose transporter in the proximal tubules. Diabetic nephropathy (DN) is a progressive disease with the pathology of glomerular filtration barrier damage and loss of podocytes. In this respect, podocyturia which is the case characterized with presence of podocytes in urine have recently been considered to be a candidate marker for glomerular damage. Therefore, we aimed to investigate effects of SGLT2 inhibitors on glomerulus through the evaluation of podocyturia in DN patients.

Method: Our study population was composed of two T2D patient groups; one of which received SGLT2 inhibitor (SGLT2 group) and the other one is control which did not received. Patients with T2D for at least 5 years, diagnosed with DN and having microalbuminuria >30 mg/day, glomerular filtration rate (GFR) >60 ml/min and HbA1c< 8.5 were involved. In addition, all patients had received angiotensin converting enzyme inhibitor or angiotension receptor blocker for at least 6 months. Nephrologic parameters of patients were monitored before and 3rd and 6th month of follow up period. Patients' age, sex, diabetes duration and HbA1c value were obtained from medical charts. GFR was calculated using the abbreviated MDRD formula. Microalbuminuria was measured in 24 hour urine. Number of podocytes in the urine was determined by immunocytochemical staining of two different markers as podocalyxin (podx) and synaptopodin (synp). Statistical analyses were carried out using Statistical Package for the Social Sciences version (SPSS) 24.0 and statistical significance was set as $p<0.05$.

Results: We evaluated a total of 29 patients (mean age: 57.59 ± 9.66). The number of patients for SGLT2 and control groups are 18 (mean age: 54.89 ± 7.73) and 11 (mean age: 62.00 ± 11.60) respectively. Between these two groups, there was no statistical difference with respect to durations of diabetes (p=0.875) and HbA1c (p=0.05) values except for age (p=0.023) in which control group is statistically higher than the SGLT receiving group. Among the patients receiving SGLT2 inhibitor, podocyturia and microalbuminuria (mca) levels in the 6th month of follow up period were statistically lower than the initial ones [p=0.039 (synp), p=0.016 (podx) and p=0.011 (mca) respectively] while there was no statistical difference for creatinine clearance rate between the initial and follow up period (p:0.371 and ;p=0.111) (**Figure-1**). For control group, although podocyturia was significantly reduced in the 6th month of follow up period [p=0.013 (synp) and p:0.005 (podx)], microalbuminuria (p=0.263) in addition to creatinine clearance (p:0.214; p=0.173) did not change significantly (p=0.263). Furthermore, while there was no significant difference for initial microalbuminuria level between the control and SGLT2 groups (p=0.353); in the 3rd and 6th month follow up period, microalbuminuria was significantly lower than the control group accordingly (p=0.011 and p=0.015 respectively).

Conclusion: According to our preliminary results; patients receiving SGLT2 inhibitors had better microalbuminuria levels than the ones did not and this parameter was correlated with podocyturia. However, even though microalbuminuria of the control group did not change during the follow up period, podocyturia was found out as reduced in the 6th month of follow up period. This discrepancy in the podocyturia level could be resulted from lower number of patients in control so that there is need for evaluation of more patients to emphasize podocyte protective effect of SGLT2 inhibitors.

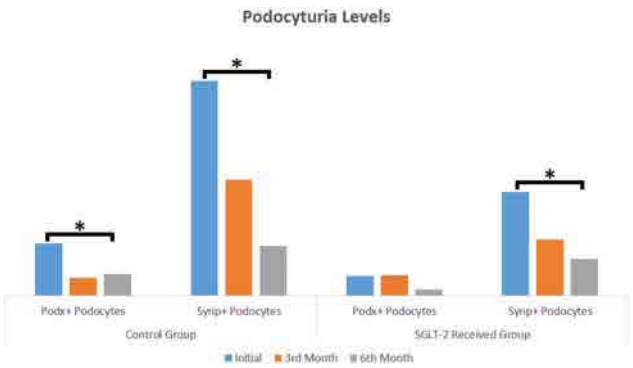


Figure-1: Podocyturia levels for control and SGLT-2 Received groups.* $p<0.05$

P1011 CARDIOVASCULAR OUTCOME TRIALS (CVOT) USING NEW ANTI-DIABETIC AGENTS IN CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Nadia Sarween[1], Nuvreen Phagura[2], Adnan Sharif[1]

[1]Queen Elizabeth Hospital Birmingham, United Kingdom and [2]University of Birmingham, United Kingdom

Background and Aims: The latest consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recommends metformin and lifestyle intervention as first-line therapy for type 2 diabetes. Second-line therapy recommendation is the use sodium-glucose cotransporter 2 (SGLT 2) inhibitors (if estimated glomerular filtration rate [eGFR] is adequate) or GLP-1 receptor agonists if eGFR is inadequate (or SGLT-2 inhibitors not tolerated). No recommendation is made for dipeptidyl peptidase-4 (DPP-4) inhibitors. Therapy choices are limited for patients with both type 2 diabetes and moderate-to-severe chronic kidney disease (CKD) and it is unclear from published data if observed cardiovascular benefits of new anti-diabetic agents extend to the CKD cohort. The aim of this study was to undertake a systematic review of all published CVOT trials using new anti-diabetic agents (GLP-1 receptor agonist, DPP-4 inhibitor, SGLT 2 inhibitor).

Method: We searched MEDLINE (via PubMed and the Cochrane Central Register of Controlled Trials) up to 1st December 2019. Data was stratified by trial entry eGFR into normal (eGFR $\geq$60 ml/min) and CKD (eGFR $<$60 ml/min), with data extracted for primary major cardiovascular event (MACE) rates such as cardiovascular death, stroke and/or myocardial infarct. A meta-analysis with random effects model was performed to estimate overall hazard ratios (HRs) for MACE with new anti-diabetic agents stratified by eGFR. Inter-study heterogeneity was assessed with the I^2 index and Cochran's Q test.

Results: We analysed 13 studies from 16 that were eligible after our search strategy, with 2 excluded due lack of data stratified by eGFR and 1 excluded due to combined MACE/renal outcomes. The studies (GLP-1 agonists, n=6; DPP-4 inhibitors, n=4; SGLT 2 inhibitors, n=3) had a combined total of 128,266 participants (22.1% with eGFR $<$60 ml/min). HR for MACE with GLP-1 agonists for participants with eGFR $\geq$60 ml/min was 0.87 (95% CI 0.77-0.98; p=0.02) and for participants with eGFR $<$60 ml/min was 0.90 (95% CI 0.78-1.04; p=0.14). HR for MACE with DPP-4 inhibitors for participants with eGFR $\geq$60 ml/min was 0.99 (95% CI 0.92-1.07; p=0.86) and for participants with eGFR $<$60 ml/min was 0.99 (95% CI 0.91-1.08; p=0.86). HR for MACE with SGLT 2 inhibitors for participants with eGFR $\geq$60 ml/min was 0.98 (95% CI 0.88-1.10; p=0.78) and for participants with eGFR $<$60 ml/min was 0.82 (95% CI 0.70-0.96; p=0.01). Significant heterogeneity was observed in the meta-analyses for each new anti-diabetic therapy drug class stratified by eGFR.

Conclusion: Among the new anti-diabetic agents, our study suggests efficacy for prevention of MACE in the setting of CKD exists only for SGLT 2 inhibitors and not with GLP-1 receptor agonists or DPP-4 inhibitors. Targeted CVOT studies incorporating participants with diabetes and CKD are critical to guide glycaemic management in these high-risk patients. Until then, we suggest recommendations for second-line therapy in patients with type 2 diabetes and renal impairment should be amended to reflect the current evidence base supporting prevention of MACE with SGLT 2 inhibitors versus other new anti-diabetic agents.

P1011A

THE SGTL-2 INHIBITORS DECREASE THE MORTALITY AND PROGRESSION OF CHRONIC KIDNEY DISEASE (CKD) IN TYPE 2 DIABETES PATIENTES. SYSTEMATIC REVIEW AND META-ANALYSIS OF THE LITERATURE.

Sebastian Cabrera[1,2], Ruben Torres[3], Leticia Elgueta[1], Erico Segovia[1], Maria Eugenia Sanhueza[1], Andres Boltansky[2], Miriam Alvo[1]

[1]University of Chile Clinical Hospital, Medicina, Chile, [2]Clínica Dávila, Nefrologia, Recoleta, Chile and [3]University of Chile, Hospital Clínico de la Universidad de Chile. Departamento de Medicina, Santiago, Chile

Background and Aims: Diabetic nephropathy is one of the main causes of chronic kidney disease (CKD) in the world. In the past years new studies using SGLT-2 inhibitors in diabetic patients have shown benefit in both mortality and progression of CKD. However, these works show heterogeneity between studies regarding the severity of CKD of patients included. All above complicates the interpretation of the benefits of SGLT-2 inhibitors.

Method: We did a systematic search of the literature in PUBMED, EMBASE, Cochrane CENTRAL trials database and in references of the selected studies. Terms used for the search were Canaglifozin, Dapaglifozin, Ertuglifozin, Empaglifozin, diabetes, mortality and CKD. Search included studies in all languages. We selected only randomized and controlled studies that reported mortality and relevant renal outcomes (doubling serum creatinine or decrease in eGFR> 40%, need for renal replacement or renal death). We included studies until September 30, 2019. For the meta-analysis, a Mantel-Haenszel model of random effects was used. The software Review Manager, Version 5.3 The Cochrane Collaboration, 2014 was used.

Results: We obtained results from 142 studies, fifteen studies met the selected criteria, but only four reported mortality and renal outcomes (EMPA-REG, CANVAS, CREDENCE AND DECLARE-TIMI 58). A total of 38,721 patients (SGTL2 inhibitors n = 21,264 and control n = 17,457) were included for the analysis. The EMPA-REG study used Empaglifozin, the CANVAS and CREDENCE studies used Canaglifozin and the DECLARE-TIMI 58 used Dapaglifozin. All studies were funded by pharmaceutical laboratories.The average age range of the studies was between 62 to 67 years. The percentage of patients with eGFR <60ml/min were 26%, 20%, 60% and 7% for the EMPA-REG, CANVAS, CREDENCE and DECLARE-TIMI 58 studies respectively.Mortality was lower in patients who used SGTL2 inhibitors **OR 0.86 (CI 0.80-0.94) Figure 1**. Renal outcomes were also lower in patients who used SGTL-2 inhibitors **OR 0.69 (CI 0.60-0.78) Figure 2.** We assessed whether the effect was related to the severity of the CKD taking out the work with patients with more severe CKD (CREDENCE study), the effect on mortality did not change **OR 0.87 (CI 0.80-0.95)** as well as renal outcome **OR 0.66 (CI 0.52- 0.83)**.

Conclusion: The SGTL-2 inhibitors decrease mortality and improve renal outcomes in patients with diabetic nephropathy. These benefits remain in patients with less severe CKD.

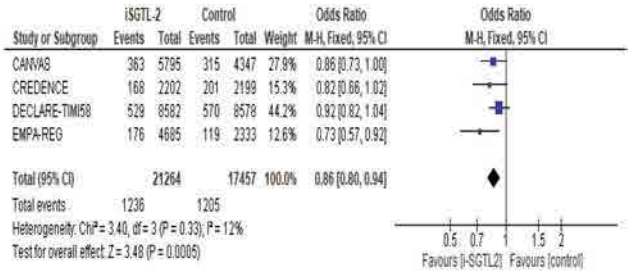


Figure 1. Mortality

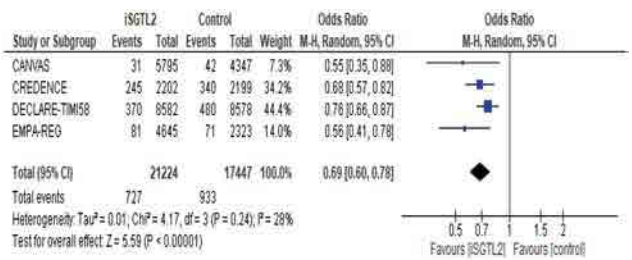


Figure 2. Renal Outcome. Doubling serum creatinine or decrease in eGFR> 40%, need for renal replacement or renal death.

P1012

NAIL CAPILLARY DENSITY DURING POSTOCCLUSIVE REACTIVE HYPEREMIA AND VENOUS CONGESTION IS MORE IMPAIRED IN DIABETIC COMPARED TO NON-DIABETIC CKD PATIENTS

Maria Schoina[1], Charalampos Loutradis[1], Evangelos Memmos[1], Eva Triantafillidou[2], Eleni Pagkopoulou[2], Theodoros Dimitroulas[2], Alexandros Garyfallos[2], Aikaterini Papagianni[1], Panteleimon Sarafidis[1]

[1]Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece and [2]Aristotle University of Thessaloniki, Fourth Department of Internal Medicine, Thessaloniki, Greece

Background and Aims: Alterations in endothelial function and capillary circulation have been associated with increased cardiovascular events and overall mortality. Both diabetes mellitus (DM) and chronic kidney disease (CKD) have been associated with microcirculatory damage. Nailfold video-capillaroscory can provide a thorough assessment of capillary density and microcirculation changes. This is the first study examining in comparison microcirculatory function parameters in diabetic and non-diabetic patients with CKD.

Method: We included 48 diabetic and 48 non-diabetic adult patients (>18 years) with CKD (eGFR: <90 and ≥15mL/min/1.73m^2), matched in a 1:1 ratio for age, sex and eGFR within each CKD stage (2, 3a, 3b and 4). All participants underwent nailfold video-capillaroscopy, during which capillary density was measured at normal conditions (baseline), after a 4-minute arterial occlusion (postocclusive reactive hyperemia) and at the end of a 2-minute venous occlusion (congestion phase).

Results: Baseline demographic, anthropometric and laboratory characteristics were similar between patients with and without diabetes in total and in CKD stages. Overall, no significant differences at baseline capillary density were observed between groups; however diabetic patients presented significantly lower capillary density during reactive hyperemia (36.3±3.8 vs 38.3±4.3 capillaries/mm^2, p=0.022) and at venous congestion (37.8±4.0 vs 39.8±4.2 capillaries/mm^2, p=0.015). When stratified according to CKD stages, the between-group differences in parameters of interest were not significant in stages 2, 3a and 4. In stage 3b, capillary density was significantly lower in diabetic compared to non-diabetic subjects at baseline (31.1±2.8 vs 33.4±3.4 capillaries/mm^2, p=0.044), during postocclusive hyperemia (36.8±2.7 vs 40.0±4.3 capillaries/mm^2, p=0.037) and venous congestion (38.3±2.8 vs 41.5±3.5 capillaries/mm^2, p=0.022).

Conclusion: Capillary density during postocclusive reactive hyperemia and after venous congestion is lower in diabetic compared to non-diabetic CKD patients, a finding indicative that diabetes is an additional factor contributing to microcirculatory functional impairment in CKD. These differences are more prominent in CKD stage 3b, and less prominent in earlier and later stages.

P1013

CANAGLIFLOZIN AND RISK OF GENITAL INFECTIONS AND URINARY TRACT INFECTIONS IN PEOPLE WITH DIABETES MELLITUS AND KIDNEY DISEASE- A POST-HOC ANALYSIS OF THE CREDENCE TRIAL

Amy Kang[1], Brendon Neuen[1], Hiddo Lambers Heerspink[1,2], Gian Luca Di Tanna[1], Bruce Neal[1], Hong Zhang[3], Carinna Hockham[1], Rajiv Agarwal[4], George Bakris[5], David M Charytan[6], Dick De Zeeuw[2], Tom Greene[7], Adeera Levin[8], Carol Pollock[9], David Wheeler[10], Bernard Zinman[11], Kenneth W Mahaffey[12], Vlado Perkovic[13], Meg Jardine[1]

[1]The George Institute for Global Health, UNSW Sydney, Newtown, Australia, [2]University Medical Center Groningen, Groningen, Netherlands, [3]Peking University First Hospital, P.R. China, [4]Indiana University - Purdue University Indianapolis, Indianapolis, United States of America, [5]The University of Chicago, Chicago, United States of America, [6]NYU School of Medicine, New York, United States of America, [7]The University of Utah, Salt Lake City, United States of America, [8]The University of British Columbia, Vancouver, Canada, [9]The University of Sydney, Camperdown, Australia, [10]University College London, United Kingdom, [11]University of Toronto - St. George Campus, Toronto, Canada, [12]Stanford University, Stanford, United States of America and [13]UNSW Sydney, Sydney, Australia

Background and Aims: To describe genital mycotic infections (GMI) and urinary tract infections (UTI) in the CREDENCE trial, determine whether canagliflozin increased the risk of these infections overall and in subgroups, and describe predictors of risk for genital mycotic infections.

Method: The CREDENCE trial randomised people with type 2 diabetes and albuminuric stage 2 and 3 chronic kidney disease to canagliflozin 100mg daily or placebo. We analysed the risk of GMI and UTI with canagliflozin compared to placebo overall and in patient subgroups. The primary analysis was conducted in the on-treatment population, as the more conservative approach with sensitivity analyses conducted using an intention-to-treat population. When canagliflozin increased risk, we determined patient risk factors for GMIs using multivariable Cox regression models adjusting for age, gender, race, markers of disease severity (body mass index (BMI), haemoglobin A1c, diabetes duration, other glucose lowering medications at baseline and kidney function).

Results: Overall 31/2905 (1.1%) men and 32/1492 (2.1%) women experienced 91 GMIs and 166/2905 (5.7%) men and 300/1492 (20.1%) women experienced 669 UTIs. Canagliflozin increased the risk of GMI (HR 3.83 [95% CI 2.08-7.06] $p<0.0001$). The hazard ratio for canagliflozin compared to placebo was consistent across most subgroups, though the risk with canagliflozin was greater in those with a higher BMI (HR 5.91 [95% CI 2.65-13.15] for BMI $\geq$30 kg/m^2 vs HR 1.36 [95% CI 0.47-3.92] for BMI$<$30 kg/m^2, p interaction=0.03) and was higher in men (HR 9.30 [95% CI 2.83-30.60] vs HR 2.10 [95% CI 1.00-4.45] for men and women respectively, p interaction=0.04). In those who were randomised to canagliflozin, independent risk factors for GMI were higher BMI (HR 1.53 [95% CI 1.29-1.83] per 5 units $p<0.0001$) and longer diabetes duration (HR 1.18 [95% CI 1.01-1.40] per 5 years p=0.04). Canagliflozin did not affect the risk of UTI over placebo (HR 1.08 [95% CI 0.90-1.29] p=0.42) overall or in any subgroup, however risk was higher in women (HR 1.23 [95% CI 0.98-1.54] vs HR 0.82 [0.60-1.11] for women and men respectively, p interaction=0.04).58/669 (8.7%) UTIs but no GMIs were reported as serious. Drug was continued in 56/63 (89%) of first GMIs, with similar frequency of subsequent GMI in those continuing on canagliflozin (13/43, 30.2%) or placebo (4/13, 30.8%). Drug was continued in 385/466 (82.6%) first UTIs, with similar frequency of subsequent UTIs in those continuing on cangliflozin (50/199 (25.1%) or placebo 49/186 (26.3%). All findings were similar when conducted using an intention-to-treat approach.

Conclusion: Canagliflozin increased the risk of genital mycotic infections but not urinary tract infections. The risk of genital mycotic infections from canagliflozin over placebo was higher in men and those with higher BMI. In those treated with canagliflozin, higher BMI and longer diabetes duration independently predicted infection. Most participants continued treatment following their first infection with similar recurrence rates in the canagliflozin and placebo groups.These findings will be useful in clinical care, and help identify those at greatest risk for genital infections with canagliflozin treatment.

P1014 INCRETIN BASED THERAPIES IN DIABETIC KIDNEY TRANSPLANT RECIPIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Theodora Oikonomaki[1], Evangelia Ntounousi[2], ANILA DUNI[2], Stefanos Roumeliotis[3], Dimitrios Divanis[4], Vassilios Liakopoulos[4]

[1]Protypo Dialysis Center, Athens, Greece, Athens, Greece, [2]Medical School, University of Ioannina, Ioannina, Greece, Nephrology Department, Ioannina, Greece, [3]AHEPA Hospital, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece, Division of Nephrology and Hypertension, 1st Department of Internal Medicine, Thessaloniki, Greece and [4]AHEPA Hospital, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece, Division of Nephrology and Hypertension, 1st Department of Internal Medicine, Thessaloniki, Greece

Background and Aims: Diabetes mellitus (DM) is the major cause of ESRD. New-onset DM after transplantation (NODAT) frequently occurs and increases the risk of infection and mortality. Kidney transplant recipients (KTR) with pre-existing risk factors for DMt2 are more prone to develop NODAT. An intriguing novel concept is the use of the incretin-based therapies including dipeptidyl peptidase-4 inhibitors (DPP-4i), glucagon-like peptide-1 receptor agonists (GLP-1-RAs) and Sodium-glucose co-transporter-2 *inhibitors* (*SGLT2i*) in solid organ transplantation. This class of antidiabetic therapy is not yet established in KTR. Our aim was to examine the efficacy and safety of incretin-based therapies in DM or NODAT in KTR.

Method: We searched without language restrictions for all publications on Kidney/Renal Transplantation and DPP-4i, GLP-1-RAs and SGLT-2i using electronic databases including Medline, Embase, Cochrane, PubMed. We hand-search the reference lists of every relevant study for additional publications. Further searches were done by reviewing abstract and review articles. We included every study (retrospective/prospective) that used these classes of antidiabetics as treatment of NODAT or DMt2 in KTR. All the primary and secondary outcomes were calculated as mean ± sd. Heterogeneity was assessed with Cochrane's Q statistics and quantified using the I stat, which indicated the proportion of variability across studies that was due to heterogeneity. We used the DerSimonian-Laird estimator for tau^2. Meta-regression was used to assess the effect of different antidiabetics on the primary and secondary outcomes. We assumed a priori the presence of heterogeneity and we used the model of random effects in all analyses. We assessed publication bias using the Begg-Mazumdar test and to nullify the estimated bias the trim-and-fill method, where it was necessary. A p-value $<$ 0.05 was considered statistical significant.

Results: On the 1512 references screened, 16 studies were included in the final analysis. In total, 310 individuals were analyzed with a mean age of 55.98 ± 8.81 years, similar between studies. In 10 of them, participants were diagnosed with NODAT, whereas in all other trials were DMt2 or NODAT. In 8 studies participants received DPP-4i, in 6 SGLT-2i i and in rest 2 GLP-1-RAs. All included KTR were stable and transplanted over 6 months. The mean follow-up of all trials included was 22,03±14.95 weeks. Glycemic control reduces HbA1c (10 studies, MD=-0.38 %, I=45%). The MD of HbA1c for the DPP-4i group was -0.3741 and for the SGLT-2i group was -0.4596 mg/dl. Within every group of each different category of drugs, there was homogeneity (QM, p-value$>$0.05) and it was explained the most of the variance of the previous meta-analysis (QE= 15.76). The Begg-Mazumdar test showed that publication bias was not present (p$>$ 0.05). Nine trials reported the difference of FPG and 5 of PPG before and after the administration of antidiabetics. The common MD estimator with a random effect model was – 25.76 for FPG and – 6.61 for PPG with a high grade of heterogeneity for both. Seven trials reported the change of body mass index (BMI) and body weight (BW) before and after the administration of this class of antidiabetics. The BW reduction, where reported, was significant in KTR on SGLT1i or DPP-4i whereas BMI wasn't significantly reduced in this group, possible due to statistical artifact. The majority of the studies showed that GFR and hepatic biochemical parameters, didn't change during therapy (DPP-4i, GLP-1-RAs, SGLT-2i).

Conclusion: Evidence concerning the efficacy of incretins in diabetes on KTR is limited. SGLT2i and DPP-4i are efficacious for glucose-lowering. The safety profile based on renal and hepatic function is indicative for the use of this class of antidiabetics in this population. More high-quality studies are required to help guide therapeutic choice for antidiabetics in KTR.

P1015 **IMPACT OF DIABETIC DISEASE ON IPTH LEVELS IN DIALYSIS PATIENTS**

Adrian Guinsburg[1], Juan Carlos Berbessi[1], Mauro Caseiro[1], Stefano Stuard[2]

[1]Fresenius Medical Care, Latinamerica, Rio de Janeiro, Brazil and [2]Fresenius Medical Care, EMEA, Bad Homburg, Germany

Background and Aims: Mineral bone disease in dialysis patients is an important predictor of morbimortality.iPTH levels had been previously associated with different parameters, but not clearly to diabetic disease (DBT). We aim to analyze relationship between DBT and iPTH levels in a large cohort of dialysis patients from Fresenius Medical Care LatinAmerica (FMC LA).

Method: Prevalent dialysis patients (more than 90 days on renal replacement therapy) by November 2019 in FMC LA dialysis units (Argentina, Brasil, Chile, Colombia, Ecuador, Perú) were included into the dataset. We obtained demographic, treatment and laboratory data by November 2019. Patients were identified as DBT when DBT was informed as etiology of renal disease or any DBT related ICD10 code was recorded as comorbid condition into the database. Use of insulin, calcitriol, paricalcitol and cinacalcet was also obtained.To evaluate association between DBT and iPTH level, Student t test for independent samples was used. Kruskal-Wallis and Mann-Whitney tests were also performed as confirmatory non-parametric tests for iPTH. Categorical variables were compared using Chi Square test. Linear regression was used to predict iPTH and analyze association with DBT. All procedures were performed on IBM SPSS Statistics© 21.

Results: A total of 31,709 prevalent patients were included. DBT prevalence was 29.7%. Main differences found between DBT and non-DBT patients are shown in table 1:

Table 1: Main differences between diabetic and non-diabetic patients.

	DBT	Non-DBT	p
Age (yrs)	64.0 ± 11.0	56.3 ± 16.7	p < 0.0001
Male/Female (%)	30,3/28,9%	69,7/71.1%	p 0.004
eKt/V	1.46 ± 0.52	1.49 ± 0.42	p < 0.0001
Ca (mg/dl)	8.77 ± 0.68	8.85 ± 0.80	p < 0.0001
P (mg/dl)	4.53 ± 1.37	4.78 ± 1.48	p < 0.0001
iPTH (pg/ml)	354.4 ± 347	540.7 ± 570	p < 0.0001
K (mEq/l)	5.07 ± 0.82	5.11 ± 0.80	p < 0.0001
Glucose (mg/dl)	173.04 ± 90.4	108.23 ± 49.2	p < 0.0001
Alb (g/dl)	3.9 ± 0.6	3.97 ± 0.4	p < 0.0001
AVF/Graft (%)	68,9%	72,0%	p < 0.0001
Catheter (%)	31,1%	28,0%	p < 0.0001
Calcitriol (%)	13,8%	18,3%	p < 0.0001
Cinacalcet (%)	3,5%	8,6%	p < 0.0001

Linear regression model to predict iPTH showed variables associated with increase in iPTH: Ca, P, K, use of calcitriol, use of cinacalcet; while others were associated with decrease in iPTH: age, dialyzate Ca, Hb, glucose, albumin, use of calcium carbonate as supplementation and DBT (table 2):

Table 2: Linear regression model to predict iPTH level

	B	Sig	Lower limit	Upper limit	Effect on iPTH
(Constant)	814.5	0.000	513.9	1115.2	
Age (yrs)	-6.0	0.000	-6.7	-5.4	Decreases
Dialyzate calcium conc (mmol/l)	-420.2	0.000	-546.3	-294.0	Decreases
eKt/V	11.8	0.230	-7.5	31.1	None
Hb (g/dl)	-6.7	0.027	-12.7	-0.8	Decreases
Ca (mg/dl)	64.9	0.000	52.2	77.5	Increases
P (mg/dl)	73.9	0.000	66.7	81.2	Increases
K (mEq/l)	19.9	0.002	7.6	32.3	Increases
Glucose (mg/dl)	-0.3	0.000	-0.5	-0.2	Decreases
Albumin (g/dl)	-102.5	0.000	-129.2	-75.7	Decreases
Gender (M/F)	-0.2	0.986	-19.8	19.4	None
Diabetes (Y/N)	-91.4	0.000	-115.2	-67.7	Decreases
Use of insulin (Y/N)	-40.4	0.507	-159.8	78.9	None
Use of calcium carbonate (binder. Y/N)	8.2	0.715	-36.1	52.6	None
Use of calcium carbonate (supplement. Y/N)	-62.2	0.000	-82.8	-41.6	Decreases
Use of cinacalcet (Y/N)	409.6	0.000	368.0	451.2	Increases
Use of calcitriol (Y/N)	54.5	0.000	32.6	76.5	Increases

Conclusion: In our population diabetic patients were older, showed higher male prevalence and higher rate of catheter use. Kt/V, Ca and P serum levels were slightly lower than non-diabetic, but not clinically significant.Remarkable differences in laboratory were higher glucose and lower K and alb in DBT. While these differences were expected and already known and well described, lower iPTH in DBT is not.Diabetic disease affects iPTH level independently from other factors increasing the risk for hypoparathyroidism. Those findings should be analyzed to determine if DBT should be considered as a different group when targeting in mineral bone disease or P-binder prescription.

P1016 EMPAGLIFLOZIN REDUCES URINARY MITOCHONDRIAL DNA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Haekyung Lee[1], Wonmi Yang[2], Hyoungnae Kim[1,2], Jin Seok Jeon[1,2], Hyunjin Noh[1,2], Dong cheol Han[1,2], Dong Won Byun[1], Hye Jeong Kim[1], Kyoil Suh[1], Hyeong Kyu Park[1], Soon hyo Kwon[1,2]

[1]Soonchunhyang University Seoul Hospital, Internal Medicine, Seoul, Korea, Rep. of South and [2]Hyonam Kidney Laboratory, Seoul, Korea, Rep. of South

Background and Aims: Recent evidences has shown that sodium-glucose co-transporter 2 (SGLT2) inhibitors improve cardiovascular and renal outcomes of type 2 diabetes mellitus (T2DM) patients. However, the mechanisms by which SGLT2 inhibitors improve clinical outcomes are unclear. Mitochondrial dysfunction plays a principal role in the pathophysiology of T2DM and its complications. We hypothesized empagliflozin, an SGLT2 inhibitor improves mitochondrial dysfunction in T2DM patients.

Method: We prospectively recruited healthy volunteers ($n = 22$) and SGLT2 naïve T2DM patients ($n = 21$). Copy numbers of urinary and serum mitochondrial DNA (mtDNA) nicotinamide adenine dinucleotide dehydrogenase subunit-1 (mtND-1) and cytochrome-c oxidase 3 (mtCOX-3) were measured using quantitative polymerase chain reaction in healthy volunteers and T2DM patients at baseline and in T2DM patients after 3 months of treatment with empagliflozin (10 mg, $n = 17$ or 25 mg, $n = 4$).

Results: Patients with T2DM were older than healthy volunteers and had higher body mass index and systolic blood pressure, but lower estimated glomerular filtration rate. Urinary mtND-1 and mtCOX-3 copy numbers were significantly higher in the T2DM group than in healthy volunteers. Urinary mtDNA copy numbers were correlated with diabetes duration (8.74 ± 7.60 years, $r = 0.54$, $P = 0.01$ for mtND-1, $r = 0.50$, $P = 0.02$ for mtCOX-3). Urinary copy numbers of mtND-1 and mtCOX-3 decreased after empagliflozin treatment. The amount of reduction of urinary mtDNA copy number did not differ according to empagliflozin dose ($P = 0.897$ for mtND-1, $P = 0.462$ for mtCOX-3).

Conclusion: In this study, we found that T2DM is associated with elevated urinary mtND-1 and mtCOX-3 copy numbers. Empagliflozin reduces the elevated urinary mtND-1 and mtCOX-3 copy numbers in patients with T2DM. Our results suggest that empagliflozin could attenuate mitochondrial damage in the kidney cells of T2DM patients.

P1017

A RANDOMIZED, PLACEBO-CONTROLLED MULTICENTER STUDY OF THE EFFECTS OF 12 WEEKS OF SODIUM ZIRCONIUM CYCLOSILICATE (SZC) ON ALBUMINURIA (UACR) IN PATIENTS WITH TYPE 2 DIABETES AND HYPERKALEMIA

Frederik Persson[1], Niels Søndergaard Heinrich[1], Rikke Borg[2], Olof Hellberg[3], Anders Fernström[4], Hans Furuland[5]

[1]Steno Diabetes Center Copenhagen, Gentofte, Denmark, [2]Zeeland University Hospital Roskilde, Nephrology, Denmark, [3]Örebro University Hospital, Nephrology, Örebro, Sweden, [4]Linköping University Hospital, Nephrology, Linköping, Sweden and [5]Uppsala University Hospital, Nephrology, Uppsala, Sweden

Background and Aims: Hyperkalemia is a frequent challenge in the treatment of type 2 diabetes and chronic kidney disease. It often leads to suboptimal dosing or discontinuation of renin-angiotensin (RAS) blockade, thus increasing the risk of renal disease progression. Furthermore, epidemiological findings indicate that high potassium levels impair the renoprotective effect of RAS blockade. We want to test whether adjunctive treatment with sodium zirconium cyclosilicate (SZC) a new treatment for hyperkalemia, improves the effect of standard RAS blocking treatment as measured by urinary albumin creatinine ratio (UACR) in individuals with type 2 diabetes.

Method: Randomized, double-blind placebo-controlled multicenter study with 2 sites in Denmark and 3 sites in Sweden. Individuals (n=100) with type 2 diabetes (age 18-85), persistent macroalbuminuria (UACR$\geq$ 200 mg/g) on chronic RAS blocking treatment and documented hyperkalemia (plasma potassium $\geq$ 5.0 mmol/L at least once within 90 days of inclusion) will be enrolled in the study. Participants with plasma potassium >5.0 mmol/L at the last assessment before randomization will be randomized to receive SZC 10 g or placebo three times a day (tid) for 2 days followed by SZC 5g or placebo once a day (qd). Participants with serum potassium $\leq$ 5.0 mmol/L will be randomized to receive SZC qd or placebo qd.UACR will be measured in three consecutive morning spot urine collections at baseline and the end of study after 12 weeks of treatment with Lokelma or placebo.

Results: The primary outcome is change in geometric mean UACR from baseline to end of studySecondary outcomes include changes in estimated glomerular filtration rate (eGFR, calculated by CKD-EPI formula) and 24-h urinary sodium and potassium excretion.In an exploratory analysis the long-term effect of potassium reduction will be modelled using the PRE-SCORE risk calculator. In addition, changes in plasma aldosterone levels will be assessed, and safety will be monitored according to good clinical practice.

Conclusion: This study will test the concept of SZC as an add-on therapy to improve the renoprotective effect of standard RAS blocking treatment. This could provide future potential for keeping more individuals on optimal dosing of RAS blockade.

P1018 **LIPID PROFILES AND RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN CKD AND DIABETES: A NATIONWIDE POPULATION-BASED STUDY**

Yeonhee Lee[1], Sehoon Park[2], Soojin Lee[1], Min Woo Kang[1], SangHyun Park[3], Kyungdo Han[3], Kwon Wook Joo[1], Yon su Kim[2], Dong Ki Kim[1], Jung-Hyun Kim[4]

[1]Seoul National University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of South, [2]Seoul National University College of Medicine, Biomedical Sciences, Seoul, Korea, Rep. of South, [3]College of Medicine, Catholic University of Korea, Medical Statistics, Seoul, Korea, Rep. of South and [4]PaiChai University, Home Economics Education, Daejeon, Korea, Rep. of South

Background and Aims: The association of lipid parameters with cardiovascular outcomes and the impact of kidney function on this association have not been thoroughly evaluated in chronic kidney disease (CKD) patients with diabetes.

Method: We reviewed the National Health Insurance Database of Korea, containing the data of 10,505,818 subjects who received routine check-ups in 2009. We analyzed the association of lipid profile parameters with major adverse cardiovascular events (MACEs) risk and all-cause mortality in a nationally representative cohort of 51,757 lipid-lowering medication-naïve patients who had CKD and diabetes.

Results: Advanced CKD patients with eGFR <30 mL/min/1.73 m2 (n=10,775) had lower serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c) but higher non-HDL-c levels and triglyceride (TG) to HDL-c ratios. There was a positive linear association between serum LDL-c and MACE risk in both early and advanced CKD patients (P <0.001 for trend). A U-shaped relationship was observed between serum LDL-c and all-cause mortality (the 4th and 8th octile groups; lowest hazard ratio [HR] 0.96, 95% confidence interval [CI] 0.87-1.05 and highest HR 1.14, 95% CI 1.04-1.26, respectively). A similar pattern remained in both early and advanced CKD patients. The TG/HDL-c ratio categories showed a positive linear association for MACE risk in early CKD (P <0.001 for trend), but this correlation disappeared in advanced CKD patients. There was no correlation between the serum TG/HDL-c ratio and all-cause mortality in the study patients.

Conclusion: The LDL-c level predicted the risk for MACEs and all-cause mortality in both early and advanced CKD patients with diabetes, although the patterns of the association differed from each other. However, the TG/HDL-c ratio categories could not predict the risk for either MACEs or all-cause mortality in advanced CKD patients with diabetes, except that the TG/HDL-c ratio predicted MACE risk in early CKD patients with diabetes.

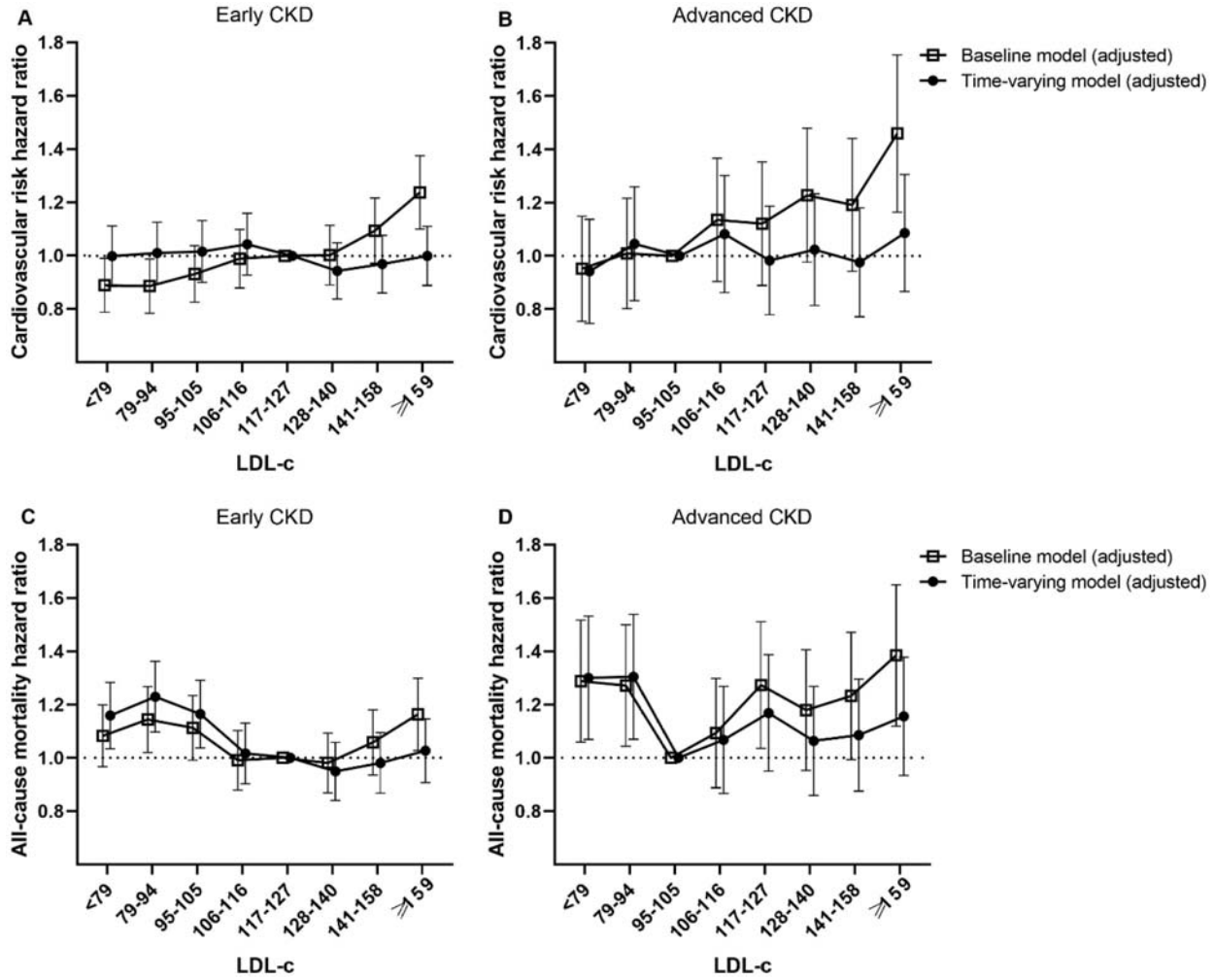


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P1019

CANAGLIFLOZIN AND RISK OF SKIN AND SOFT TISSUE INFECTIONS IN PEOPLE WITH DIABETES MELLITUS AND KIDNEY DISEASE - A POST-HOC ANALYSIS OF THE CREDENCE TRIAL

Amy Kang[1], Brendan Smyth[1], Brendon Neuen[1], Hiddo Lambers Heerspink[1,2], Gian Luca Di Tanna[1], Bruce Neal[1], Hong Zhang[3], Carinna Hockham[1], Rajiv Agarwal[4], George Bakris[5], David M Charytan[6], Dick De Zeeuw[2], Tom Greene[7], Adeera Levin[8], Carol Pollock[9], David Wheeler[10], Bernard Zinman[11], Kenneth W Mahaffey[12], Vlado Perkovic[13], Meg Jardine[1]

[1]The George Institute for Global Health, UNSW Sydney, Newtown, Australia, [2]University Medical Center Groningen, Groningen, Netherlands, [3]Peking University First Hospital, P.R. China, [4]Indiana University - Purdue University Indianapolis, Indianapolis, United States of America, [5]The University of Chicago, Chicago, United States of America, [6]NYU School of Medicine, New York, United States of America, [7]The University of Utah, Salt Lake City, United States of America, [8]The University of British Columbia, Vancouver, Canada, [9]The University of Sydney, Camperdown, Australia, [10]University College London, United Kingdom, [11]University of Toronto - St. George Campus, Toronto, Canada, [12]Stanford University, Stanford, United States of America and [13]UNSW Sydney, Sydney, Australia

Background and Aims: The skin's hypertonic microenvironment has a hypothesized protective antimicrobial function that may be disrupted by SGLT2i. The association between sodium glucose cotransporter inhibitors (SGLT2i) and genital mycotic infections is well established, but it is not known if these agents increase the risk of other skin and soft tissue infections (SSTI). We aimed to describe SSTI in the CREDENCE trial, and determine whether canagliflozin affects the risk of skin and soft tissue infections (SSTIs) overall and in subgroups.

Method: We performed a post-hoc analysis of the CREDENCE trial that randomised people with type 2 diabetes and albuminuric stage 2 and 3 chronic kidney disease to either canagliflozin 100mg daily or placebo. Infections reported as adverse events were assessed by two blinded authors following predetermined criteria for SSTI with discrepancies resolved by consensus. We analysed the risks of SSTIs in the on-treatment population as the more conservative approach, with a sensitivity analysis conducted in the intention-to-treat population. Univariable time-to first-event regression models were assessed.

Results: Overall 373/4397 (8.5%) participants experienced 478 events comprising 252 bacterial skin infections (including 2 episodes of necrotising fasciitis), 94 fungal skin infections, 109 other skin infections and 23 soft tissue infections. Of these, 136/478 (28%) were serious. Drug was continued in 290/373 (78%) of first events, with similar frequency of subsequent events between groups (31/133 (23%) and 33/157 (21%) for those continuing canagliflozin and placebo respectively). In both cases of necrotising fasciitis, drug was withdrawn and the participants recovered.Canagliflozin did not increase the risk of SSTI (HR 0.85 [95% Confidence Interval (CI) 0.69-1.04] p=0.11) (Figure 1). Results were similar in the intention-to-treat population (HR 0.88 [95% CI 0.73-1.07] p=0.20), in analyses confined to serious SSTI (HR 0.83 [95% CI 0.58-1.21] p=0.33), and in the predefined subgroups.

Conclusion: Although other studies suggest that SGLT2i may reduce the sodium content of the skin, we found that canagliflozin does not increase the risk of skin and soft tissue infections, overall or in any subgroup, in people with type 2 diabetes mellitus and albuminuric chronic kidney disease.

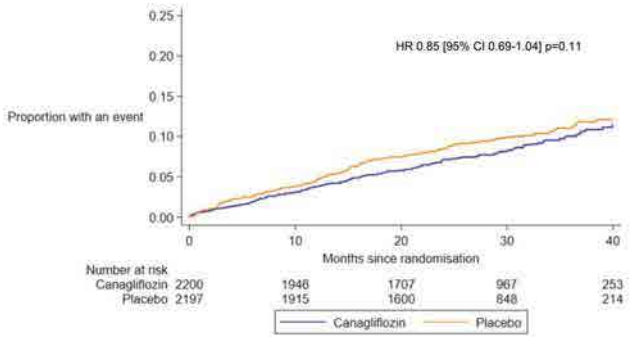


Figure: Kaplan Meier Failure Curve of Skin and Soft Tissue Infections

P1020

ROLE OF CHRONIC KIDNEY DISEASE AND ASSOCIATED BIOCHEMICAL ALTERATION ON ARTERIAL STIFFNESS IN T2 DIABETIC PATIENTS WITHOUT CARDIOVASCULAR DISEASE

Silverio Rotondi[1,2], Lida Tartaglione[1], Marzia Pasquali[3], Maria Luisa Muci[4], Sandro Mazzaferro[1], Luca D'onofrio[1], Angela Carbone[1], Gaetano Leto[1], Carmen Mignogna[1]

[1]Sapienza University of Rome, Roma, Italy, [2]Alma Mater Studiorum - Università di Bologna, Bologna, Italy, [3]Policlinico Umberto I, Roma, Italy and [4]ICOT, Latina, Italy

Background and Aims: DMT2 and its complications such as chronic kidney disease (CKD) lead to increase vascular stiffness, measurable with CAVI, and biochemical alterations in substances implicated in vascular damage like Klotho, FGF23, and Sclerostin. The aim of the study was to evaluate the role of CKD stage 1-2 and possible alterations of 25 (OH)Vitamin-D, FGF23, Klotho, and Sclerostin on early vascular damage in DMT2 patients

Method: Patients included: DMT2 from <10 years, age <60 years, no insulin therapy, eGFR≥60 ml/min/1.73m2, absence of vascular complications. We have evaluated CAVI, albumin-excretion-rate (ACR), 25(OH)Vitamin-D, Klotho, FGF23, and Sclerostin. 30 healthy subjects were the control for CAVI, Klotho, FGF23 and Sclerostin.

Results: We enrolled 40 women and 60 men, average age 56 years (IQR: 52-59), 5-year DMT2 (IQR: 2.7-7), HbA1c 6.3% (5.8-6.7), eGFR of 95 ml/min/1.73m^2. FGF23 (42±10 vs controls 29.8±11 pmol/l, p<.05) and Sclerostin (36.2±7 vs 26.6±1 pmol/l, p<.05) were increased and Klotho reduced (673±300 vs 845±330 pg/ml, p<.05). CKD (ACR≥30mg/gr; eGFR between 60-90 ml/min /1.73m^2) was present in 12.6%. The mean CAVI value was normal. Patients with borderline (≥8, 33%) and pathological (≥9, 13%) CAVI were older (p.001), with longer duration of DMT2 (p.022) and lower 25(OH)Vitamin-D (p.041). CAVI correlated positively with age (p.001), Hb1Ac (p.036), systolic blood pressure (SBP) (p.012) and diastolic blood pressure (DBP) (p.001) and correlated negatively with 25(OH)Vitamin-D (p.046). The multivariate analysis showed positive predictors of CAVI age (p.001), DBP (p.0001), ACR (p.008) and Klotho (p.017).

Conclusion: In our DMT2 population, borderline and pathological CAVI is associated with increased ACR, elevated DBP and reduced 25(OH)Vitamin-D. Furthermore the alterations of FGF23, Sclerostin and Klotho, secondary to CKD, are an early sign of possible vascular damage. ACR, 25(OH)Vitamin-D and DBP can be modifiable risk factors for early vascular damage in DMT2

P1021

MARKERS OF "METABOLIC MEMORY" AND KIDNEY GRAFT FUNCTION IN PATIENTS WITH TYPE 1 DIABETES MELLITUS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

Irina Larina[1], Anastasia Severina[1], Minara Shamhalova[1], Marina Shestakova[1], Larisa Nikankina[1], Ekaterina Artemova[1], Darya Egorova[1], Gulya Musaeva[2], Ilya Dmitriev[3], Aleksey Pinchuk[3], Michael Kaabak[4]

[1]Endocrinology Research Centre, Institute of diabetes, Moscow, Russia, [2]I.M. Sechenov First Moscow State Medical University, Moscow, Russia, [3]Scientific and Research Institute for Emergency Care named.after N.V. Sklifosovsky, Moscow, Clinical Department of Kidney and Pancreas Transplantation, Moscow, Russia and [4]B.V. Petrovsky Russian Research Center of Surgery, Department of Kidney Transplantation, Moscow, Russia

Background and Aims: To evaluate the relationship between oxidative stress markers and advanced glycation end products receptor (RAGE) with kidney graft function and complications of end-stage renal disease (ESRD) in patients with type 1 diabetes mellitus (T1DM), who reached stable euglycemia after simultaneous pancreas-kidney transplantation (SPKT).

Method: The study included 27 patients with T1DM duration for 21 [19; 28] years, diabetic nephropathy (DN) duration 7,0 [5,5; 13,5] years and duration of renal replacement therapy (dialysis) for 2 [1; 4] years after successful SPKT. The posttransplantation period at the time of inclusion was 61 [20; 90] months. Assessment included examination of oxidative stress markers (3-nitrothyrosine (3-NT), superoxide dismutase (SOD) and RAGE, analysis of the main kidney transplant dysfunction markers (KIM-1, NGAL, podocin, IL-18) and state of carbohydrate metabolism with monitoring for 1 year. All patients received three-component immunosuppressive therapy.

Results: SPKT allowed to achieve *stable euglycemia (HbA1c* 5.5 [5.1; 5.9] %, 5.5 [5.3; 5.7] % and C-peptide 2,9 [2,1; 3,6] ng/ml, 2,6 [2,0; 3,4] ng/ml at baseline and after 1 year of follow – up, respectively) and the restoration of graft function to the rate of estimated glomerular filtration rate (eGFR) CKD-EPI stage C2, albuminuria stage A1 of chronic kidney disease (CKD). However, 22% of patients experienced an increase of albumin-to-creatinine ratio to A2 at different times after surgical treatment. There was a statistically significant increase in SOD level (p=0.0005) and RAGE level (p=0.011) after 12 months of observation. Significant correlations of kidney transplant function parameters with "metabolic memory" markers (oxidative stress and RAGE) were also found: RAGE & creatinine (R=0.50, p=0.02), RAGE & KIM-1 (R=0.43, p=0.047), 3-NT& eGFR (R= - 0.40, p=0.046), IL-18 & SOD baseline (R=0.43, p=0.047). Attention is drawn to the correlations of RAGE & HbA1c+12 month (R=0.47, p=0.01), podocin with HbA1c (R=-0.46, p=0.03), which may probably reflect the direct influence of carbohydrate metabolism compensation to the kidney graft condition and also the correlation of SOD baseline & RAGE +12 month (R= - 0.70, p=0.0008), which may demonstrate the relative influence of components of "metabolic memory".

Conclusion: SPKT as the way to achieve compensation of carbohydrate metabolism remains just one of factors of stable kidney graft function. The results of analysis of "metabolic memory" markers could indicate not only their direct contribution to the persistence of metabolic consequences of DM and DN, but also their possible participation in the development of recurrent nephropathy.

P1022

HEMATURIA AND ABSENCE OF RETINOPATHY ARE NOT INDICATIVE OF NON -TYPE 2 DIABETES ASSOCIATED RENAL DISEASE IN PATIENTS WITH OTHERWISE TYPICAL DIABETIC KIDNEY DISEASE

Jonathan Chemouny[1,2,3], Valentin Maisons[4], Aurélie Sannier[5,6], Noemie Jourde-Chiche[7,8], Jean-Michel Halimi[4], Cécile Vigneau[1,3,9], Nathalie Rioux-Leclercq[3,9,10], Christophe Barba[11], Laurent Daniel[12], Mickael Bobot[7,8], Francois Vrtovsnik[6,11,13]

[1]CHU de Rennes, Nephrology, Rennes, France, [2]INSERM, CIC 1414, Rennes Cedex 9, France, [3]IRSET, Rennes, France, [4]Chru Hôpitaux De Tours, Nephrology, Tours, France, [5]Bichat-Claude Bernard Hospital, Pathology, Paris, France, [6]University of Paris, Paris, France, [7]Aix-Marseille University, INSERM, INRAE, C2VN, Marseille, France, [8]Ap-Hm, Nephrology, Marseille, France, [9]University Rennes 1 - Ufr Médecine, Rennes, France, [10]CHU de Rennes, Pathology, Rennes, France, [11]Bichat-Claude Bernard Hospital, Nephrology, Paris, France, [12]Ap-Hm, Pathology, Marseille, France and [13]INSERM, 1149, Paris, France

Background and Aims: Diabetic Nephropathy (DN) is usually a presumptive diagnosis based on clinical and biological evidences. However, Renal Biopsies (RB) may be performed when the suspicion of Non-Diabetic Renal Disease (NDRD) with potential specific treatment arises from atypical features mainly identified through studies focusing on the power of individual clinical and biological features to predict NDRD. We aimed to assess the actual value of RB indications (RBi) to discriminate NDRD from Type 2 Diabetes (T2D) Associated Renal Disease (T2D-ARD) such as DN and Hypertensive nephropathy which are frequently associated, seen in similar patients with high cardiovascular risk, lack for specific treatment and might be therefore be considered as "failure events" in the context of RB performed to diagnose NDRD with specific treatment.

Method: We conducted a retrospective multicenter study in four nephrology units and reviewed the charts of patients with T2D who underwent a first RB from 2006 to 2015. Clinical and biological characteristics, RBi and diagnoses were retrospectively collected from the patients' medical charts. RBi were defined according to the sequence in Figure 1. As such, diabetic retinopathy may be absent in patients of all indication groups, conversely, patients in group 6 and 7 had stable proteinuria and renal function. Similarly, patients with monoclonal gammopathy were all included in group 1.We considered missing data regarding the absence/presence of Diabetic Retinopathy (DR) as meaningful, suggesting the data was unneeded to reach a decision of RBi. We performed univariate and multivariate logistic regression analyses to identify clinical or biological features associated with the diagnosis of NDRD. We also compared the number and percentage of actual NDRD diagnosed for each of the RBi.

Results: 464 first renal biopsies were performed in 464 patients during the study period. Two RB were excluded because the RBi could not be clearly identified through careful reviewing of the patients' medical charts. Of the 462 remaining RB, 40% revealed NDRD. The most frequent were acute interstitial nephritis, IgA nephropathy and acute tubular necrosis (8.7%, 5.8% and 4.1% respectively). Patients with NDRD were more frequently >65yo (55 vs 44%), with serum creatinine (SCr) >250 µmol/l (52 vs 30%), hematuria (58 vs 36%), non-retrieved DR status (45 vs 17%), and less frequently with urinary-to-protein ratio (UPCR) >3g/g (33 vs 57%), HbA1c >7% (32 vs 50%) and duration of diabetes >5 years (52 vs 72%).Logistic regression analyses identified high SCr, UPCR, hematuria and low diabetes duration as predictive of NDRD. Surprisingly, missing RD status rather than absence of RD was predictive of NDRD.

Adjusted model	Odd ratio	pvalue
Creatininemia > 250 µmol/l	3.02	2.57E-04
UPCR > 3g/g	0.29	3.80E-05
Hematuria, Not retrieved	0.66	7.28E-01
Hematuria, Yes	2.51	1.71E-03
Diabetic retinopathy Not retrieved	3.73	2.19E-03
Diabetic retinopathy, Yes	1.23	5.62E-01
Diabetes duration > 5 years	0.45	7.72E-03

As expected NDRDs were frequent in patient with RBi 1 to 3 (53%, 40% and 21%), infrequent in patients with RBi 5 (7%) and totally absent from patients with RBi 6 and 7 despite their predictive value as regards with NDRD.

Conclusion: Our study confirms several well-known facts on the subject of renal biopsy in patients with T2D: 1) Renal biopsy is useful in selected patients with T2D and renal disease to diagnose NDRD with specific treatment. 2) Hematuria and short duration of diabetes are predictive of NDRD. On the other hand, our study suggests two novel and antidogmatic findings: 1) Assessing the presence of diabetic retinopathy is not required for RBi. 2) Hematuria is not indicative of NDRD in patients with otherwise typical diabetic kidney disease. Of course, our study is limited by its retrospective design precluding us of precisely defining what was considered rapid evolution of DFG or proteinuria emphasizing the need for prospective studies.

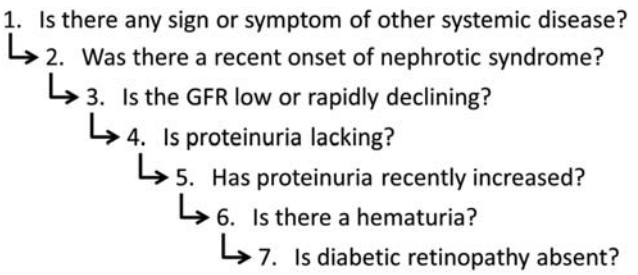


Figure:

P1023

DEPRESSION IS A MAJOR DETERMINANT OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH DIABETIC KIDNEY DISEASE

Suhyun Kim[1,2], Hyo jin Boo[2], Jeunseok Jeon[2], Hye Ryoun Jang[2], Wooseong Huh[2], Yoon-Goo Kim[2], Dae Joong Kim[2], Jung Eun Lee[2]

[1]Hanil General Hospital, Nephrology Division; Department of Internal Medicine, Korea, Rep. of South and [2]Samsung Medical Center, Sungkyunkwan University School of Medicine, Nephrology Division; Department of Internal Medicine, Korea, Rep. of South

Background and Aims: Poor health-related quality of life (HRQOL) is associated with increased cardiovascular risk and mortality in patients with kidney disease. Therefore, it is critical to identify and modify clinical contributors of poor HRQOL. This study examined modifiable factors associated with poor HRQOL in patients with diabetic kidney disease (DKD) focusing on depression, anxiety, sleep quality, and physical activity.

Method: Between April 2017 and March 2018, 141 adults (aged ≥18 years) with DKD were recruited in single tertiary hospital. HRQOL was assessed at baseline with the Short Form 36 of life Health Survey Question (SF-36) questionnaire. Poor HRQOL was defined as a score below the median value at baseline. Depression and anxiety were assessed with the Hospital Anxiety and Depression Scale. Sleep quality and physical activity were measured using Korean version of the Pittsburgh Sleep Quality Index and International Physical Activity Questionnaire respectively.

Results: The age was 65 [57-72] years old, and 73% (n=103) of participants were men. Prevalence of anxiety and depression were 8% (n=11) and 17% (n=24) respectively. Forty-eight (34%) subjects corresponded to poor sleepers and 40 (28%) subjects showed low physical activity. SF-36 scores were decreased with advanced CKD stages (stage 3, 79 [71-82]; stage 4, 71 [56-82]; stage 5, 70 [57-82]; $p = 0.029$ for trend) progressively. Anxiety, depression, and poor sleep quality were negatively correlated with SF-36 scores ($p < 0.05$). eGFR and physical activity were positively correlated with HRQOL scores ($p < 0.05$). In multivariable logistic analysis, depression scores were associated poor HRQOL independently of age, sex, comorbidity, eGFR, anemia, sleep quality, anxiety and physical activity (odds ratio per 1-score increment, 1.51; 95% confidence interval, 1.27-1.80, $p < 0.001$).

Conclusion: In patients with DKD, depression was a major determinant of poor HRQOL among the modifiable clinical factors such as anxiety and sleep. Active surveillance of depression and psychosocial intervention should be considered to improve the well-being of these patients.

Table. The effect of clinical factors on poor HRQOL: multiple logistic regression analyses

Variable	Odds ratio	95% CI	*P*
Age, year	1.00	0.97 – 1.04	0.851
Sex	2.67	0.96 – 7.39	0.059
CCI*, score	1.37	0.95 – 1.97	0.096
Hb, g/dL	0.93	0.70 – 1.24	0.636
eGFR, mL/min/1.73m2	1.00	0.96 – 1.03	0.791
PSQI-K, score	1.03	0.91 – 1.17	0.619
HADS-A, score	1.04	0.87 – 1.23	0.695
HADS-D, score	1.51	1.27 – 1.80	<.0001
IPAQ, score	1.00	1.00 – 1.00	0.771

*Comorbidity was measured using the modified Charlson Comorbidity Index (CCI)

Abbreviations: CCI, Charlson Comorbidity Index; eGFR, estimated glomerular filtration rate; IPAQ, International Physical Activity Questionnaire; HADS-A, Hospital Anxiety and Depression Scale-anxiety subscale; HADS-D, Hospital Anxiety and Depression scale-depression subscale; Hb, hemoglobin; PSQI-K, Korean version of the Pittsburgh Sleep Quality Index.

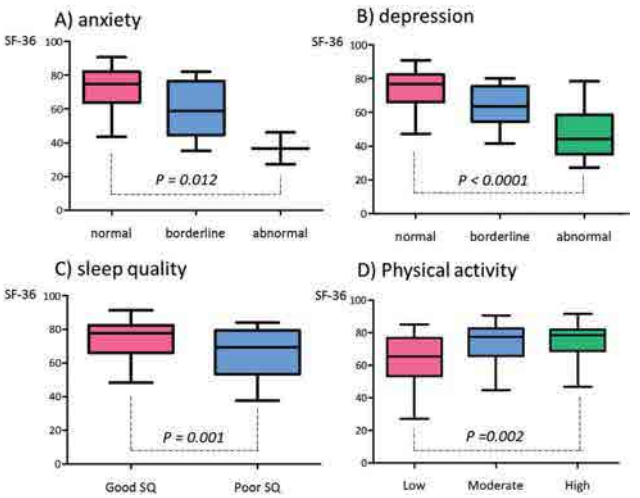


Figure: Distributions of SF-36 scores according to anxiety, depression, sleep quality, and physical activity status

P1024 INFLUENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN THE EVOLUTION OF RENAL FUNCTION IN DIABETIC PATIENTS

Lucia Aubert[1], Justo Sandino[1], Florencio Garcia[1], Elena Gutiérrez[1], Julian Segura[1], Teresa Bada[1], Maria Fernandez-Vidal[1], Manuel Praga[1], Enrique Morales[1]

[1]*Hospital Universitario 12 de Octubre, Nephrology, Madrid, Spain*

Background and Aims: Nowadays, there is growing evidence that non-alcoholic fatty liver disease (NAFLD) may be associated with renal impairment and have an impact on the evolution of renal function in patients with type 2 diabetes mellitus (DM). Our aim was to compare the effect on renal function and proteinuria in patients with type 2 DM according to the presence of NAFLD.

Method: Retrospective and observational study, including patients with type 2 DM, < 70 years of age and with estimated glomerular filtration rate (eGFR) > 30 ml/min/1,73 m^2. NAFLD was defined with the presence of compatible ultrasonography and/or presence of fibrosis using NAFLD score. Metabolic syndrome (MSd) was defined as: obesity (body mass index (BMI) > 30 kg/m^2), hypertension and dyslipidaemia. Patients were classified according to the presence or absence of NAFLD. We analysed different clinical and analytical variables along the follow up.

Results: A total of 71 patients were included (66% males) with mean age of 57.4 ± 7.8 years. The median evolution of type 2 DM was 72.2 months (34.7 - 125.5 months) and 90.1% of the patients were treated with renin-angiotensin blockade. When comparing patients with (group 1, n=38) and without (group 2, n=33) NAFLD at the beginning of this study, we found no significant difference in eGFR (80.2 ± 40.4 ml/min vs 71.4 ± 31.8 ml/min), proteinuria (1.4 ± 2.7 g/24h vs 0.8 ± 1.0 g/24h) and glycated haemoglobin (6.8 ± 1.4% vs 7.2 ± 1.6%). On the other hand, we found significant difference in the presence of higher BMI (33.8 vs 29.3 kg/m^2; .001) and presence of MSd (67.7 vs 32.3%; .03) in those patients with NAFLD. After a mean follow-up time of 74 months, we found significant differences in the loss of eFGR (-33.8 vs -13.9 ml/min; .003), but no difference in increase of proteinuria. We found an increase in incidence of chronic kidney disease in group 1 (50%) vs group 2 (10.5%). There were no differences in the need to initiate renal replacement therapy or all-cause mortality.

Conclusion: NAFLD in type 2 DM caused a mayor decline in renal function. We should, therefore, take into consideration the presence of NALFD and the presence of MSd to optimise treatment of associated risk factors.

P1025 **HISTOLOGICAL AND CLINICAL FINDINGS IN ADULT AUTOPSIES OF TYPE 2 DIABETES MELLITUS PATIENTS WITH OR WITHOUT DIABETIC KIDNEY DISEASE**

Elena Gimenez-Civera[1], Maria Jesã°s Puchades Montesa[1], Liria Terrádez[2], Anais Moscardo[2], Luis D'Marco[1], Aurora Pérez Ys[1], Francesc Moncho[1], Elisa Perez-Bernat[1], Nayara Panizo Gonzalez[1], Patricia Tomas[1], Miguel Gonzalez-Rico[1], Jose Luis Gorriz[1]

[1]University Hospital Clinico. INCLIVA. Universidad de Valencia. GEENDIAB. Valencia. Spain, Nephrology, València, Spain and [2]University Hospital Clinico. Valencia. Spain, Anatomia Patológica, València, Spain

Background and Aims: Few studies have analyzed early lesions of diabetic nephropathy (DN) in those patients who do not have clinical signs of this involvement, since the indication of renal biopsy is usually performed in patients with significant renal manifestations.The aim of the study was to analyze renal histological lesions from autopsies of diabetic patients with or without clinical expression of DN. Thus, we analyze their correlation according to the presence or absence of proteinuria (albumin/creatinine to ratio > 300). Autopsies from non-diabetic patients was used as a control group.

Method: Kidneys from autopsies of 21 patients with type 2 diabetes mellitus (T2DM) and 4 non-diabetic controls were analyzed by two pathologists. The histological lesions score of DN was performed according to the classification of Tervaert et al. (JASN. 2010; 21: 556–63), and a description of histological findings, clinical and analytical data were made.

Results: The mean glomeruli per sample was: 170 ±88. Patient demographics of autopsies: mean age 76 ± 11 years, mean duration of diabetes 6.08 ± 3.2 years (20%> 10 years). Last known eGFR: 51 ± 28, HbA1c: 7.3 ± 1.9%. Albuminuria and cardiovascular disease were present in 42% and 60% of patients with T2DM. Histological and clinical data are shown in **Table and Graphics**.

Conclusion: A high percentage of diabetics without early clinical lesions of DN (albuminuria) already express moderate to severe histological changes, especially severe mesangial expansion and severe glomerular vascular lesions. The control group showed minimal histological lesions except for mild expansion of the mesangium and inflammation associated with IFTA. Our data suggest renal involvement in T2DM is present in earlier stages (patients without albuminuria). Therefore, early metabolic control is important, as well as other risk factors that may influence in the development of DN. Large sample size studies are pending to confirm these data.

Table:

	No albuminuria (n=12)	Albuminuria (n=9)	Control (n=4)
Age (median) , years	76 ± 8	76 ± 3	74 ± 13
eGFR < 60 ml/min/1,73 m2	33 %	83 %	25 %
Cardiovascular disease	41 %	44 %	25 %
Caoronary heart disease	17 %	22 %	50 %
Cerebrovascular disease	25 %	11 %	25 %
BMI (kg/m2)	30 ± 4	31 ± 5	28 ± 9
Glomeruli number analyzed	197 ± 95	150 ± 85	132 ± 54
% GMB expansion	81%	69%	4%
% interstitial fibrosis	67%	80%	25%
Mesangial expansión: mild	58 %	83 %	50 %
Mesangial expansion >50%	33 %	17 %	0 %
Severe glomerular lesions	83 %	100 %	0 %
Interstitial fibrosis > 25 %	33 %	20 %	0 %
Inflammation non associated to IFTA	11 %	33 %	25 %
Inflammation associated to IFTA	78 %	68 %	0 %
intima > media arteriosclerosis	25 %	44 %	25 %

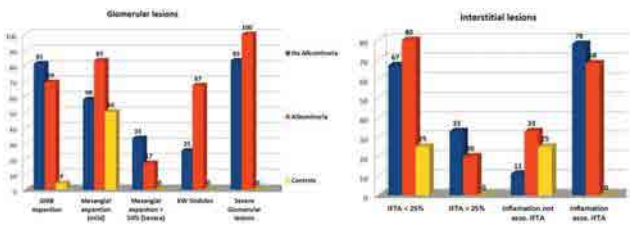


Figure:

P1026

THE EFFECT OF DAPAGLIFLOZIN ON 24-HOUR BLOOD PRESSURE IN PATIENTS WITH TYPE-2 DIABETES MELLITUS: A DOUBLE-BLIND RANDOMIZED CLINICAL TRIAL

Eirini Papadopoulou[1,2], Charalampos Loutradis[2], Glyceria Tzatzagou[3], Kalliopi Kotsa[4], Ioanna Zografou[1], Ioanna Minopoulou[2], Marieta Theodorakopoulou[2], Apostolos Tsapas[5], Asterios Karagiannis[1], Pantelis Sarafidis[2]

[1]Aristotle University of Thessaloniki, Second Propaedeutic Department of Internal Medicine, Thessaloniki, Greece, [2]Aristotle University of Thessaloniki, Department of Nephrology, Thessaloniki, Greece, [3]Papageorgiou Hospital, First Department of Internal Medicine, Thessaloniki, Greece, [4]Aristotle University of Thessaloniki, First Department of Internal Medicine, Thessaloniki, and [5]Aristotle University of Thessaloniki, Second Department of Internal Medicine, Thessaloniki, Greece

Background and Aims: Arterial hypertension is present in >90% of patients with type-2 diabetes mellitus (DM). Previous evidence suggests that sodium-glucose transporter 2 (SGLT-2) inhibitors can effectively manage hyperglycemia, but also reduce office blood pressure (BP) levels. The aim of this study is to evaluate the effects of dapagliflozin on ambulatory brachial BP in patients with type-2 DM.

Method: This is a double-blind, randomized, placebo-controlled clinical trial including 85 adult patients with type-2 DM on monotherapy or combination therapy with two of: metformin, sulphonylurea, DDP-4 inhibitor, or insulin. Patients were randomized in a 1:1 ratio to oral dapagliflozin 10 mg per day or placebo for 12 weeks. Study participants underwent 24-h ambulatory BP monitoring with the Mobil-O-Graph NG monitor at baseline and study-end.

Results: Baseline demographic, clinical and laboratory parameters were similar in the two groups (age 61.74±6.73 vs 60.64±9.35; p=0.534). During follow-up, 24-hour brachial SBP decreased in the active (128.97±12.57 vs 123.17±12.35; p<0.001) but was similar in the control group (128.95±12.41 vs 128.86±13.45; p=0.942). Corresponding changes in 24-hour SBP levels was greater in the dapagliflozin group compared with the placebo group (-5.80±9.48 vs -0.10±8.70 mmHg; p=0.005). Similarly, 24-hour DBP decreased in the active (77.33±7.30 vs 75.11±6.37; p=0.008) and was unchanged in the placebo group (78.86±8.66 vs 78.96±7.64; p=0.911). Decrease in brachial pulse pressure (PP) was greater in the active group (-3.57±6.67 vs -0.21±6.31 mmHg; p=0.019), while 24-hour heart rate was stable in both groups. Dapagliflozin and placebo treatments were associated with similar rates of generally mild adverse effects.

Conclusion: Treatment with dapagliflozin can produce statistically significant and clinically meaningful reductions in 24-hour BP levels in type-2 diabetics. These agents can improve BP control in this population.

P1027

THE DIFFERENCES EFFECTS OF GLUCAGON LIKE PEPTIDE-1(GLP-1) ANALOGUES AND SODIUM-COTRANSPORTER 2 (SGLT-2) INHIBITORS ON TYPE 2 DIABETES PATIENTS WITH RENAL IMPAIRMENT

TAKEYUKI HIRAMATSU[1], SHOTA OKUMURA[1], Daiki Iguchi[1], Shinji Furuta[1]

[1]*Konan Kosei Hospital, Nephrology, Konan, Japan*

Background and Aims: Diabetes mellitus (DM) is a progressive multifactorial disease associated with cardiovascular complications. To prevent the progression of cardiovascular complications in DM patients, glycemic control is important. In this study, we examined impact on cardiac function between glucagon like peptide-1(GLP-1) analogue and sodium-glucose cotransporter-2 (SGLT-2) inhibitors to treat type 2 diabetes patients with renal impairment.

Method: A total of 125 type 2 DM patients with renal impairment were recruited for this study. All patients were divided into two groups according to the anti-diabetic agents at baseline: Group G; 0.9mg/day liraglutide, n=53, Group S; n=72; 5mg/day dapagliflozin, n=32, empagliflozin n=14, 20mg/day tofogliflozin n=19, or 50mg/day ipragliflozin n=16. Blood glucose levels, glycosylated hemoglobin (HbA_1c), serum creatinine, and albuminuria were obtained 12 months before and every 3 months for 36 months. Echocardiography, ankle brachial pressure index(ABI) and cardio-ankle vascular index(CAVI) were obtained every 12 months for 36 months.

Results: At baseline, the mean age was 68.5±6.0 years, DM vintage was 12.0±6.0 years, and mean total oral pill counts was 12.0±6.0. Compared with baseline, mean total pill counts were reduced at 12 months after initiation of new anti-diabetic agents (ADA) and remained afterward (Group G; 12.3±5.3 at baseline, 8.9±4.0 at 12 months ($p<0.05$), Group S; 11.8±4.2 at baseline, 8.6±3.4 at 12 months ($p<0.05$)). The counts of ADAs were also decreased (Group G; 3.85±2.61 at baseline, 1.41±2.01 at 12 months ($p<0.01$), Group S; 3.48±2.43 at baseline, 2.41±1.44 at 12 months ($p<0.05$)). HbA1c and systolic blood pressure were significantly decreased after initiation of GLP-1 analogue or SGLT-2 inhibitor in both groups. Nevertheless, eGFRs were gradually decreased in both groups. Albuminuria indicated by urinary albumin creatinine ratio were decreased significantly after initiation of anti-diabetic agents. Left ventricular mass index (LVMI) (Group G; 135.8 at baseline, 110.2 at 12 months,114.5 at 24 months, 107.2 g/m^2 at 36 months, Group S; 130.0 at baseline, 113.2 at 12 months,106.4 at 24 months, 115.9 g/m^2 at 36 months) and left atrial volume index (LAVi) (Group G; 25.6 at baseline, 22.3 at 12 months, 21.4 at 24 months, 20.8 mL/m^2 at 36 months, Group S; 24.0 at baseline, 21.8 at 12 months,21.7 at 24 months, 22.7 mL/m^2 at 36 months) were significantly decreased in both groups. Cardiac systolic function indicated by ejection fraction (EF) and diastolic function indicated by E/e' (Group G; 12.9 at baseline, 10.4 at 12 months, 9.4 at 24 months, 9.5 at 36 months, Group S; 12.4 at baseline, 10.6 at 12 months, 12.5 at 24 months, 12.9 at 36 months) or left atrial dimension were remained or improved only in group G. Moreover, arterial stiffness indicated by cardio-ankle vascular index (CAVI) was improved in group G (Group G; 10.2 at baseline, 9.9 at 12 months, 9.9 at 24 months, 9.9 at 36 months, Group S; 10.3 at baseline, 10.5 at 12 months, 10.6 at 24 months, 10.6 at 36 months) (Table1). With respect to admission due to cardiovascular events, cerebrovascular infarction were occurred higher in group S (3.8% vs 1.3% / yea; $p<0.05$), congestive heart failure were higher in group G (1.9%. vs 0.5% / year; $p<0.05$).

Conclusion: These findings suggest that liraglutide and SGLT-2 inhibitor for type 2 DM patients with renal impairment have similar effects on renal function including eGFR and albuminuria and left ventricular and atrial volume. However, liraglutide could provide more benefit for arterial stiffness than SGLT-2 inhibitors.

Table 1. Clinical data

		at baseline	after 12 months	after 24 months	after 36 months
HbA1c (%)	Group G (n=53)	7.14 ± 1.28	6.67 ± 0.99*	6.61 ± 0.82*	6.51 ± 0.74*
	Group S (n=72)	7.33 ± 0.73	7.08 ± 0.71*	7.03 ± 0.93* †	7.05 ± 1.02* †
eGFR (mL/min/1.73m^2)	Group G (n=53)	44.4 ± 10.0	43.4 ± 10.2	42.0 ± 10.0	40.1 ± 9.9**
	Group S (n=72)	46.9 ± 10.3	45.5 ± 11.3	44.6± 12.5	42.0 ± 10.0
ACR (mg/gCr)	Group G (n=53)	257.1 ± 215.4	155.4 ± 149.2**	142.8 ± 112.3**	139.4 ± 107.0**
	Group S (n=72)	237.9 ± 199.6 †	161.3 ± 182.7**	170.9 ± 170.3**	182.0 ± 159.2**
Systolic Blood Pressure (mmHg)	Group G (n=53)	140.8 ± 14.1	133.5 ± 12.7*	129.7 ± 14.8**	113.2 ± 11.1**
	Group S (n=72)	136.2 ± 15.9	1127.3 ± 14.1*	128.2 ± 13.0**	130.7 ± 10.7**
LVMI (g/m^2)	Group G (n=53)	135.8 ± 45.8	110.2 ± 30.3**	114.5 ± 41.5**	107.2 ± 38.2**
	Group S (n=72)	130.0 ± 43.9	113.2 ± 36.5**	106.4 ± 34.2**	115.9 ± 29.5**
LAVi (mL/m^2)	Group G (n=53)	25.6 ± 6.7	22.3 ± 5.2**	21.4 ± 5.7**	20.8 ± 5.8**
	Group S (n=72)	24.0 ± 3.5	21.8 ± 3.8**	21.7 ± 3.5**	22.7 ± 4.3*
Ejection Fraction (%)	Group G (n=53)	69.0 ± 10.3	67.0 ± 12.6	66.7 ± 11.3	66.7 ± 11.4
	Group S (n=72)	71.3 ± 6.7	70.5 ± 8.7	67.5 ± 10.9*	64.9 ± 13.8*
E/e'	Group G (n=53)	12.9 ± 3.0	10.4 ± 2.5**	9.4 ± 2.4**	9.5 ± 3.1**
	Group S (n=72)	12.4 ± 3.3	10.6 ± 3.9**	12.5 ± 3.7	12.9 ± 3.9
CAVI	Group G (n=53)	10.2 ± 1.7	9.9 ± 1.3	9.9 ± 1.1	9.9 ± 1.2
	Group S (n=72)	10.3 ± 2.0	10.5 ± 1.9	10.6 ± 1.7* †	10.6 ± 1.7* †
		* : p <0.05, ** : p <0.01 vs at baseline, † : p <0.05 vs Group G			

Figure:

P1028

EFFECTS OF CANAGLIFLOZIN ON MAJOR ADVERSE CARDIOVASCULAR OUTCOMES IN PATIENTS WITH DIFFERENT BASELINE LEVELS OF TYPE 2 DIABETES MELLITUS DISEASE SEVERITY: RESULTS FROM THE CANVAS PROGRAM

Tamara Young[1], Jing-wei Li[1], Amy Kang[1], Hiddo Heerspink[1], Carinna Hockham[1], Clare Arnott[1], Brendon Neuen[1], Sophia Zoungas[1,2], Kenneth W Mahaffey[3], Vlado Perkovic[1], Dick De Zeeuw[4], Gregory Fulcher[5], Bruce Neal[1], Meg Jardine[1,6]

[1]The George Institute for Global Health, Newtown, Australia, [2]Monash University, Melbourne, Australia, [3]Stanford University, Stanford, United States of America, [4]University Medical Center Groningen, Groningen, Netherlands, [5]University of Sydney, Sydney, Australia and [6]Concord Repatriation General Hospital, Concord, Australia

Background and Aims: Patient with type 2 diabetes mellitus (T2DM) included in trials of sodium-glucose cotransporter 2 inhibitors are heterogeneous in terms of disease severity. We assessed the effects of canagliflozin compared to placebo on cardiovascular and renal outcomes in the CANVAS program according to severity of T2DM as indicated by intensity of treatment, duration of diabetes and glycaemic control.

Method: We compared effects on major adverse cardiovascular events ([MACE], defined as cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) according to three indicators of T2DM severity at study baseline: number of oral glucose lowering treatments or insulin therapy (0-1, 2, 3+, insulin), duration of diabetes (<10, 10-16, >16 years) and HbA1c (<7.0, 7.0-7.5, 7.5-8.0, 8.0-8.5, 8.5-9, >9.0%). We also assessed effects on other pre-specified cardiovascular outcomes, and an adjudicated composite of end-stage kidney disease, renal death or sustained 40% decline in estimated glomerular filtration rate. We assessed for constancy of hazard ratios across subgroups by fitting an interaction term that tested for linear trend.

Results: Of 10,142 participants in the CANVAS Program, 1011 experienced a MACE during a mean follow-up of 3.6 years. Event rates for MACE were higher in those with longer duration of diabetes and higher HbA1c at baseline. The effect of canagliflozin on MACE in the overall population (HR 0.86, 95 % CI 0.75-0.97) was consistent irrespective of the number of glucose lowering treatments (p=0.509), duration of diabetes (p=0.174) and baseline HbA1c (p =0.314). Effects were also consistent across different levels of T2DM disease severity for all other outcomes studied.

Conclusion: Higher event rates were observed in those with longer disease duration and higher HbA1c. The proportional risk reductions achieved with canagliflozin were comparable regardless of diabetes duration, number of therapies or HbA1C at baseline.

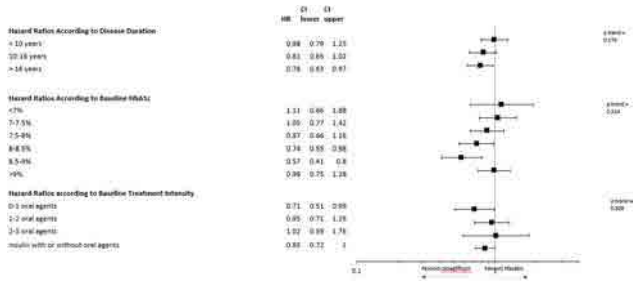


FIGURE 1: Effects of canagliflozin compared to placebo on major adverse cardiovascular events in patient subgroups according to different parameters of disease severity:

P1029

SAFETY AND EFFICACY OF LONG-TERM ADMINISTRATION OF DPP-4 INHIBITORS IN PATIENTS WITH NEW ONSET DIABETES AFTER KIDNEY TRANSPLANTATION.

Adamantia Mpratsiakou[1], Marios Papasotiriou[1], Konstantinos Tsiotsios[1], Theodoros Ntrinias[1], Evangelos Papachristou[1], Dimitrios Goumenos[1]

[1]*University Hospital of Patras, Department of Nephrology, Patras, Greece*

Background and Aims: New onset diabetes (NODAT) is a common complication after kidney transplantation. The available treatment options in this patient population have limitations due to reduced renal function, possible interactions with immunosuppressive drugs and side effects such as hypoglycemic events. The aim of this study was to investigate the long term safety and efficacy profile of dipeptidyl peptidase-IV (DDP-4 inhibitors) administration in renal transplant recipients with NODAT.

Method: The study included 12 patients treated with DPP-IV inhibitors monotherapy as well as 5 patients receiving insulin monotherapy as initial treatment immediately after NODAT diagnosis. All patients were monitored at every scheduled outpatient visit and for 12 months after diagnosis by measuring glycosylated hemoglobin (HbA1c), serum creatinine (eGFR calculation with CKD-EPI formula), plasma immunosuppressive trough levels, serum lipids, blood pressure, and body weight. The mean values of the aforementioned parameters for the last six months of follow up were compared to the ones at diagnosis.

Results: Patients receiving DPP-IV inhibitors were treated with either linagliptin (4 patients), sitagliptin (4 patients), vildagliptin (2 patients) or halogliptin (2 patients). These patients had a mean age of 59.4 $\pm$ 12 years, a mean HbA1c of 6.6% and a mean fasting glucose of 114.5 mg/dl at diagnosis. The mean HbA1c the last 6 months of one year of follow up after initiation of treatment, decreased to 6.1% (p=0.03). Renal function remained stable (mean eGFR from 58.8 to 61.7 ml/min/1.73m^2, p=ns) while plasma tacrolimus levels did not appear to be affected (from 6.2 to 5.5 ng/dl, p=ns). Patients received a slightly reduced mean dose of tacrolimus during the last six months of follow up in comparison to the one at initiation of treatment (from 2.9 to 2.6 mg/24h, p=ns). No significant difference was shown in serum total, LDL, and HDL cholesterol before and after treatment, nevertheless, triglyceride levels were significantly reduced (from 214.4 to 174.9 mg/dl, p=0.0039). A decrease in body weight was observed (from 79.9 to 77.9 kg, p=ns) which was however not statistically significant. Finally, achieving the goal of lowering HbA1c levels was better in patients treated with DPP-IV inhibitors than in those treated with insulin (6.1% vs 7.1%, respectively, p=0.01).

Conclusion: Administration of DPP-IV inhibitors appears to be a safe and effective option for the treatment of NODAT in renal transplant recipients with the benefit of avoiding hypoglycemic episodes and possibly better diabetes control than with insulin therapy.

P1030

ENDOTHELIAL DYSFUNCTION AND CARDIAC VALVE CALCIFICATION IN PATIENTS WITH DIABETIC KIDNEY DISEASE UNDERGOING CHRONIC HEMODIALYSIS

Zoriana Litovkina[1], Oleksandr Susla[1,1], Ihor Mysula[1], Bohdan Susla[1]

[1]*I. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine*

Background and Aims: The character of endothelial dysfunction (ED), especially of nitric oxide (NO) system, in patients with diabetic kidney disease (DKD) undergoing chronic hemodialysis (HD) was not asserted enough. In this condition not clearly established the relationship of structural and functional activity of endothelium with the presence and severity of cardiac valve calcification (CVC) as independent predictor of cardiovascular morbidity and mortality. The purpose of the current study was to determine the role of ED in mechanisms of mitral (MVC) and aortic (AVC) valve calcification in HD patients with DKD.

Method: We enrolled 136 patients undergoing HD (male/female, 78/58; age, 53.9±1.0 years; HD duration, 47.6±4.2 month) in this observational cross-sectional study. According to the study design, depending on the presence of type 2 diabetes mellitus with kidney injury patients were divided into two groups: the 1st one – without DKD (n=88); the 2nd one – with DKD (n=48). All subjects underwent echocardiographical examination for detection of CVC; the MVC and AVC degree were scored as follows: 1, no calcification; 2, valve thickening without calcification; 3, valve annulus or cusps calcification. Vasomotional function of endothelium was assessed using a test with reactive hyperemia (brachial artery flow-mediated dilatation (FMD)). Plasma content of nitrites (NO_2), circulating endothelial cells (CECs) and serum concentration of C-reactive protein (CRP) were measured as markers of ED. Data are expressed as means±SEM. Used nonparametric statistics methods: Mann-Whitney U-test, χ^2-test, Spearman's rank R correlations.

Results: In group of HD patients with DKD indices of CECs (22.3±1.3 vs. 14.2±0.7 × 10^4/L, Z=4.98, p<0.001), CRP (9.94±1.12 vs. 7.07±1.09 mg/L, Z=3.47, p<0.001) were higher, and NO_2 (4.16±0.41 vs. 9.01±1.37 umol/L, Z=3.15, p=0.002), FMD (2.27±0.66 vs. 5.13±0.52%, Z=3.26, p=0.001) – lower compared to the group without diabetes. CVC was detected in 66.6% of patients with DKD with predominance of calcification of both valves (35.4%) over isolated MVC (20.8%) and AVC (10.4 %). Combined valve calcification in the HD patients of the 2nd group was observed 2.6 times more often (χ^2=8.78, p=0.003) than in the 1st one. For the first time it was established that in DKD the presence of CVC closely associated with indices of FMD (Rs=-0.59, p<0.001), NO_2^- (Rs=-0.56, p<0.001), CECs (Rs=0.63, p<0.001) and CRP (Rs=0.54, p<0.001). The MVC as well as AVC degree were related with the level of FMD (Rs=-0.47, p<0.001; Rs=-0.43, p=0.003), content of NO_2^- (Rs=-0.40, p=0.005; Rs=-0.62, p<0.001), CECs (Rs=0.47, p<0.001; Rs=0.62, p<0.001) and CRP (Rs=0.48, p<0.001; Rs=0.41, p=0.004) concentrations respectively.

Conclusion: (1) HD patients with DKD are combined with damaged endothelium, disturbance of vasoreactivity and lack of NO. (2) Type 2 diabetes mellitus with kidney injury is characterized by the large-scale combined MVC and AVC, which in turn are closely associated with the ED markers. (3) Complex estimation of the character of CVC and endothelium activity in HD patients with DKD permits a better identification of their cardiovascular risk.

P1031

CHADS2 AND CHAD2DS2-VASC SCORES IN THE PREDICTION OF PERIPHERAL ARTERIAL DISEASE IN DIABETIC PATIENTS

Yi-Hsin Chen[1,2]

[1]Taichung Tzu Chi Hospital, Nephrology, Taichung, Taiwan, R.O.C. and [2]Tzu Chi University, Medicine, Hualian, Taiwan, R.O.C.

Background and Aims: Peripheral arterial disease (PAD) is more often seen in diabetic patients, accounting for 25-30%. Diabetic patients suffered more lower limb amputations in Unites States as high as 60% and patients with PAD suffer higher risk for amputations. We want to use CHADS2 and CHA2DS2-VASc scores to predict the risk of PAD in diabetic patients.

Method: We analysed data from the Taiwan National Health Insurance Research Database between January 1st, 2002 and December 31st, 2009. A total of 5,6732 diabetic patients were selected as the study cohort. The CHADS2 score and CHA2DS2-VASc score were calculated for each patient.

Results: During the follow-up period, 228 (0.4%) patients experienced new-onset PAD. The rate of PAD increased from 0.3% (CHADS2 score 1-2) to 1.4% (CHADS2 score 4-6) ($p<0.001$). The rate of PAD increased from 0.2% (CHA2DS2-VASc score 1-3) to 3.5% (CHADS2 score 7-9) ($p<0.001$). According to a multivariate analysis, the hazard ratio of each point increment in the CHADS2 score for predicting PAOD was 1.67 ($p<0.001$), CHA2DS2-VASc score was 2.03($p<0.001$).

Conclusion: The CHADS2 and CHA2DS2-VASc scores are useful predictors of new-onset PAD in diabetic patients.

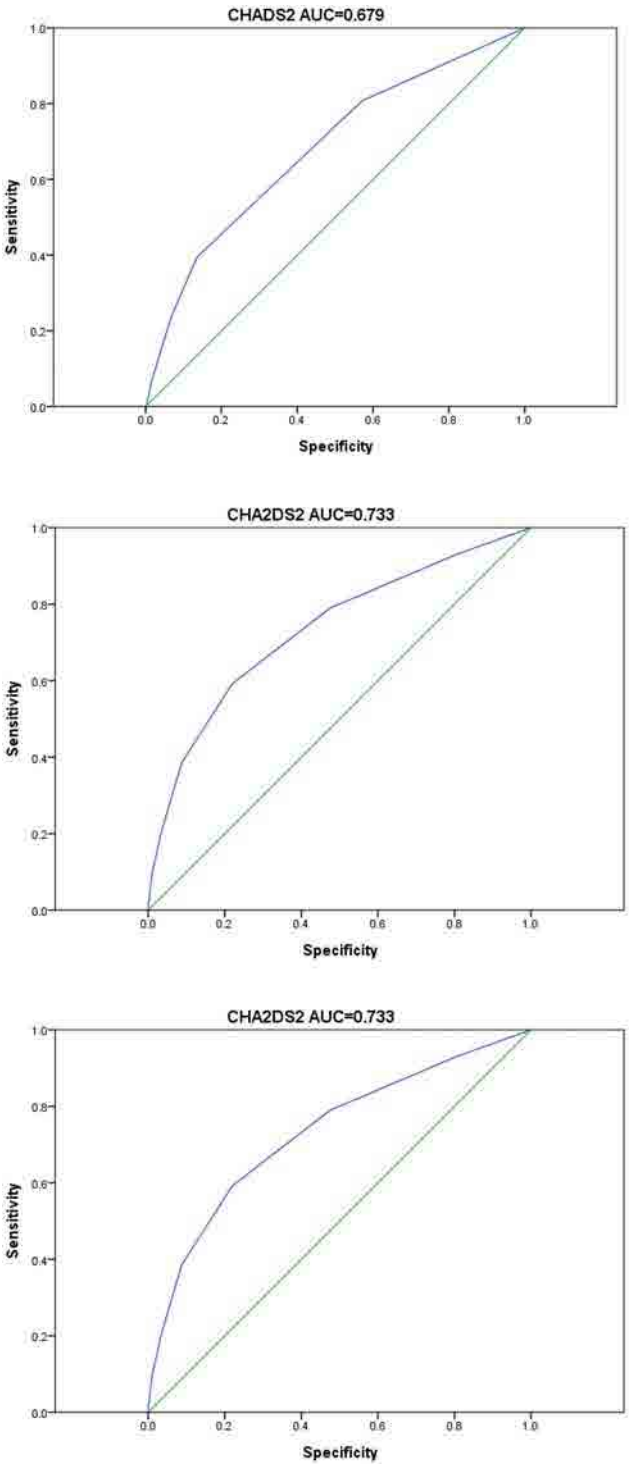


Figure 1: Receiver operating characteristics curve for $CHADS_2$ and CHA_2DS_2-VASc in prediction of peripheral arterial disease in diabetes patients.

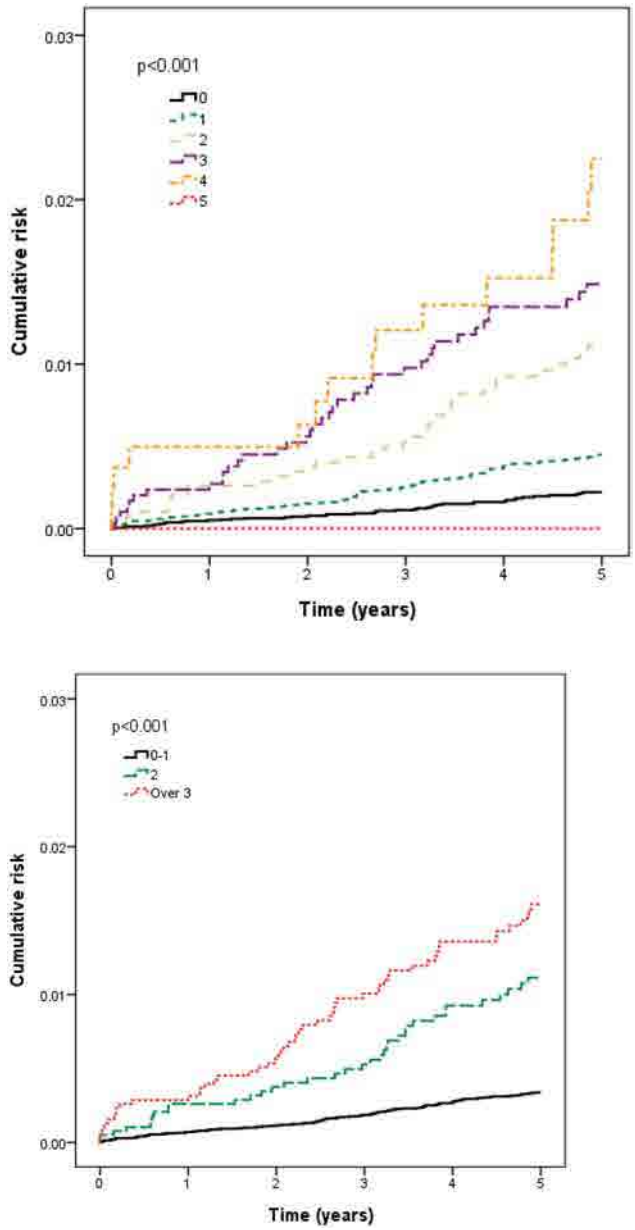


Figure 2. (a) Peripheral arterial disease risk stratified by $CHADS_2$ score. (b) Peripheral arterial disease risk stratified by $CHADS_2$ score categories.

P1032 CMV INFECTION & RISK OF NEW ONSET DAIBETES AFTER TRANSPLANTATION

MUHAMMAD TASSADUQ KHAN[1]

[1]*DOW UNIVERSITY HOSPITAL, RENAL TRANSPLANT UNIT, KARACHI, Pakistan*

Background and Aims: NODAT is a frequent complication among kidney transplant recipients and is considerably associated with risk of allograft rejection and allograft loss. The present research study was aimed to identify whether CMV infection acts as risk factor for NODAT development in kidney transplant recipients.

Method: This retrospective study recruited 59 kidney transplant recipients (43 males and 16 females). The diagnosis of NODAT was established if two fasting plasma glucose readings were $\geq$126 mg/dL after the 3rd month of post-transplantation. We carefully monitored recipients for CMV viremia (CMV DNA copies/mL) in the plasma through quantitative Polymerase Chain Reaction (qPCR). The 1 year post-transplantation allograft outcomes due to CMV viremia were also measured; eGFR (CKD-EPI method), allograft and transplant patient survival.

Results: In this study, 14 (23.7%) patients were diagnosed with NODAT. The CMV load and CMV viremia was elevated in NODAT cohort in comparison with their counterparts (4000 versus 3600 and 51.1 versus 47.6, respectively); however, no statistical relationship was observed ($P = 0.79$ and $P = 0.84$, respectively). We witnessed significantly high CMV DNA replication in first (1-6 months) half of the post-transplant period in both controls and NODAT patients; however, statistically significant CMV DNA replication was only observed for NODAT cohort ($P<0.001$). Majority of the NODAT diagnoses; 9 out of 14 (64.3%), in our cohort was made during the first six months of kidney transplantation ($P<0.001$). Overall, 7 (11.9%) of the kidney transplant recipients recruited in our study progressed to symptomatic CMV infection. We also witnessed that a greater CMV viremia load was worsening the kidney allograft function at 12 months post-transplantation. The allograft and patient survival (censored for death) was poor in the NODAT cohort; however, without any statistical significance.

Conclusion: The present study demonstrated that CMV infection is not a risk factor for NODAT development among kidney transplant recipinets.

P1033

VALUE OF ADDING PENTOXIFYLLINE IN COMPARISON TO ANGIOTENSIN CONVERTING ENZYME INHIBITORS IN TYPE 2 DIABETIC PATIENTS AMONG EGYPTIAN POPULATION

Magdy ElSharkawy[1], Mohamed Mostafa[1], Mohamed Ezzat[2]

[1]faculty of Medicine, Ain shams University, internal medicine and nephrology, cairo, Egypt and [2]faculty of Medicine, Ain shams University, Internal Medicine and Nephrology, Cairo, Egypt

Background and Aims: Microalbuminuria is one of the early presentations of diabetic kidney disease that may progress to macroalbuminuria, progressive loss of glomerular filtration rate and eventually end stage renal disease. Early recognition and management of microalbuminuria can avert irreversible complications. Antihypertensive medications and antihyperlipidemic medications are medications that have been used to control diabetic nephropathy, but the reports of some side effects limited the usage of some of these drugs in diabetic patients. Pentoxifylline is an anti-inflammatory medication that have been experienced for clinical trials in diabetic patients with diabetic kidney disease. Effect of Pentoxifylline on albuminuria has been evaluated in several studies with different outcomes where a significant decrease in albuminuria in the Pentoxifylline group compared with placebo was the final conclusion. The aim of our study is the assessment of the value of Pentoxifylline addition in diabetic patients.

Method: Of 90 patients aged between 20 and 55 years old with a history of diabetes mellites type II for more than 5 years with normal serum creatinine and had a spot urinary albumin/creatinine ratio of $>$ 300 mg/g on two consecutive measurements with HBA1C $<$ 7% and lacking any history of glomerular disease, immunological, malignant nor cardiovascular disease in the previous 6 months nor using pentoxifylline for the past 3 month attending Ain Shams University clinics in Egypt from October 2017 to September 2018, 61 patients were eligible and randomly assigned in prospective, randomized, parallel-group, non-blind study after obtaining written informed consent from studied patients into 2 groups either the Pentoxifylline group (n = 30) receiving 400 mg thrice daily for 6 months or Ramipril group (n = 31) receiving 2.5 mg once daily on the same schedule. Blood samples and single first morning void urine samples were collected before breakfast after an 8–12 hours overnight fast. Plasma glucose, HbA1c, serum Creatinine, AST, ALT, and urinary protein / Creatinine levels were measured. All biochemical analyses were performed. Participants were followed up after 1, 3 and 6 months during the treatment period to evaluate the outcome

Results: Highly Statistically significant differences were noted as regard the reduction of the proteinuria levels at the same measurement points in both groups where the mean ranges of proteinuria in group 1 were found to be 2.2$\pm$1, 1.8$\pm$0.7, 1.4$\pm$0.6 mg\g at the start of the study, 3 and 6 month later respectively while in group 2 the mean range was found to be 2.6$\pm$1.2, 2$\pm$0.8, 1.6$\pm$0.7 mg\g with marked reduction of 20.6% after 3 month and 37.6% after 6 month from the start of the trial in group 1 in contrast to 20.7% and 40.2% respectively in group 2, also the effect of both drugs on the level of HbA1c has been studied in both group, in group 1 there was no reduction in the level of HbA1c after 6 month of drug administration in contrary to group 2 which showed a reduction of 4% where these results were found to be statistically significant in group 2 only. we also found statistically significant differences in both groups as regard the decline in eGFR throughout the trial duration which was 4% in group 1 and 6% in group 2.

Conclusion: We concluded that Pentoxifylline has a promising role as an antiproteinuric agent in comparison with ACEI from our statistical analysis of the study data with a more decline in eGFR throughout the trial duration in the study population using ACEI in comparison to Pentoxifylline. Due to restrictions of the study design these observations need further confirmation by prospective studies.

Figure:

Figure (1): showing comparison between both groups as regard the level of proteinuria and its reduction rate over 6 months

Figure (2): showing eGFR levels at 0, 6 months in both groups

Figure (3): showing comparison between both groups as regard HbA1C at baseline and after 6 months.

P1034

EVALUATION OF RISK FACTORS FOR DIABETIC NEPHROPATHY AMONG NEWLY DIAGNOSED TYPE 2 DIABETIC SUBJECTS

Muhammad Abdur Rahim[1], Shahana Zaman[2], Samira Humaira Habib[3], Faria Afsana[4], Wasim Md. Mohosin Ul Haque[1], Sarwar Iqbal[1], Md. Jakir Hossain[5]

[1]Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Nephrology, Dhaka, Bangladesh, [2]National Institute of Cardiovascular Diseases (NICVD), Cardiology, Dhaka, , [3]Bangladesh Diabetic Somiti, Health Economic Unit, Dhaka, Bangladesh, [4]Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Endocrinology, Dhaka, Bangladesh and [5]United Hospitals Ltd., Cardiology, Dhaka, Bangladesh

Background and Aims: Diabetes mellitus (DM) is the leading cause of chronic kidney disease in developed as well as in developing countries, principally resulting from the increasing prevalence of type 2 DM (T2DM). Patients with T2DM pass through pre-diabetic stages and half of the T2DM patients remain undiagnosed. During diagnosis, one-third to half of the T2DM patients may have different macro- and micro-vascular complications including diabetic nephropathy. This study was designed to evaluate risk factors for diabetic nephropathy among newly detected T2DM subjects.

Method: A case-control study was done at out-patient department of a tertiary care hospital in Dhaka, Bangladesh from October 2016 to June 2017. Newly detected (<3 months) adult (≥ 18 years) T2DM patients of either sex, who underwent test for urine albumin-to-creatinine ratio (UACR) at least twice, at least 6 weeks apart, within a 6-month period, were included in this study. Patients with diagnosed kidney diseases, features of glomerulonephritis, systemic diseases like systemic lupus erythematosus and vasculitis, history of recent fever and exercise, urinary tract infection and pregnancy were excluded. Patients with UACR ≥ 30 mg/g in at least two (of three, if done) samples were cases and those with UACR <30 mg/g were controls.

Results: Total patients were 100, including 35 cases [moderately increased proteinuria (previously, microalbuminuria) (UACR 30-299 mg/g) = 33 and severely increased proteinuria (previously, overt proteinuria) (UACR ≥ 300 mg/g) = 2] and 65 controls. Mean age was 46.6 ± 12.3 years and there was female predominance (male:female ratio was 1:2). Twenty four percent patients were smokers, 50% were hypertensive and 46% had dyslipidaemia. Seventy five percent of the study participants had positive family history of DM and 39% had family history of diabetic nephropathy. Mean body mass index (BMI) was 26.3 ± 2.9 kg/m^2. Mean fasting blood glucose (mmol/L), 2-h post glucose value (mmol/L) and mean glycated haemoglobin (HbA1c) (%) were 9.2 ± 2.9, 14.5 ± 4.1 and 7.9 ± 1.3 respectively. Eighty percent of the patients were asymptomatic regarding DM. Besides nephropathy, other chronic complications of DM were diabetic retinopathy (17%), neuropathy (11%), coronary artery disease (11%) and cerebrovascular disease (4%). Regarding risk factors for diabetic nephropathy, family history of DM (OR 1.62, p 0.0001) and diabetic nephropathy (OR 25.13, p 0.003), presence of hypertension (OR 4.93, p 0.001) and coexisting diabetic retinopathy (OR 14.18, p 0.046) were significant. On multivariate logistic regression, family history of DM (OR 1.77, p 0.001) and diabetic nephropathy (OR 24.31, p 0.001), higher BMI (>25 kg/m^2) (OR 2.11, p 0.013), hypertension (OR 4.31, p 0.003) and diabetic retinopathy (OR 14.09, p 0.021) were significant.

Conclusion: One-third of the newly detected type 2 diabetic subjects had diabetic nephropathy in this study. Family history of DM and diabetic nephropathy, higher BMI, presence of hypertension and diabetic retinopathy were significant risk factors for diabetic nephropathy.

P1035 URINARY HEME OXYGENASE 1 AS A MARKER FOR EARLY DIAGNOSIS OF DIABETIC NEPHROPATHY

Fatma Ahmed[1], Hesham Abo el Ieel[1], Hayam Ahmed Hebah[1], Aya Magdy[1]
[1]*ain shams university, nephrology, Egypt*

Background and Aims: Heme oxygenase 1 is an essential enzyme in heme catabolism induced by oxidative stress.It induced in avariety of kidney substructres in response to injury, including proximal tubules, glomeruli and renal interstitium.We aimed to assess the possible role of heme Oxygenase-1 as a potential marker in early diagnosis of diabetic nephropathy.

Method: This case control study was conducted in Ain Shams university hospital, Cairo, Egypt**. It included** 80 type 2 diabetic patients diagnosed according to the American Diabetes Association (ADA) criteria, with and without DN ,and 20 healthy control subjects matched in age and sex .Patients were divided into two groups according to the value of the urinary albumin-to-creatinine ratio (ACR) : Group I: 40 normoalbuminuric patients(16 M and 24 F) with ACR<30 mg/g, and Group II: 40 microalbuminuric patients (18M and 22 F) with ACR 30-300mg/g. We excluded patients with history of diabetic ketoacidosis or hypoglycemic coma in the past 3 months preceding the study. Patients with glomerulonephritis, nephrolithiasis, tumors or any other renal diseases were excluded as well. For all studied groups,full history **taking** and clinical examination were done. **We assessed g**lycosylated hemoglobin (HbA_1**C**),**b**lood urea, serum creatinine, **urine creatinine, u**rinary albumin-to creatinine ratio (ACR mg/g) ,and urinary hemeoxygenase 1(**UHO**-1) by ELISA . Glomerular filtration rate (eGFR) was estimated by modification of diet in renal disease formula(MDRD)and uHO-1/cr was calculated.

Results: Group I patients were diabetic for 6.18±0.75 years, while group II patients for 6.05±0.81 years($p = 0.477$). Normoalbuminuric patients had significantly higher levels of uHO-1 compared to control (3.01ng/ml vs 0.3 ng/ml,$p<0.001$).UHO-1 reached highest value among the microalbuminuric group (5.02 ng/ml) with $P<0.001$.UHO-1/cr ratio was significantly positively correlated with urinary ACR ($r = 0.61$,$p<0.001$) and significantly negatively correlated with eGFR($r = -0.71$,$p <0.001$). There was highly significant correlation between uHO-1and eGFR by linear regression. ROC curves showed that AUC of uHO-1is comparable to uHO-1/ Cr ratio (0.957 vs 0.954) respectively with equivocal sensitivity 100 % and specificity 95% and cut off value of uHO-1 >0.46 ng/mland > 0.7 for uHO-1/ Cr ratio.

Conclusion: UHO-1 is increased in normoalbuminuric patients before the presence of any proteinuria and level increased with the progression of proteinuria and falling of eGFR as well as with the uncontrol of diabetes. UHO-1 is more sensitive than albumin for the detection of early diabetic nephropathy.

P1036

THE SHORT-TERM EFFICACY AND SAFETY OF THE APPLICATION OF SGLT2I AS A DIURETIC MEDICATION ON THE DIURETIC RESISTANCE IN PATIENTS WITH DIABETIC NEPHROPATHY ON CKD STAGE 3-4

Wei Liang[1]

[1]*Renmin Hospital of Wuhan University, nephrology, Wuhan, P.R. China*

Background and Aims: At stage 3-4 of chronic renal disease, patients with diabetic-induced renal dysfunction are not sensitive to the conventional diuretic therapy based on loop diuretics and thiazide diuretics, leading to the earlier renal replacement at stage CKD 3-4. The lower sodium excretion could contribute to the development of diuretic resistance. The protective effects of SGLT2 inhibitors on cardiovascular is contributed by metabolic regulation and osmotic diuretic effect of glucose due to extra excretion of Glucose. The present study aim to investigate the efficacy and safety of SGLT2 inhibitors on the diuretic resistance of diabetic nephropathy at CKD 3-4 stage.

Method: Patients with Diabetic nephropathy at CKD3-4 stage were administrated with furosemide + hydrochlorothiazide for 3 days with urine volume <1000ml, urine sodium excretion <90mmol followed by Dapagliflozin/Canagliflozin once a day for 7 days.

Results: 3 male and 7 female patients with diabetic nephropathy were included, aged 51-80 years, with eGFR 60-4.6ml/min, and 3 patients presented with cardiac insufficiency. Urine volume was 800±300ml/24 hours before treatment and 2000±500ml/24 hours after treatment. Sodium excretion in urine was 80±20mmol/24 hours before treatment and 150±50mmol/24 hours before treatment. The average net weight change was -3.5±2.2kg. The Scr increased by 30%±5% before and after treatment, and the renal function in 2 patients increased by >30% after 7 days of treatment, and returned to the level of Scr before treatment after 7 days of withdrawal of Dapagliflozin/Canagliflozin. Electrolyte levels were comparable before and after treatment.

Conclusion: The diuretic regimen based on SGLT2i could significantly improve the resistance of diabetic nephropathy patients to loop diuretics, increase urinary sodium excretion, and slightly elevate renal function in the short term without affecting blood electrolyte level. The efficacy and safety of long-term use of SGLT2i in diabetic nephropathy patients at CKD3-4 stage need further investigate in larger sample size.

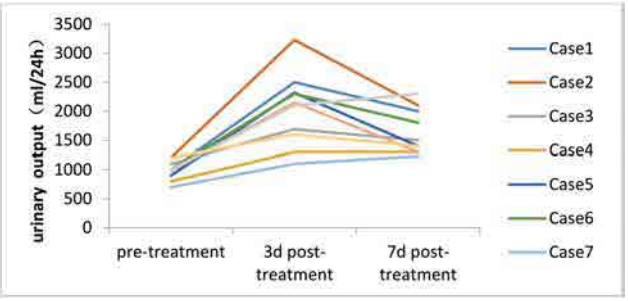


Figure:

P1037

EFFECT OF VITAMIN D SUPPLEMENTATION ON PROTEINURIA, LIPID STATUS, GLICOREGULATION, C-REACTIVE PROTEIN, VEGF-A, TGF-BETA1 AND NEPHRIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Marijana Petroviä‡[1,2], Stanko Petrovic[3], Katarina Obrencevic[4], Tamara Dragovic[5], Nemanja Rancic[6], Neven Vavic[4], Danilo Vojvodic[7], Dejan Petrovic[8], Violeta Rabrenovic[4], Jelena Tadic[4], Mirjana Mijuskovic[4], Brankica Terzic[4], Dejan Pilcevic[4]

[1]Military Medical Academy, Clinic of Nefrology, Belgrade, Serbia, [2]Faculty of Medicine of the Military Medical Academy, University of Defence, Belgrade, Serbia, [3]Military Medical Academy, Clinic of Gastroenterology and hepatology, Belgrade, Serbia, [5]Military Medical Academy, Clinic of Endocrinology, Belgrade, Serbia, [6]Military Medical Academy, Centre for Clinical Pharmacology, Belgrade, Serbia, [7]Military Medical Academy, Institute for Medical Research, Belgrade, Serbia and [8]Faculty of Medical Sciences University of Kragujevac, Department of internal medicine, Kragujevac, Serbia

Background and Aims: Vitamin D insufficiency/deficiency is often present in patients with Type-2 diabetes mellitus and could present a risk factor for rapid progression of diabetic nephropathy and higher incidence of cardiovascular events. The aim of this study was to examine the influence of vitamin D supplementation on glucoregulation, inflammation, cholesterol, triglycerides, albuminuria and biomarkers of renal injury – nephrin, VEGF-A and TGF- β_1 in patients with Type-2 diabetes mellitus and vitamin D insufficiency/deficiency.

Method: We included 90 patients with Type-2 diabetes mellitus and vitamin D insufficiency/deficiency in this prospective, cohort study. Patients are divided in 3 equal groups: 30 patients with normal albuminuria, 30 with microalbuminuria and 30 with macroalbuminuria. Therapy included 6 months of supplementation with cholecalciferol drops: first 2 months with 20000 IU twice weekly, than if vitamin D level remained below normal range, we procedeed with same dose next 4 months. If the level of vitamin D normalized, we proceeded with 5000 IU twice weekly. At the beginning and at the end of the study we measured levels of albumin, hemoglobin, serum iron, urea, creatinine, fasting blood glucose, hemoglobin A1c, calcium, phosphorus, total cholesterol, triglycerides, C-reactive protein, intact parathyroid hormone, and urine analysis: 24-hour urine protein, albumin/creatinine ratio and creatinine clearance. Biomarkers are measured in serum and urine. Levels of calcium, phosphorus and vitamin D are also checked 2 months after beginning of therapy due to possible correction of cholecalciferol dose. Results are analysed according to the vitamin D level at the beginning and at the end of the study.

Results: The lowest level of vitamin D, before therapy, is found in patients with macroalbuminuria, while at the end of the study we found significantly higher level of vitamin D in all three groups. After 6 months of therapy we found significant decrease of 24-hour urine protein, total cholesterol, triglycerides, hemoglobin A1c and VEGF-A in urine, in all three groups, and C-reactive protein in patients with normal albuminuria and microalbuminuria, nephrin in urine in patients with microalbuminuria and TGF- β_1 in urine in patients with macroalbuminuria.

Conclusion: vitamin D supplementation with high-dose cholecalciferol in patients with Type-2 diabetes mellitus (with or without albuminuria) decreases C-reactive protein, hemoglobin A1c, total cholesterol, triglycerides in serum, and albumin/creatinine ratio, 24-hour urine protein, VEGF-A, TGF- β_1 and nephrin in urine.

Figure:

P1038 **NEPHROPROTECTIVE EFFECT OF SGLT2 INHIBITORS DURING FIRST YEAR OF TREATMENT**

Catarina Almeida[1], Leonor Silva[2], Tiago Costa[2], Daniela Lopes[1], Luís Andrade[2]

[1]Centro Hospitalar Vila Nova Gaia Espinho, Nephrology, Vila Nova de Gaia, Portugal and [2]Centro Hospitalar Vila Nova Gaia Espinho, Internal Medicine, Vila Nova de Gaia, Portugal

Background and Aims: SGLT2 inhibitors, the most recent glucose-lowering oral agents, have the potential to exert nephroprotection not only through improving glycemic control but also through glucose-independent effects. Recent studies demonstrate this effect with decreased albuminuria and lowering the progression of chronic kidney disease. The aim of our study was to evaluate the effect of iSGLT2 on glomerular filtration rate and albuminuria during the first year of treatment.

Method: This was a retrospective cross-sectional study that included patients diagnosed with DM2 and treated with an iSGLT2 during 1 year in a Diabetic Clinic. Demographic and clinical variables were collected, including HbA1c, disease duration and cardiovascular risk factors (CVRF). Patient glucose-control therapy as well as RAAS inhibitor drugs were gathered. The estimated Glomerular Filtration Rate (eGFR) by the formula CKD-EPI and albuminuria, using the urinary albumin-to-creatinine ratio, were evaluated at the iSGLT2 introduction date and at 3, 6, 9 and 12 months of treatment.

Results: We analyzed 208 patients, 53.8% male, mean age 65.5 years, median baseline HbA1c 8.4% and median duration of DM2 14 years. Of all patients, 94.2% had at least 1 CVRF, 71.6% were hypertensive, 83.2% had dyslipidemia, 48.1% were obese, and 25.2% had past/current smoking habits. Regarding glucose-control therapy, only 20.2% were treated with one oral drug class and the remaining with 2 or more classes, with 81.7% of the patients receiving metformin and 51.4% being on insulin therapy. Overall, 63.5% of patients received dapaglifozin therapy and 36.5% empaglifozin. Also, 56.3% were on a RAAS inhibitor. Regarding eGFR, 15.6% patients had an eGFR between 30 and 60 and 84.4% patients had an eGFR greater than 60 ml/min/1.73m2. As for albuminuria, 37 patients had normal albuminuria (<30mg/g), 18 patients had moderate albuminuria (30-300mg/g) and 6 patients had severe albuminuria (>300mg/g). In 12 months, there was a significant reduction in HbA1c (mean variation 0.5%) (p<0.001). Evaluating eGFR throughout the year, a decrease was observed in the first 6 months from an average of 81.6 to 78.5 ml/min/1.73m2 (p=0,001). Although on the second semester, there was an increase in eGFR to 83.4 ml/min/1.73m2 (p<0.001). These were similar in patints treated with dapagliflozin and empagliflozin. In patients with eGFR <60ml/min at the admission, there was an increase in eGFR from 49.6 to 53.4ml/min/1.73m2 after one year of treatment (p=0,260). A decrease in albuminuria levels was observed in the first year of iSGLT2 use, either in the case of moderate albuminuria (initial median of 80.52mg/g to 54.88mg/g) (p=0,758) or severe albuminuria (initial mean 650.40mg/g to 420.28mg/g) (p=0,213).

Conclusion: This data shows that after an initial reduction in eGFR during the first 6 months of treatment, the use of iSGLT2 after one year improved the eGFR, promoting a **nephroprotective effect** in type 2 diabetic patients.

	Dapaglifozin		Empaglifozin		Total	
Basal HbA1c median (IQR)	N: 132	8,3 (1,7)	N: 76	8,4 (2,3)	N: 208	8,4 (1,9)
Final HbA1c median (IQR)	N: 118	7,9 (2,1)	N: 51	7,8 (2,3)	N: 169	7,9 (2,1)
Initial eGFR ml/min/1.73m2	N: 132	84,2±1,7	N: 76	77,1±2,5	N: 208	81,6±1,4
eGFR at 6 months ml/min/1.73m2	N: 87	81,3±2,0	N: 54	74,0±3,3	N: 141	78,5±1,8
eGFR at 12 months ml/min/1.73m2	N: 104	85,3±2,0	N: 45	79,0±3,6	N: 149	83,4±1,8

	Dapaglifozin	Empaglifozin	Total
eGFR variation in first semester (mean ml/min/1.73m2)	-2,6 (p=0,034)	-3,1 (p=0,008)	-3,1 (p=0,001)
eGFR variation in the second semester (mean ml/min/1.73m2)	4 (p=0,001)	5 (p=0,085)	4,9 (p<0,001)

Total and Subgroup Analysis of HbA1c and estimated Glomerular Filtration Rate.
IQR stands for Interquartile range. N stands for number of patients. ± stands for standard deviation. eGFR stands for estimated glomerular filtration rate

Figure:

P1039

BARIATRIC SURGERY AND RISKS OF RENAL DISEASES, CARDIOVASCULAR DISEASES AND MORTALITY AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS

Carlos Wong[1], Tingting Wu[1], Simon Wong[2], Betty Law[3], Eleanor Grieve[4], Olivia Wu[4], Cindy Lam[1]

[1]University of Hong Kong, Department of Family Medicine and Primary Care, Hong Kong, P.R. China, [2]Chinese University of Hong Kong, Department of Surgery, Hong Kong, P.R. China, [3]University of Hong Kong, Department of Surgery, Hong Kong, P.R. China and [4]University of Glasgow, Health Economics and Health Technology Assessment, United Kingdom

Background and Aims: To measure and compare the risks of end-stage renal diseases (ESRD), cardiovascular diseases (CVD), all-cause mortality between obese type 2 diabetes mellitus (T2DM) patients with and without bariatric surgery.

Method: A retrospective population-based cohort of 1,690 obese T2DM patients who were free of ESRD and CVD were assembled based on 2006-2017 Hospital Authority database. One-to-five propensity-score matching was used to balance baseline covariates between patients in bariatric surgery and control groups. Incidence rates (IR) of stage 4/5 chronic renal diseases, ESRD, CVD and all-cause mortality events for two groups were calculated. Hazard ratios (HR) for stage 4/5 chronic renal diseases, ESRD, CVD events were assessed using Cox proportional hazard models. Changes in estimated glomerular filtration rate (eGFR), and urine albumin-creatinine ratio (UACR) were measured up to 60 months.

Results: Over a mean follow-up period of 34 months with 863 person-years, cumulative incidences of mortality, stage 4/5 chronic kidney diseases, ESRD and CVD for surgical patients were 0, 0.050, 0.017, and 0.036, respectively. Surgical patients had reduced IR of all-cause mortality, stage 4/5 chronic kidney diseases, ESRD and CVD (IR=0, 1.784, 0.587 and 1.321 per 100 person-years, respectively) than control patients (IR=1.954, 2.028, 0.914 and 2.814 per 100 person-years, respectively). Surgery group had a significant reduction in risk of CVD events (HR=0.464, P=0.015), and no occurrence of mortality events. However, the IR of stage 4/5 chronic kidney diseases and ESRD of the two groups were not significantly different. Surgical patients had significantly higher eGFR within 12 months, and had significantly lower until 48 months.

Conclusion: Among obese T2DM patients, bariatric surgery lowered the risk of CVD and mortality, and was beneficial towards the kidney outcomes of eGFR up to 36 months.

Figure:

P1040 PREGNANCY IN WOMEN WITH DIABETIC NEPHROPATHY: COMPLICATIONS AND OUTCOMES

Elena Prokopenko[1], Andrey Vatazin[1], Vera Gurieva[2], Irina Nikolskaya[2], Fatima Burumkulova[2], Aleksei Zulkarnaev[1]

[1]M.F. Vladimirsky Moscow Regional Research Clinical Institute, Postgraduate Medical Faculty, Department of transplantology, nephrology and artificial organs, Moscow, Russia and [2]Moscow Regional Research Institute of Obstetrics and Gynecology, Obstetrics Department, Moscow, Russia

Background and Aims: Pregnancy in patients with diabetic nephropathy (DN) is characterized by an increased incidence of complications and adverse outcomes. The aim of the study was to determine the nature and incidence of pregnancy complications and maternal and fetal outcomes in women with DN.

Method: 61 pregnant women with diabetes mellitus (DM) type 1 and CKD 1-4 stages: 1 st. –29 patients, 2 st. - 19, 3-4 st. – 13 (age 29.7±4.9 years, DM duration 18.6 ± 5,3 years) and 72 pregnant patients with pre-existing (type 1) DM without CKD (age 28.2±4.8 years, DM duration 11.4 ±3.7 years) observed in 2010-2017 were included. The incidence of chronic arterial hypertension (AH), preeclampsia (PE), fetal macrosomia, fetal growth restriction, preterm delivery, cesarean section, stillbirth and the effect of pregnancy on kidney function were evaluated.

Results: Chronic AH was detected in 19.4% of women w/o CKD, in 10.3% – CKD 1 st, 17.6% – CKD2, 61.3% – CKD 3-4 (p &lt 0.05 CKD3-4 vs CKD1). The incidence of PE in patients w/o CKD was 12.5% (2-3% for general population), with CKD 1 – 24.1%, CKD 2 – 41.2%, CKD 3-4 – 38.5% (p &lt 0.001 when comparing all groups). Macrosomia was common in pregnant diabetic women w/o CKD (30.6%), patients with CKD 1 (41.4%) and CKD 2 (52.9%), but was not observed in CKD 3-4 (0%). In contrast, the incidence of fetal growth restriction was highest with CKD 3-4 (61.5%) compared women w/o CKD (5.6%) and with CKD1(13.8%) and CKD2 (11.8%), p &lt 0.05.Preterm delivery was more common in women with CKD, and its frequency increased with increasing severity of CKD: w/o CKD – 18.1%, CKD 1 – 48.3%, CKD2 – 61.3%, CKD 3-4 –84.6% (p &lt 0.05). Incidence of cesarean section was high and did not differ significantly between groups: w/o CKD – 62.5.1%, CKD 1 – 55.2%, CKD2 – 82.4%, CKD 3-4 –92.3% (p &gt 0.05). Stillbirth was observed only with CKD stage 3-4 in 15.4% of cases.Four out of 13 (30.8%) patients with pre-existing CKD 3-4 and none of the patients with CKD1-2 reached stage 5 CKD and started regular hemodialysis with a median follow-up period of 43.3 months (min 29.7 - max. 81.5).

Conclusion: DN has a negative effect on pregnancy outcomes, increasing the frequency of preeclampsia, fetal growth restriction, preterm birth and stillbirth, however, fetal macrosomia practically does not occur with CKD 3-4. The rapid achievement of CKD 5D after delivery is typical for diabetic women with advanced stages of CKD.

P1041 KIDNEY BIOPSY IN DIABETIC PATIENTS ALLOWS A BETTER DEFINITION OF DIAGNOSIS AND OUTCOME

Vittoria Esposito[1], Yasser Ode[2], Ettore Pasquinucci[2], Massimo Torreggiani[1], Luca Semeraro[1], Giuseppe Sileno[2], Marco Colucci[1], Ciro Esposito[2]

[1]ICS Maugeri SpA SB, Nephrology, Pavia, Italy and [2]ICS Maugeri, University of Pavia, Nephrology, Pavia, Italy

Background and Aims: The WHO has defined type II Diabetes Mellitus (DMII) as an epidemic disease. Indeed worldwide, diabetic patients are estimated to be 400 millions and this number is bound to grow in the next decades [1].Diabetic nephropathy (DN) develops in 20-40% of patients with DM [2].It is a condition generally characterized by presence of proteinuria and leads to a progressive reduction in kidney function and ultimately to End Stage Renal Disease (ESRD). Although DN represents a frequent complication in patients with DM it is well known that diabetic patients may develop kidney disease due to any other cause. Several studies have shown that about 30% of diabetic patients undergoing a kidney biopsy will be diagnosed with a non diabetic renal disease (NDRD) [3].This suggests the importance of kidney biopsy in patients with DM.. Aim of our study was to evaluate the frequency of NDRD in our population, to identify pre-existing clinical or humoral parameters in patients with histological diagnosis of DN vs NDRD also evaluating the different clinical outcomes in patients with diagnosis of DN vs NDRD and identifying histological patterns of DN which may be associated to worst clinical outcomes.

Method: In this single centre retrospective observational study we evaluated all type II diabetic patients having undergone kidney biopsy in ICS Maugeri Spa SB in Pavia from May 2002 to December 2018

Results: Our population included 71 patients with diagnosis of DMII having undergone kidney biopsy. Among these 36 (51%) had a histological diagnosis of DN, 29 (40%) of NDRD and 6 (9%) had both DN+NDRD. Of the NDRD patients 21% were diagnosed with membranous nephropathy 17% with nephroangiosclerosis, 10% with focal segmental glomerulosclerosis and 10% acute tubular necrosis.We found DN patients compared to NDRD had a greater DM II vintage (12 years vs 9,5 years), higher HbA1C (7,4% vs 6,5%, $p<0.001$), were more frequently on insulin(67% vs 14%, $p<0.002$) and were more frequently affected by diabetic retinopathy (89% vs 3,5% $p<0.001$)There was no difference between DN and NDRD in terms of hypertension diagnosis or degree and proteinuria or creatinine value at biopsy (proteinuria median value in both groups 3 g/24 h and creatinine DN (1,48 mg/dL), vs NDRD (1,43 mg/dL)).Interestingly, 24 months post biopsy however proteinuria values in NDRD reduced significantly while remaining stable in DN, with a significant difference from DN at 24 months ($p<0.018$). Consistently with this data also creatinine values were higher in DN vs NDRD. We postulated this could be a consequence of targeted therapeutic intervention in NDRD .We next evaluated in DN the exhistence of a correlation between degree of histological damage and clinical outcome.We analyzed biopsies from 10 DN patients having a follow up of at least 24 months and assigned to each a score based on degree of glomerulosclerosis (0-3), tubulointerstitial(0-5) and vascular damage (0-5). Our data shows a correlation between severity of glomerular damage (score>2) and worsening of proteinuria and creatinine over a 24 month period although not statistically significant probably due to small sample size

Conclusion: In a population of DMII patients undergoing kidney biopsy 40% of patients had NDRD. NDRD appeared to have better clinical outcome (lower proteinuria and lower creatinine) over time probably as a result of targeted therapy, also degree of gloerular damage in DN correlated with worse prognosis. Although some pre-exhisting conditions such as diabetic retinopathy are highly predictable of DN diagnosis our data supports the essential role of kidney biopsy in diabetic patients.Alltogether our data demonstrates the value of performing kidney biopsy in DMII patients

P1042

CHEMERIN, INFLAMMATION AND DIABETIC KIDNEY DISEASE PROGRESSION IN PATENTS WITH TYPE 2 DIABETES MELLITUS

Fatima El-Tahir[1], Ali Moustafa Shendi Mohamed[1], Marwan Elgohary[2], Asmaa Mohammed Esh[3], Adel Ghorab[2]

[1]Faculty of Medicine, Zagazig University, Nephrology unit, Zagazig, Egypt, [2]Faculty of Medicine, Zagazig University, Internal Medicine Department, Zagazig, Egypt and [3]Faculty of Medicine, Zagazig University, Clinical Pathology Department, Zagazig, Egypt

Background and Aims: Diabetic kidney disease (DKD) is the leading cause of end-stage renal diseases worldwide. The development of DKD includes immunologic and inflammatory mechanisms which involve activation of the innate immune system and participation of inflammatory cytokines such as tumor necrosis factor (TNF)-α. Chemerin is an adipokine that has been suggested to be related to inflammation and has been correlated with the development of diabetic complications.We aimed to explore the potential links between chemerin, inflammation and the development of DKD in patients with type 2 diabetes mellitus (DM).

Method: The study population included 94 subjects: 84 patients with type 2 DM (89.4%), classified into 3 groups according to the 24 hr urinary albumin, and 10 normoalbuminuric non-diabetic controls (10.6%). Demographic, clinical and analytical data, and chemerin and TNF-α levels were collected.

Results: A total of 84 diabetic patients were enrolled, 32 males (38.1%) and 52 females (61.9%), mean age 57.9±10.7 years. They were divided into 3 groups: 14 with normalbuminuria, 27 with microalbuminuria, and 43 with macroalbuminuria (24 h urinary albumin <30, 30-300 and >300 mg/dl respectively). Chemerin levels increased significantly with the rise in albuminuria (control: 21.3 (10.8 –180), normoalbuminuria: 794 (556.9-1066), microalbuminura: 1155.5 (718 – 1877) and macroalbuminuria: 1619 (705 – 8067) ng/ml; p< 0.001, Kruskal Wallis test), yet with no significant difference between the control and normoalbuminuria groups. Serum TNF-α was significantly elevated in macroalbuminuria compared to control groups (p=0.017) with no significant difference between normoalbuminuria, microalbuminuria and macroalbumenuria groups (control: 77.85 (59 – 124.7), normoalbuminuria: 85.15 (59-146), microalbumenuria: 89 (68 – 180) and macroalbuminuria: 100 (66 – 556) pg/ml) (Figure). Among the diabetics, a significant association was evident between serum chemerin and serum TNF-α (r= 0.84; p<0.001). Both biomarkers were significantly associated with the inflammatory markers ESR and CRP, serum creatinine, BUN, 24 hour urine albumin, HbA1c, and diabetes duration and negatively with eGFR and serum albumin (p<0.05). On linear stepwise regression analysis, chemerin was significantly associated with TNF-α (unstandardized β 9.954, p<0.001) and ESR (unstandardized β 19.596, p<0.001); and TNF-α was significantly correlated with chemerin (unstandardized β 0.059, p<0.001), 24 hour urine albumin (unstandardized β 0.004, p<0.001) and HbA1c (unstandardized β -13.699, p=0.014).

Conclusion: Chemerin increased progressively with the rise in albuminuria, and was associated with the inflammatory milieu in patients with DKD, given the significant association with the inflammatory markers TNF-α and ESR. TNF-α, as surrogate of inflammation, was strongly associated with albuminuria. As such, our results suggest a potential role of Chemerin and TNF-α in the development and progressions of DKD. Larger studies are warranted to further explore the potential links between chemerin, inflammation and DKD.

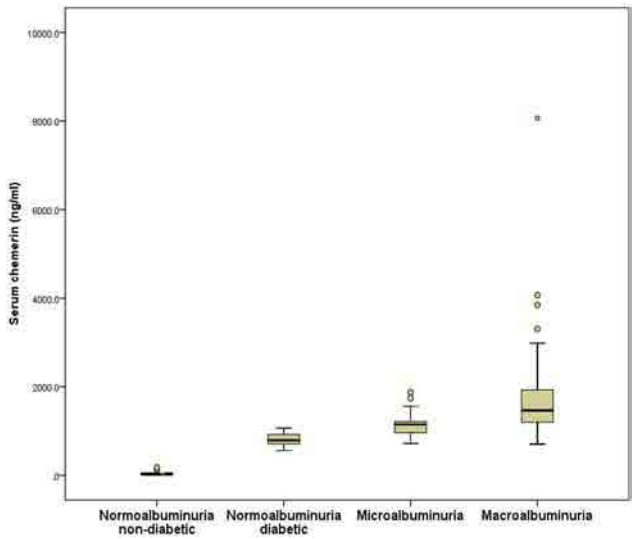


Figure: C hemerin levels among the different studied groups.

P1043 **CORRELATION OF ANEMIA AND THYROID HORMONES DISTURBANCES IN PATIENTS WITH TYPE 1 DIABETES AND CHRONIC KIDNEY DISEASE**

ALENA SAZONAVA[1,2], Tatiana Mokhort[1], Natalia Karlovich[1,2]

[1]Belarusian State Medical University, Endocrinology, Minsk, Belarus and [2]Republican Center for Medical Rehabilitation and Balneotherapy, Endocrinlology, Minsk, Belarus

Background and Aims: Impaired thyroid function is a common endocrine pathology among patients with chronic kidney disease (CKD), affecting metabolic parameters, including iron metabolism. The purpose of the study was to investigate potential relationship between thyroid status and iron metabolism profile in patients with type 1 diabetes (T1D) and DKD.

Method: We recruited 155 patients with T1D. GFR was estimated by CKD-MDRD formula. All patients were divided into 3 groups: the group 1 comprised 59 patients with GFR>60 ml/min; group 2-77 patients with GFR<60 ml/min, group 3- 19 patients, receiving renal replacement therapy (RRT). Biochemical parameters, HbA1c, thyroid hormones, iron homeostasis parameters were measured. Nonparametric statistical methods were used. A P-value <0,05 was considered significant.

Results: Groups were matched by age of T1D manifestation, HbA1c, BMI, CKD duration in groups 2 and 3. Duration of T1D differed by groups. Comparative analysis of patients in the subgroups revealed reliable differences in TSH levels only between patients from group 1 (p= 0.009), however, in the whole sample and in RRT patients its levels remained within the reference interval. Groups differed by FT4 values (group 1 - 14.12 (12.70-16.25) pmol / L, group 2 - 14.52 (13.27-16, 21), 3 group - 12.25 (11.38-13.48), p1,2 = 0.143, p1,3 = 0.035, p2,3 = 0.003) and FT3 (1 group - 4.43 (4,02-4.89) pmol / L, 2 group - 4.27 (3.98-4.78), 3 group - 1.43 (1.31-1.57), p1,2 = 0.712, p1,3 = 0.002, p2,3 = 0.012) with a tendency to maximum decrease when receiving RRT. No significant differences were obtained according to the levels of total T4 and T3, TG, Ab-TG, AbTPO. Significant decrease in Ab-R-TSH levels (group 1 - 0.70 (0.44-1.67) IU / l, group 2 - 0.40 (0.30-0.88), group 3 - 0.30 (0.30-0, 52), p1,2 = 0.492, p1,3 = 0.009, p2,3 = 0.035) confirms the absence of the influence of autoimmune component on the genesis of thyroid disorders in patients with CKD. No differences were obtained between groups in terms of serum iron levels and total iron binding capacity. Patients significantly differed in ERYTHROCYTES levels (group 1 - 4.68 (4.41-5.01) 109 / l, group 2 - 4.59 (3.96-4.83), group 3 - 3.84 (3, 32-4.27), p1,3 <0.001, p2,3 <0.001), HEMOGLOBIN (group 1 -139.00 (129.00-154.00), group 2 - 135, 00 (115.50-145.00), group 3 - 115.00 (103.00-124.00), p1,2 = 0.025, p1,3 <0.001, p2,3 <0.001), HCT (1 group - 41.90 (39.20-45.10)%, group 2 - 40.75 (35.65-43.70), group 3 - 36.25 (32.90-41.20), p1,3 <0.001, p2,3 = 0.055), TRANSFERRIN (group 1 - 32.90 (30.80-35.60) µmol / L, group 2 - 31.60 (19.20-35, 45) 3 group - 2.45 (2.14-3.65), p1,2 = 0.049, p1,3 <0.001, p2,3 <0.001) and FERRITIN (1 group - 54.00 (33.00- 74.97) µg / L, group 2 - 74.85 (37.18-109.90), group 3 - 152.60 (92.80-329.60), p1,3 < 0,001, p2,3 = 0.001), which reflects the highest sensitivity of these indicators to decrease in renal function. HCT correlated with levels of total T3 (ρ = 0.489), AbTPO (ρ = -0.490), total T4 (ρ = 0.536). Hb levels correlated with total T4 levels (ρ = 0.811), fT3 (ρ = 0.483). Ferritin levels correlated with fT4 (ρ = 0.510), and transferrin with fT3 (ρ = 0.523). Serum iron levels correlated with AbTPO (ρ = -0.656).

Conclusion: According to revealed changes, possibly anemia contributes to the development of thyroid dysfunctions in patients with diabetic genesis of CKD, due to the involvement of iron in the processes of deiodination and peripheral conversion of thyroid hormones.

P1044

RENAL DIABETIC FOOT: DIFFERENT PATTERNS AND CHARACTERIZATION OF PERIPHERAL ARTERY DISEASE BETWEEN NON-UREMIC AND UREMIC DIABETIC PATIENTS.

Michele Ferrannini[1], Giulia Marrone[2,3], Georgia Wilson Jones[2], Marco Meloni[2], Annalisa Romani[4], Luigi Uccioli[2], Nicola Di Daniele[2], Annalisa Noce[2]

[1]Policlinico Tor Vergata, Roma, Italy, [2]University of Tor Vergata, Systems medicine, Roma, Italy, [3]University of Tor Vergata, PhD School of Applied Medical, Surgical Sciences, Roma, Italy and [4]University of Firenze, 4PHYTOLAB (Pharmaceutical, Cosmetic, Food Supplement, Technology and Analysis)-DiSIA, Sesto Fiorentino (FI), Italy

Background and Aims: The diabetic foot (DF) was traditionally considered a local foot problem due to diabetes; however many observations support the concept that the DF is actually a part of a more complex diabetes related syndrome which includes several long-term complications and co-morbidities. In recent years, an increase in the incidence of ischemic diabetic foot ulcers (DFUs) amongst dialyzed subjects has been observed, going up from approximately 5-10% fifteen years ago to the current rate of approximately 30-35%. Today it is well recognized that end stage renal disease (ESRD) is an independent risk factor for non-healing ulcers and amputation in diabetic subjects. In clinical practice, the presence of foot problems in ESRD diabetic patients is identified as a specific entity termed "renal-diabetic foot". The aim of this study is to describe the angiographic characteristics of peripheral arterial disease (PAD) in patients with DFUs receiving chronic dialysis treatment.

Method: The study group was composed of patients with DFUs and PAD who referred to our diabetic foot unit. All patients have been managed with a pre-set limb salvage protocol including revascularization of the affected limb. Arterial lesions (stenosis between 50-99% and occlusions) were retrospectively evaluated through angiogram analysis. According to the presence of dialytic treatment, patients were divided in two subgroups: renal-diabetic foot (RDF) and diabetic foot (DF). Patterns of PAD and immediate revascularization outcome (technical revascularization outcome) for RDF and DF were separately reported and compared

Results: The demographic and clinical characteristics were reported in Table 1.RDF reported greater number of affected vessels (n= 5±1.6 *vs* 3.9±1.5, p<0.0001), greater involvement of the superficial femoral artery (90.2 *vs* 75.8%, p=0.003), tibial-peroneal trunk (53.7 *vs* 25.5%, p=0.01), anterior tibial artery (93.9 *vs* 80.9%, p=0.03) and below-the-ankle arteries (70.7 *vs* 35.7%, p=0.0001) than DF patients. RDF showed a higher rate of revascularization failure (43.9 *vs* 15.3%, p<0.0001) in comparison to DF patients (Table 2). Below-the-ankle (BTA) arterial disease [OR 9.5 (CI 95% 3.5-25.4) p=0.0001] resulted as the only independent predictor of revascularization failure.

Conclusion: It was interesting to highlight that the above mentioned findings could be specifically related to the effect of renal disease on the arteries of the lower extremity because the two groups, RDF and DF, did not report any difference in terms of other traditional cardiovascular risk factors (age, smoke, arterial hypertension, dyslipidemia, diabetes duration) which could influence the characteristics of PAD. RDF patients showed a widespread distribution of arterial lesions with a higher involvement of foot arteries in comparison to DF subjects. BTA arterial disease is an independent predictor of revascularization failure.

Table 1. Demographic and clinical characteristics of whole population, renal-diabetic foot and diabetic foot patients.

Variables	Whole population n=239	Renal-diabetic foot patients RDF n=82	Diabetic foot patients DF n=157	P values RDF vs DF
Age, *years*	71.8±12*	69.4±11*	73.1±13*	p=0.07
Sex (man), *n (%)*	173/239 (72.4)	68/82 (82.9)	105/157 (66.9)	0.006
Diabetes type (2)	209/239 (87.4)	74/82 (90.2)	135/157 (86)	ns
Diabetes duration (years)	21.4±12	20.6±10.8	21.8±12.7	ns
HbA1c, *mmol/mol*	63±22	64±15	62±25	ns
Coronary artery disease, *n (%)*	158/239 (83.1)	66/82 (80.4)	92/155 (59.3)	0.0008
Hypertension, *n (%)*	222/239 (92.9)	75/82 (91.4)	147/155 (94.8)	ns
Dyslipidemia, *n (%)*	184/239 (77)	61/82 (74.4)	123/155 (79.3)	0.07
Smoking, *n (%)*	41 (17.1)	13/82 (15.8)	28/155 (18.1)	ns

*Data expressed as mean ± standard deviation

Figure:

P1045

MISALIGNED EXPECTATIONS ON INTEGRATIVE MEDICAL SERVICE FOR DIABETES AND DIABETIC KIDNEY DISEASE: A COMPARATIVE FOCUS GROUP SERIES OF PATIENTS AND PHYSICIANS

Kam Wa CHAN[1], Pak Wing Lee[1], Crystal Pui Sha Leung[2], Gary Chi Wang Chan[3], Loretta Yuk Ying Chan[1], Joseph Chi Kam Leung[1], Tai Pong Lam[4], Kar Neng Lai[1], Sydney Tang[1]

[1]The University of Hong Kong, Department of Medicine, Hong Kong, P.R. China, [2]Hospital Authority Hong Kong East Cluster, Department of Family Medicine and Primary Healthcare, Hong Kong, P.R. China, [3]Queen Mary Hospital, Department of Medicine, Hong Kong, P.R. China and [4]The University of Hong Kong, Department of Family Medicine and Primary Care, Hong Kong, P.R. China

Background and Aims: Difference of perspective between patients and physicians over integrative medicine (IM) research and service provision remains unclear despite significant use worldwide. We sought to explore the barriers and recommendations regarding IM service among diabetes and diabetic kidney disease (DKD) patients and physicians.

Method: A 10-group, 50-participant semi-structured focus group interview series was conducted. Twenty-one patients with diverse severity of disease, comorbidities and education levels; and 29 physicians (14 western medicine (WM) and 15 Chinese medicine (CM)) with diverse clinical experience, academic background and affiliation were purposively sampled from private and public clinics. The perspectives were qualitatively analysed by constant comparative method with grounded theory approach.

Results: Seven subthemes regarding barriers towards IM service were identified including finance, service access, advice from medical professionals, uncertainty of service quality, uncertainty of CM effect, difficulty in understanding CM epistemology and access to medical records. Patients underreported the use of CM due to the concern over neutrality of medical advice among physicians. Practical issues including inconvenience of access to service, frequent follow-up, use of decoction and long-term financial burden were identified as key obstacles among patients. Regarding research design, WM physicians emphasized standardization and reproducibility while CM physicians emphasized personalization. Some CM-related outcome measurements were suggested as abstract and non-communicable. Both WM and CM physicians acknowledged the discordance in epistemology should be addressed by pragmatic approach.

Conclusion: Further assessment on IM should be pragmatic to balance between standardisation, reproducibility and real-world practice. Evidence-based IM programs and research should merge with existing infrastructure.

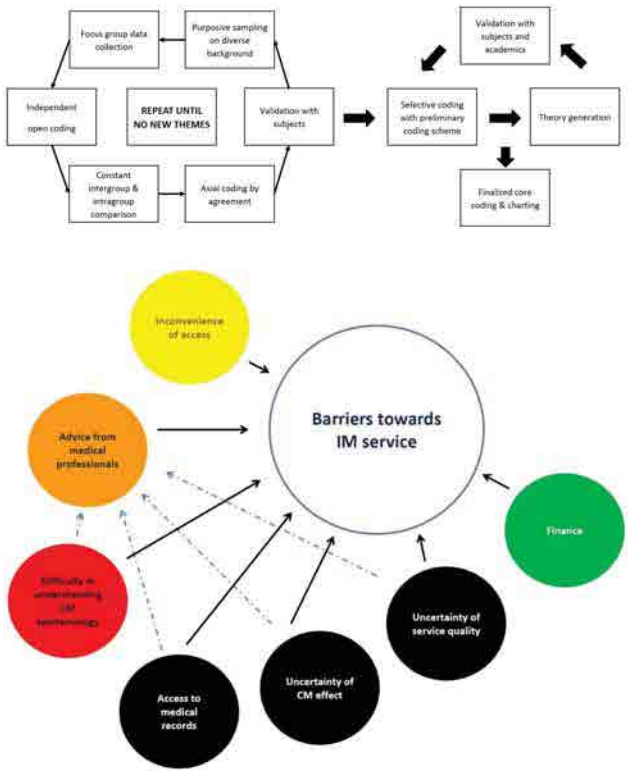


Figure:

P1046

GENDER DIFFERENCES IN CORRELATIONS BETWEEN THE LEVEL OF NT-PROBNP AND PLATELET PARAMETERS IN PATIENTS WITH EARLY DIABETIC NEPHROPATHY AND CHRONIC HEART FAILURE

Ivan Pchelin[1], Alexander Shishkin[1], Petr Vasilev[1], Volha Vasilkova[2], Tatyana Kulibaba[1], Liudmila Slepykh[1], Marina Sheveleva[1]

[1]Saint Petersburg State University, Department of Faculty Therapy, Saint Petersburg, Russia and [2]Gomel State Medical University

Background and Aims: Many studies have shown that platelet parameters represent important markers of cardiovascular risk, but the data on gender differences are limited. In this study, we aimed to assess correlations between the level of NT-proBNP and platelet parameters in men and women with early diabetic nephropathy and chronic heart failure.

Method: We investigated 65 patients with type 2 diabetes who also had chronic kidney disease (stage 1-3) and chronic heart failure (42 women and 23 men). eGFR was calculated using CKD-EPI formula. In addition to routine clinical tests, we assessed mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW) and serum levels of NT-proBNP and erythropoietin. Mann-Whitney U-test and Spearmen's correlation coefficient (rs) were used for statistical analysis.

Results: Mean levels of NT-proBNP were similar in men and women: 1019±267 and 1192±176 pg/ml ($p>0.05$), respectively, and there were no significant differences in platelet count, MPV, PCT and PDW between the groups. In women platelet indices were not related to age, body mass index, GFR, erythropoietin and hemoglobin levels, while in men PDW was positively correlated with body mass index ($rs=0.600$, $p=0.009$) and hemoglobin level ($rs=0.506$, $p=0.021$). Only in the female group serum level of NT-proBNP was interconnected with platelet count ($rs= -0.419$, $p=0.006$) and plateletcrit ($rs= -0.559$, $p<0.001$). Both in men and in women serum concentration of NT-proBNP was not correlated with the values of MPV and PDW.

Conclusion: The results of the study suggest that platelet count and plateletcrit are negatively correlated with serum level of NT-proBNP in women, but not in men with early diabetic nephropathy and chronic heart failure. Further studies are needed to clarify clinical implications of these findings.

P1047 **URICOSURIA AND URINARY GLUCOSE EXCRETION ON DIABETIC KIDNEY DISEASE (DKD) PATIENTES TREATED WITH SGLT2 INHIBITORS**

Maria Marques Vidas[1], Alba Maroto[1], Ignacio Sanz[1], Paula López[1], Jose' M. Portoles[1]

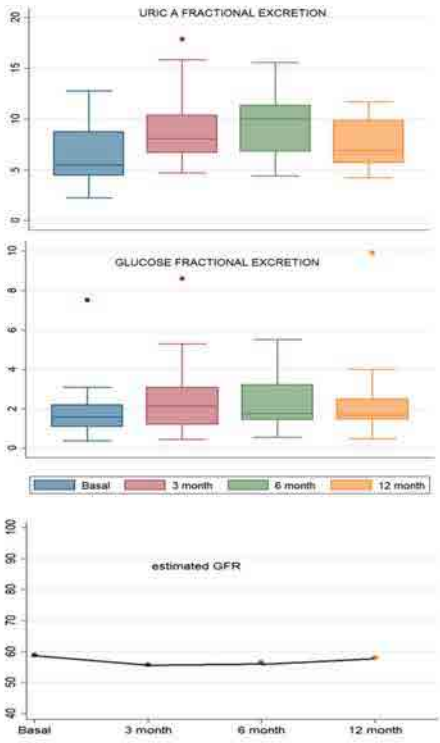
[1]*Hospital Universitario Puerta de Hierro Majadahonda, Nephrology, Majadahonda, Spain*

Background and Aims: The use of sodium glucose co-transporter 2 inhibitors (SGLT2i) is consistently associated with decrease of serum uric acid levels due to increase uricosuria coupled to glucosuria by mechanisms that are still incompletely understood. In diabetic kidney disease these drugs had shown only modest effects on HbA1c control allegedly due insufficient glucosuric effect. However, renal patients also benefit from hypouricemic effect of SGLT2 inhibitors. The aim of this study was to evaluate glucosuria and uricosuria in DKD patients treated with SGLT2i

Method: We prospectively analyzed glucose and urate fractional excretions of patients that were to initiate treatment with an SGLT2i, using fractional excretion classical formulas. Patients on GLP1ar or any uricosuric agent including losartan were excluded. All participants gave written consent.

Results: 37 patients (75.7% male) diagnosed from DKD were included, median age 69.6 years IQR [65.6-73.4], median CKD-EPI eGFR 54,10 ml/min/1,72 m^2 [41,12-69,68 IQR] and UACR 137 [49-443] mg/g. SGLT2i used was 53.3% dapagliflozin, 24.4% empagliflozin or 22.2% canagliflozin and mean follow- up was 1.5 years.Serum uric acid levels didn't show any significative difference along time in this group of patients (6.8 vs 6.3; p 0.4) and %HbA1C was only slightly decreased by month 12 (7.1 vs 6.7; p0.03). Urinary uric acid fractional excretion increased by month 3 and was stabilized till month 12 when this effect seemed to decrease (figure and table) Glucosuria exhibit a similar effect: Urinary glucose fractional excretion increased immediately after the addition of the drug and stabilized over time decreasing at the end of the observation period. Spearman rank correlation test indicated dependency glucosuria and uricosuria (Spearman's rho 0,24, p 0,03). GFR estimated by CKD-EPI kept stable along the study indicating that loss of uricosuric and glucosuric effect are independent of GFR

Conclusion: We conclude that uric acid renal excretion is significantly increased in patients treated with SGLT2i even in the presence of DKD but tends to diminish over time, feature that was also observed on urinary glucose excretion and that showed no correlation with GFR. Over-expression of SGLT1 after SGLT2 inhibition has been described in animal models of DKD. Whether this extends to human tubule and explains these results need to be further investigated



	basal	3 months	6 months	12 months	24 months
Uric A Urinary Frac Exc (%)	6,76 SD 3,26	9,11 SD 3,82	9,63 SD 3,39	7,61 SD 2,54	7,71 SD 3,44
Glucose Urinary Frac Excre (%)	1,8 SD 1,5	2,4 SD 1,9	2,2 SD 1,0	2,3 SD 2,1	2,7 SD 1,9
CKD EPI eGFR (ml/min/173m²)	55,3 [42,3-75,0 IQR]	50,7 [41,4-69,7 IQR]	51,2 [39,6-72,1 IQR]	56,7 [44,8-70,5 IQR]	60,3 [47,9-76,9 IQR]

Figure:

P1048 EMPHYSEMATOUS PYELONEPHRITIS IN TYPE 2 DIABETES - CLINICAL PROFILE AND MANAGEMENT

Dr Sanjay Bhat[1], Alok Srivastava[2], Nisar Ahmad[3], Priyanka Rai[1], R .P Singh[1], Rohit Srivastava[1], A K ROY[4], Jalees Fatima[5]

[1]RML Institute of Medical Sciences, Surgery, Lucknow, India, [2]RML Institute of Medical Sciences, Urology, Lucknow, India, [3]Era Medical College, Surgery, Lucknow, India, [4]Era Medical College, Surgery, Lucknow, India and [5]Era Medical College, Medicine, Lucknow, India

Background and Aims: Emphysematous pyelonephritis (EPN) is a rare but life-threatening acute suppurative infection of the kidney.60-70% are associated with uncontrolled diabetes mellitus (DM) with or without obstructive uropathy and superimposed with infection caused by gas-forming organisms. Conventional treatment of EPN is parenteral antibiotics with percutaneous or open surgical drainage and/or nephrectomy. There is no current consensus on management of EPN as to whether present day antibiotics alone good enough or is surgical intervention necessary and if surgical intervention required when should one go for nephrectomy.

Method:A prospective observational study was conducted at Tertiary care hospital, Lucknow from 2015-2018 to look for clinical, microbial profile and treatment outcome of diabetic patients with emphysematous pyelonephritis.The clinical features and laboratory data at the initial presentation, management and outcomes were analyzed .Contrast enhanced computerized tomography (CECT) was performed in case of suspected renal abscess and nonrecovering pyelonephritis

Results: A total of 76 Diabetic patients diagnosed with pyelonephritis were identified, of which 15 patients were diagnosed with EPN (26.3%) Renal papillary necrosis and renal abscess was seen in 1 and 3 patients, respectively. The mean age of the patients was 58.4 $\pm$ 6.5 years (age range 22-79 years). Pyelonephritis was more common among males. Duration of symptoms prior to hospitalization ranged from 16.34 $\pm$ 7.32 (range 8-32) days. Renal dysfunction at presentation was seen in 15 (100%) patients. Bilateral involvement was seen in 5 (33.3%) patients. Fever was the most common presenting symptom followed by dysuria. Urine and blood cultures were positive in 13 (88.3%) and 3 (20 %) patients respectively. Gram-negative bacilli were the most frequent organisms isolated, Escherichia coli in 11 (73.3%), *Klebsiella* sp. in 1 (6.6%), *Pseudomonas* in 1 (6.6%), and 1 each with polymicrobial and fungal UTI respectively. The fungus included *Candida albicans* managed with fluconazole. Good, moderate, and poor glycemic control was seen in 13 (12.3%), 16 (15.2%) and 76 (72.3%), respectively.Of 15 EPN patients, 13 (86.6 %) survived and 2 (13.3%) expired. 2 of them underwent Nephrectomy both survived.All patients with Stage I, II and IIIa EPN ($n = 12$) were managed with antibiotics with or without PCD. In EPN Stage IIIb/IV ($n = 3$), all the 3 (20 %) patients were managed with antibiotics and PCD and later 2 (13.3%) needed nephrectomy.Of different variable only altered sensorium and shock at presentation were associated with poor outcome in EPN patients ($P < 0.05$)

Conclusion: EPN in diabetics needs good multidisciplinary approach with adequate antibiotics and surgical management as and well required for better patient outcomes.

P1049

LOWER ACCEPTANCE RATE FOR PANCREAS OR ISLET TRANSPLANTATION AFTER INTRODUCTION OF A MULTIDISCIPLINARY APPROACH FOR TRANSPLANT ELIGIBILITY

Espen Nordheim[1], Jørn Petter Lindal[2], Espen Nordheim[2], Anders Åsberg[2], Kåre Birkeland[2], Rune Horneland[3], Turid Birgitte Boye[3], Trond Geir Jenssen[2]

[1]Oslo University Hospital, Rikshospitalet, Department of Transplantation Medicine, Norway and [3]Oslo University Hospital, Rikshospitalet, Psycosomatic unit, Norway

Background and Aims: β-cell replacement therapy, with either pancreas or islet transplantation, is a treatment option for selected patients with brittle type 1 diabetes. All patients referred to the national transplant centre for assessment of this treatment, are evaluated in the outpatient clinic before any work-up for transplantation is initiated. Before 2015, this assessment was performed by a nephrologist alone, while from 2015 the assessment has also included an endocrinologist, a transplant surgeon and a psychiatrist in a multidisciplinary team.

Method: The proportion of patients accepted for transplantation before and after the multidisciplinary approach were compared. A chi square test was used for comparing the groups in the two periods; 2010-2014 versus 2015-2019 vs. P-values are reported according to two- tailed analysis, and p- values < 0.05 were considered statistically significant.

Results: From 2010 to December 2019, 144 patients were assessed for β-cell replacement therapy eligibility. Out of all patients referred, 64 out of 79 (81%) and 22 out of 65 (34%) were listed for transplantation before and after the multidisciplinary assessment was introduced (p-value < 0.005). The main reasons for not being listed after the introduction of a multidisciplinary team were suboptimal diabetes treatment and that the patients withdrew their interest after the outpatient clinic visit with thorough information about advantages and risks.

Conclusion: The rate of patients who were accepted for islet or single pancreas transplantation declined after a multidisciplinary approach was introduced for transplant candidate eligibility. We suggest that a broader, multi-disciplinary approach revealed previously undetected medical issues and improved patient information that subsequently resulted in fewer patients listed for transplantation.

P1050

THE EFFICACY AND RENAL SAFETY OF SWITCHING FROM DAPAGLIFLOZIN TO EMPAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES

Al-YU YANG[1], Hung-Chun Chen[2,3]

[1]Kaohsiung Medical University Hospital, Kaohsiung Medical University, Department of Pharmacy, kaohsiung, Taiwan, R.O.C., [2]Kaohsiung Medical University Hospital, Kaohsiung Medical University, Division of Nephrology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C. and [3]Kaohsiung Medical University, Faculty of Medicine, College of Medicine, Kaohsiung, Taiwan, R.O.C.

Background and Aims: Both dapagliflozin (DPG) and empagliflozin (EPG) are highly selective sodium-glucose cotransporter-2 (SGLT-2) inhibitors that inhibit glucose reabsorption and increase its excretion in urine. Previously, DPG was limited to patients with an estimated glomerular filtration rate (eGFR) $\geq$ 60 mL/min/1.73 m2, while EPG can be used for those with an eGFR $\geq$ 45 mL/min/1.73 m2. Therefore DPG was switched to EPG in many patients when eGFR decreased. However, the clinical efficacy and safety of these switches are not clear. In this study, we compared the efficacy and renal safety between patients switching from DPG to EPG and those continuing DPG in patients with type 2 diabetes mellitus (T2DM).

Method: This retrospective observational study included patients with T2DM who were treated with DPG for more than 6 months. This study included patients who switched to EPG and those who continued using DPG. All other hypoglycemic drugs were maintained at the same dosage before and after the study period. The primary outcome measure was the change in hemoglobin A1c (HbA1c) level after 6 months. The EPG group was evaluated for whether the hypoglycemic effect remain effective after drug switching. Patients with HbA1c levels at or lower than the baseline value after 6 months were defined as effective and patients with levels higher than the baseline were defined as invalid. Safety was evaluated by comparing the difference of eGFR between the baseline value and six months after treatment.

Results: This study included 169 patients. Among them, 72 patients continued DPG and 97 patients switched to EPG. HbA1c level decreased significantly only in EPG group. In EPG group, 59 patients belong to the effective group (60.8%) and 38 patients were invalid (39.2%). There was no significant change in eGFR after treatment in both groups. Ten patients in DPG group develop adverse reactions (three patients felt uncomfortable and seven patients had urinary tract symptoms), but all continued treatment. In EPG group, five patients lacked follow-up records during the study period and it was difficult to determine whether the patient's willingness to continue treatment was affected by adverse reactions.

Conclusion: Our study showed that switching from DPG to EPG in patients with T2DM was effective for blood glucose maintenance and caused no significant changes in renal function. In addition, no severe drug-related adverse reactions were found.

DIALYSIS. EXTRACORPOREAL DIALYSIS: TECHNIQUES AND ADEQUACY

P1051 WHICH MODEL OF DIALYSATE SODIUM PRESCRIPTION TO CHOOSE?

Natasha Eftimovska-Otovikj[1], Natasha Petkovikj[1], Elizabeta Poposka[1], Olivera Stojceva-Taneva[2]

[1]General City Hospital 8th September, department of nephrology, Skopje, Republic Of North Macedonia and [2]Dialysis center Diaverum, dialysis, Skopje, Republic Of North Macedonia

Background and Aims: The dialysate sodium prescription remain unclear as an important component of sodium balance in HD patients Pre-hemodialysis (pre-HD) serum sodium levels can vary among different patients, therefore, a single dialysate sodium prescription may not be appropriate for all patients. Dialysate sodium is one of the most easy changeable parameter which can influence hemodynamic stability. The aim of the study was to investigate whether dialysis patients will have some beneficial effects of prescription of different models of dialysate sodium

Method: 77 nondiabetic subjects (41 men; 36 women) performed 12 months hemodialysis (HD) sessions with dialysate sodium concentration set up at 138 mmol/L, followed by additional 3 models of dialysate sodium (each model performed 2 months sessions with 2 months standard dialysate sodium between each model) wherein dialysate sodium was set up: model 1: according to pre-HD serum sodium concentration, model 2: according to sodium concentration in UF fluid, model 3: sodium profiling (from 144 to 136 mmol/L). Blood pressure (BP), interdialytic weight gain (IDWG), thirst score, sodium gradient were analysed. After the standard dialysate sodium hemodialyses, the subjects were divided into 3 groups: normotensive (N=58), hypertensive (N=14) and hypotensive (N=5) based on the average pre-HD systolic BP during the standard dialysate sodium hemodialyses.

Results: Model 1: resulted in significantly lower blood pressure (133,61±11.88 versus 153.60±14.26 mmHg; p=0.000) and IDWG (2.21±0.93 versus 1.87±0.92 kg; p=0.018) in hypertensive patients, whereas normotensive patients showed only significant decrease in IDWG (2.21±0.72 versus 2.06±0.65, p=0,004). Hypertensive patients had significant highest sodium gradient compared to other patients ($p<0.05$), followed by significant increase of 0,6% IDWG confirmed with univariate regression analysis. Thirst score was significantly lower in all patients with individualized-sodium HD and the use of antihypertensive drugs significantly reduced in hypertensive patients during the individualized phase. Model 2: resulted in significantly lower BP in normotensive and hypertensive patients (126.92±9.71 versus 124.08±8.71 mmHg; p=0.000; 153.60±14.26 versus 138.91±8.48 mmHg, accordingly), with no influence on IDWG, thirst score compared to standard dialysate sodium. Model 3: significantly higher BP and IDWG in all 3 groups (normotensive 126.92±9.71 versus 130.20±9.5 mmHg; p=0.001; IDWG 2.21±0.72 versus 2.34±0.82 kg, p=0,005; hypertensive 153.60±14.26 versus 157.58±5.0 mmHg; IDWG 2.21±0.93 versus 2.39±0.74 kg; p=0.005; hipotensive 79.81±11.78 versus 91.09±24.98 mmHg, IDWG 2.53±0.57 versus 2.73±0.15 kg, p=0.005) and significantly higher thirst score in normotensive and hypotensive patients, with no influence in hypertensive patients.

Conclusion: A reduction of the dialysate sodium concentration based on the pre HD serum sodium level of the patient, reduced the BP, IDWG, thirst score and use of antihypertensive drug compare to dialysate sodium according to sodium concentration in UF or sodium profiling. We recommend prescription of dialysate sodium according to pre HD serum sodium concentration.

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P1051A

SINGLE SESSION AND WEEKLY BETA 2 MICROGLOBULIN REMOVAL DURING SHORT FREQUENT HEMODIALYSIS USING PHYSIDIA TECHNOLOGY

MICHEL THOMAS[1], Eric Vincent[2], Veliana Todorova[3]

[1]Physidia, Medical affairs, Saint Barthélémy d'Anjou, France, [2]Physidia, Research and Development, Saint-Barthélemy-d'Anjou, France and [3]Physidia, Marketing, Saint-Barthélemy-d'Anjou, France

Background and Aims: S^3 Physidia monitor is a dedicated system for short frequent hemodialysis at home based on push pull dialysis mode. Clinical data is provided to show the Beta 2 microglobulin elimination, used as a model for middle molecule removal. The aim of the study is to compare Beta 2 microglobulin removal between hemodialysis systems with low dialysate flow rate and conventional hemodialysis or hemodiafiltration.

Method: Analyzed data is collected during multicentric clinical study performed to evaluate the safety and performances level with S^3 Physidia system.

This clinical investigation has been conducted in accordance with the Good Clinical Practices (Helsinki Declaration), every patient was informed by the investigator and has signed the consent form prior to the completion of the study. The project has been approved by the local Committee and authorities.

Anonymized data of 10 patients (age: 55.3 +/- 12.3 years, weight: 72.8 +/- 17.2 kg) is collected during 126 dialysis sessions (blood flow rate: 293 +/- 24 ml/min, dialysate flow rate: 190 +/- 14 ml/min).

The convection volume (Ultrafiltration and back filtration generated by the push pull technique) is between 1 to 8 l per session (dialyzer used: Smartflux HFP190).

For each session, Beta 2 microglobulin (β2M) removal rate is calculated by using pre and post dialysis β2M blood concentrations. Post concentration is corrected by using Bergström formula to take into account the hemoconcentration and rebound. Both single session (2hours) and weekly (12 hours/week) β2m removal rates were calculated.

Single session and weekly β2m removal levels are compared to published data with conventional hemodialysis or post dilution hemodiafiltration.

Weekly dialysis performance is evaluated according to the standardized Kt / V (sdt) according to the Gotch calculation method.

Results: Using S^3 daily hemodialysis, weekly dialysis diffusive performance for urea (standardized Kt / V is 2.56 +/- 0.39, higher than KDIGO recommendations for frequent dialysis (min 2.1).

β2M removal rate per session is 52.9 +/- 6.6 % with pre dialytic concentration average value of 25 mg/l corresponding to 73 mg of β2M removed per session. Calculated weekly β2M removal is 438 mg.

These results are compared to β2M removal obtained by standard treatment procedures (ref1) and by short frequent hemodialysis using diffusive low dialysate flow (Nx Stage system One, ref 2).

During conventional hemodialysis (4h, 3 sessions per week), the β2M removal rate is between 60 to 80 % corresponding to a removal of 300 to 380 mg/week (ref 1)

During high volume post dilution hemofiltration (4h, 3 sessions per week, convection $>$ 20 l per session), the average β2M removal rate is 80% corresponding to a removal of 380 mg/week (ref 1)

With Nx Stage device, without convective component, single session β2M removal rate is between 40 and 50 % depending on blood flow rate (maximum obtained with blood flow rate 400 ml/min) (ref 2)

Ref 1: J. Potier et al, Int J Artif Organs. 2016 Nov 11;39(9):460-470

Ref 2 : M. Leclerc et al, Blood Purif 2018;46:279–285

Conclusion: β2M reduction rate obtained with the S^3 Physidia system is greater than 50%, removing any dowry concerning the performance of a low dialysate flow rate system. The convective component, provided by the push pull technique, must be confirmed, but these initial results are encouraging (reduction rate $>$ 50% despite a relatively low blood flow rate).

Due to the frequency, the quantity of β2M weekly removed is higher than that obtained with conventional treatment methods.

Figure:

P1052

EXPANDED HEMODIALYSIS (HDX) DOES NOT AFFECT EPIGENETIC INTERCELLULAR SIGNALS INVOLVED IN INFLAMMATION AND CARDIOVASCULAR DISEASE

Carmen Vida[1], Matilde Alique[1,2,2], Patricia De Sequera Ortiz[3,4], Guillermo Bodega[5], Carlos Oliva[6], Julia Carracedo[6,7], Manuel Ramírez Chamond[1,2]

[1]Universidad de Alcalá, Dpto. Biología de Sistemas, Alcalá de Henares, Spain, [2]Instituto Ramón y Cajal de Investigación Sanitaria, (IRYCIS), Madrid, Spain, [3]Universidad Complutense de Madrid, [4]Hospital Universitario Infanta Leonor, Nefrología, [5]Universidad de Alcalá, Dpto. de Biomedicina y Biotecnología, Alcalá de Henares, Spain, [6]Universidad Complutense de Madrid (UCM), Dpto. Genética, Fisiología y Microbiología (Sección Fisiología), Madrid, Spain and [7]Instituto de Investigación Hospital 12 de octubre (I+12), Madrid, Spain

Background and Aims: Epigenetic signals play a principal role in homeostasis, but also may promote diseases including cardiovascular diseases (CVDs) when are altered. Extracellular vesicles (EVs) or plasma circulating DNA and RNA may have relevant functions in both physiological and pathophysiological contexts related to the epigenetic intercellular communication. Thus, changes in the endothelial or platelet EVs, or the plasma circulating methylated DNA may contribute to the chronic inflammation and the subsequent CVDs in chronic kidney disease patients, particularly when are in hemodialysis (HD). Dialysis membranes do not usually allow the passage of molecules larger than 30-40 kDa. However, the new system of expanded hemodialysis (HDx) with a medium-cut-off membrane (MCO), due to its characteristics, could alter the plasma content of these EVs and DNA methylation, and thereby, promote the development of CVDs. Therefore, our study evaluates whether global plasma DNA methylation and EVs content are modified during an HDx session.

Method: For this study, we selected 12 dialysis patients: HDx patients (n=6; dialyzed with MCO) and control group (n=6; dialyzed with other HD membranes). Before and after a dialysis session, plasma samples were obtained. EVs were isolated by ultracentrifugation, and the total number of EVs and platelet and endothelial-derived EVs were characterized and quantified by flow cytometry. RNA and DNA extraction and quantification were carried out using different kits and NanoDrop spectrophotometer. DNA methylation was assessed with a 5-methyl cytosine (5-mC) DNA assay kit.

Results: As shown in the figure, after a dialysis session with the HDx, no significant differences were observed in the total number of EVs, as well in the number of platelet- and endothelial-derived EVs, in comparison to those observed in HDx patients before the dialysis session. By contrast, patients dialyzed with other HD membranes presented differences in the number of total EVs and platelet and endothelial EVs, which decreased significantly ($p<0.05$) after the dialysis session. Concerning DNA methylation, no statistically significant changes in total DNA 5-mC (%) were observed in both HDx and control patients after the dialysis session. However, a slight tendency to decrease methylated DNA was observed with the HDx compared to other HD membranes (control). Moreover, no significant changes in DNA and RNA % were observed after dialysis session in both HDx and control group.

Conclusion: To our knowledge, this is the first study to investigate the influence of the HDx technique on the content of plasma cellular EVs and DNA methylation status. HDx does not affect EVs levels, although it shows a tendency to purify plasma methylated DNA. Although this study was not designed to analyze the comparative effectiveness between different membranes, interestingly this effect in epigenetic signals was not observed with other HD membranes, where patients showed a marked reduction of EVs content. The differential activity of HDx about other HD membranes deserves further investigation.

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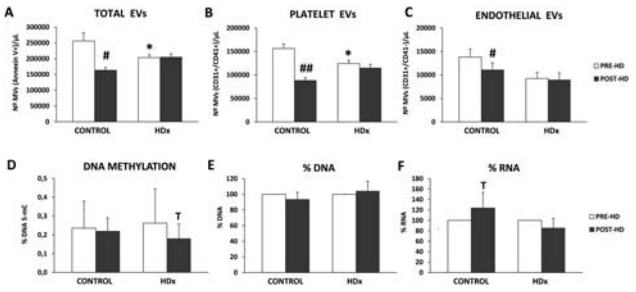


Figure:

Plasma levels of (A) total number of extracellular vesicles (EVs) (annexin V+), (B) platelet-(annexin V+/ CD31+/CD41+) and (C) endothelial-(annexin V+/CD31+/CD41-) derived EVs. (D) DNA methylation content (DNA 5-mC), and normalized percentage (%) of (E) DNA and (F) RNA, from CKD patients undergoing to a session of expanded hemodialysis (HDx) or with other membranes HD modalities (control group). All parameters were studied before (pre-HD) and after (post-HD) HD session. Each column represents the mean ± SD. # $p<0.05$, ## $p<0.01$ vs. to pre-HD group. * $p<0.05$ vs. to control group. T: statistical trend ($0.5<p<0.2$)

P1052A

SUPPRESSION OF BLOOD COAGULATION ON THE SURFACE OF A DIALYSIS MEMBRANE USING A DIALYSATE CONTAINING 800 PPM OF NITRIC OXIDE

Kozue Kobayashi[1,2], Maho Sato[1], Yuhei Yoshida[2], Kokubo Kenichi[1,2], Hirosuke Kobayashi[1,2], Masaru Kubota[1,2]

[1], Kitasato University School of Allied Health Sciences, Sagamihara, Japan and [2], Kitasato University Graduate School of Medical Sciences, Sagamihara, Japan

Background and Aims: Activation of platelets and leukocytes when blood comes in contact with a dialysis membrane surface leads to increased oxidative stress and release of proinflammatory cytokines, which may result in complications in dialysis patients. Within the blood vessels, nitric oxide (NO) generated by nitric oxide synthase on the endothelial cells suppresses both aggregation/activation of platelets and migration/adhesion of leukocytes. We previously showed in a rat hemodialysis model that NO (800 ppm) gas added to the dialysate can suppress blood coagulation on the surface of a dialysis membrane. The aim of the present study was to determine, using a rat hemodialysis model, the appropriate concentration of NO that would most effectively prevent blood coagulation without causing any adverse effects.

Method: Male Sprague Dawley rats weighing 300 to 400 g were used for the experiments. After the rats were anesthetized (isoflurane, 1.5%-3.0%), extracorporeal circulation was established by removal of blood from the carotid artery and returning it to the tail vein. During the experiment, the blood flow rate was kept at 1.0 mL/min, and the dialysate flow rate at 3 mL/min. Heparin was administered by bolus injection (0.7 unit/g-mouse) at the start of the hemodialysis, and no further heparin was added during the 4-hour hemodialysis session. A cellulose triacetate membrane and polymethylpentene membrane were used for making the small dialyzer and gas exchanger, respectively (the prototype module was manufactured by NIPRO, Co., Japan). NO (200 ppm, 400 ppm, or 800 ppm) was added to the dialysate via the gas exchanger in the NO groups, and N_2 gas was added to the dialysate in the control group. During the experiment, the arterial pressure, dialyzer inlet pressure, venous pressure, activated whole blood clotting time (ACT) and methemoglobin (met-Hb) concentration were measured. After circulation, the amount of coagulated blood was measured by the hemoglobin (Hb) content and lactate dehydrogenase (LDH) activity in the eluate from the residual blood clotting in the dialyzer.

Results: The 4-hour hemodialysis session achievement rate was highest in the NO-800 ppm group (control, 54%; NO-200 ppm, 66%; NO-400 ppm, 77%; NO-800 ppm, 85%). The blood met-Hb content was below 10% in all the NO groups. The Hb content and LDH activity in the eluate were significantly lower in the NO groups than in the control group. These results indicate that addition of higher concentrations of NO was associated with a lower likelihood of coagulation on the dialyzer and in the dialysis circuit and a higher likelihood of smooth and successful 4-hour dialysis sessions. Addition of NO was associated with little risk of adverse effects such as met-Hb accumulation and reduction of blood pressure. Therefore, 800 ppm is considered as the most appropriate concentration of NO to be added to the dialysate for effectively inhibiting blood coagulation without causing any adverse effects.

Conclusion: Our experiment in a rat hemodialysis model showed that 800 ppm was the most appropriate concentration of NO to be added to the dialysate to suppress blood coagulation on the surface of the dialysis membrane without causing any adverse effects.

P1053 **SHORT-TERM CLINICAL RESULTS WHEN COMPARING EXPANDED HEMODIALYSIS THERAPY VERSUS ONLINE HEMODIAFILTRATION THERAPY.**

Fernando Hadad Arrascue[1], Lars-Göran Nilsson[2], Angelito Bernardo[3], Angela Rivera[3], Lourdes Guardiola Belmonte,[1], Florentina Rosique[4], Antonio Perez Perez[4], Alberto Andreu Muñoz[4], Juan Cabezuelo-Romero[5]

[1]Clínicas de Diálisis RTS, Murcia, Spain, [2]Baxter International, Lund, Sweden, [3]Baxter Healthcare Corporation, Deerfield, United States of America, [4]Hospital General Universitario Reina Sofía, Murcia, Spain and [5]Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain

Background and Aims: HDx is a dialysis therapy that uses dialyzers with newly designed medium cut-off membranes (MCOs), which show a greater capacity for purification of middle molecules than conventional dialyzers and requires less technical resources than OL-HDF. However, it is not well known if HDx has comparable clinical results with OL-HDF. Therefore, the aim of this study was to evaluate the clinical differences between patients dialyzed with HDx and OL-HDF.

Method: A 24-week prospective study that included 43 patients between 18 and 80 years old, in OL-HDF at least 3 months before the start of the study, stratified by residual function; and randomized for HDx or HDF-OL therapy. Twenty-one patients assigned to HDx used the Theranova® 500 dialyzer with MCO membrane; and 22 patients with HDF-OL with Polyflux® 170H dialyzer.

Variables related to dialysis were analyzed: blood flow rate (Qb), ultrafiltration volume (VUF), dialysis time, Kt/V, and complications; anemia [Hemoglobin (Hb), transferrin saturation (TSAT), Ferritin, erythropoietin stimulating agent (ESA) dosage (IU/week), erythropoietin resistance index (ERI), iron dose]; the bone mineral metabolism [calcium (Ca), phosphorus (Pi), product CaxPi, Paratohormone (PTH), fibroblast growth factor 23 (FGF-23)]; and healthcare resource utilization (hospitalization, cardiovascular events, infectious events and death).

Results: The substitution volume in the OL-HDF group was 24.4±3.2 liters. No significant differences were found in time of treatment, QB, residual diuresis or VUF. The Kt/V was similar in both groups HDx: 1.8±0.26; OL-HDF: 1.8±0.28. No significant differences in the number of adverse events during hemodialysis between the two groups.

No differences in the levels of P, Ca, PTH between both groups. However, there were differences in FGF-23 at week 12 compared to baseline (HDx: -188±1351 pg/mL; OL-HDF: +218±1293 pg/mL, p=0.48).

The iron dose showed no significant differences between both groups. The use of ESA was lower in the HDx group at the end of the study (HDx: 5605±7115 IU/Week; OL-HDF: 7667±5867 IU/Week), maintaining hemoglobin values stable throughout the study in both treatment groups (HDx: 11.2±1; OL-HDF: 11.7±0.8 g/dl at 24-week).

Serum TSAT was comparable between the groups at all timepoints in the study. Serum ferritin levels were slightly higher in HDx group and showed an overall increase at Week 24.

Both treatments were effective in maintaining pre-dialysis albumin levels. At 12 weeks (HDx: 0.06±0.47; OL-HDF: -0.01±0.26, p=0.889) and 24 weeks of treatment (HDx: -0.02±0.25; OL-HDF: - 0.02±0.34, p=0.5948) versus baseline.

The assessment of rates of hospitalizations, cardiovascular events, infective episodes and death showed no substantial differences between both groups.

Conclusion: In our experience, HDx with Theranova® 500 is a safe and effective hemodialysis technique. A short-term HDx therapy decreases FGF23 levels and the needs of EPO compared to OL-HDF. Both techniques are similar in the other parameters analysed.

P1054 **COMBINING A HEPARIN-GRAFTED DIALYZER WITH A CITRATE ENRICHED DIALYSATE OFFERS ADEQUATE HEMODIALYSIS EFFICACY AVOIDING SYSTEMIC ANTICOAGULATION: RESULTS OF THE NON-INFERIORITY RANDOMIZED EVOCIT STUDY.**

Karlien François[1], Dieter De Clerck[1], Annelies Tonnelier[1], Marie-Laure Cambier[1], Wilfried Cools[2], Karl Martin Wissing[1]

[1]Vrije Universiteit Brussel, Universitair Ziekenhuis Brussel, Division of Nephrology and Hypertension, Brussels, Belgium and [2]Vrije Universiteit Brussel, Interfaculty Center Data processing & Statistics, Brussels, Belgium

Background and Aims: The combined use of a heparin-grafted membrane with a citrate enriched dialysate is an effective hemodialysis strategy with low circuit clotting rates while avoiding systemic anticoagulation. Whether this technique results in dialysis efficacy that is non-inferior to regular hemodialysis using systemic anticoagulation has not been investigated up to now.

Method: Prevalent hemodialysis (n=26) patients were recruited for a randomized crossover non-inferiority trial powered at >90% to detect a prespecified non-inferiority threshold of 10% spKt/V_{urea} (NCT03887468). Hemodialysis using a heparin-grafted dialyzer in combination with a 1.0 mmol/L citrate enriched dialysate ("evocit") was compared to hemodialysis using a heparin-grafted dialyzer, systemic unfractionated heparin and regular bicarbonate-based dialysate ("evohep"). Each treatment arm lasted 4 weeks with a 3x4hours weekly hemodialysis regimen. All sessions were standardized with fixed blood- and dialysate flow rates. Biological analyses were done during midweek sessions. The primary endpoint was spKt/V_{urea}. Secondary endpoints included alternative adequacy markers, premature treatment termination, retransfusion failure and loss of total cell volume of the dialyzer after dialysis.

Results: A total of 617 hemodialysis sessions were performed: 307 sessions according to evocit and 310 sessions according to evohep protocol. Mean spKt/V_{urea} was 1.45±0.25 for evocit sessions and 1.50±0.26 for evohep sessions. In a paired analysis, mean of the difference in spKt/V_{urea} between both study arms was 0.05 with a 95%CI of 0.012-0.098 (p=0.01), the upper bound of the estimate lying within the prespecified non-inferiority threshold (i.e. <0.15).

Processed blood volume was 75.4±3L vs 75.8±1.5L and online Kt was 47.3±5L vs 48.3±4L for all evocit and evohep sessions respectively. Urea reduction rate (RR) was 71.3±5.7 vs 72.3±5.8, bèta2microglobulin RR 37.1±8 vs 37.9±8 and myoglobin RR 30.9±9.8 vs 34.5±12.5 for midweek evocit and evohep sessions respectively. Circuit thrombosis leading to premature treatment end occurred in 13/307 (4.23%) of evocit sessions in 6/26 patients but in none of the evohep sessions (p=0.03). Treatment time of evocit sessions complicated with circuit thrombosis (n=13) was reduced with 36 minutes (IQR 20-46 minutes) without impact on effective treatment times overall (236±12 vs 238±4 minutes for evocit and evohep sessions respectively). Retransfusion failure occurred in 3/307 (0.98%) of evocit sessions and none of the evohep sessions. Dialyzers' total cell volume was reduced with 17% (IQR 11-33%) and 9% (IQR 6-17%) (p<0.0001) after evocit and evohep sessions respectively.

Conclusion: Hemodialysis avoiding systemic anticoagulation using a heparin-grafted dialyzer with a citrate enriched dialysate is an adequate technique for maintenance hemodialysis offering spKt/V_{urea} results within recommended dose, and is not inferior to standard hemodialysis using systemic anticoagulation with heparin in terms of spKt/V_{urea}.

Circuit clotting complications occurred at low frequency during evocit sessions and did not have clinically significant repercussions on dialysis efficacy.

P1055 **REMARKABLE REMOVALS OF BETA-2-MICROGLOBULIN AND PHOSPHATE WITH SHORT-DAILY HOME HEMODIALYSIS USING LOW DIALYSATE FLOW RATE.**

Mercedes Gonzã¡lez Moya[1,2], Pablo Molina[1,2], Belén Vizcaíno[1,2], María Rodrigo[1], Pilar Pascual[1], Sandra Beltrán[1], Alejandra Yugueros[1], Emma Calatayud[1], Maria Jesús Lidón[1], Cristela Moncho[1], Marisa Santaolaria[3], Araceli Carbonell[3], Guillermo Sáez[3,4], Nuria Estañ[3], Luis M. Pallardó[1,2]

[1]Hospital Universitari Dr Peset, Department of Nephrology. FISABIO, Valencia, Spain, [2]Universitat de València, Department of Medicine, València, Spain, [3]Hospital Universitari Dr Peset, Department of Clinical Analysis, Valencia, Spain and [4]Universitat de València, Department of Biochemistry and Molecular Biology, Valencia, Spain

Background and Aims: Short-daily hemodialysis (HD) with low-dialysate volume is an appealing portable dialysis approach for home use. Although this type of HD has proved being effective for the volume control and the clearance of low molecular-weight uremic toxins, limited data are available on the impact on the removal rates of other uremic toxins like β_2-microglobulin (β_2M) or phosphate (P), whose clearance is limited by sequestration into compartments, poor diffusion, high time-dependency, or protein binding. We evaluated the impact of short-daily HD with slow dialysate flow rate on the removal of solutes of different molecular weights and distribution volumes.

Method: Single-session and weekly balances of β_2M, P, urea, and creatinine were prospectively assessed with total dialysate collection and serum measurements before and after 341 dialysis sessions (mean dialysate volume: 30963 ± 862 mL; mean length of dialysis session: 153 ± 8 min) in 31 stable patients (female; 9, 29 %; mean age: 55.6 ± 13.6 y; dry weight: 74.9 ± 13.3 kg) undergoing short-daily home HD with NxStage cycler, between July 2014 and October 2019. The mean blood flow rate was 365 ± 17 mL/min, whereas the mean dialysate flow rate was 194 ± 12 mL/min.

Results: Single-session β_2M, P, urea, and creatinine removals were 0.138 ± 0.050 g, 0.610 ± 0.161 g, 18.89 ± 6.07 g and 1.07 ± 0.31 g, respectively, whereas the reduction rates (%) were 38.0 ± 13.0, 46.8 ± 8.6, 48.2 ± 7.0 and 46.6 ± 6.6, for β_2M, P, urea and creatinine, respectively. The estimated weekly β_2M, P, urea and creatinine removals in HDD patients dialyzing 5-6 days per week were comparable with 4-h in-center thrice-weekly on-line hemodiafiltration according to previous studies (Table 1).

Conclusion: Treating patients with short-daily HD with low-dialysate volume at a 5-6 days per week prescription may achieve an efficient weekly β_2M and P removal.

Table:

	Estimated weekly solute mass eliminated (g)		Estimated weekly reduction rate (%)	
	5 d / week	6 d / week	5 d / week	6 d / week
β_2-microglobulin	0.687 ± 0.249	0.825 ± 0.298	190 ± 65	228 ± 78
Phosphate	3.05 ± 0.81	3.66 ± 0.97	234 ± 43	281 ± 52
Urea	94.43 ± 30.34	113.31 ± 36.41	241 ± 35	289 ± 42
Creatinine	5.36 ± 1.55	6.44 ± 1.86	233 ± 33	279 ± 39

P1056 **SUSTAINED LOW EFFICIENCY DIALYSIS (SLED) WITH STANDARD HEMODIALYSIS MACHINE AND CITRATE AS CIRCUIT ANTICOAGULANT IN CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY INJURY**

Francesca Di Mario[1], Filippo Fani[2], Paolo Greco[1], Caterina Maccari[1], Maria Teresa Farina[1], Tommaso Di motta[1], Elisabetta Parenti[1], Giuseppe Regolisti[1], Enrico Fiaccadori[1]

[1]UO Nefrologia, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy and [2]UO Nefrologia e Dialisi, Ospedale San Giovanni di DIO ASL Toscana centro, Firenze, Italy

Background and Aims: Sustained-Low Efficiency Dialysis (SLED) is a Renal Replacement Therapy (RRT) modality characterized by excellent efficiency and hemodynamic stability that is increasingly used in critically patients with Acute Kidney Injury (AKI). SLED can be performed with either continuous RRT or conventional hemodialysis machines. Even in the case of SLED, avoiding extracorporeal circuit clotting is a mainstay of treatment, and a rational approach to this issue is represented by regional citrate anticoagulation. The present pilot study is aimed at a preliminary evaluation of safety and efficacy of a simplified regional anticoagulation protocol based on ACD-A for SLED performed by using a conventional hemodialysis machine in critically ill patients with AKI in the ICU.

Method: SLED was performed for 8-12 hours (daily or every other day) with a Surdial X Nipro® hemodialysis machine, with a standard hemodialysis circuit, and a triacetate of cellulose filter (Sureflux-19L, 1.9 m2, KUF 19 ml/mmHg/h). Blood flow was set at 200 ml/min and dialysis fluid flow at 100 ml/min. The citrate was infused in pre-dilution as ACD-A solution (citrate 2.2%, 112.9 mmol/L) at rates ranging from 200 to 400 ml/h, to obtain an estimated pre-filter citrate concentration between 2 and 4 mmol/L. The treatment was monitored by serial evaluations of ionized calcium (Ca ++) and ACT (Hemochron Jr) at the following times: at the beginning of the SLED (sampling at the arterial line representative of patient's blood), at the 2nd hour (arterial line and post-filter) and at the end of SLED (arterial line). Laboratory targets for monitoring were as follows: normal values of ACT and calcium ionized (Ca^{++}) not less than 0.9 mmol/L in the patient blood (systemic circulation), ionized calcium values not less than 0.6 mmol/L in the post-filter blood. The blood of the extracorporeal circuit was then recalcified in the filter by dialysis fluid itself (Ca^{++} 1.5 mmol/L) through Ca back-filtration. The protocol does not request routine calcium infusion to the patient until Ca^{++} values in the post-filter blood at the 2nd hour is < 0.6 mmol/L.

Results: A total of 41 SLED sessions were performed in 12 patients (mean age 69 $\pm$ 18 SD, 7 males and 5 females, mean APACHE II 22); 6 patients were on mechanical ventilation, and 6 had severe hemodynamic instability requiring high-dose vasoactive drugs. Patients had an average fluid overload of 6 Kg, as estimated by the usual weight values reported. Average pre-SLED urea was 94 mg/dL, and 32 mg/dL at the end of treatment. Most of the sessions were completed for elapsed prescribed time. Only in three cases a premature interruption was observed for clotting of circuit or of the filter (in all cases after at least 6 hours of treatment); in one case only blood restitution was not complete. No statistically significant differences were observed between systemic ACT values during SLED as compared to baseline values of the patients. Calcium infusion (calcium gluconate at fixed rate, 5 ml/h) was started in 10 treatments (10/42, 23.8%). No new cardiac arrhythmia episode or hemorrhagic events were observed during treatments or shortly after.

Conclusion: Our preliminary data suggests that a simplified citrate-based SLED protocol using a conventional dialysis machine is easy and safe, also ensuring a good match between prescribed and actual dialysis dose administered.

P1057 **UNTARGETED 1H NMR-BASED SERUM METABOLIC PROFILE ANALYSIS OF PATIENTS TREATED WITH HIGH VOLUME HEMODIAFILTRATION (HDF)**

Andressa Flores[1,2], Elberth Manfron Schiefer[2,3], Guilherme Sassaki[4], Leociley Menezes[4], Renato Fonseca[2], Regiane Cunha[2], Maria Eugenia Canziani[5], Murilo Guedes[6], Andrea N Moreno-Amaral[6], Wesley Souza[1], Roberto Flavio Silva Pecoits Filho[6], Andréa E. M. Stinghen[2]

[1]Universidade Federal do Paraná, Clinical Analysis Department, Curitiba, Brazil, [2]Universidade Federal do Paraná, Experimental Nephrology Laboratory, Pathology Department, Curitiba, Brazil, [3]Universidade Tecnologica Federal do Paraná, Physics Department, Curitiba, Brazil, [4]Universidade Federal do Paraná, Biochemistry Department, Curitiba, Brazil, [5]Universidad Federal de São Paulo, Nephrology Department, São Paulo, Brazil and [6]Pontifícia Universidade Católica do Paraná, Programa de Pós-Graduação em Ciências da Saúde, Curitiba, Brazil

Background and Aims: Uremic toxins (UTs) accumulate in the circulation of patients with chronic kidney disease (CKD), contributing to poor outcomes. One of the main objectives of renal replacement therapies is the removal of UTs, and while HD is restricted to the clearance of low molecular weight UTs, hemodiafiltration (HDF) adds efficiency to the removal of medium molecular weight UTs through the association of diffusion and convection methods. Metabolomic analysis from nuclear magnetic resonance (NMR) spectra offers efficient data about metabolites profile, indicating the main features of HDF, and possibly highlighting the positive effects of this modality. Thus, the aim of the present study is to evaluate the profile of metabolites in the circulation of a cohort of patients undergoing HDF.

Method: From 97 individuals participating in the HDF arm of a randomized control trial (ClinicalTrials.gov Identifier: NCT02787161), we randomly (using Python language; NumPy library) selected 6 patients (mean age 49, 6 males, 44% diabetics, average duration of 245 minutes, blood flow of 400 mL/min, target convective volume of 22 L per treatment). Patient's serum samples were collected in the beginning of the study (baseline) and 6 months. The samples were prepared with deuterium oxide, sodium trimethylsilylpropanesulfonate as internal standard (ð=0.0 ppm), and further submitted to ^{1}H NMR spectra recorded with Bruker 600 MHz AVANCE III spectrometer in order to identify the patient's metabolomic profile. Data was evaluated with *t*-test and results were then compared with the Human Metabolome Database (HMDB) for descending order of the Jaccard similarity score.

Results: A total of 50 metabolites were investigated. Interestingly, 2 metabolites were significantly ($P<0.05$) reduced in the serum after 6 months compared to baseline, acetate (3.3 ± 0.1) % and dimethylglyoxal (7.6 ± 0.1) % (Figure 1). In order to confirm the presence of these metabolites in human serum, further studies will be conducted with 2D ^{1}H-^{13}C-HSQCed NMR.

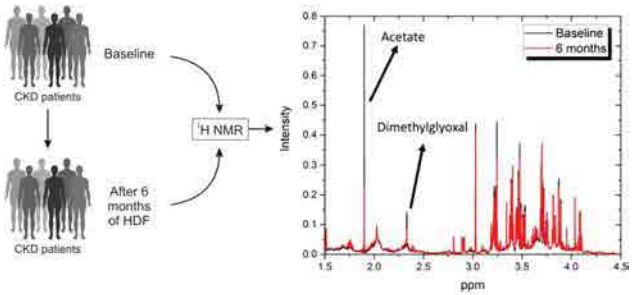


Figure 1: Conclusion: We observed a reduction of acetate and dimethylglyoxal levels after six months of HDF treatment, in comparison to baseline, most likely as a consequence of the increase in clearance of these molecules. Hypothetically these changes in solute removal could explain the positive effects of HDF on clinical outcomes, and further studies should address this potential benefit of the modality.

P1058 **COMPARISON OF THE REMOVAL EFFICIENCY AND THE BIOCOPATIBILITY BETWEEN PRE- AND POST-DILUTION ON-LINE HEMODIAFILTRATION**

Kenji Sakurai[1], Takeshi Saito[1], Hiromi Hosoya[1], Yoshitaka Kurihara[1], Fumi Yamauchi[1], Yoshiko Iwadate[1], Minami Yoshinaga[1], Kazunari Yoshida[2], Kokubo Kenichi[3], Daisuke Ishii[4], Toru Hyodo[5]

[1]Hashimoto Clinic, Dialysis Center, Sagamihara, Japan, [2]Kitasato University School of Medicine, Oran Transplant Medicine, Sagamihara, Japan, [3]Kitasato University School of Allied Health Science, Chemical Sciences and Technology, Sagamihara, Japan, [4]Kitasato University School of Medicine, Urology, Sagamihara, Japan and [5]Eijin Clinic, Dialysis Center, Hiratsuka, Japan

Background and Aims: On-line HDF (OL-HDF) performed in Japan is characterized by the fact that pre-dilution OL-HDF (pre-HDF) accounts for 95% of the cases. In Europe, post-dilution OL-HDF (post-HDF) is the mainstream mode, and particularly high-volume post-HDF is reportedly associated with a favorable prognosis in patients. Last year, we reported favorable biocompatibility and removal efficiency of low-volume post-HDF using high-performance hemodiafilters. Here, we performed pre-HDF and post-HDF for 4 weeks each under the same conditions in the previous study and compared the removal efficiency and the biocompatibility.

Method: Nine stable dialysis patients who had received pre-HDF for at least 6 months (age, 60.8±15.4 years; dry weight, 54.5±9.5 kg) were included in this study. Fineflux-210 Seco (asymmetric triacetate membrane, NIPRO) was used as a hemodiafilter. Post-HDF (replacement fluid rate, 12 L/session) was performed in the first session and pre-HDF (replacement fluid rate, 60 L/session) in the second, each lasting 4 weeks. Each study parameter was evaluated on the last day of each session. In either session, HDF was performed at a blood flow rate of 250 mL/min and a total dialysate flow rate of 500 mL/min. Each HDF cycle lasted 4 h. The removal efficiency was evaluated in terms of Kt/V, as well as the removal rates and removal volumes of urea, creatinine, β2-microglobulin (MG), and α1-MG. Biocompatibility was evaluated in terms of the rates of changes in the levels of CRP, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), pentraxin-3 (PTX3), and intercellular adhesion molecule-1 (ICAM-1) before and after dialysis. Changes in the levels of CD62P during dialysis were also examined. Paired *t*-test was used for statistical analysis.

Results: Removal efficiency results: The removal efficiency for small molecular weight solutes was significantly higher in post-HDF. The removal rate (%) and removal volume (g/session) of β2-MG were 81.4±3.6 and 0.224±0.051 in post-HDF and 80.7±3.3 and 0.218±0.029 in pre-HDF, respectively. The removal rate (%) and removal volume (g/session) of α1-MG were 37.0±4.0 and 0.151±0.024 in post-HDF and 33.3±4.1 and 0.133±0.026 in pre-HDF, respectively. The amount of albumin leakage (g/session) was 3.7±0.6 in post-HDF and 3.1±0.7 in pre-HDF, indicating a significant difference. Biocompatibility results: There were no significant differences between the two modes in the rates of changes in the levels of CRP, PTX3, IL-6, TNF-α, or ICAM-1 before and after treatment. The rate of expression of CD62P was also not significantly different.

Conclusion: Under the present conditions using high-performance filters, post-HDF and pre-HDF demonstrated favorable removal efficiency for both small and large molecular weight solutes, and the biocompatibility was also favorable, indicating no significant differences between the two modes.

		Pre-HDF	Post-HDF	
Kt/V		1.66±0.29	1.82±0.33***	
Reduction Rate (%)	Urea	74.0±5.4	76.7±5.5**	
	Creatinine	68.9±5.1	70.5±5.7*	
	β_2-MG	80.7±3.3	81.4±3.6	*** p<0.001
	α_1-MG	33.3±4.1	37.0±4.0*	** p<0.01
Removal Amount (g)	Urea	11.6±2.8	10.7±3.1	*p<0.05 paired t-test
	Creatinine	1.8±0.5	1.8±0.4	
	β_2-MG	0.218±0.029	0.224±0.051	
	α_1-MG	0.133±0.026	0.151±0.024	

Figure:

P1059 **REMOVAL OF LOW MOLECULAR WEIGHT AND PROTEIN-BOUND UREMIC RETENTION SOLUTES WITH ALLO-HEMODIALYSIS: RESULTS FROM EX VIVO STUDY**

Vaibhav Maheshwari[1], Nadja Grobe[1], Joshua Chao[1], Xia Tao[1], Stephan Thijssen[1], Peter Kotanko[1,2]

[1]Renal Research Institute, Research, New York City, United States of America and [2]Icahn School of Medicine at Mount Sinai, Department of Nephrology, New York City, United States of America

Background and Aims: It is projected that in 2030, 14.5 million people will have end stage kidney disease and need kidney replacement therapy, yet only 5.4 million will receive it due to economic, social, and political factors. We have proposed allo-hemodialysis (alloHD) as a simple and low-cost HD alternative (https://www.kidneynews.org/kidney-news/features/buddy-dialysis-probed-hemodialysis-alternative). In alloHD, the patient's blood is dialyzed against the blood of a healthy subject ('buddy'), who receives the excess fluid and uremic solutes and excretes them via his/her healthy kidneys.

Method: We conducted *ex vivo* experiment with bovine whole blood, 4L in a patient and buddy bucket, respectively. In this setup, buddy blood flows through the dialyzer fiber lumen, while patient blood flows in the dialysate space (Nipro Cellentia 17H dialyzer). The patient blood was spiked with urea, creatinine, potassium chloride, indoxyl sulfate (IS), and p-cresyl sulfate (pCS); solute levels on the buddy side were not altered. The alloHD session lasted for 3 hours, the ultrafiltration (UF) volume was 750 mL. The blood flow rates were kept constant at 150 and 200 mL/min on the patient and buddy side, respectively. Heparin (5000 IU/L) was added to either bucket. The alloHD machine prototype comprises 2 pumps on the buddy side and one on patient side (**Figure 1A**). UF is controlled by the blood flow rate differential between the buddy-sided arterial and venous pumps, respectively.

Results: The levels of small unbound solutes (urea, creatinine, potassium) equilibrate quickly between patient and buddy buckets (**Fig. 1B, top panel**). Of note, the buddy-sided potassium equilibrium concentration is lower, because ongoing UF dilutes albumin in the buddy bucket and concentrates it in the patient bucket, resulting in a Gibbs-Donnan potential. The protein-bound uremic solutes IS and pCS equilibrate towards lower total concentrations on the buddy side due to the earlier mentioned UF-induced albumin dilution. Of note, the levels of free IS and pCS, respectively, converge on both sides of the dialyzer membrane (**Fig 1B, bottom panel**).

Conclusion: Our *ex vivo* data suggest that alloHD can be used to treat hyperkalemia, a major cause of death in acute and chronic kidney failure. Both unbound and protein-bound low molecular weight uremic solutes are also removed. With elimination of "classical" dialysate, we simplify the HD procedure and reduce machine size and costs significantly, making it an affordable HD alternative. Feasibility and efficacy studies in animal models are the next step.

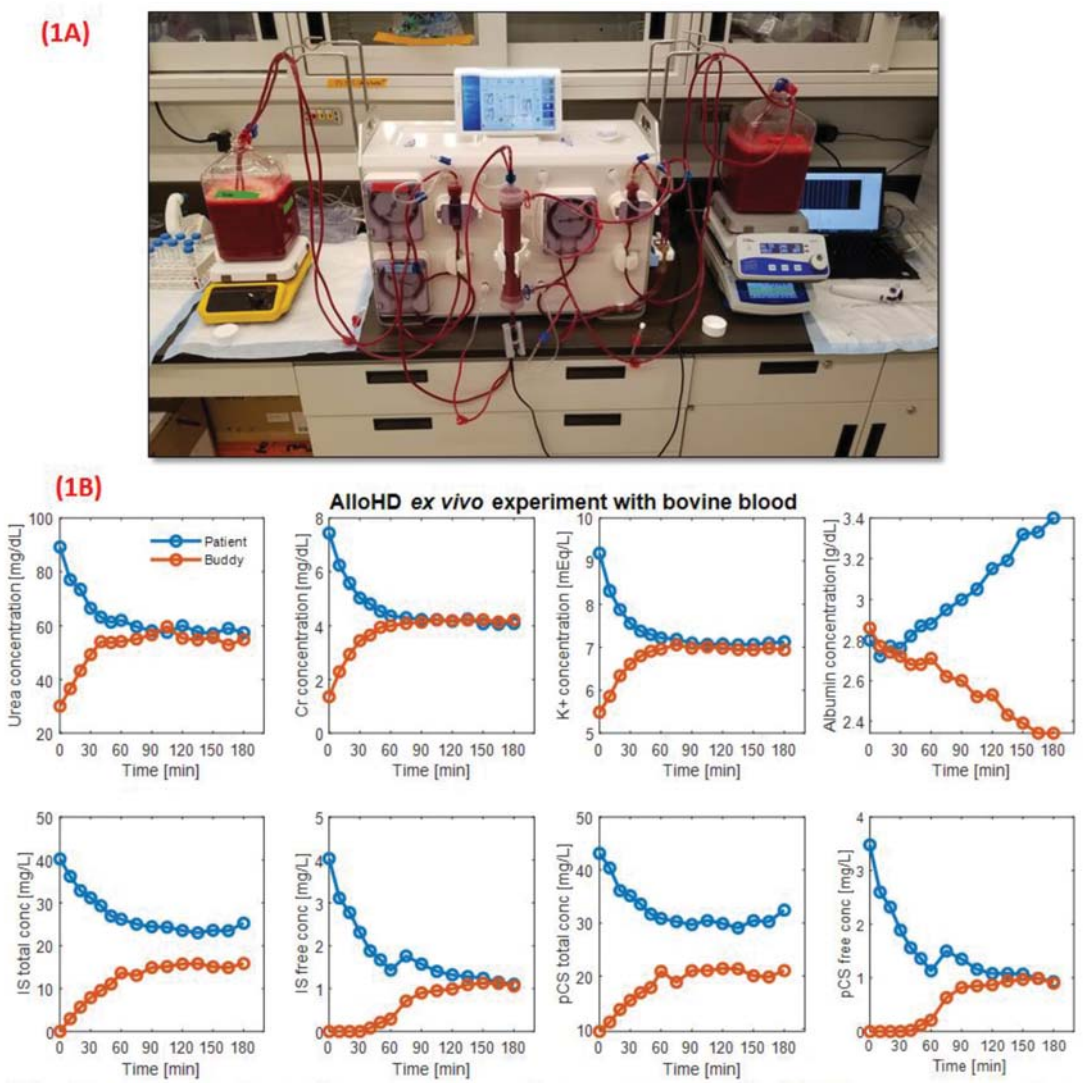


Figure 1: Top panel: Setup of the alloHD machine prototype in the ex vivo experiments; (B) Solute levels in the patient and buddy buckets, respectively, during a 3-hours alloHD session. Both buckets contained 4L bovine blood.

Figure:

P1059A

COULD INFERIOR VENA CAVA DIAMETER REFLECT THE VOLUME STATUS OF THE PATIENT WITH INTERMITTENT HEMODIALYSIS ?

Salwa Elwasif[1], Ahmed Naguib[1], Samar Elshahat[1], Ibrahim Galalah[1], Khaled Eldahshan[1]

[1]Mansoura urology and nephrology center, renal transplantation and dialysis unit, Mansoura, Egypt

Background and Aims: In 1960, Clyde shields (1st chronic hemodialysis patient) developed severe hypertension under treatment.His physician "Dr.scribner" decided to treat this complication using ultrafiltration to deplete the extracellular volume which was thought to be responsible for the increased blood pressure.It was successful, blood pressure decreased to normal and Clyde remained alive for 11 years.from these coming the rationale of dry body weight and its value in improving dialysis patient and improving his survival and decreasing his suffering.

Several different techniques have been used to derive more standard methods of assessment dry weight, however optimal methods for adjusting fluid volume status and ideal dry weight remain uncertain.

AIM: To assess value of using IVC diameter and collapsibility index in modification of dry body weight in hemodialysis patient.

Method: A single center study included 98 patients hemodialysis patient unit in our center. all patients were subjected to assessment of IVC diameter before and after one hour of the first hemodialysis session of the week using ultrasound. We choose muscle cramps as an indicator for hypovolemia . Patients were allocated in two groups. Group 1 : patients with muscle cramps (hypotension) at last hour of session& Group 2 :without muscle cramps (normotensive or hypotensive) at last hour of session. Patients with other causes of muscle cramps rather than hypovolumia were excluded (e.g. hypocalcaemia, l-carnitine deficiency ,etc) .

Results: Patients with muscle cramps in last hour of session were 8 patients with average ivc diameter 0.7 cm & collapsibility more than 80%.Patients without muscle cramps in last hour of session were 84 patient with average ivc diameter 1.3 cm & collapsibility more than 50%.

On interpretation of the eight patient :one patient had bilateral lower limb edema 2ry to local cause (varicose vein) not as a part of overload, three patient had uncontrolled blood pressure cannot tolerate more UF and was hypovolemic but on need to increase antihypertensive medication, two Patients had improved nutritional status with increased lean body mass, one patient had prepare for transplantation and during coarse of preparation NCCT chest showed bilateral diffuse ground glass opacities (overload versus interstitial lung disease). There was marked improvement, however NCCT still revealed ground glass opacities, in spite of patient become hypovolemic (clinically and confirmed by IVC diameter), so patient investigated for the cause of interstitial lung disease and unfortunately diagnosed by further investigation as latent TB.

Conclusions: Using of ultrasound in assessment of IVC diameter is a promising method for estimating dry body weight in hemodialysis patient because it is simple, quick ,non-invasive and helpful especially in debatable cases.

Conclusion: Using of ultrasound in assessment of IVC diameter is a promising method for estimating dry body weight in hemodialysis patient because it is simple, quick ,non-invasive and helpful especially in debatable cases.

P1060 USING ARTIFICIAL INTELLIGENCE TO PREDICT HOME THERAPY CANDIDATES

Jerry Yu[1], Andrew Long[1], Maria Hanson[2], Aleetha Ellis[2], Michael Macarthur[2], Dinesh Chatoth[3], Joseph Turk[3], Michael Buck[2], Len A Usvyat[1], Robert J. Kossmann[3], Franklin Maddux[4]

[1]Fresenius Medical Care, Global Medical Office, Waltham, United States of America, [2]Fresenius Medical Care North America, Fresenius Kidney Care, Waltham, United States of America, [3]Fresenius Medical Care North America, NA Medical Office, Waltham, United States of America and [4]Fresenius Medical Care AG & Co. KGaA, Global Medical Office, Bad Homburg, Germany

Background and Aims: There are many benefits for performing dialysis at home including more flexibility and more frequent treatments. A possible barrier to election of home therapy (HT) by in-center patients is a lack of adequate HT education. To aid efficient education efforts, a predictive model was developed to help identify patients who are more likely to switch from in-center and succeed on HT.

Method: We developed a model using machine learning to predict which patients who are treated in-center without prior HT history are most likely to switch to HT in the next 90 days and stay on HT for at least 90 days. Training data was extracted from 2016–2019 for approximately 300,000 patients. We randomly sampled one in-center treatment date per patient and determined if the patient would switch and succeed on HT. The input features consisted of treatment vitals, laboratories, absence history, comprehensive assessments, facility information, county-level housing, and patient characteristics. Patients were excluded if they had less than 30 days on dialysis due to lack of data. A machine learning model (XGBoost classifier) was deployed monthly in a pilot with a team of HT educators to investigate the model's utility for identifying HT candidates.

Results: There were approximately 1,200 patients starting a home therapy per month in a large dialysis provider, with approximately one-third being in-center patients. The prevalence of switching and succeeding to HT in this population was 2.54%. The predictive model achieved an area under the curve of 0.87, sensitivity of 0.77, and a specificity of 0.80 on a hold-out test dataset. The pilot was successfully executed for several months and two major lessons were learned: 1) some patients who reappeared on each month's list should be removed from the list after expressing no interest in HT, and 2) a data collection mechanism should be put in place to capture the reasons why patients are not interested in HT.

Conclusion: This quality-improvement initiative demonstrates that predictive modeling can be used to identify patients likely to switch and succeed on home therapy. Integration of the model in existing workflows requires creating a feedback loop which can help improve future worklists.

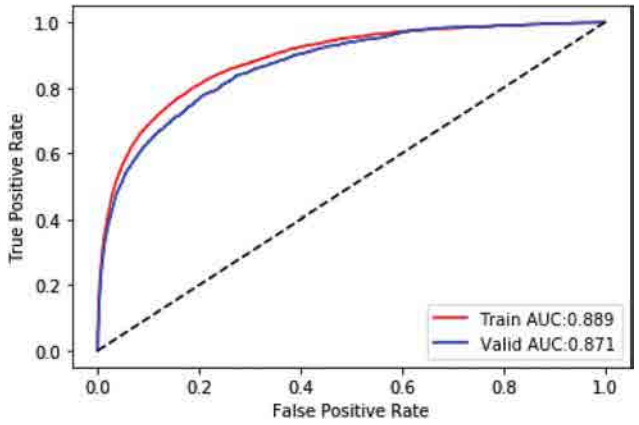


Figure:

P1061 ACID-BASE MODELLING AND TREND IN CENTRAL VENOUS OXYGEN SATURATION IN HEMODIALYSIS

Pietribiasi Mauro[1], John (Ken) Leypoldt[1], Jacek Waniewski[1]

[1]*Nalecz Insitute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland*

Background and Aims: Central venous oxygen saturation (sO2cv) is commonly used as a proxy of cardiac output in non-uremic populations. Recently, the decrease in sO2cv commonly observed in many hemodialysis (HD) sessions was correlated with ultrafiltration volume (UFV) and was suspected to be linked with a treatment-induced decrease in cardiac output (Zhang et al, NDT 2018). High variability in sO2cv has also been associated with all-cause mortality in this group of patients (Zhang et al, Blood Purif 2019). We adapted a comprehensive mathematical model of whole body oxygen (O2) and carbon dioxide (CO2) biochemistry, storage and transport and applied it to simulate the changes in sO2cv during bicarbonate hemodialysis to test their connection with changes in CO.

Method: The original model of biochemistry and transport of base excess, CO2 and O2 was originally developed by Rees and Andreassen (Crit Rev Biomed Eng 2005), and describes in detail the chemical and respiratory mechanisms that regulate the biochemical status in different physiological compartments of the patients' body (venous blood, arterial blood, tissue cells, interstitial fluid). The model was modified to include the effect of the HD treatment on these systems, allowing to calculate the variations in venous and arterial sO2. Treatment perturbations included the removal via ultrafiltration of interstitial fluid and plasma volume (and consequent hemoconcentration), and infusion of bicarbonate. Simulation experiments of 4h HD sessions were carried out with bicarbonate dialysate concentration = 35 mmol/L and dialysance = 198 mL/min, and various ultrafiltration volumes (UFV); CO was assumed to decrease by 2% for each 1% change in blood volume. The initial biochemical status of the patient was defined assuming 20 mEq/L bicarbonate concentration, 7.4 pH, and 97% oxygen saturation in the arterial compartment, resulting in initial sO2cv equal to 66.6%. Both artero-venous and veno-venous access were simulated.

Results: The model predicted a negative linear trend for sO2cv with variable slope depending on UFV, as shown in the table:

UFV	Δ sO2cv	Slope sO2cv (%/h per 10 mL UFV/Kg)	Δ CO
2 L	-2.55 %	-0.26	-14.6 %
3 L	-4.39 %	-0.29	-21.8 %
4 L	-6.59 %	-0.33	-29.1 %

The trend in sO2cv was directly proportional to the decrease in CO during HD and inversely proportional to UFV. In case of constant CO, the simulated sO2cv would actually increase during the session. Although the type of vascular access determined changes in other simulated quantities, partial pressures of CO2 and O2 and oxygen saturation in both arterial and venous blood were practically unchanged.

Conclusion: Our model confirmed the correlation between the trend in sO2cv and UFV already highlighted in previous works. Moreover, it showed that the decrease in cardiac output is a major determinant of the decrease in sO2cv during the HD session. The developed mathematical model may provide physiological insights in the development of new technologies to monitor changes in cardiac performance during HD.

P1062 **EXPANDED DIALYSIS (HDX): IS THERE AN IMPACT ON PATIENT REPORTED SYMPTOM?**

Jarrin Penny[1,2], Fabio R Salerno[1], Lisa Hur[1], Christopher McIntyre[1,3,4]

[1]Western University, Medical Biophysics, London, Canada, [2]Western University, Kidney Clinical Research Unit, London, Canada, [3]Lawson Health Research Institute, Medicine, London, Canada and [4]London Health Sciences Centre, Division of Nephrology, London, Canada

Background and Aims: High flux dialysis membranes sufficiently remove smaller sized uremic toxins however, the accumulation and retention of larger middle molecular weight toxins, which are associated with chronic inflammation, cardiovascular disease and suboptimal outcomes are poorly cleared. The recent advent of medium-cut-off dialysis membranes, labelled "expanded dialysis" (HDx) are permeable to molecules of larger size responsible for poor clinical outcomes. However, it remains unclear if HDx can directly impact the symptoms associated with hemodialysis (HD).

Symptom burden plays a significant role in quality of life (QOL) and mortality rates in the HD population. The London Evaluation of Illness (LEVIL), an application-based platform has been developed to measure patient reported outcomes (PROM). In comparison to cross-sectional PROM's, LEVIL more accurately represents the fluctuations in daily symptoms and the impact of intervention. LEVIL evaluates general well-being, energy, sleep, appetite, pain and breathing, all of which are outcomes of interest on symptom burden in chronic kidney disease. Our aim was to determine if HDx therapy had any effect on symtoms/QOL domains using LEVIL.

Method: 28 patients from two dialysis centers in London Ontario were consented to participate. Patients were required to be over 18 years of age and on conventional thrice weekly maintenance HD for at least three months. 23 participants completed study and analyzed (five lost for various reasons).

Baseline (BL) symptom characteristics were obtained while using high flux membrane for two weeks. Symptoms continued to be measured throughout the 12 weeks of HDx therapy two-three times weekly using LEVIL. Laboratory biomarkers including beta-2 microglobulin and free-light chains were collected at baseline and after 12 weeks of HDx therapy.

Results: Patients were stratified into tertiles (high/middle/low) using mean values of BL symptoms scores in each domain (wellbeing, energy, sleep, appetite, pain, breathing). Those in the high BL group were labeled as "control". Low and middle BL measures were further stratified into responders vs. non-responders (responders were considered to have a 50% increase in any symptom domain by $\geq$50%). Of those domains which responded to HDx, 76% also had low BL scores with 27% having middle BL scores. General wellbeing, energy and sleep were domains with the greatest response reaching statistical significance after eight weeks of therapy. HDx had limited effect on appetite, pain and breathing. Although stratification was per domain, overall, 74% of the population studied did respond in at least one domain, with some responding in as many as five.

Conclusion: HDx using Theranova (Baxter) shows the most benefit in domains with low BL measures. Additionally, not everyone who had low BL scores responded after 12 weeks of therapy, leaving us to question whether HDx may have a latent effect in some individuals/populations. Those who had no response to therapy in certain domains also had greater baseline quality of life respectively. This information may assist in decision making/rationale for the utilization and implementation of such therapy. Although more work is required to further stratify symptoms in relation to demographic/biochemical finding and clinical outcomes. It is evident that HDx improves patient reported symptoms and QOL.

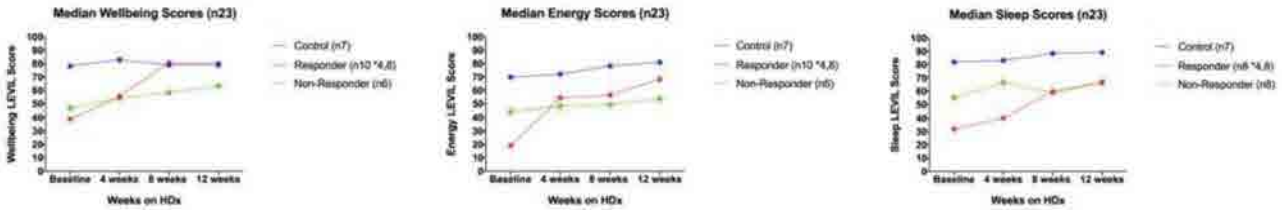


Figure 1 Median LEVIL scores for Wellness, Energy, Sleep for control, responders, non-responders at baseline, 4 weeks, 8 weeks and 12 weeks of HDx therapy.

P1063 **PERFORMANCE OF MEDIUM CUT-OFF DIALYZERS IN EXPANDED HEMODIALYSIS PATIENTS IN COLOMBIA**

Roberto D'Achiardi[1], Eduardo Zuñiga[1], Alejandra Molano[1], Ha Tran[2], Rhea Parreno[2], Jasmin Vesga[3], Angela Rivera[4]

[1]Renal Therapy Services (RTS) Colombia, Medical, Bogota, Colombia, [2]Baxter Healthcare Corporation, Global Clinical Development, Deerfield, United States of America, [3]Renal Therapy Services (RTS) Colombia, Clinical Research, Bogota, Colombia and [4]Baxter Healthcare Corporation, RCS Medical & Quality, Deerfield, United States of America

Background and Aims: Uremic toxins which are retained in ESRD include small solutes to large middle molecules. Large middle molecules play significant roles in immune modulation and cardiovascular morbidity and mortality. Expanded hemodialysis (HDx) enabled by innovative medium cut-off (MCO) membrane more effectively removes large uremic toxins vs current dialytic therapies.

Aims: To evaluate the efficacy of MCO dialyzer in large middle molecules removal and pre-dialysis albumin levels after 24 weeks of treatment.

Method: This was an exploratory, prospective observational, multicenter cohort study. Prevalent patients on HD therapy for at least 90 days at the Renal Care Services (RCS) were included between June 6, 2018, to June 14, 2018. Uremic toxins removal was evaluated by measuring the reduction ratio (RR) of free light chains (FLC) κ, λ, Interleukin (IL) 6, IL-10, β2 Microglobulin (β2 M) and fibroblastic factor 23 (FGF-23) at 12 weeks (w) of treatment, as well as the change in predialysis midweek serum level of β2M, FGF-23, factor XIV activity, and VII at baseline, 12 w and 24 w of treatment. A mixed-model repeated measures analysis (MMRM) was performed to identify statistical differences over time

Results: The RR of κ-FLC, λ-FLC, β2 M, and FGF-23 at week 12 showed a reduction between 46-72%; while in IL-6 RR was not significantly changed (Table 2). Predialysis serum levels decreased for β2m, FLCs and IL-6 and FGF 23 (Table 3). The decrease in albumin was within 5% from baseline.

Twenty-two adverse events (AEs) occurred during the follow-up period; No AEs during HDx were deemed related to MCO membrane use.

Conclusion: MCO dialyzers are safe and effective in removing large MMs and decrease in the uremic toxins levels.

Table 1. Baseline characteristics of the study population

Baseline Characteristic	*N*= 52
Age, mean (SD), yr	61 (13)
Sex, % (*n*)	
Men	65 (34)
Women	35 (18)
BMI, kg/m^2, mean (SD)	25.7 (4.4)
CKD cause % (*n*)	
Hypertension	44 (23)
Diabetes	33 (17)
Autoimmune	6 (3)
Obstructive	4 (2)
Unknown	4 (2)
Other	10 (5)
Dialysis vintage, median (IQR), months	68.05 (72.7)
Vascular access, % (*n*)	
AV fistula	88 (46)
Catheter	10 (5)
Graft	2 (1)
Duration of a dialysis session, median (IQR), hr	4 (0)
Dialysate flow, media (SD), ml/min	468 (47)
Blood flow, media (SD), ml/min	323 (43)

BMI, body mass index; CKD, chronic kidney disease; IQR, interquartile range; SD, standard deviation.

Table 2. Reduction Ratios of Lambda-FLC, Kappa-FLC, IL-6, ß2M, and FGF-23 at Week 12

Parameter	n	Reduction Ratio % (SD)	Reduction Ratio 95% CI
Lambda FLC[a], Mean (SD)	47	45.7 (29.0)	[37.2, 54.2]
Kappa FLC[a], Mean (SD)	47	72.4 (9.6)	[69.5, 75.2]
IL-6[b], Mean (SD)	47	-6.2 (99.2)	[-35.4, 22.8]
Beta-2 Microglobulin, Mean (SD)	47	73.6 (10.0)	[70.6, 76.5]
Fibroblast Growth Factor 23, Mean (SD)	47	48.9 (43.1)	[36.2, 61.5]

a: Free Light Chain; SD: Standard deviation; CI: Confidence Interval; IL: Interleukin

Table 3. Change of clinical parameters over time

Clinical Parameters	Follow-up	n	Mean, SD	Change from baseline, 95% CI*	P value
Beta-2 Microglobulin, mg/L	Baseline	52	28.5 (8.8)	NA	—
	Week 12	47	23.8 (7.7)	-4.42 [-5.25, -3.60]	<.0001
	Week 24	41	24.5 (6.6)	-3.52 [-4.57, -2.46]	<.0001
Kappa FLC, mg/L	Baseline	52	276.8 (142.7)	NA	—
	Week 12	47	283.1 (209.0)	14.21 [-41.91, 70.34]	0.6126
	Week 24	41	178.6 (61.1)	-83.47 [-99.73, -67.21]	<.0001
Lambda FLC, mg/L	Baseline	52	156.2 (75.6)	NA	—
	Week 12	47	179.6 (96.4)	26.56 [12.32, 40.80]	0.0005
	Week 24	41	128.7 (51.1)	-20.29 [-25.93, -14.66]	<0.0001
Interleukin-6, pg/mL	Baseline	52	7.6 (6.9)	NA	—
	Week 12	47	6.8 (3.8)	0.52 [-0.49, 1.53]	0.3083
	Week 24	41	8.9 (7.8)	3.41 [0.85, 5.97]	0.0102
Fibroblast Growth Factor 23, kRU/L	Baseline	52	6200.8 (12440.5)	NA	—
	Week 12	47	3760.0 (5172.3)	-1542.00 [-2404.32, -679.70]	0.0008
	Week 24	41	4392.9 (6154.2)	-1173.18 [-2753.57, 407.21]	0.1413
Albumin, g/dL	Baseline	52	3.8 (0.3)	NA	—
	Week 12	47	3.7 (0.2)	-0.11 [-0.14, -0.07]	<0.0001
	Week 24	41	3.8 (0.2)	-0.09 [-0.15, -0.04]	0.0011

*Mixed-effect repeated measures model

P1064 HEPARIN-FREE DIALYSIS: A PHASE II PILOT STUDY USING ASYMMETRIC TRIACETATE (ATA) CELLULOSE DIALYZERS

Björn Meijers[1], Ines Vandenbosch[2], Bert Bammens[1], Katrien De Vusser[1], Amaryllis Van Craenenbroeck[1], Kathleen Claes[1], Pieter Evenepoel[1]

[1]University hospitals Leuven, Immunology, microbiology and transplantation, Leuven, Belgium and [2]GZA Antwerpen, Nephrology, Wilrijk, Belgium

Background and Aims: Not all dialysis patients tolerate heparin anticoagulation. Heparin should be avoided in patients at high risk of bleeding. Strategies include saline infusion, citrate-containing dialysate, regional citrate anticoagulation and heparin-coated membranes. We recently studied the combination of a heparin-coated membrane and citrate-containing dialysate, with a success rate of 94% . Although this combination resulted in low rates of clotting, heparin-coated membranes are not ubiquitously available. The quest for easy to perform, safe and affordable heparin-free dialysis is on. Asymmetric cellulose triacetate (ATA) dialyzers have a low degree of platelet contact activation and might be an alternative to heparin-coated dialyzers.

Method: We performed a phase II pilot study in maintenance dialysis patients. The 'Strategies for Asymmetrical Triacetate dialyzer heparin-Free Effective hemodialysis (SAFE study)' was a two-arm open-label cross-over study. In Arm 1, patients were dialyzed using a 1.9 m2 ATA membrane (Solacea^{TM}-19H, Nipro Corp., Japan) in combination with citrate (1 mM) containing dialysate. In Arm 2, patients were dialyzed with the same 1.9 m2 ATA membrane, in combination with high volume predilution hemodiafiltration. The primary endpoint was the success rate to complete 4 hours of hemodialysis without preterm clotting.

Results: We scheduled 240 dialysis sessions (120 per arm) in twenty patients. Ten patients were randomized to start in Arm 1, the others to Arm 2. All patients crossed to the other arm halfway the study. 232 (96.7%) study treatments were delivered. Overall, 23 clotting events occurred, 7 in Arm 1 and 16 in Arm 2. Success rate in Arm 1 (ATA + citrate containing dialysate) was 90.8 / 94.0 % (intention to treat/ as treated). Success rate in Arm 2 (ATA + predilution HDF) was 83.3 / 86.2 % (intention to treat/ as treated). Therapy survival was borderline significantly better in Arm 1(Mantel-Cox log rank P = 0.05).

Conclusion: Asymmetric cellulose triacetate (ATA) dialyzers have a low clotting propensity. In combination with citrate-containing dialysate, asymmetric cellulose triacetate (ATA) may be a suitable alternative to heparin-coated membranes for systemic heparin-free hemodialysis.

P1065 EXTRACORPOREAL CYTOKINE ADSORPTION IN PATIENTS WITH AKI AND SEPTIC SHOCK AFTER CARDIAC SURGERY

Kristina Boss[1], Michael Jahn[1], Daniel Wendt[2], Ender Demircioglu[2], Matthias Thielmann[2], Arjang Ruhparwar[2], Andreas Kribben[1], Bartosz Tyczynski[1]

[1]University Hospital Essen, Department of Nephrology, Essen, Germany and [2]University Hospital Essen, Department of Thoracic- and Cardiovascular Surgery, Essen, Germany

Background and Aims: Extracorporeal cytokine adsorption is a new option in septic shock as an additional measure to prevent severe cytokinaemia. The purpose of this study was to investigate the effects of extracorporeal cytokine adsorption on hemodynamics in patients with acute kidney injury (AKI) and septic shock after cardiac surgery.

Method: In this retrospective study 64 patients with AKI and septic shock after cardiac surgery were investigated for the effect of extracorporeal cytokine adsorption by CytoSorb® columns on hemodynamics. In all patients CytoSorb®-treatment was applied in addition to continuous renal replacement therapy (CRRT) with citrate anticoagulation. A paired t-test has been performed to determine statistical significance.

Results: Before treatment, the mean noradrenalin dose to reach a mean arterial pressure (MAP) > 65 mmHg was 0.49 µg/kg bw/min, the mean adrenalin dose was 0.1 µg/kg bw/min. 24 h after treatment, significantly reduced catecholamine doses were necessary to maintain a MAP > 65 mmHg (0.23 µg/kg bw/min noradrenalin; $p^{***} < 0.0002$ and 0.06 µg/kg bw/min adrenalin; $p^{*} < 0.02$). The mean SOFA-score for these patients with AKI and septic shock 24 h before CytoSorb®- treatment was 16.6 points. The mean predicted in-hospital mortality rate based on this SOFA-score of 16.6 points was 77 % while the all-cause mortality rate of the patients in this study was 59.4 %.

Conclusion: In patients with AKI and septic shock after cardiac surgery, 24 h after extracorporeal cytokine adsorption by CytoSorb® the catecholamine dose required to maintain a MAP > 65 mmHg was halved. Additionally, observed in-hospital mortality was lower than SOFA-score predicted mortality.

P1066 **OBJECTIVIZATION OF "DRY WEIGHT" CLINICAL ASSESSMENT IN HEMODIALYSIS PATIENTS BY MULTI-FREQUENCY BIOIMPEDANCE SPECTROSCOPY WITH VECTOR ANALYSIS**

Konstantin Vishnevskii[1], Ekaterina Dudash[1], Olga Domashenko[1], Olga Volkova[1], Elena Turbasova[1], Ekaterina Frolova[1]

[1]*St. Petersburg State Healthcare Institution "City Hospital № 15", Dialysis department, St.-Petersburg, Russia*

Background and Aims: Hydration status is an important prognostic factor in patients receiving hemodialysis (HD). An accurate hydration status assessment and determination of the euvolemia ("dry weight", DW) target value is a difficult task and need to be objectified by instrumental methods. One of these methods is the vector analysis of multi-frequency bio-impedance spectroscopy (MBIS). The aim of the study was to assess the effect of DW correction according to the results of a vector analysis of MBIS on the blood pressure dynamics and the frequency of intra-dialysis complications.

Method: Total 104 patients were included in the study. The mean age was 63±11 years, mean duration of renal replacement therapy was 91±68 months. Patients were randomly (block randomization) divided into the study (SG, N=52) or control (CG, N=52) groups. In the SG, the correction of DW performed according to the results of the MBIS vector analysis using the Bodystat MultiScan 5000 analyzer (Bodystat Ltd) with specially developed correction algorithm (figure). In the CG the correction of DW was carried out only according to clinical indicators. Within 3 months before and 3 months after the initial assessment of DW the blood pressure during HD and the number of intradialytic complications were recorded in all patients.

Results: In the SG, DW was increased in 13 patients by an average of 1.0±0.9 kg, decreased in 26 patients (-1.1±0.7 kg) and did not change in 13 patients. In the CG, DW increased on average by 1.3±0.9 kg in 19 patients, in 27 decreased (-1.2±0.8 kg) and in 2 did not change. In patients who had a history of increased blood pressure during dialysis, in SG the frequency of hypertension episodes decreased from 3.8 to 1.1 episodes per month (p=0.02), in contrast to CG (from 2.4 up to 2.3 episodes per month, p=0.87). Also, among patients initially prone to hypertension in SG, in contrast to CG, a decrease in systolic blood pressure was observed both before the HD (from 163±16 to 143±10 mm Hg, p=0.004) and after the HD (from 151±23 to 130±15 mmHg, p=0.02). No changes in the frequency of episodes of hypotension and diastolic blood pressure during HD were observed either in the study or in the control group

Conclusion: Objectification of the dry weight clinical assessment of in HD patients using multifrequency bioimpedance spectroscopy with vector analysis can help to reduce the complications rate and arterial hypertension severity.

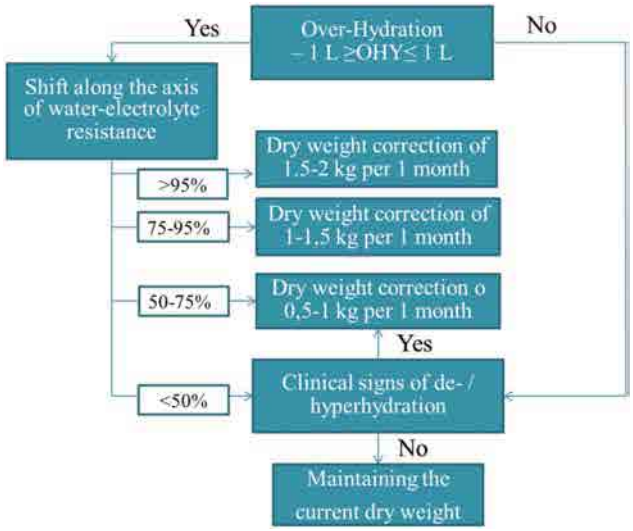


Figure:

P1067 **CONDUCTIVITY BASED ONLINE MONITORING OF PREDIALYTIC HYPONATREAMIA AS DIAGNOSTIC TOOL IN HEMODIALYIS**

Joachim Harlos[1], Andreas Maierhofer[2], Bernard Canaud[3]

[1]Dialysezentrum Schweinfurt, Schweinfurt, Germany, [2]Fresenius Medical Care Deutschland GmbH, Global Research & Development, Schweinfurt, Germany and [3]Fresenius Medical Care Deutschland GmbH, Global Medical Office, Bad Homburg, Germany

Background and Aims: Hyponatremia in dialysis patients is a strong indicator of poor outcome in dialysis patients that requires early detection to facilitate clinical workup and management. However, plasma sodium concentration as determined by lab methods (Na-Lab) is measured at the best monthly in clinical practice.

Recently, online monitoring of predialytic plasma Na (pPlNa) as estimated from dialysate conductivity using an electrolyte model has become available at every hemodialysis session, thus providing an unprecedented close and almost continuous monitoring of this crucial indicator. This could be used as diagnostic tool to identify changes in patient status and alert earlier the physician.

Method: In a monocentric retrospective clinical study in 114 patients on maintenance hemodialysis (>90% online postdilution HDF) for whom online pPlNa was available for a period of at least 12 months at least once a week, kinetics of pPlNa were analyzed. For 10 patients with hyponatremic episodes as manifested in pPlNa, the agreement between time course of pPlNa and Na-Lab and the correlation to the manifestation of clinical findings was explored.

Results: Time course of pPlNa and Na-Lab showed very good agreement. Hyponatremia onset was clinically related to diagnoses such as fluid overload and congestive heart failure, diarrhea secondary to inflammatory bowel disease, sepsis, liver cirrhosis, cancer and use of loop diuretics.

Conclusion: The clinical examples show that due to the good agreement of the time course of online monitoring of pPlNa and Na-Lab, pPlNa can be used as adjuvant diagnostic tool for the early detection of onset and progression of morbid events. Due to its routine availability variations in pPlNa could be used to timely trigger clinical workup and investigations.

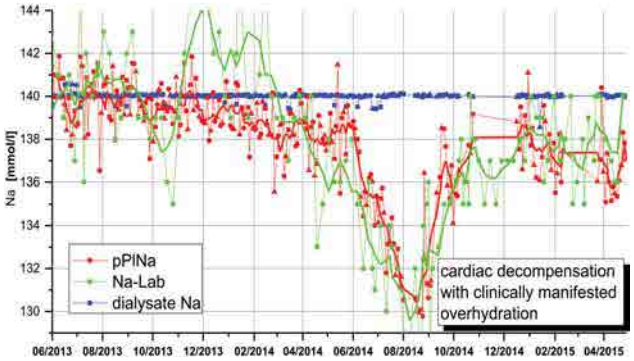


Fig.: I llustrative example for the agreement between pPlNa and Na-Lab, and to clinical findings during a period of hyponatremia

P1068 LUNG ULTRASONOGRAPHY IS MORE EFFECTIVE THAN BIOIMPEDENCE OR NT-PRO BNP AT ASSESSING POST-DIALYSIS VOLUME CHANGES

Hazel Teng[1], Yan Ting Chua[1], Weng Kin Wong[1,2], Lee Ying Clara Ngoh[1,2]

[1]National University Hospital, Division of Nephrology, University Medical Cluster, Singapore, Singapore and [2]National University of Singapore, Department of Medicine, Yong Loo Lin School of Medicine, Singapore, Singapore

Background and Aims: At present, there are no precise and quantitative clinical indices for assessing fluid status in haemodialysis (HD). Existing modalities such as plasma B-type natriuretic peptide (NT-pro BNP), measurement of inferior vena cava diameter (IVCD) by ultrasound or bioimpedance spectroscopy (BIS) have limitations and do not always give quantitative measurements to guide dry weight titration. Lung ultrasonography (LUS) has emerged as a novel real-time technique to assess extravascular lung water (EVLW) on HD. Current studies comparing the above techniques often lack standardized dialysis days and timepoints for sampling volume assessment methods. This study aims to compare the performance of LUS against existing methods (NT-pro BNP, IVCD, BIS) of volume assessment in an Asian HD cohort, using a standardised protocol for sampling. The secondary aim was to measure the turnover time required for performing each volume assessment method.

Method: This was a prospective study of 50 chronic HD patients in a single dialysis unit. In this cohort, 34 (68%) had diabetes, and 43 (86%) were on at least 1 antihypertensive. Patients aged more than 21 years, on thrice weekly dialysis with a high flux dialyser for more than 3 months with residual urine output less then 500 ml per day were recruited.

NT-pro BNP, IVCD and BIS were sampled immediately pre- and post- midweek dialysis. 28-intercostal space LUS was performed by a Nephrologist with appropriate certification immediately pre- and 30 minutes after midweek dialysis. EVLW produces lung artefacts (B-lines), which is summated into a B-line score (BLS). We also measured the time required, from performing each volume assessment methodology, to the point of result acquisition.

Results: Pre-HD, lung congestion was classified as mild (BLS $\leq$ 15) in 6 patients (12%), moderate (BLS 15 – 30) in 12 patients (24%) and severe (BLS $>$ 30) in 32 patients (64%). Median BLS reduced from 46.5 (22.5 – 77.0) pre-HD to 15.5 (9.9 – 21.5) post-HD. There was a linear correlation between changes in BLS and ultrafiltration on HD, with UF 500ml approximately equal to 8.2 B-lines.

There were significant but weak to moderate correlations between pre-HD LUS and BIS ($r = 0.457$, $p = 0.004$), IVCD indexed to body surface area during expiration (IVCDimax) (r = 0.371, $p = 0.026$) and NT-pro BNP ($r = 0.406$, $p = 0.004$). Post-HD, correlations between LUS and IVCDimax remained similar ($r = 0.353$, $p = 0.02$), but weakened with BIS ($r = 0.329$, $p = 0.021$) and became non-significant with NT-pro BNP. This was related to a paradoxical increment in NT-pro BNP and BIS overhydration values post-HD, in up to 40% of the cohort.

Separately, the mean execution time for the various volume measurements were LUS: 6 $\pm$ 0.2 minutes, BIS: 5.9 $\pm$ 0.4 minutes, IVCD: 4.1 $\pm$ 0.3 minutes and the laboratory turnaround time to obtain a NT-pro BNP result was 125 $\pm$ 10.6 minutes.

Conclusion: LUS was able to demonstrate a linear correlation with UF volume, and may be more effective then NT-pro BNP or BIS at real-time assessment of fluid changes post-HD. The execution of LUS was no more time-consuming then BIS. LUS is hence likely to be a useful clinical tool for dry weight titration in HD patients.

P1069 **COMPARISON OF BIOCOMPATIBILITY OF REGULAR AND INCREASED DOSE OF CITRATE IN CHRONIC HEMODIALYSIS - PRELIMINARY RESULTS OF A RANDOMIZED TRIAL**

Alesa Orsag[1], Mojca Bozic-Mijovski[2], Sasa Simcic[3], Jakob Gubensek[1,3]

[1]University Medical Center Ljubljana, Department of Nephrology, Ljubljana, Slovenia, [2]University Medical Centre Ljubljana, Department of Vascular Diseases, Ljubljana, Slovenia and [3]University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

Background and Aims: The dose of citrate that is needed in regional citrate anticoagulation (RCA) to achieve optimal biocompatibility of the extracorporeal circuit is not known. Insufficient biocompatibility is related with increased inflammation and oxidative stress and therefore higher risk for cardiovascular events, as well as decreased dialysis dose. Biocompatibility is multifaceted and includes activation of coagulation and complement cascades, as well as degranulation of leukocyte and platelets. We performed a randomized control trial (ACTRN12613001340729) to compare regular and increased dose of citrate in RCA.

Method: 30 chronic hemodialysis patients were randomly assigned to a single hemodialysis session with RCA using either regular (2.7 mmol/l) or increased dose of citrate (4.0 mmol/l). Markers of activation of complement system (C5a), activation of hemostasis (thrombin – antitrombin complex (TAT)), activation of platelets (platelet factor 4 (PF4)) and activation of leukocyte (myeloperoxidase (MPO)) were taken at the beginning (time 0), after 30 minutes (arterial line) and after 4 hours (arterial and venous line) of dialysis. Results were corrected for changes in hematocrit, and compared between groups using T test.

Results: There was no significant difference in any of the measured biocompatibility parameters between the two citrate dose groups at any of the time points. We have observed a significant, but transient increase in PF4 after 30 minutes (28 +/- 17 to 47 +/-29 IU/mL vs. 30 +/-17 to 54 +/- 33 IU/mL, $p<0.05$ for both groups), which was parallel in both groups ($p=0.76$ for between group comparison). No significant changes in TAT, MPO or C5a were observed during dialysis. There were no clotting problems or significant hypocalcemia observed in either group.

Conclusion: Given the absence of significant increase in the majority of biocompatibility parameters at the standard dose of citrate and absence of blunting of PF4 increase by the higher dose of citrate, the standard dose of citrate (2.7 mmol/l) seems sufficient in RCA for chronic hemodialysis.

P1070

ONLINE HIGH-VOLUME HEMODIAFILTRATION REDUCES PRE-DIALYSIS LEVELS OF INDOXYL SULFATE COMPARED TO HIGH-FLUX HEMODIALYSIS: RESULTS FROM HDFIT MULTICENTRIC RANDOMIZED CONTROLLED TRIAL

Jordana Lima[1], Murilo Guedes[2], Silvia Rodrigues[1], Ana Clara Flórido[2], Ana Beatriz Barra[3], Maria Eugênia Canziani[4], Américo Cuvello[5], Carlos Eduardo Poli De Figueiredo[6], Roberto Pecoits-Filho[2], Lia Nakao[1]

[1]Universidade Federal do Paraná, Department of Basic Pathology, Curitiba PR, Brazil, [2]Pontifícia Universidade Católica do Paraná, School of Medicine, Curitiba PR, Brazil, [3]Fresenius Medical Care Brazil, [4]Universidade Federal de São Paulo, São Paulo SP, Brazil, [5]Hospital Alemão Oswaldo Cruz, São Paulo SP, Brazil and [6]Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil

Background and Aims: Online High-Volume Hemodiafiltration (OL-HDF) combines convective and diffusive clearances and is associated with better outcomes compared to standard hemodialysis (HD). Although HDF has been shown to improve the clearance and pre-dialysis concentration of middle size uremic toxins, little is known about its effect on concentration of protein-bound uremic toxins (PBUT), particularly in comparison to high-flux HD. Here, we investigated whether high-volume post-dilution OL-HDF impacts pre-dialysis plasma levels of PBUT indoxyl sulfate (IxS), *p*-cresyl sulfate (pCS) and indole 3-acetic acid (IAA) compared to high-flux HD over time, since accumulation of these PBUT has been associated with increased overall mortality of CKD patients.

Method: This is post hoc analysis of the multicentric randomized controlled trial (RCT) studying the impact of post-dilution high-volume OL-HDF *versus* high-flux HD on measured physical activity (HDFit - clinicalTrials.gov: NCT02787161), which included clinically stable HD patients with a vintage >3 to <24 months. Total plasma levels of IxS, pCS and IAA were determined by high performance liquid chromatography (HPLC) with fluorescence detection at baseline, 3 and 6 months. The difference between HDF and HD in respect to changes in the PBUT concentrations during the follow up, analyzed using linear mixed effect models, was compared. Results are presented as mean differences between groups in the change from baseline along with 95% confidence intervals (CI).

Results: 193 patients (mean age 53 years old, 70% males and 60% white – no differences between groups) were analyzed. There were no differences between HD and OL-HDF groups regarding clinical and biochemical characteristics at the baseline. In the OL-HDF group, 99% of patients achieved a convective volume higher than 22 L and both groups had similar dialysis session duration and blood flows throughout the follow up. The mean differences (95% CI) in concentrations over time for PBUTs among HDF and HD groups are shown in Figure 1. HDF group presented a significantly lower trajectory of IxS levels and a lower trajectory of pCS levels than HD group. Trajectories of IAA levels were not different between groups.

Conclusion: OL-HDF reduced the pre-dialysis concentration of IxS and pCS through 6 months-period compared to high-flux HD.

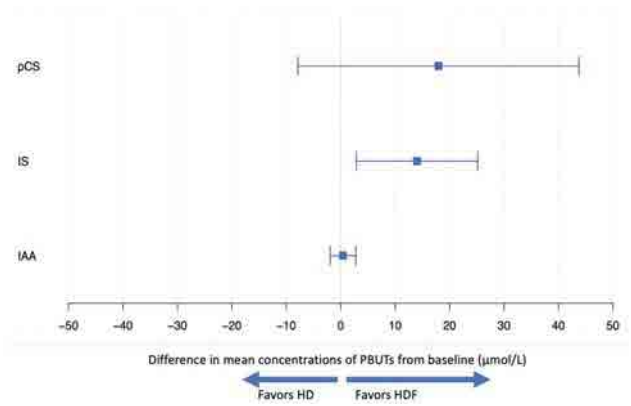


Figure 1: Differences in the mean reduction of PBTUs concentrations from baseline (95% confidence intervals) favoring high-volume OL-HDF compared to high flux-HD for pCS and IxS.

P1071 WITHIN-PATIENT RELATIONSHIPS BETWEEN ULTRAFILTRATION AND FLUID GAINS IN HAEMODIALYSIS PATIENTS

Mai Nguyen[1], Richard Corbett[1], Neill Duncan[1], Damien Ashby[1]

[1]*Hammersmith Hospital, United Kingdom*

Background and Aims: Despite the now-widespread use of haemodialysis treatment, optimal fluid management in long-term dialysis patients remains challenging. Whilst the between-patient factors affecting target weight and ultrafiltration have been well studied, little is known regarding the within-patient factors affecting these relationships.

Method: Dialysis data for a group of stable haemodialysis patients, from 4 dialysis units, were analysed over a period of one year. All weights and volumes are expressed as percentage of target weight.

Results: From 100 patients (aged 28–89, mean 65.4, 54% male) observed over a year, complete data were available for 15530 dialysis sessions, and 13027 combinations of dialysis session plus the following inter-dialytic interval.

Mean arterial pressure dropped by 3.5(+/-14.6)mmHg during dialysis, with a significant correlation ($p<0.05$) between pressure drop and ultrafiltration volume in 26 patients (mean R=0.09, mean regression gradient 3.2).

In 87 patients, inter-dialytic fluid gain correlated strongly ($p<0.05$) with the previous dialysis session's ultrafiltration volume (mean R=0.37, mean regression gradient 0.20) suggesting a significant role of ultrafiltration volume in driving subsequent fluid intake behaviour (thirst).

Unsurprisingly, more fluid was gained over longer inter-dialytic intervals: mean(sd) weight at the start of dialysis was 103.2(1.0)% after a 3-day gap and 102.5(1.0)% after a 2-day gap, with this difference being significant ($p<0.05$) in 87 patients. However, fluid gain was non-linear, diminishing during longer inter-dialytic intervals: mean(sd) daily inter-dialytic fluid gain was 1.13(0.38)% during the 3-day gap vs 1.21(0.53)% during the 2-day gap ($p<0.05$ in 36 patients), implying that at least a third of patients consume less fluid during the 3rd post-dialysis day.

Conclusion: Inter-dialytic fluid gain is strongly dependent on ultrafiltration during the previous dialysis session, and diminishes during the inter-dialytic interval. Large ultrafiltration volumes, which have historically been perceived as the inevitable result of large fluid intakes, are actually a cause of thirst and large fluid intakes in haemodialysis patients. These data, derived from within-patient analyses, strongly challenge our conventional understanding of dialytic fluid management.

P1072 **COMPARISON OF UREMIC TOXINS, INFLAMMATORY MARKERS AND VEGF LEVEL WITH MEDIUM CUT-OFF MEMBRANES AND HIGH-FLUX MEMBRANES IN HEMODIALYSIS: THERANOVA IN SISLI HAMIDIYE ETFAL (THE SHE) STUDY**

Mustafa Sevinç[1], Nuri Baris Hasbal[2], Vuslat Yilmaz[3], Perin Nazif Ozcafer[1], Elbis Ahbap Dal[1], Tamer Sakaci[1], Taner Basturk[1], Abdulkadir Unsal[1]

[1]Sisli Hamidiye Etfal Education and Research Hospital, Nephrology, İstanbul, Turkey, [2]Hakkari State Hospital, Nephrology, Hakkari, Turkey and [3]Aziz Sancar Institute of Experimental Medicine, Neuroscience, Istanbul, Turkey

Background and Aims: Mortality in hemodialysis have not changed since last 30 years which may be caused by inflammation and accumulation of middle and large uremic toxins. Medium cut-off (MCO) membranes are able to perform hemodialysis as effective as hemodiafiltration. Their effect on inflammatory molecules and vascular endothelial growth factor-C (VEGF), an independent factor effective on mortality, are not well known. The aim of the study was to compare intra and inter dialyzer performances of MCO and high-flux dialyzers regarding middle and large uremic toxin, inflammatory marker, VEGF and serum albumin level.

Method: This is a randomized, prospective, open-label, cross-over study (ClinicalTrials.gov: NCT03836508) approved by local ethic committee. Patients had hemodialysis with either 36 sessions of high-flux dialyzer followed by 36 sessions of medium cut-off dialyzer or vice versa. Pre and postdialysis levels for urea, creatinine, albumin, total protein, free kappa light chain, free lambda light chain, beta-2 microglobulin, myoglobulin levels were determined at first and last sessions of every dialyzer. Postdialysis level of middle and large uremic molecules have been determined by a formula to prevent hemoconcentration effect. Reduction rate for uremic toxins were calculated. Serum level of human VEGF, fibroblast growth factor-23 (FGF-23), interferon gamma (IFN-g), interleukin-6 (IL-6), interleukin-10 (IL-10), interleukin-17A (IL-17A) levels were determined at first and last session of the each dialyzer.

Results: Fifty-two patients were enrolled to the study. Median age of patients was 56.40 (43.87-67.39) years. Median dialysis vintage was 4.77 (3.08-10.09) years. Reduction rates and postdialysis levels of free kappa and lambda light chain, myoglobulin, beta-2 microglobulin were lower both at first and last sessions in medium cut-off dialyzers compared to high-flux dialyzers ($p<0.05$ for all) (Table 1). Last session predialysis free kappa, free lambda, beta-2 microglobulin level was lower than first session predialysis levels in medium cut-off dialyzers ($p<0.05$ for all) (Table 2). Last session IL-6, IL-10, IL-17, IFN-gamma levels did not differ between dialyzers ($p>0.05$ for all). Vascular endothelial growth factor levels were 500.91 (363.80-679.15) pg/ml in medium cut-off group and 610.60 (450.63-1021.93) pg/ml in high-flux group (p=0,043). Predialysis serum albumin level at first session for MCO and high-flux groups were 3.88 (3.71-4.04) g/L and 3.75 (3.59-3.95) g/L, respectively (p=0.086) (Figure 1). After 3 months of hemodialysis, it was 3.62 (3.45-3.88) g/L in MCO group and 3.78 (3.58-4.02) g/L in high-flux group (p=0.04). Serum albumin level has decreased from 3.88 (3.71-4.04) g/L to 3.62 (3.45-3.88) g/L in 3 months during hemodialysis with MCO dialyzers (p=0.0001). It did not change significantly in high-flux group in the same time period (p=0.861).

Conclusion: MCO membranes not only decrease post dialysis levels of free kappa, free lambda, beta-2 microglobulin, myoglobulin but also decrease the third month predialysis levels of free kappa, free lambda, beta-2 microglobulin. They do not let the increase in myoglobulin level as seen in high-flux dialyzers. Even though the IL-6, IL-10, IL-17, IFN-gamma, FGF-23 levels did not differ, VEGF levels were lower in MCO dialyzer. The most important side effect of hemodialysis with MCO membranes is decreased serum albumin level.

Molecule	Timing		MCO dialyzer	High-flux dialyzer	p
Free kappa	First session	Predialysis (mg/L)	237.50 (176.75-291.75)	243 (160.75-301.50)	0.809
		Postdialysis (mg/L)	49.51 (38.75-66.90)	101.65 (76.99-159.60)	**0.000**
		Reduction rate (%)	79 (74-82)	47 (38-66)	**0.000**
	Last session	Predialysis (mg/L)	150.50 (124.50-249.25)	176.50 (124.75-259.75)	0.517
		Postdialysis (mg/L)	38.60 (26.95-51.72)	102.20 (76.40-139.75)	**0.000**
		Reduction rate (%)	77 (70-82)	40 (19-54)	**0.000**
Free lambda	First session	Predialysis (mg/L)	135.50 (118-181.50)	133.50 (109.50-150.25)	0.446
		Postdialysis (mg/L)	82.45 (70.21-103.40)	109.85(85.30-139.29)	**0.000**
		Reduction rate (%)	42 (32-49)	20 (32-27)	**0.000**
	Last session	Predialysis (mg/L)	124 (96.65-151)	132.50 (117.75-157.75)	0.135
		Postdialysis (mg/L)	76 (59.52-87.62)	120.05 (94-147.37)	**0.000**
		Reduction rate (%)	42 (30-49)	6 [(-18)- (-19)]	**0.000**
Myoglobulin	First session	Predialysis (mg/L)	226.50 (189-334.75)	214 (182-318.50)	0.556
		Postdialysis (mg/L)	83.18 (62.32-119.84)	186.29 (153.05-274.37)	**0.000**
		Reduction rate (%)	64 (59-69)	8 (4-23)	**0.000**
	Last session	Predialysis (mg/L)	239 (185-331.50)	234.50 (173.25-342)	0.944
		Postdialysis (mg/L)	86.25 (64.57-114.75	217.40 (165.35-336.90)	**0.000**
		Reduction rate (%)	62 (58-70)	7 [(-5)-12]	**0.000**
Beta-2 microglobulin	First session	Predialysis (mg/L)	34.80 (31.07-38.15)	33.40 (28-37.05)	0.299
		Postdialysis (mg/L)	7.62 (6.80-8.73)	10.49 (9.43-12.50)	**0.000**
		Reduction rate (%)	77 (73-80)	67 (62-71)	**0.000**
	Last session	Predialysis (mg/L)	31 (27.80-34.95)	33.35 (30.70-38.07)	**0.028**
		Postdialysis (mg/L)	7.20 (5.90-8.55)	11.30 (10.20-13.85)	**0.000**
		Reduction rate (%)	78 (73-80)	65 (59-69)	**0.000**

MCO: Medium Cut-Off

Figure 1. Predialysis serum albumin levels of MCO and high-flux dialyzer groups at first and last sessions of the study.

P1073 NF-U OF A NEW POLYMETHYLMETHACRYLATE MEMBRANE IMPROVES THE NUTRITIONAL STATUS AND PATIENT-REPORTED SYMPTOMS OF ELDER DIALYSIS PATIENTS

Tetsuro Chida[1], Hiroyuki Igarashi[1], Ikuto Masakane[2]

[1]Tendo-Onsen Yabuki Clinic, Tendō, Japan and [2]Yabuki Hospital, yamagata, Japan

Background and Aims: Malnutrition is the most powerful prognostic factor in dialysis patients, and elder dialysis patients have a higher risk of malnutrition because of multiple comorbidities and daily inactivity. Hence, it is very important to set up a dialysis prescription for preventing progression of malnutrition. We reported nutritional advantage of polymethylmethacrylate (PMMA) membrane for preventing dialysis patients from the progression of malnutrition in the previous report. NF-U has been developed with better hemocompatibility and lesser albumin leakage during the dialysis session than conventional PMMA membranes. We studied additional advantages of NF-U on the nutritional status, patient-reported symptoms and other clinical parameters in elder dialysis patients.

Method: This study was a retrospective one. 10 elder chronic dialysis patients of greater than 75 years old were enrolled into the study; 5 males and 5 females, the mean age was 82.8 years old, and the average dialysis vintage was 11.2 years. NF-U were installed because of low albuminemia, dry weight (DW) loss and other signs of malnutrition. The previous membrane materials were polyether polymer alloy (6), vitamin E coated polysulfone (1), on-line HDF with polyethersulfone (2) and polysulfone (1). On-line HDF were performed in predilution with the substitution volume of 12L/hr. During the observation period the dialysis prescription except dialysis membrane was not changed.

Serum albumin, β_2MG, CRP, nPCR, GNRI, %CGR, DW, CTR were compared one month and four month after the replacement with NF-U. In consideration of the seasonal variation of nutritional status, DW and CTR were compared with that of one year before the study. The changes in body composition were analyzed by Inbody770® (Inbody Japan, Tokyo, Japan)at three months before and after the replacement with NF-U. We also evaluated patient-reported subjective symptoms by our original tool as "Patient-oriented Dialysis (POD)" system three months before and after NF-U installation.

Results: Serum albumin increased from 3.0g/dl to 3.3g/dl. GNRI increased from 87.7 to 91.4. %CGR increased from 91.9% to 102.8%. No significant changes were observed in β_2MG, CRP and nPCR. Although DW had continuously decreased from 52.7kg to 51.7kg before NF-U installation, DW increased from 52.0kg to 52.7kg by NF-U. CTR did not change. Muscle volume and body fat mass also increased. Regarding subjective symptoms, total POD score was significantly improved and especially dialysis related fatigue was remarkably reduced by NF-U.

Conclusion: The current study clearly showed that NF-U of a new PMMA membrane improved the nutritional status of elder dialysis patients with higher risk of malnutrition although the study was a limited retrospective one. Furthermore, NF-U also improved patient-reported subjective symptoms such as fatigue which was reported as a mortality risk factor and the most important patient's outcome. We have not yet established a golden standard or parameter to set up dialysis prescriptions properly to elder dialysis patients. However, improvement of nutritional status and fatigue are one of the most important parameters to expect better outcome of them. We conclude that NF-U should be one of the best choices to treat elder dialysis patients.

P1074 **SIMPLIED REGIONAL CITRATE ANTICOULATION USING A CALCIUM-CONTAINING REPLACEMENT SOLUTION FOR RENAL REPLACEMENT THERAPY: A RANDOMIZED CONTROLLED CLINICAL TRIAL.**

Tiantian Wei[1], Ping Fu[2], Ling Zhang[2]

[1]West China Hospital, Sichuan University, Department of Nephology, Chengdu, P.R. China and [2]West China Hospital, Sichuan University, Deparament of Nephrology, Chengdu, P.R. China

Background and Aims: A simplified protocol for Regional citrate anticoagulation (RCA) using a commercial calcium-containing replacement solution, without a continuous calcium infusion, is more efficient to be used in continuous renal replacement therapy (CRRT). We aim to design a randomized prospective pilot trial to compare the safety and efficacy between calcium-free and calcium-containing replacement solution in CRRT with RCA.

Method: Of the 59 patients who requiring CRRT and being treated with RCA-based continuous venovenous hemodiafiltration (CVVHDF) enrolled, 31 patients were randomized to calcium-containing group and 28 to calcium-free replacement solution group. Primary endpoints were filters lifespan. Secondary endpoints were mortality, kidney function recovery and severe complications rates. Time spent on fluids preparation before CRRT and the amount of 4% trisodium citrate solution pumped during CRRT were recorded. Serum and effluent citrate and calcium concentration during CVVHDF were measured during CRRT.

Results: Filters lifespan were superior for calcium-containing group (mean 58.06 versus 47.12 hours, P=0.05). Mortality and renal outcome were comparable between groups during hospitalization: 10/31 (33.26%) of calcium-containing group patients died versus 13/28 (46.43%) of calcium-free group patients, and 16/31 (51.61%) of calcium-containing group patients had kidney function recovery versus 15/28 (53.57%) of calcium-containing group (P = 0.265). Only 5 patients showed the symptoms and signs of hypocalcemia or citrate toxicity in this study. The mean CRRT preparation time in calcium-containing group: 25.5 minutes, was significantly shorter than calcium-free group: 43.7 minutes ($p<0.001$). The serum and effluent calcium concentration was slightly lower in calcium-containing group during CRRT. While, the mean 4% trisodium citrate solution infusion rate was similar between groups (161.5 mL/h versus 157.4 mL/h, P=0.376).

Conclusion: Patients treated with calcium-containing or calcium-free replacement solution have similar clinical outcomes. Since the calcium-containing replacement solution based RCA has longer filter lifespan and obviates the need for a separate venous catheter and intravenous calcium preparation for continuous intravenous calcium infusion, it is more efficient to be used in clinical practice and superior to the calcium-free replacement solution.

P1075 CONTROL AND MONITORING OF DIAGNOSTIC AND TREATMENT PROCESS IN HEMODIALYSIS CLINIC USING TELEMEDICINE TOOLS

Dmitriy Zinovev[1], Vladimir Novitskiy[1,2], Andrey Malkoch[1,3,4]

[1]Nephrology Expert Council, Moskva, Russia, [2]Moscow State University of Food Production, Informatics and computing technology of food production, Moskva, Russia, [3]Moscow State University of Food Production, Therapy and children diseases, Moskva, Russia and [4]Russian Medical Academy of Continuous Professional Education, Nephrology and Hemodialysis, Moskva, Russia

Background and Aims: Quality of life of hemodialysis patients and adequacy of hemodialysis therapy in general, is defined by the number and duration of incidents during hemodialysis procedures. In this study we examined the effect of telemedical system for control and monitoring of hemodialysis procedures on patients' condition and their quality of life.

Method: The system described in this work included: doctor/patient video call functionality initiated from both ends; functionality of hemodialysis procedure parameters and patient's condition parameters monitoring and registration; functionality of alerting medical staff about registered incidents, functionality of visual control of hemodialysis procedure. The effect of control and monitoring system usage was studied on population of 2300 hemodialysis patients (at the start of the study) with median follow-up of 2 years. The primary end-point was doctor's reaction time on patient's complaint, medical staff reaction time on intradialysis hypertension incidents. Secondary end-points were: number of patients who left the clinic due to reasons besides lethality, patients' satisfaction by hemodialysis therapy (according to survey), number of incidents of intradialysis and interdialysis hypertension.

Results: During the study we observed that as a result of system deployment average doctor's reaction time on patient's complaint (defined as the time from emergence of the complaint to start of patient/doctor communication) reduced from 8 to 1.5 minutes, average staff reaction time on intradialysis hypertension incidents (defined as time from registration of hypertension incident to start of blood pressure normalization actions) reduced from 5 to 2 minutes. Number of patients who left the clinic due to reasons besides lethality reduced from 2.5 per 100 patients before system deployment to 1.7 per 100 patients at the end of the study. Average value of patient's satisfaction by dialysis therapy increased from 7.2 to 9.1 points on 10-point scale (according to survey conducted at the beginning and at the end of the study). By the end of the study, average number (across population) of hypertension incidents per month reduced from 8.3 to 6.2 and from 20.7 to 16.5 episodes for intradialysis and interdialysis hypertension correspondingly.

Conclusion: The use of telemedical tools of hemodialysis procedures control and monitoring has positive impact on patients' satisfaction level by the dialysis procedure and on duration/frequency of incidents registered by these tools, which, in return may improve the quality of patient's life.

P1076 **HEMODYNAMIC TOLERANCE TO INTERMITTENT DIALYSIS IN CRITICALLY ILL PATIENTS: THE CLINICAL JUDGMENT OF HIPERVOLEMIA IS ABLE TO PREDICATIT?**

Erica Melo[1], Marcelo Silveira[1,2], Fábio Dutra[1,3], Ana Baptista[1,3], Filipe Miranda[1,3], Carolina Nascimento[1,3], Fernanda Coelho[1,2,3], Maurício Teixeira[1], Marcel Gomes[1], Sérgio Souza[1], Paulo Benigno[1,2,3], Octavio Messeder[3], Augusto Farias[3], Juliana Caldas[1,2], Rogério Passos[1,2,3]

[1]Hospital São Rafael, Nephrology, Salvador, Brazil, [2]D'Or Institute for Research and Education, Rio de Janeiro, Brazil and [3]Hospital Português, Nephrology, Salvador, Brazil

Background and Aims: Evaluation and management of fluid balance are a key challenge in caring for the critically ill requiring renal replacement therapy. As intradialytic hypotension is a common complication and can be associated ultrafiltration rate. Usually the nephrologist and critical care physician have relied in their subjective clinical judgment and clinical data to calculate ultrafiltration. The aim of this study was to assess the prediction of clinical judgment of fluid overload and other clinical and dialysis data as predictors of hemodynamic tolerance to intermittent dialysis.

Method: This prospective observational single-center study was performed in critically ill patients with acute kidney injury undergoing intermittent hemodialysis. Before hemodialysis, clinical judgement of Hypervolemia from nephrologists and intensivists were assessed and posterior-anterior views of chest-X-rays done within three hour before of beginning of dialysis were collected for measurement of vascular pedicle width (VPW). Factors predicting intradialytic hypotension were identified by multiple logistic regression analysis.

Results: 248 AKI patients requiring intermittent dialysis were considered eligible. The clinician judgement of hypervolemia was not different between hypotensive and non hypotensive sessions. Multiple logistic regression showed that the size of VPW was independently associated with the development of hypotension during IHD session. A VPW value of $>$ 70 mm had an 86.1 % sensitivity, 55 % specificity for identifying non hypotensive sessions with an area under the curve (AUC) = 0.81, 95 % CI 0.75–0.84, $p < 0.001$.

Conclusion: Clinical judgment of hypervolemia and other clinical and demographic variables that are used by nephrologists and critical care physicians at bedside did not predict hypotensive hemodialysis sessions. The high predictive ability of VPW measurement can help physicians to avoid inductive and deductive thinking and may assist critical thinking.

P1077 **PERSISTENCE OF CIRCULATING RESIDUAL HEPARIN IN ESRD PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS**

Vinod Bansal[1], Melissa Mazariegos[2], Arjun Grewal[2], Jasdeep Bajwa[2], Emily Bontekoe[2], Debra Hoppensteadt[2], Omer Iqbal[2], Jawed Fareed[2]

[1]Loyola University Medical Center, Nephrology, Maywood, United States of America and [2]Loyola University Medical Center, Pathology, Maywood, United States of America

Background and Aims: ESRD patients who receive routine maintenance hemodialysis are administered with unfractionated heparin to prevent thrombotic complications. The hemostatic dysregulation along with detectable levels of circulating heparin may cause them to be in a hypocoagulable state. The purpose of this study is to determine the circulating levels of heparin in ESRD patients and its characterization using heparinase digestion methods.

Method: Blood plasma samples collected at routine pre-dialysis sessions from 95 ESRD patients undergoing maintenance hemodialysis were analyzed for the presence of residual heparin utilizing standard laboratory methods such as aPTT, Anti-Xa and Anti-IIa activities On a centrifugal analyzer (ACL-Elite: Instrumentation Laboratory, Bedford, MA). The levels of heparin were calculated in terms of units per ml relative to the USP reference standard. Heparinase digestion was used to confirm the presence of heparin.

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Conclusion: The presence of residual heparin was demonstrated by both clot- based and amidolytic assays in the plasma samples collected from ESRD patients prior to their next-dialysis session. Since these samples were obtained 3 days following the last dialysis session the presence of significant levels of heparin was surprising. Upon heparinase treatment of these samples, the aPTT and the anti-Xa and IIa tests were restored to near normal levels. Our studies confirm the presence of residual heparin in pre-dialysis plasma samples obtained from ESRD patients. The Anti-IIa activity was greater pre-heparinase and it was not decreased to the same extent as Anti-Xa after heparinase digestion. These results suggest that heparin found in ESRD patient's plasma is of high molecular weight origin with delayed clearance.

P1078 IMPACT OF A MEDIUM CUT-OFF DIALYZER ON SKIN AUTOFLUORESCENCE IN HAEMODIALYSIS PATIENTS.

Daniela Viramontes Horner[1], Nitin Kolhe[2], Janson Leung[2], Richard Fluck[2], Nicholas Selby[1,2], Maarten Taal[1,2]

[1]University of Nottingham, Centre for Kidney Research and Innovation, Division of Medical Sciences and Graduate Entry Medicine, Derby, United Kingdom and [2]Royal Derby Hospital, Renal Medicine, Derby, United Kingdom

Background and Aims: Advanced glycation end-products (AGEs) are middle-sized uraemic toxins that accumulate in haemodialysis (HD) patients due to increased production, impaired excretion and insufficient removal. Previous studies have reported that the use of a medium cut-off (MCO) dialyzer promotes a greater removal of larger middle molecules (such as AGEs) than conventional high-flux HD and haemodiafiltration. However, to our knowledge, there is no published evidence regarding the effect of an MCO dialyzer on skin autofluorescence (SAF), a measure of long-term tissue AGE accumulation and independent risk factor for mortality in the HD population. We aimed to investigate the impact of using an MCO dialyzer on change in SAF over time in HD patients.

Method: HD patients were enrolled in a prospective observational study. SAF was measured using a validated Autofluorescence Reader at baseline, 12 and 24 months. During the initial 12 months patients dialysed using high-flux polysulphone, polyarylethersulfone or polyvinylpyrrolidone dialyzers. At a variable time after 12 months patients were switched to an MCO dialyzer (Theranova; Baxter®). Forty patients who had been using the MCO dialyzer for at least 3 months were included in this analysis.

Results: Mean age, baseline SAF levels and time on MCO dialyzer were 63±13 years, 3.5±0.9 arbitrary units (AU) and 124±49 days, respectively. SAF increased significantly from baseline to 12 months (3.5±0.9 vs. 3.9±1.1 AU; $p<0.0001$) but tended to decrease between 12 and 24 months, after conversion to an MCO dialyzer (3.9±1.1 vs. 3.7±0.7 AU; p=0.06). Additionally, mean ΔSAF from baseline to 12 months was positive (0.41±0.68 AU) whereas ΔSAF from 12 to 24 months was negative (-0.18±0.76 AU; p=0.002 for comparison). Furthermore, SAF at 24 months correlated negatively and significantly with time on MCO dialyzer (r= -0.384; p=0.01) though second year ΔSAF (delta from 12 to 24 months) did not (r= 0.061; p=0.7).

Conclusion: We found in this observational study that SAF levels decreased/stabilised in HD patients after switching to an MCO dialyzer compared to the time when patients were using conventional high-flux HD and haemodiafiltration, during which SAF levels increased. Future prospective and interventional studies with larger sample sizes and longer follow-up are needed to confirm these findings and to evaluate the impact of using an MCO dialyzer on long-term outcomes, including survival.

P1079

NOVEL ULTRAFILTRATION RATE FEEDBACK CONTROLLER FOR ATTAINMENT OF RELATIVE BLOOD VOLUME TARGETS DURING HEMODIALYSIS

Lemuel Rivera-Fuentes[1], Leticia Tapia[1], Stephan Thijssen[1], Sabrina Rogg[1], Peter Kotanko[1]

[1]*Renal Research Institute, Clinical Research, New York, United States of America*

Background and Aims: Preciado et al. have identified half-hourly relative blood volume (RBV) targets (at 30, 60. . .180 min) during hemodialysis (HD) that are associated with significantly improved patient survival. Attainment of these RBV targets would necessitate incessant adjustments to the ultrafiltration rate (UFR) by the dialysis nurse, which is logistically not feasible. We developed a novel proportional-integral controller that takes RBV data from the commercially available CLiC® device as an input and provides UFR suggestions to guide the RBV curve into the desired targets. The clinician specifies the desired UF goal and the maximum allowed upward/downward deviation from this goal, and the Controller then optimizes the RBV trajectory within the limits allowed by the clinician's prescription. The present study is aimed to characterize the behavior of this novel feedback controller.

Method: We conducted a single-arm, prospective, interventional pilot study in subjects on chronic HD at three Avantus Renal Therapy Dialysis Centers in New York City. Subjects were treated with Fresenius 2008T HD machines. RBV was measured with the CLiC® device. CLiC® and HD machine data were fed into a research laptop running the UFR Feedback Controller software. The UFR recommendations (generated every 10 minutes) were evaluated by dialysis nurses who then either implemented or rejected them as they deemed clinically appropriate. The nurses were instructed to only override Controller recommendations if medically indicated, but not in an attempt to manage the subjects' RBV trajectories themselves.

Results: Fifteen subjects (58.9 ± 15.3 years, 33% white, 53% black, dialysis vintage 4.1 ± 2.4 years, baseline interdialytic weight gain 2.6 ± 0.8 L, treatment time 222 ± 28 min) were studied (63 study visits, 4.2 ± 1.9 visits per subject). Of 300 analyzed RBV target timepoints, 63% had RBVs within the desired target range, 33% of the RBVs were above and 4% were below target. Stratified by timepoint, the on-target percentage increased from 37% at 30 min to 73% at 180 min into HD, while the proportion of RBVs above or below target decreased. In subjects with at least 4 complete study visits (N=8), looking at each of their first 4 complete visits, on average 71.8% of subjects were within the desired RBV target at 180 min into HD. The rate of intradialytic morbid events did not appear to be outside of the ordinary. There was no indication of adverse events related to the use of the UFR Feedback Controller. The Figure shows an example study visit where the UFR Feedback Controller modulates the UFR on an ongoing basis throughout the treatment to keep the RBV curve close to the ideal target trajectory (red line, defined by connecting the RBVs associated with the lowest all-cause mortality). Solid black line: RBV curve (left y-axis); dashed black line: UFR (right y-axis); green boxes: half-hourly RBV target ranges associated with improved survival.

Conclusion: The UFR Feedback Controller behaves as expected, steering the patients' RBV curves toward the predefined target ranges where possible, while simultaneously guaranteeing that the prescribed fluid removal goal will be achieved. Preciado et al. had reported approx. one third of patients within the favorable RBV target range at 3h into HD. In contrast, while our pilot study was relatively small, with use of our novel UFR Feedback Controller, approx. 72% of subjects were within the desired RBV target range at 3h into HD. This novel UFR feedback control technology holds great promise for improving fluid management and clinical outcomes in HD patients without requiring additional staff time.

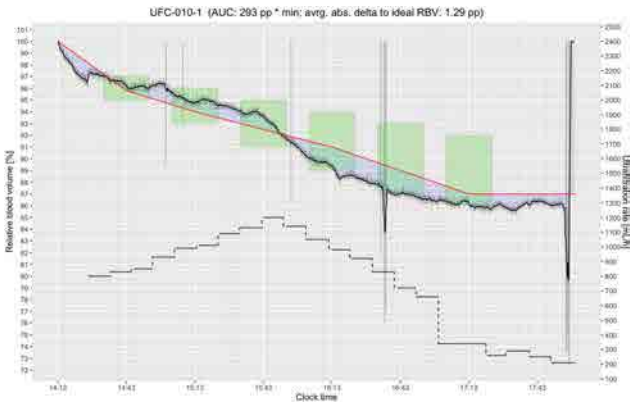


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P1080

INCREASE OF POST DIALYSIS HEMOGLOBIN CONCENTRATION IS MORE APPROPRIATELY EXPLAINED BY PLASMA VOLUME CHANGE THAN INTRADIALYTIC WEIGH LOST

Elena Babalj Banskolieva[1], Risto Grozdanovski[1], Katerina Spaseska Gjurovska[1], Marko Ilievski[1], Biljana Filipovska[1], Sasho Gelev[1], Angel Oncevski[1]

[1]*Special Hospital for nephrology and dialysis Diamed, dialysis, Skopje, Republic Of North Macedonia*

Background and Aims: It is well known that haemoglobin significantly increases after haemodialysis and it is associated with the rate of weight loss during dialysis. However, it has been shown that the increase in haemoglobin is not always proportional to the rate of body weight loss during haemodialysis (ultrafiltration). The purpose of the study was to investigate the correlation between haemoglobin changes, body weight loss and plasma volume changes during haemodialysis

Method: A prospective study was performed on 92 patients in mid-week treatments. Pre-dialysis and post-dialysis haemoglobin and weight were measured. 27 patients were excluded because clinical instability, no change or a decrease in Hb and low pre-dialysis haemoglobin (< 9 g/dL). The correlation was statistically significant between %ΔPV and ΔHb in both groups (R^2=0.59), whereas the correlation between %ΔBW and ΔHb was lower (R^2=0.19). So, analysis show that only 19% of the variability in haemoglobin is explained by %ΔBW, and that 59% of the variability in haemoglobin is explained by %ΔPV.

Results: The mean age was 61.16 ± 13.11 year. The men were 52 (56%). The mean pre-dialysis Hb was 11.31 ± 1.16 g/dL, the mean post-dialysis Hb level was 12.53 ± 1.47 g/dL. The mean absolute change of haemoglobin (ΔHb g/dL) and percent of change of haemoglobin (%ΔHb) were 1.22 ± 0.76 and 9.44 ± 5.31, respectively. Average percent of weight change (%ΔBW) was - 2.44 ± 1.01. Percent of plasma volume change was - 9.22 ± 5.46. The patients were divided in two groups according post-dialysis haemoglobin level: Group A with haemoglobin Hb $<$ 13 g/dL (64 patients) and group B with Hb $\geq$13 g/dL (28 patients).

The mean time average haemoglobin concentration (TAC Hb) in all patients was 11.68 ± 1.11 g/dL.(Predicted Hb TAC was calculated according Krisper′s formula)

In both groups there was an increase in %ΔHb, but in the group with post dialysis Hb $\geq$ 13 g/dL, %ΔHb was greater than in group B with post dialysis Hb $<$ 13 g/dL (13.08 ± 5.11 versus 7.87± 4.61, P = 0.000) despite the relatively small difference of %ΔBW between the two groups (- 2.85 ± 0.95 versus - 2.23 ± 1.02; P = 0.010). However, the difference in %ΔPV between the two groups was significant (- 12.90 ± 5.63 versus - 7.61 ± 4.57; P $<$ 0.000).

Conclusion: The intradialytic changes in haemoglobin levels are predominantly determined by changes in plasma volume. Changes in body weight are of little predictive value in evaluation of variation of haemoglobin levels. TAC Hb determination should be performed in patients with large variations in plasma volume, because the plasma volume has very little effect on TAC Hb.

Hb-post g/dL	%ΔBW	%ΔPV	Hb-pre g/dL	% ΔHb	TAC Hb g/dL	ΔHb g/dL
Group B ≥13.0 (n=28)	- 2.85 ± .95	-12.90 ± 5.63	12.50 ± 1.17	13.08 ± 5.11	12.98 ± .95	1.88 ± .76
Group A <13.0 (n=64)	-- 2.23 ± 1.02	- 7.61 ± 4.57	10.79 ± .68	7.95 ± 4.61	11.12 ± .57	0.93 ± .56

Figure: Changes of plasma volume, body weight, TAC Hb, percent of change of Hb and difference of pre- and post-dialysis haemoglobin. P $<$ .000 in both group for all comparisons, except for %ΔBW P = .010

P1081 DIALYSATE SODIUM ALLIGNMENT AND SODIUM SET-POINT STABILITY IN HEMODIALYSIS PATIENTS: TWO-YEAR OBSERVATION

Daria Matveeva[1], Roman Gerasimchuk[1,2], Anastasia Sabodash[3], Ara Grigoryan[1], Alexander Zemchenkov[1,2,3]

[1]City Mariinsky hospital, dialysis department, Saint Petersburg, Russia, [2]North-Western State Medical University named after I.I.Mechnikov, Internal diseases, clinical pharmacology and nephrology, Saint Petersburg, Russia and [3]Pavlov First Saint Petersburg State Medical University, department of nephrology and dialysis, Saint Petersburg, Russia

Background and Aims: The low dialysate sodium (NaD) reduces intradialytic weight gain (IDWG) and blood pressure (BP), which are associated with improved outcomes. However, the intervention probably also increases intradialytic hypotension and reduces serum sodium (NaS), that are associated with increased mortality risk, so NaD should be individualized and brought closer to NaS. Predialysis natraemia in hemodialysis (HD) patients is considered constant (set-point) but some observations contradict this statement. The significance of clinical parameters, dialysis parameters and body water distribution is not clear.

Method: We undertake the retrospective observation among 45 HD patients for 24 months before large-scale prospective intervention investigation for individualization of NaD. We used two-year routinely monthly fixed data: NaS, NaD, IDWG, frequency of intradialysis hyper- and hypotension and seizures, peri- and intradialysis BP, home BP estimates, clinically and by bioimpedance estimated dry weight, ultrafiltration rate, frequency and duration of HD sessions.

Results: We included 27 males and 18 females of 60 (34-83) years old, with median HD vintage of 63 (29÷93) months. 1048 NaS measurements revealed mean natraemia of 137.1±2.8 (Q5-Q95 132-141) mmol/l (corrected for glucose). No differences in mean NaS according to gender, age, HD vintage, cardiac or liver dysfunction and residual renal function were found. Intraindividual NaS mean varied from 132 to 141 mmol/l and median of coefficient of variation (CV) was 1.4% (1.2÷1.6) (range 0.9-2.0%) which could be attributed mainly to measurement accuracy. The intraindividual NaS Q10-Q90 did not exceed 6 mmol/l with its median 3.0 (2.7÷3.7). Among whole group we revealed slow decreasing NaD trend (-0.12 mmol/l per year, R?0.45) which was accompanied by more prominent trend in systolic BP (-3.3 mmHg/year, R?0.64) and diastolic BP (-1.6 mmHg/year, R?0.49). In parallel, the frequency of intradialytic hypotension increased by 1.6 episodes/100HD per year (mean 2.3±0.6 after excluding the trend). 33 patients (73%) showed no significant individual trend in NaS (<1 mmol/l per year) for 24 months, 8 (18%) demonstrated decreasing trend (mean -1.5 mmol/l per year) while only 4 (9%) - increasing trend (mean +1.6 mmol/l per year). We observed no trend in prescribed bicarbonate level in dialysate. There were no significant associations between intraindividual deviations from individual mean weight before HD and from mean individual NaS. In whole group, intraindividual variations in NaS had no link with mean NaS. We observed the significant variations in NaS only in patients with large CV of predialysis weight (Q90-Q10>5 kg over 2 years). Overall mean of sodium serum to dialysate gradient (NaG) was slightly positive (+0.15±3.0 mmol/l) while 58% of patients had negative or neutral NaG. The latter had lesser IDWG but no difference in intradialytic hypotension frequency. We evaluated the number of random consecutive monthly predialysis NaS need to get acceptable estimation of real mean two-year predialysis NaS: five values gave 94% hit in range -1÷ +1 mmol/l.

Conclusion: Serum sodium is stable over time in HD patients with the only exception of patients with large intraindividual predialysis weight variation. Pre-HD serum sodium may be used as a parameter for individualizing dialysate sodium prescription.

P1082

COMPARISON OF THE REMOVAL OF PROTEIN-BOUND TOXINS AND LARGE MIDDLE MOLECULES WITH HIGH-FLUX PMMA AND MEDIUM CUT-OFF DIALYZERS.

Pablo Molina[1,1,2], Julio Peiró[3], María Amparo Martínez-Gómez[4], Belén Vizcaíno[1,2], Mercedes Gonzã¡lez Moya[1,2], Cristina Esteller[3], Sandra Beltrán[1], Julia Kanter[1], Erika Pérez-Zafra[3], Silvia Alcover[3], Jonay Pantoja[1], Asunción Sancho Calabuig[1,2], Nuria Estañ[3], Mónica Climente[4], Luis M. Pallardó[1,2]

[1]Hospital Universitari Dr Peset, Department of Nephrology. FISABIO, Valencia, Spain, [2]Universitat de València, Department of Medicine, Valencia, Spain, [3]Hospital Universitari Dr Peset, Department of Clinical Analysis, Valencia, Spain and [4]Hospital Universitari Dr Peset, Department of Pharmacy. FISABIO, Valencia, Spain

Background and Aims: Dialytic clearance of protein-bound toxins and large middle molecules is poor by diffusive treatment and limited by high-flux hemodialysis (HD) and on-line hemodiafiltration (OL-HDF), and only a few studies have examined how to improve their removal by other extracorporeal strategies. Since 2017, there is a new generation of polymethyl methacrylate (PMMA) membranes that suppress platelet adhesion on the membrane surface improving hemocompatibility and permeability, while also maintaining adsorption properties related to conventional PMMA membranes. Expanded HD (HDx) with medium cut-off (MCO) membranes has also recently been incorporated into clinical practice and may improve the removal of uremic toxins in HD treatments. The aim of this pilot study was to compare the efficacy of a new high-flux PMMA dialyzer (Filtryzer® NF-2.1H) in a post-dilution OL-HDF session with a new MCO membrane (Theranova® 400) in a HDx session.

Method: In an open, cross-over, single-center, controlled, prospective clinical study, 40 adult stable HD patients were assigned to be treated by post-dilution OL-HDF with the NF-2.1H dialyzer or by HDx with the Theranova 400 dialyzer. All other dialysis parameters, including blood and dialysate flow rates, length of dialysis session, and ultrafiltration rate remained unchanged during both sessions. P-cresyl sulfate (PCS), indoxyl sulfate (IS), and kappa (κ) and lambda(λ) free light chains (FLC) reduction rates were intraindividually compared for the two dialyzer types (primary outcomes). Secondary outcomes included the kt and the reduction ratio of blood urea nitrogen, phosphate and β2 -microglobulin (β 2-m).

Results: The reduction ratio of protein-bound toxins ranges from 60% to 67%, with no differences between membranes (Figure). PMMA membrane achieved greater FLC reduction ratios than MCO membrane, reaching significance for λFLC (56.6% vs. 77.4%; $p < 0.001$). Conversely, β2M reduction ratio was slightly but significantly higher with MCO membrane (68.5 vs. 72.1%; $p = 0.002$). Small molecules removal including urea and phosphate were similar in both groups, achieving an optimal Kt with no differences between groups (61.3±9.2 Vs. 59.7±9.3; p=0.16). Albumin reduction ratio tended to be higher with PMMA membrane without reaching significance (10.1±5.9% Vs. 7.8±12.3%; p=0.17). The mean convective volume achieved with PMMA was 23.5±4.4 L.

Conclusion: This study suggested that new high-flux PMMA dialyzer in post-dilution OL-HDF mode might achieve better FLC reduction ratios than MCO dyalizer in HDx mode, whereas both techniques may equally remove protein-bound toxins. OL-HDF with new PMMA membranes could be a good dialysis strategy for adding convective transport to the well-known mechanisms of diffusion and absorption previously described with conventional PMMA membranes, enabling an adequate substitution volume.

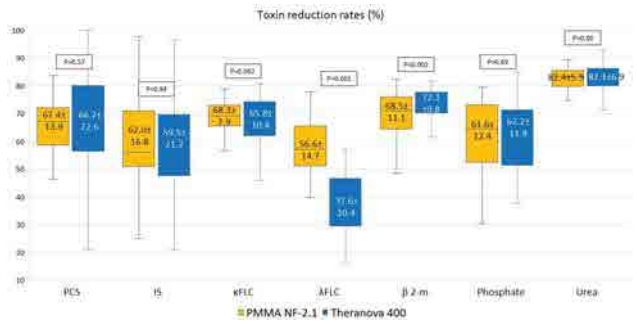


Figure:

P1083

A TRANSITIONAL REGIME OF INCREMENTAL HAEMODIALYSIS IN PATIENTS WITH END-STAGE RENAL DISEASE (ENDURE): A FEASIBILITY TRIAL

Adil Hazara[1,2], Victoria Allgar[2], Sunil Bhandari[1]

[1]Hull University Teaching Hospitals NHS Trust, Academic Renal Research, Hull, United Kingdom and [2]University of York, Hull York Medical School, York, United Kingdom

Background and Aims: Mortality rates are high in patients starting long-term haemodialysis (HD) therapy, particularly in the first 6-months. Incremental HD has been proposed as a means of making patients' transition into long-term HD treatment less physiologically demanding with reduced burden of treatment at the start. A feasibility study is being conducted with the primary aim of evaluating the acceptability, tolerance and safety of a novel incremental HD regime. The secondary aims are to study the effect of incremental HD on residual renal function (RRF), fluid load, quality of life, functional status, blood pressure and blood markers of renal anaemia, secondary hyperparathyroidism and cardiac load.

Method: The regime being tested aims to start patients on twice-weekly HD with progressive increases in the duration and frequency of sessions over approximately 15 weeks (figure 1). 40 patients from pre-dialysis clinics, who have been referred for start of long-term HD therapy, will receive the study regime (incremental HD group). They will be followed-up for 12 months.

Acceptability and tolerance will be gauged by documenting rates of participation and retention in the study. Completion rate of each study test will be recorded to evaluate the feasibility of their inclusion in a future trial; these tests include: 24-hour urine collection to measure RRF, bio-impedance analysis for estimation of overhydration, six-minute walk test to monitor performance status and a quality-of-life questionnaire.

Rates of pre-defined safety events will be recorded and compared to a cohort of 40 matched patients who previously started conventional HD (historical controls, conventional HD group). Blood tests for estimation of RRF and markers of renal anaemia, bone disease and cardiac load will be performed at regular intervals and compared to the conventional HD group.

Results: Eight months in to the 18-month recruitment period, 106 patients have been screened for participation in the trial. Of these, 47 (43%) met eligibility criteria. Reasons for exclusions were: patient choosing other dialysis modalities over HD, 34; clinically unsuitable for incremental HD, 7; dialysis modality undetermined, 6; already started HD, 5; for conservative (non-dialysis) management, 4; non-compliant with treatment, 3.

Of the 47 eligible patients, 35 have been approached by the study team. Of these, 16 (46%) have been consented, 10 (28%) declined and 9 (26%) remain undecided. Patients who consented were relatively older compared to those who declined (68 vs. 58 years) and to all eligible patients (68 vs. 63 years). Men were more likely to decline than women (M:F ratio 1.3 vs 4.0 among participants and decliners respectively). Not all study participants have started treatment yet. Baseline characteristics of the first 6 patients starting incremental HD and their matched controls are shown in table 1.

Table 1: Baseline demographic characteristics and laboratory values of the first 6 active participants and their matched controls (AVF, arteriovenous fistula; HDF, haemodiafiltration)

	Active (n=6)	Control (n=6)
Age, median (range)	70 (66-81)	70 (65-80)
% Male	83%	83%
Diabetes	33%	33%
AVF Vascular access type	100%	100%
Modality	HDF	HDF
Laboratory values		
eGFR (mL/min/1.73m^2)	9.2	8.8
Haemoglobin (g/L)	104.7	96.0
Albumin (g/L)	32.7	32.3
Adjusted Calcium (mmol/l)	2.3	2.4
Phosphate (mmol/l)	1.7	1.8

Conclusion: The ENDURE study tests the feasibility of starting patients on a novel incremental HD regime. This regime is relatively short and has fixed increments in treatment times. It aims to make patient transition smoother in to dialysis dependency. Early data point towards an encouraging levels of patient interest in the study. The outcome of this trial will be used to design a future RCT of incremental HD vs. conventional treatment.



Figure 1: The ENDURE study incremental HD regime

P1084 LONG TERM EVALUATION OF THE EXPANDED HEMODIALYSIS (HDX) ON DIALYSIS ADEQUACY, ANEMIA AND QUALITY OF LIFE

Giuseppe Gernone[1], Francesca Partipilo[1], Francesco Detomaso[1], Vito Pepe[1], Stefania Pietanza[1], Adele Mitrotti[1]

[1]*"S. Maria degli Angeli" and "S. Giacomo" Hospital, Nephrology and Dialysis, Putignano-Monopoli, Italy*

Background and Aims: The High-Flux (HF) dialyzer in standard hemodialysis (HD) allow the removal of a wider spectrum of uremic toxin. However, the HD can remove mostly low molecular weight solutes while the HDF can remove solutes around 15kDa, so-called Middle Molecules (MM), improving morbidity and mortality by exchange volumes >23L per session. The new medium cut-off (MCO) filter Theranova® is designed to expand the removal of toxins up to 45kDa in HD compared to HF membranes (HemoDialysis eXpanded, HDx) even with conventional blood flows and without exchange fluid infusion. The aim of this study is to evaluate the performance of HDx and its impact on anemia and quality of life (QoL) in haemodialysis patients.

Method: 11 stable HDs patients were enrolled (M/F 8/3, age 70.8±9) with Qb ≤300 ml/min in a 12 months observational case-control study. Each patient was evaluated first with HF filter (T0) and then in HDx for 12 months (T12). At T0-T6-T12 were evaluated: urea, phosphate (P), beta2-microglobulin (B2m), myoglobin (Myo), free light-chains k and λ (FLC- K and FLC- λ), C-Reactive Protein (CRP), hemoglobin (Hb) and albumin as well. Furthermore Kt/V, dose of EPO, ERI and SF-36 questionnaire were evaluated at the beginning and end of observation. We treat HD patients accordingly to the KDIGO Guideline for Anemia in CKD. The values have been reported as mean ±SD.

Results: HDx (Qb = 275 ± 41 ml/min, TT 215 ± 21 m) shows a significant increase in KT/V (T0 1,33 ± 0,19; T12 1,57 ± 0,16; p = 0.001) with relevant RR of: Urea 73.5%; P 58.4%; B2m 66,1 % (p< 0.05); Myo 55,1% (p< 0.05); FLC-k 64.1 % (p< 0.05); FLC-λ 59.9% (p< 0.05). There is a significant reduction at 12months for PCR (Tab.1). HDx reduced ERI [T0 10.1 ± 11.2; T6 4.1 ± 5.3 (p <0.05); T12 6±9.8] and EPO dose [T0 8182 ± 9141; T6 3545 ± 4547 (p <0.05); T12 5273±8912], keeping the Hb unchanged. QoL is significantly improved (ISF: T0 27.3 ± 10.1; T12 40.2 ± 8.4 p = 0.0001) (ISM: T0 43.8 ± 14.2; T12 51.1 ± 9.8 p = 0.001).

Conclusion: HDx effectively removes uremic toxins up to 45kDa, even with Qb <300 ml/min, without reducing serum albumin and with interesting results on inflammation. Reduction of ERI and improvement of QoL are encouraging and suggest the use of HDx even in patients who cannot benefit from convective techniques because of vascular access or intolerance to high volumes of exchange.

Months	Kt/V	RR Urea (%)	RR Fosfati (%)	RR B2m (%)	RR Myog (%)	RR FLC k (%)	RR FLC λ (%)	PCR mg/l	Hb g/dl	Albumin g/dl
T0	1,33	68,2%	48,1%	46,3%	24,9%	35,2%	25,1%	13,6±14,4	11,7±1,2	3,1±0,4
T6	1,61 *	74,1%	58,2%	63,0% *	52,5% *	62,2% *	61,1% *	5,8±4,9	12,2±0,9	3,2±0,3
T12	1,57 *	73,5%	58,4%	66,1% *	55,1% *	64,1% *	59,9% *	4,5±2,8*	12,2±0,9	3,3±0,3

Figure: Tab. 1 (Values of parameters examined in the study ; * p<0.05)

P1085

EFFECT OF INTRAVASCULAR FLUID REMOVAL ON THE RATE OF CHANGE OF THE INFERIOR VENA CAVA DIAMETER, EARLY DIASTOLIC MITRAL VALUE INFLOW AND NUMBER OF LUNG ECHO B-LINES IN HEMODIALYSIS PATIENTS

Shigeru Otsubo[1], Katsuya Kajimoto[2]

[1]Tohto Sangenjaya Clinic, Blood Purification, Tokyo, Japan and [2]Sekikawa Hospital, Cardiology, Tokyo, Japan

Background and Aims: In hemodialysis therapy, intravascular fluid is removed first. As intravascular water is removed, the circulating serum protein concentrations increase, resulting in a marked increase in the driving force which pulls water from the extravascular space into the blood vessels, by a process called plasma refilling. We examined the effect of total fluid removal and intravascular fluid removal as estimated by the change of the hematocrit value during dialysis on the rate of change of the inferior vena cava (IVC) diameter, early diastolic mitral valve inflow (E wave), and lung echo B-lines.

Method: We enrolled 59 patients under maintenance hemodialysis for this study. Lung ultrasound was performed at the first session of the week. Bilateral scanning of the anterior and lateral chest walls was performed with the patient in a supine position. The chest wall was divided into 8 areas (2 anterior and 2 lateral areas per side), and 1 scan was obtained for each area. The total number of B-lines was estimated. Echocardiographic measurements were obtained at the same time and the IVC dimensions and E wave were estimated. We performed each ultrasound examinations at two time-points (just after the start and just before the end of the hemodialysis therapy). We then investigated the rate of change ((post-pre)/post) of the IVC diameter, E wave, and number of B-lines. A peripheral blood sample was obtained before and after the hemodialysis session and the hematocrit was measured. We estimated the intravascular fluid volume as pre body weight /13, and estimated intravascular fluid removal as (post hematocrit – pre hematocrit)/post hematocrit x estimated intravascular fluid. We also defined estimated extravascular fluid removal as total fluid removal – estimated intravascular fluid removal. We investigated the relationship between the total, intravascular and extravascular fluid removals and the rate of change of the IVC diameter, E wave, and number of B-lines.

Results: The rate of change of the IVC diameter was negatively related to the estimated intravascular fluid volume (r=-0.285, P=0.033), but not to the estimated extravascular fluid or total fluid removal. The rate of change of the E wave was negatively related to the estimated intravascular fluid volume (r=-0.422, P=0.001), and the estimated extravascular fluid (r=-0.369, P=0.006) and total fluid removal (r=-0.419, P=0.002). Among these, the rate of change of the E wave was most closely related to the estimated intravascular fluid volume. The rate of change of the number of B-lines was not associated with the estimated intravascular fluid volume, but was negatively correlated with the estimated extravascular fluid (r=-0.368, P=0.005) and total fluid removal (r=-0.353, P=0.008). The estimated extravascular fluid removal was the most closely related to the rate of change of the number of B-lines.

Conclusion: The rates of changes of the IVC diameter and E wave were strongly associated with the estimated intravascular fluid removal, whereas the rate of change of the number of B-lines was correlated with estimated extravascular fluid removal. The E wave represents the flow to the left ventricle, which occurs after left ventricular diastole, reflecting the preload status. The IVC dimensions are strongly associated with the right atrial pressure and blood volume and therefore reflect the intravascular volume. Therefore, both the E wave and the IVC diameter may represent the intravascular fluid volume. On the other hand, the number of B-lines has been reported to be correlated with the amount of extravascular lung water. Our results were consistent with these reports.

P1086 **REVERSE INCREMENTAL HEMODIALYSIS IS A GOOD METHOD FOR SETTING DIALYSIS DOSE CONSIDERING THE INDIVIDUAL RESIDUAL RENAL FUNCTION**

TOSHIMASA TAKAHASHI[1,2], Yoshie Kanazawa[2], Toshiyuki Nakao[2]

[1]Bosei Shinjuku Minamiguchi Clinic, Department of Nephrology, Tokyo, Japan and [2]Organization for Kidney and Metabolic Disease Treatment, Research Department, Tokyo, Japan

Background and Aims: We previously reported on Planned Incremental Hemodialysis (PIHD) for patients with good adherence to a prescribed diet and consideration of residual renal function (RRF), and some reports have been suggested that IHD in ESRD patients may have a positive effect on survival rates and RRF. On the other hand, the ESRD patients are commonly started on thrice-weekly HD at hospitals in Japan. However, and interestingly, careful observation of our ESRD patients whose CKD was gradually increased, and in some cases, we detected some recovery of their RRF. If there is RRF, IHD can be performed and potentially reduce dialysis frequency. We named this method "Reverse Incremental Hemodialysis (RIHD)."

Method: One hundred thirteen patients who were started on thrice-weekly HD in other hospitals and who had been referred to our clinic since 2013, we selected 11 patients (9 males and two females) on the basis of their laboratory data and careful physical examination. The number of patients by the causes of their ESRD is as follows: 3 patients with Chronic glomerulonephritis, two patients with Nephrosclerosis, one patient with Diabetic kidney disease, one patient with Polycystic kidney disease, one patient with Chronic interstitial nephritis, one patient with Interstitial nephritis, one patient with Nephrotic syndrome, and one patient with Fabry disease. In order to reduce the number of dialysis sessions for patients, we considered the following laboratory data were required to be within the control standards before dialysis at the maximum dialysis interval, as follows: BUN<100mg/dL, serum creatinine<20.0 mg/dL, K<5.5mEq/L, HCO3->20.0mmol/L, respectively. To avoid over-volume, we also restricted the patient's weight gain as the Once-weekly HD patient is within 3.0 kg/week, and Twice-weekly HD patient is within 6.0 kg/week. We also checked physical examination and X-rays, if necessary, we sometimes checked the patient's hANP. We also considered the dialysis volume evaluated like Peritoneal Dialysis (PD) such as weekly Kt/V urea above 1.7 together with RRF as an appropriate dialysis volume.

Results: The average dialysis duration of 11 patients was 35.2 months (M) as 5-97M. Eight patients were able to reduce their HD from thrice-weekly to twice-weekly HD, and the average dialysis duration was 9.9M (1-32M). Three patients gradually reduced from thrice-weekly to once-weekly HD, and their average dialysis duration was 26.3M (10-37M). Eight patients who reduced their number of HD to twice-weekly HD, the average RRF weekly Kt/V urea was 0.10, actual HD weekly standardized (std) Kt/V urea was 1.37 and total weekly Kt/V urea was 1.47. Three patients who decreased their number of HD to once-weekly HD, the average RRF weekly Kt/V urea was 0.83, actual HD weekly std Kt/V urea was 0.56, and total weekly Kt/V urea was 1.39. Two patients (18.2%) had exceeded their weekly weight restriction, but no one had clinical symptoms of over-volume such as hypoxia, pulmonary edema, and pleural effusion. The laboratory data that we considered to be within the control standards before dialysis at the maximum dialysis interval was respected as 97.8% (11patients' BUN, s-Cr, K, and HCO3- laboratory datas:43 out of total 44 points) were observed. Their total weekly Kt/V urea data were lower than that of the weekly Kt/V urea recommended for PD patients, but our patient's clinical status was within a controllable range.

Conclusion: Some patients can gradually reduce the number of dialysis sessions with careful follow-up with considered their RRF and total weekly Kt/V urea, and setting weight gain limits individually. We still need to consider adjusting the treatment of total weekly Kt/V urea, as indicated by PD treatment recommendation for their prognosis. However, RIHD is a flexibly responds to insufficient renal function for RRT individually and might be suitable for QOL and cost-effective treatment for some ESRD patients.

P1087 **HOME HEMODIALYSIS THROUGH THE YEARS**

Verica Todorov Sakic[1], Zivka Djuric[1], Petar Djuric[1], Ana Bulatovic[1], Jelena Tosic Dragovic[1], Radomir Naumovic[1,2], Nada Dimkovic[2]

[1]Zvezdara University Medical Center, Clinical Department for Renal Diseases, Belgrade, Serbia and [2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia

Background and Aims: Outcome of dialysis patients differ considerably across the globe and many studies confirmed that home-based treatments offer some advantages, not only in regard of quality of life but also regarding of patients' outcome. History of home hemodialysis (HOHD) in our country dates from 1971. and since that time many patients were treated with this dialysis modality. HOHD changed over the time together with general improving of dialysis techniques and we aimed to analyze the results of treatment of our population treated by HOHD during different time points.

Method: We analyzed patients characteristics, dialysis and uremia-related complications and survival of patients on HOHD during three different time points: 2001. (No=70), 2011. (No=29) and 2019. (No=22).

Results: The most frequent reason for ESRD in 2001, 2011 and 2019. was glomerulonephritis (48%, 45%, 36% respectively), followed by polycystic kidney disease 24% in 2011. and 36% in 2019. Diabetes mellitus (DM) was rarely cause of ESRD: in 2001. 2.1%; 4.5% in 2019. and none in 2011. In 2001. the patients were more frequently treated using high flux membranes (HF) as compared to HDF (87.1% vs.12.9%), and through years this changed in favor of HDF (48% vs. 52% in 2011, and 13.6% vs. 86.4% in 2019). Anti HCV prevalence was 27.4%, 38%, 27%, in 2001, 2011. and 2019. respectively. Anemia status was better controlled in recent years revealed by Hb level: 10.5±2.0 g/dl in 2001, 12.1±1.6 in 2011. and 11.9±2.3 in 2019. with almost similar percentage of patients treated with ESA (31%, 28% and 36% respectively). In 2001, parathyroid hormone level (iPTH) was 379±236 pmol/l and only 20% of patients underwent parathyroidectomy while in 2011. and in 2019. parathyroidectomy was performed in 69% and 59% of patients respectively. Therefore, in 2011. and in 2019. mean iPTH level was 33.8±48.5 and 40±46.2pmol/l respectively. Kaplan-Mayer analysis confirmed ten-year survival of 42% for period 1982-2001, and the most frequent reasons for death were infection and cardiovascular diseases. During the period 2011. to 2019., ten-year survival was 88% and cardiovascular diseases led to death in most of the cases.

Conclusion: our results have shown that HOHD treatment improved through the years considering patients' survival, anemia status and secondary hyperparathyroidism treatment. Apart from HDF, the other factors have to be taken into consideration.

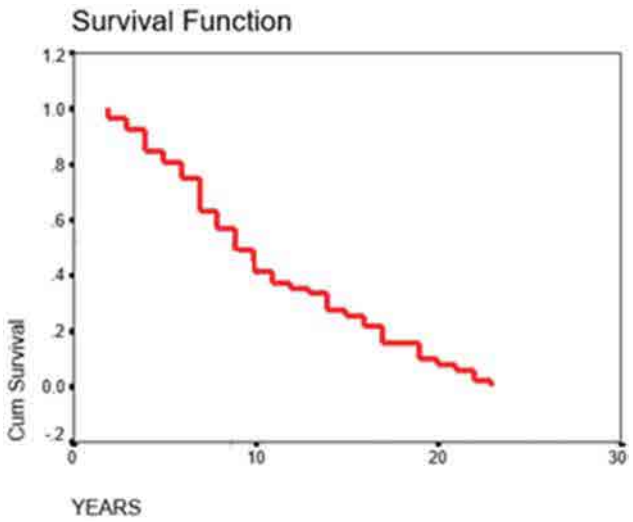


Figure 1. Kaplan-Mayer survival analysis of patients on Home-HD (1982-2001)

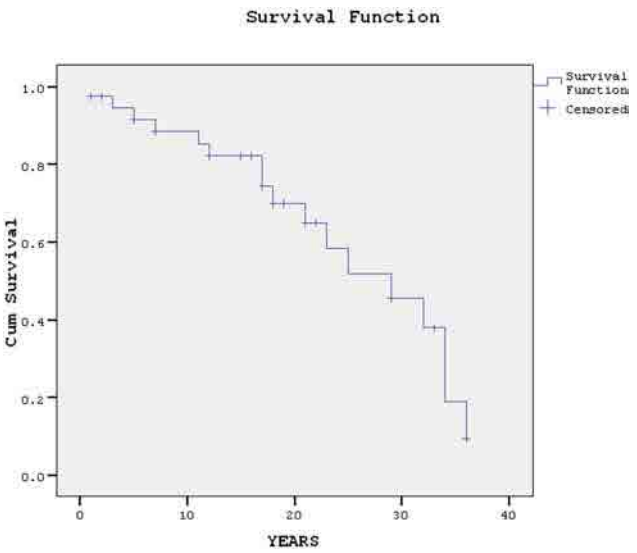


Figure 2. Kaplan-Mayer survival analysis of patients on Home-HD (2011-2019)

P1088 **BRAND NEW METHOD TO CALCULATE THE VOLUME OF EXTRA CELLULAR FLUID IN HEMODIALYSIS PATIENT ONLY FROM REGULAR BLOOD TEST**

Kazuhiko Shibata[1], Shigeru Nakai[2], Ikuto Masakane[3], Takahito Ito[4], Kiyoshi Ozawa[5], Kanenori Maeda[6], Teppei Matusuoka[7], Takahiro Shinzato[8]

[1]Yokohama Minami Clinic, Yokohama, Japan, [2]Fujita Health University, [3]Yabuki Hospital Group , [4] Kataguilli Medical Center, [5]Yokosuka Clinic, [6]Maeda Clinic, [7]Ogaki Kita Clinic and [8]Daiko Medical Engineering Research Institute

Background and Aims: Uric acid is a small molecule with molecular weight 168, but has an electrical pole which enables pass through the phospholipid bilayers of cell membranes by simple diffusion. Urate transport proteins of cell membranes (URAT1, GLUT9, OAT, MRP4, MCT9, NPT4, ABCG2) are expressed only in uric acid-excreting tissues. These findings suggest that uric acid does not pass through the cell membrane, either by diffusion or active transport. Since uric acid does not pass through cell membranes, the uric acid distribution volume (UDiV) would reflect the extracellular volume (ECV). At ASN 2018, we reported that UDiV significantly correlated with ECV predicted by the bio-impedance method measured by InBody, *S* 20 (Biospace Co., Ltd, Korea). However, both data were correlated, there was a large fixed error. This time, we examined the correlation with the UDiV again using the Fresenius BCM (Fresenius Medical Care, Bad Homberg, Germany), which is trusted worldwide.

Method:

1. Calculation of UDiV

We calculated UDiV from regular blood test results by uric acid kinetic modeling.

1. Study design

This study was performed in Yokohama Minami Clinic. One hundred nine patient under hemodialysis was consented and enrolled in this study. The HD patients were 59males and 50females. 68.0±10.9years old.

We performed UDiV calculation from blood samples obtained before and after hemodialysis. Then, after the hemodialysis session, 30minutes interval was made to measure the BIA-ECV using BCM. Then, we compared UDiV with BIA-ECV .

1. Statistics

We used least squares regression analysis and Bland–Altman analysis to compare the UDiV method and the BIA-ECV method, and the Steel test for multiple comparisons of UDiV and symptoms. All analyses were performed using JMP 9.0.2 (SAS Institute, Inc., Cary, NC, USA).

Results: There was a significant correlation between UDiV(x) and BIA-ECFV (y): ($y = 0.70x + 3.02$, r-square = 0.61, $p < 0.0001$, Figure 1a). The regression line closely coincided with the line of identity. Bland–Altman analysis showed a systematic error for UDiVvs. BIA-ECV (Figure 1b). There was a significant difference between UDiVand BIA-ECV (mean difference 1.32 L, 95% CI -2.6 to 5.2 L).

Conclusion: UdiV could be a viable alternative marker of BIA-ECV for the assessment of hydration status of patients with HD.

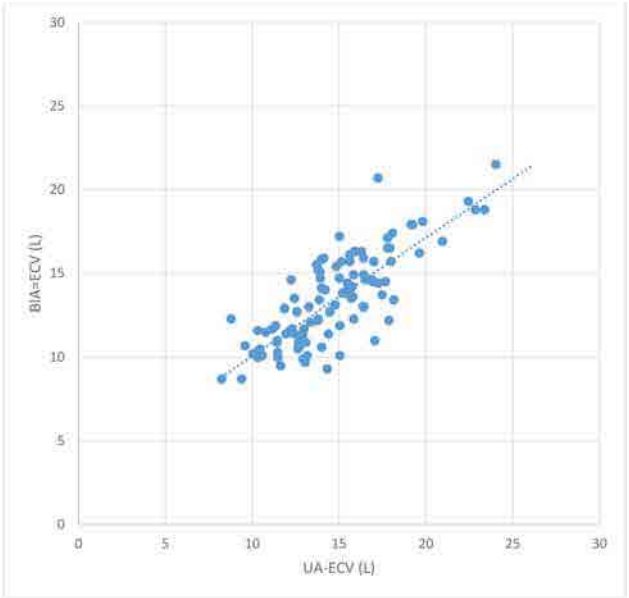


Figure: Scatter plot of UDiV(x) and BIA-ECFV (y)

P1089

REGIONAL CITRATE ANTICOAGULATION VERSUS LOW MOLECULAR WEIGHT HEPARIN ANTICOAGULATION FOR CONTINUS VENOVENOUS HEMOFILTRATION IN PATIENTS WITH SEVERE HYPERCALCEMIA: A RETROSPECTIVE CASE-CONTROL STUDY

Shiren Sun[1], Ming Bai[1,1,1], Yan Yu[1], Wei Zhang[1], Yangping Li[1]

[1]*Xijing Hospital, Fourth Military Medical University, Nephrology, Xi'an,*

Background and Aims: Severe hypercalcemia, poor conservative treatment effect, or combined with renal dysfunction, heart failure, intermittent hemodialysis treatment is recommended. But calcium-free hemodialysis could cause rebound of serum calcium, hypovolemia and hypotension. Continuous renal replacement therapy (CRRT) is the most commonly used treatment in critically ill patients with severe AKI. Some case reports showed that CRRT successed control calcium with stable hemodynamics, no rebound hypercalcemia, but there was only one case used continuous venovenous hemofiltration (CVVH). During CVVH treatment, clotting in the extracorporeal circuit shortens the filter and catheter lifespan, causes blood loss, and decreases solute clearance, consequently, reduces the effectiveness of CVVH and increases the treatment cost and medical stuff's workload. So how to safely decrease calcium level and how to choose appropriate anticoagulants during CVVH in esvere hypercalcemia patients is a challenging work. We conducted a retrospective study to evaluate the efficacy and safety of regional citrate anticoagulation (RCA) versus low molecular weight heparin (LMWH) anticoagulation for CVVH in severe hypercalcemia patients.

Method: Between January 2014 and May 2019, severe hypercalcemia patients requiring CVVH were screened and divided into the RCA and LMWH-anticoagulation group according to the CVVH anticoagulation strategy they accepted. Serum calcium reduction rate (RRSeCa), filter lifespan, bleeding, totCa/ionCa ratio, citrate accumulation, and catheter occlusion were evaluated as outcomes.

Results: Of the 33 included patients, RCA and LMWH-anticoagulation were employed for CVVH in 14 and 43 filters, respectively. The serum calcium reduction rate (RRSeCa) was not significantly different between the LMWH-anticoagulation and RCA group (P = 0.320). Compared to LMWH-anticoagulation, RCA significantly prolonged the filter lifespan (> 72 hours vs. 24.0 hours [IQR, 15.0-26.0], P = 0.012). The incidence of filter failure was 55.8% (24/43) in the LMWH -anticoagulation group and 21.4% (3/14) in the RCA group (P = 0.033), respectively. The adjusted results demonstrated that RCA could significantly reduce the risk of filter failure (P = 0.028, 95% CI 0.076-0.859, HR = 0.255). No citrate accumulation was observed in RCA-CVVH patients.

Conclusion: In patients with severe hypercalcemia who underwent CVVH, both RCA CVVH and LMWH-anticoagulation CVVH could effectively decrease calcium levels. RCA CVVH had better filter lifespan and no obvious adverse events, compared with the LMWH-anticoagulation CVVH. Further prospective, randomized, control studies are warranted to obtain robust evidences.

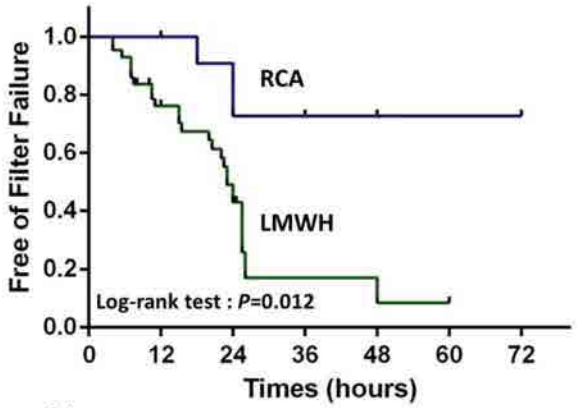


Figure: Survival curves of the filters with the use of RCA versus the filters with the use of LMWH-anticoagulation in the cohort.

P1090 DETERMINATION OF ABSOLUTE BLOOD VOLUME USING ONLINE DIALYSATE DILUTION: WHEN SHOULD BE MEASURED?

Susanne Kron[1], Daniel Schneditz[2], Til Leimbach[3], Joachim Kron[3]

[1]Charite - Universitätsmedizin Berlin, Department of Nephrology and Internal Intensive Care Medicine, Berlin, Germany, [2]Medical University Graz, Otto Loewi Research Center, Graz, Austria and [3]KfH Kidney Center, Berlin-Köpenick, Berlin, Germany

Background and Aims: Current on-line haemodiafiltration (HDF) machines equipped with a blood volume monitor (BVM) and an on-line bolus function have the potential for measuring absolute blood volume (aBV). Recently, we developed a simple method to determine absolute BV in everyday dialysis sessions. The aim of the present study was to evaluate the reproducibility of measurements.

Method: Intra-individual reproducibility was studied in 10 patients during a single dialysis session by 4 measurements of absolute BV: immediately after beginning before ultrafiltration (UF) was started, and after one, two and three hours.

ABV was determined by indicator dilution. A defined volume bolus of 240 mL dialysate was infused into the venous blood line by pressing the emergency button of the HDF machine 5008 (FMC). For this reason, total UF volume was increased by 1L. UF was automatically stopped during and after the infusion. The resulting increase in relative blood volume (RBVpost-RBVpre) was measured by the ultrasonic relative BVM incorporated in the dialysis machine. ABV was measured in hourly intervals and for assessment of reproducibility the volume at treatment start (t=0) where RBV is 100% was calculated for all measurements as:

aBV in mL = bolus volume 240 mL x 100% / increase RBV in %

ABV data were normalized for body mass at dry weight (in mL/kg).

Additionally, in 5 patients the RBV graph was monitored immediately at the beginning of dialysis without UF in a separate dialysis session.

Results: ABV at t=0 were consistently larger when calculated from measurements done immediately after the beginning compared to measurements obtained after 1 h (6.52 $\pm$ 1.40 L or 80.6 $\pm$ 14.5 mL/kg vs. 5.16 $\pm$ 1.40 L or 63.9 $\pm$ 14.3 mL/kg). Specific BV derived from 2 and 3 h measurements did not significantly differ from the measured volumes after 1 hour (61.4 $\pm$ 13.8 mL/kg, and 60.9 $\pm$ 13.9 mL/kg). The standard deviations of the 3 examinations in the same study patient during a further course of dialysis were between 0.6 and 5.3 ml/kg (ø 2.6 ml/kg).

In a separate session, RBV decreases without UF at the beginning of dialysis in the first 3 minutes by 0.5 % and in 5 minutes by 0.6 %.

Conclusion: If BV is diluted by additional priming volume and bolus volume, a part of this volume will leave the circulation. This represented the time frame where the bolus was initially infused and the measurements were carried out. This loss is caused by the reduction in plasma colloid osmotic pressure induced by the dilution thereby changing the microvascular filtration equilibrium. The increase in RBV display is not solely caused by the bolus volume in this time and, and therefore, calculated BV would be overestimated by about 17 mL/kg.

If measurement is performed at a later time, UF will take place and, consequently, refilling. This inward drive matches the outward bolus escape as a counterforce. BV measurement during a further course of dialysis is well reproducible with a deviation of only $\pm$ 2.6 ml/kg. The method would therefore be sufficiently precise in clinical practice. Therefore, we propose the determination of aBV only after 1 hour dialysis when a sufficient refilling takes place. With a software modification, the BV measurement could be routinely automated during each dialysis treatment. Manufacturers are asked to implement this technology in their devices.

P1091 DYNAMICS OF VASCULAR REFILLING IN EXTENDED NOCTURNAL HAEMODIALYSIS

Susanne Kron[1], Daniel Schneditz[2], Til Leimbach[3], Joachim Kron[3]

[1]Charite - Universitätsmedizin Berlin, Department of Nephrology and Internal Intensive Care Medicine, Berlin, Germany, [2]Medical University Graz, Otto Loewi Research Center, Graz, Austria and [3]KfH Kidney Center, Berlin-Köpenick, Berlin, Germany

Background and Aims: Refilling volume had not been a measurable parameter in clinical practice so far, because the knowledge of absolute blood volume (BV) is necessary. Recently, we developed a simple method to determine absolute BV, thus enabling quantification of the refilling volume. The overnight dialysis is particularly suitable for studying the refilling process due to negligible external influences and the extended treatment time.

Method: At the beginning of the dialysis (t=0), before starting the ultrafiltration (UF), a defined online bolus of 240 ml dialysate was infused by pressing the emergency button on the haemodiafiltration (HDF) machine (5008, FMC). The subsequent increase in relative BV (RBVpost-RBVpre) was measured with the integrated BV monitor, and absolute BV at t=0 was calculated:

absolute BV in ml = bolus volume 240 ml x 100% / increase in relative BV in%.

Absolute BV at any other time t was calculated as: $V_t = V_0 \times RBV_t$ (in %) / 100

At constant UF rate refilling volume (Vref) is given for every hour (h) as:

$Vref_h = UFV_h$ – drop in absolute $BV_{h\ (beginning - end)}$

The refilling fraction is expressed as refilling/UF ratio:

Ref% = Vref/UFV x 100, in %

Before treatment, volume overload was evaluated by bioimpedance spectroscopy (BIS) using the body composition monitor (FMC).

Results: Refilling volume and refilling fraction were studied in 10 stable chronic haemodialysis (HD) patients during an extended (7 hour) nocturnal HD session. Specific BV at treatment start was 74.9 ± 11.8 mL/kg and dropped to 68.6 mL/kg at dialysis end. The constant UF rate was set to 406 ± 120 mL/h (specific UF rate 4.81 ± 1.83 mL/kg/h). In the first hour refilling volume amounted only to 23% of UF volume. Refilling fraction reached its maximum in the 2nd, 3 rd and 4th hour at about mean 90% (91.5%, 88.7%, and 91.1% respectively) of UF volume. From the 5th hour on, refilling volume and refilling fraction decreased (5th hour 81.3%, 6th hour 72.5%, and 7th hour 70.0% of UF volume). In the 5th hour, cumulative UF volume exceeded volume overload (1.1 ± 1.0 L) measured by BIS in 9 of 10 patients. Refilling fraction cumulatively increased up to the 4th hour. Thereafter, cumulative ratio remained constant at 70 – 75% due to the decrease in refilling volume. This did not change during the further course of dialysis. Cumulative refilling volume showed a strong correlation ($r^2 = 0.88$; $p<0.001$) with UF volume.

Conclusion: After the first hour, when sufficient refilling takes place, refilling volume is in a stable ratio of approximately 90 % of UF volume. Refilling is low in the first hour, and, therefore, refilling volume amounted cumulatively only about 70 to 75% of UF volume during usual dialysis duration. Thereby, absolute BV will be reduced by approximately 250 to 300 ml per liter UF. This must be taken into account in volume management in order to avoid intradialytic complications.

As expected, refilling decreases when volume overload in the interstitial space is removed. Due to the reduced refilling, there will be an additional gap in BV.

P1092 **THE ENVIRONMENTAL IMPACT OF DISPOSABLES IN A NEW CONFIGURATION OF HEMODIALYSIS (HD) SYSTEM**

Carlo Alberto Lodi[1], Marcello Malagoli[2], Maurizio Gilioli[1], Roberta Bandini[3], Nicolas Goux[4]

[1]BAXTER GAMBRO DASCO S.P.A, System Support, San Giacomo Roncole, Italy, [2]BAXTER GAMBRO DASCO S.P.A, Bloodlines R&D, San Giacomo Roncole, Italy, [3]Baxter SPA, Marketing EMEA, Roma, Italy and [4]Baxter, Global Marketing, Meyzieu, France

Background and Aims: A new configuration of **Artis** Dialysis System, namely **Artis Physio Plus** (AP+), has been recently released for chronic HD market.

The AP+ Dialysis System features 3 stationary ultrafilters integrated in the hydraulic flow path and designed to retain bacteria and endotoxins, in order to provide fluid suitable for infusion to be used for on-line hemodiafiltration (HDF), hemofiltration (HF) or on-line bolus, priming and rinse-back also in HD.

With this new fully internal filtration process, no external single-use filter is needed on the infusion lines, resulting in a simplified configuration of the extra-corporeal circuit (EC).

HD has a considerable environmental impact because it uses large volumes of water, energy and medical supplies, and hence a significant amount of waste is produced. The aim of this study was to provide a comparison of the plastic waste amount between the previous Artis Dialysis System configuration (i.e., **Artis Physio**, AP) and the new one (AP+).

Method: The weight of the EC components (i.e., the blood tubing set, the related infusion lines for HD or HDF/HF and the dialyzer) after their discharge from dialysis machine was measured. In particular, the EC components for AP includes the Ultra Prime Line for HD (Fig. 1a) and Ultra HDF Line for HDF/HF in Pre or Post dilution (Fig. 2a). The EC components for AP+ includes the ULTRALINE HD for HD (Fig. 1b) and ULTRALINE HDF for HDF/HF in Pre or Post dilution (Fig. 2b).

For simplicity, the same blood tubing set (**ArtiSet** PrePost) has been assumed for all treatment types. The dialyzers used were **Revaclear** 400 for HD and **Polyflux** 210H for HDF/HF.

Other plastic waste, like concentrates and disinfectant cartridges, were not considered since their consumption is the same for AP and AP+.

Results: Table 1 shows the weight of the EC components before (i.e., components dry) and after dialysis (i.e., after patient rinse-back and automatic draining by AP/AP+).

Table 2 reports an estimation of the total weekly amount of plastic waste for a single Artis Dialysis System performing 3 shifts a day with a mix of different dialysis treatments (i.e., 60% of HD, 30% of HDF Post, 10% of HDF/HF Pre).

The results show a significant decrease of the disposable waste weight.

Conclusion: The new AP+ infusion lines, dealing with the ready to use infusion fluid delivered from the machine, are much simpler: this leads not only to a significant usability improvement, but also to a better shipment packing factor for the goods, a better storage in the dialysis unit, and a reduction of plastic waste. In particular, a weight decrease of 10.2% is achieved considering the EC items used on a single Artis Dialysis System during a week. Higher reduction of plastic waste will be achieved in clinics running higher number of HDF treatments.

This contributes to have a more eco-friendly dialysis and to reduce the expenditures for the hospitals, both in terms of goods delivery and of waste disposal.

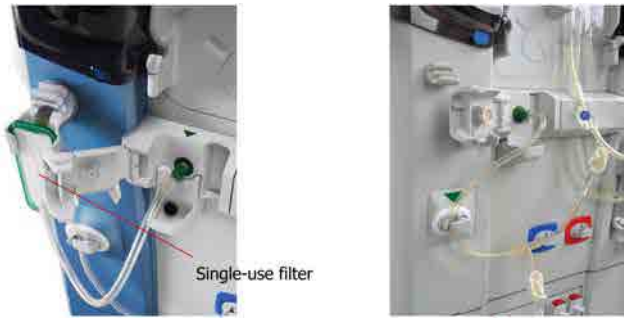


Fig. 1a: Ultra Prime Line on the AP Dialysis System ***Fig. 1b:*** ULTRALINE HD on the AP+ Dialysis System

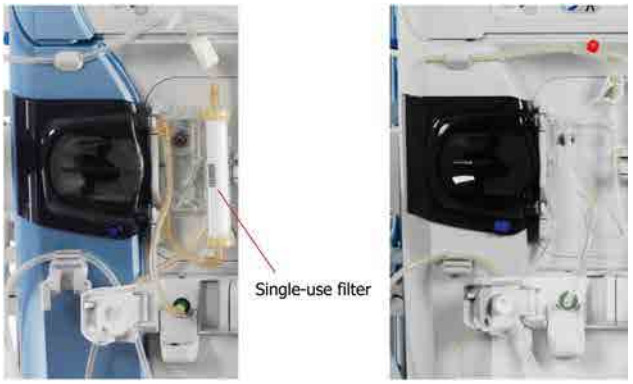


Fig. 2a: Ultra HDF Line on the AP Dialysis System ***Fig. 2b:*** ULTRALINE HDF on the AP+ Dialysis System

Table 1: Individual weights of EC components before and after dialysis

Dialysis System:	Weight of unused infusion line [g][1]	Weight of unused blood tubing set [g][1]	Weight of unused dialyzer [g][1]	Total weight of unused EC components [g]	Total weight of EC components after their discharge [g][2]
AP	**57**(Ultra Prime Line)	**295**	**150**	**502**	**626 ± 7**
	136(Ultra HDF Line)	**295**	**250**	**681**	**873 ± 10**
AP+	**21**(ULTRALINE HD)	**295**	**150**	**466**	**579 ± 1**
	64(ULTRALINE HDF)	**295**	**250**	**609**	**757 ± 2**

[1] As per specification

[2] Mean value and standard deviation derived from 5 runs of measurement.

Table 2: Total amount of EC components waste weekly produced by a machine

Dialysis System:	Total weight of EC components after their discharge [kg]
AP	**10.867**
AP+	**9.754**

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P1093 BENEFITS OF HOME HEMODIALYSIS

Verica Todorov Sakic[1], Zivka Djuric[1], Petar Djuric[1], Ana Bulatovic[1], Jovan Popovic[1], Radomir Naumovic[1,2], Nada Dimkovic[2]

[1]Zvezdara University Medical Center, Clinical Department for Renal Diseases, Belgrade, Serbia and [2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia

Background and Aims: Home hemodialysis (HOHD) has been available as a modality of renal replacement therapy since the 1960s, in our center since 1972. Despite better patients' outcome provided by HOHD comparing to hospital hemodialysis (HHD), its adoption has been limited worldwide. The aim of this study was to compare anemia, nutrition, mineral metabolism and morbidity in patients on HOHD and HHD.

Method: we analyzed dialysis and uremia related complications and morbidity in 19 HOHD patients in comparison with patients on HHD (N= 57). Each HOHD patient was previously matched with three patients on HHD by sex, age and reason for end stage renal disease (ESRD). Patients on HHD were on dialysis 3x4 h per week while patients on HOHD had dialysis on consecutive days in duration of 5-6 hours. Also, patients on HOHD were more frequent on hemodiafiltration (HDF), 89.5% of them, as compared to HHD patients (only 21.4%).

Results: All patients on HOHD were using AVF as vascular access for HD, and most of the analyzed HHD patients (only 5.3% used AVG). As revealed by hemoglobin level (Hgb) patients on HOHD had significantly better anemia control than HHD patients (12±2.3 vs. 10.2±1g/dl, p=0.004), despite the lower ferritin level (94±117 vs. 256±175ng/ml, p=0,001) and less frequent use of erythropoietin-stimulating agents (ESA), (and only 31% on HOHD vs 80% patients on HHD, p=0,001). By analyzing patients that used ESA therapy, we revealed that HOHD patients had lower weekly dose of ESA (5333±3265 IU vs. 6068±4145 IU). The values of intact parathyroid hormone (iPTH), did not differ significantly between HOHD (311±419pg/ml ; min 5,25, max 1529) and HHD (233±212pg/ml; min 19,25, max 926), but higher percentage of patients in HOHD group underwent parathyroidectomy (63% vs. 3.5%). The average values of calcium, and phosphorus did not significantly differ between HOHD and HHD patients (2.4±0.3 vs. 2.3±0.2mmol/l; 1.5±0.5 vs. 1.6±0.5mmol/l, respectively). HOHD patients had significantly higher albumin level (43±4.5 vs. 40.6±4g/l, p=0,035). There was no difference in annual hospital admission rate (0.4±0.5 vs. 0.6±0.7, p=0.35) between groups, but HHD patients had longer in-hospital stay. (4.8±5.3 days for HOHD vs. 7.3±9.3 days for HHD; p=0.16). Vascular access complications were most frequent reason for hospitalization in both groups (37%), followed by cardiovascular complications 13.6%, in HOHD group and infectious complications in HHD group 24%.

Conclusion: Our study has shown that HOHD provides some advantages over HHD including better quality of life and better anemia and nutrition control, better control of parathyroid function and shorter in-hospital stay. More frequent and longer dialysis sessions may be possible reason including HDF.

P1094 **PULSE AMPLITUDE OF THE TOE MEASURED WITH A PORTABLE LASER DOPPLER FLOW METER IS USEFUL FOR SCREENING OF DIALYSIS PATIENTS FOR PERIPHERAL ARTERIAL DISEASE**

Makoto Saito[1], Hiroomi Jingu[1], Yusuke Oyama[2], Toshiyuki Tanaka[2], Akihiko Shiono[2], Masami Machida[2]

[1], Department of Clinical Engineering, Public Tomioka General Hospital, Gunma, Japan, Tomioka-shi, Gunma prefecture, Japan and [2], Department of Urology, Public Tomioka General Hospital, Gunma, Japan, Tomioka-shi, Gunma prefecture, Japan

Background and Aims: Peripheral arterial disease (PAD) occurs at a high frequency in hemodialysis (HD) patients and is known to be associated with poor outcomes. Measurement of the ankle-brachial blood pressure index (ABI) or toe brachial index (TBI) has been used for screening, diagnosis and severity determination of PAD. However, the procedures for measurement of these indices are complicated and the measurements cannot be performed during dialysis sessions. The purpose of the present study was to clarify the ability of the toe blood flow and pulse amplitude measured with a portable laser Doppler flow meter (LDF) to detect PAD in dialysis patients, in comparison with the diagnostic abilities of ABI and TBI.

Methods: Fourteen patients on maintenance HD participated in this study. The mean age was 65.2 years old and the mean duration of HD was 9.1 years. We measured the ABI and TBI before HD, and the blood flow and pulse amplitude on the ventral side of the first toe with a portable LDF (pocket LDF®, JMS Co., Ltd., Tokyo, Japan) during the HD session on the same day. The correlations between the blood flow / pulse amplitude in the toe and the ABI / TBI were investigated. The sensitivity and specificity of the blood flow and pulse amplitude in the toe for PAD detection were determined by a receiver operating characteristic curve analysis. Statistical analysis was performed using the Fisher's exact test. A p value of $<5\%$ was considered to indicate a significant difference.

Results and Discussion: No significant correlation was found between the blood flow and the pulse amplitude in the toe ($p = 0.454$). The blood flow was not correlated with either the ABI or the TBI ($p = 0.286$, $p = 0.115$, respectively). However, the pulse amplitude showed significant correlations with both the ABI and TBI ($p < 0.001$, $p < 0.05$). When we used the general reference cutoff values for ABI and TBI of 0.9 and 0.6, respectively, the sensitivity and specificity of ABI for the detection of PAD were 0.75 and 0.75, respectively, and those of TBI were 1.0 and 0.75, respectively. On the other hand, the sensitivity and specificity of blood flow in the toe were 0.50 and 1.0, respectively, when the cutoff value was set at 23.8 mL/min. The sensitivity and specificity of the pulse amplitude were 0.75 and 1.0, respectively, when the cutoff value was set at 7.6 mL/min. These results indicate that the pulse amplitude in the toe showed a high diagnostic ability, like ABI and TBI, for the detection of PAD. Although our results in this study were obtained from a small sample size and further investigation is warranted, the pulse amplitude measured with the portable LDF was correlated well with both the ABI and TBI, and its sensitivity and specificity for the detection of PAD were also high, indicating the high diagnostic ability of the pulse amplitude for PAD. As compared to the measurement of ABI or TBI, the pulse amplitude in the toe can be easily measured with a portable LDF, even during a dialysis session. Thus, we believe that the use of a portable LDF might be of great benefit as a screening tool for PAD.

Conclusion: The pulse amplitude in the toe measured with a portable LDF may have the potential to become a novel easily measurable index in the screening of dialysis patients for PAD.

P1095 USE OF CYTOKINE ADSORBING MEMBRANES IN PATIENTS WITH ACUTE RENAL FAILURE IN INTENSIVE CARE UNITS

Eva Jakopin[1], Martin Hren[2], Masa Knehtl[1,3], Benjamin Dvorsak[1], Nina Hojs[1,3], Tadej Zorman[2], Tina Stropnik Galuf[2], Andreja Sinkovic[3,4], Franci Svensek[4], Zvonko Borovsak[5], Jozica Wagner Kovacec[5], Robert Ekart[2,3], Radovan Hojs[1,3], Sebastjan Bevc[1,3]

[1]Maribor University Medical Centre, Department of Nephrology, Maribor, Slovenia, [2]Maribor University Medical Centre, Department of Dialysis, Maribor, Slovenia, [3]UNIVERZA V MARIBORU MEDICINSKA FAKULTETA, Maribor, Slovenia, [4]Maribor University Medical Centre, Medical intensive care unit, Maribor, Slovenia and [5]Maribor University Medical Centre, Surgical intensive care unit, Maribor, Slovenia

Background and Aims: Use of cytokine adsorbents has been proposed as a novel therapeutic approach in sepsis management. Our aim was to evaluate laboratory markers, clinical parameters and SOFA (Sequential Organ Failure Assessment) score in patients who were treated with cytokine adsorbing membrane (CytoSorb®, CytoSorbents Corp. New Jersey, USA) and continuous veno-venous haemodialysis.

Method: We included adult patients with septic shock and acute renal failure. We retrospectively collected laboratory results (leukocytes, thrombocytes, C-reactive protein, procalcitonin, lactate, urea, creatinine, bilirubin, PaO2), clinical parameters (mean arterial pressure (MAP), FiO2, residual diuresis), SOFA score and vasopressor use at the beginning and at the end of the procedure.

Results: We included 69 patients, 51 men, aged 56.6 ± 15 years. 51 patients had 1 procedure, 14 patients had 2 procedures, 3 patients had 3 procedures and 1 patient had 4 procedures. Median time from admission to initiation of procedure was 47 hours, median treatment time was 23.6 hours.

We discovered significant improvement in procalcitonin (35.36 ± 37.33 ng/mL vs. 24.25 ± 31.18 ng/mL; $p<0.001$), creatinine (345.06 ± 174.65 μmol/L vs. 233.11 ± 108.82 μmol/L; $p<0.0001$), SOFA score (14.20 ± 2.64 vs. 12.69 ± 3.52; $p<0.001$) and FiO2 (48.17 ± 21.17 % vs. 44.63 ± 21.45 %; p=0.020).

Patients with more than 1 procedure showed statistically significant reduction in lactate level (5.40 ± 4.74 mmol/L vs. 2.46 ± 1.74 mmol/L; p=0.010) and vasopressin dose (1.26 ± 1.61 vs. 0.88 ± 3.2 IU/h; p=0.022).

Conclusion: We observed potential beneficial effect of adsorptive membrane use in septic patients. According to our results two or more procedures were associated with improved laboratory markers and lower vasopressor requirement.

P1096 **SAFETY AND EFFICACY OF A NEW SIMPLIFIED REGIONAL CITRATE ANTICOAGULATION PROTOCOL FOR SUSTAINED LOW EFFICIENCY DIALYSIS FOCUSED ON PREVENTION OF RRT-INDUCED HYPOPHOSPHATEMIA IN CRITICALLY ILL RENAL PATIENTS**

Francesca Di Mario[1], Paolo Greco[1], Francesco Peyronel[1], Tommaso Di motta[1], Maria Rosaria Varì[1], Vincenzo Oliva[1], Elisabetta Parenti[1], Giuseppe Regolisti[1], Enrico Fiaccadori[1]

[1]*UO Nefrologia, Azienda Ospedaliero-Universitaria Di Parma, Parma,, Italy*

Background and Aims: Sustained-Low Efficiency Dialysis (SLED) is a hybrid Renal Replacement Therapy (RRT) increasingly used in critically ill patients with Acute Kidney Injury (AKI). Usually lasting 8-12 hours, this modality combines several advantages of both intermittent and continuous RRT (CRRT). Regional citrate anticoagulation (RCA) represents the most adequate anticoagulation strategy to avoid the extracorporeal circuit clotting. Hypophosphatemia (serum phosphorus, s-P, levels $\leq$ 2.5 mg/dl) is a common electrolyte disorder in critically ills, with an increased incidence in course of prolonged RRTs, especially when standard dialysis/replacement solutions and highly intensive modalities are employed. Given the potentially negative impact of hypophosphatemia on patients' outcomes, strategies aimed at preventing its onset should be appropriately implemented. This pilot study is aimed at evaluation of safety and efficacy of a simplified RCA protocol for SLED, based on the combination of a low-concentrated citrate solution with a phosphate-containing solution.

Methods: a prospective observational study was conducted on critically ill patients with AKI requiring RRT or End Stage Renal Disease (ESRD) previously on RRT admitted to our renal Intensive Care Unit (ICU). SLED was performed by the Prismax system (Baxter) and polyacrylonitrile AN69 haemofilters (ST 150, 1.5 m2, Baxter). 8-hours SLED sessions were prescribed, in the SLED-f variant, by using a 18 mmol/l pre-dilution trisodium citrate solution (Regiocit 18/0, Baxter) combined with a phosphate-containing solution acting as dialysate (Ca^{2+} 0, HPO_4^{2-} 1, Mg^{2+} 0.75, HCO_3^- 22 mmol/l; Biphozyl, Baxter) and a standard RRT solution acting as post-dilution replacement fluid (Prismasol 4, Baxter). Calcium chloride (CaCl 10%) was infused in a separate central venous line to maintain the systemic Ca^{2+} (s-Ca^{2+}) within a normal range. Each patient underwent three consecutive daily SLED sessions. The activated coagulation time (ACT), acid–base parameters, s-Ca^{2+} and potassium were measured at SLED start and every 2 h. Phosphorus and magnesium losses with RRT were replaced, when needed, with sodium glycerophosphate pentahydrate (Glycophos^{TM} 20 mmol/20 ml, Fresenius Kabi Norge AS, Halden, Norvegia) and magnesium sulphate.

Results: a total of 60 SLED-f sessions were performed in 20 ICU patients. At ICU admission, the average APACHE II score was 21.8 and half of patients were mechanically ventilated. Many of them showed hemodynamic instability and AKI was oliguric in 90% of cases. No premature interruptions for irreversible filter clotting occurred and the prescribed dialysis dose was delivered in 95% of cases. No statistically significant differences were observed between systemic ACT at SLED start and during RRT sessions, and no major hemorrhagic events were observed. Regarding RCA, no clinically relevant episode of hypo or hypercalcemia was observed, and calcium infusion rate remained constant in course of treatments. Acid-base status was effectively maintained during the entire period of treatment and no episodes of clinically relevant metabolic acidosis or alkalosis were registered. The analysis of the main laboratory variables at SLED start, in course and after 24 h of treatment did not show statistically significant differences. Regardless of starting values, s-P and s-Mg were progressively corrected and maintained within the normality range, limiting the need for exogenous supplementations.

Conclusions: These preliminary data suggest that our simplified RCA protocol for SLED, combining a low-citrate solution with a phosphate-containing solution, is safe and efficacious allowing to optimizing acid-base balance and to preventing RRT-related hypophosphatemia.

P1097 **INITIATING MAINTENANCE HAEMODIALYSIS USING INCREMENTAL HAEMODIALYSIS REGIME - A SINGLE CENTRE EXPERIENCE**

Tijana Azasevac[1], Violeta Knezevic[1,2], Sonja Golubović[1,2], Bojana Ljubiä[N/A]ïä‡[3], Mira Markovic[1], Marija Sibalic Simin[1], Dejan Celic[1,2]

[1]Clinical Centre of Vojvodina, Novi Sad, Clinic of Nephrology and Clinical Immunology, Novi Sad, Serbia, [2]University of Novi Sad, Faculty of medicine Novi Sad, Novi Sad, Serbia and [3]Clinical Centre of Vojvodina, Novi Sad, Departement of immergency internal medicine, Novi Sad, Serbia

Background and Aims: Most patients with end stage renal disease (ESRD) initiate maintenance dialysis in three times per week regime irrespectively of residual kidney function (RKF). Incremental haemodialysis (IHD) showed benefits of starting and maintaining patients on less than three times per week regime, most importantly preserving urine volume output (UVO) and RKF. The aim of this study was to assess the main differences between a group of patients initiating dialysis once-weekly (1xHD) and twice-weekly (2xHD), to evaluate time to dialysis regime change, UVO and patients volume status at the end of study period.

Method: Patients with ESRD who started haemodialysis through the planned IHD (once-weekly and twice-weekly) and were undergoing IHD for at least 4 months (M) were enrolled (n=44) in the study. Study was conducted from January 2016 to December 2019 at dialysis department of our hospital. Patients were divided into two groups: 1xHD (20 pts) and 2xHD (24 pts). They were excluded from the study at the end of study period or earlier if they transitioned to thrice-weekly haemodialysis or died. Patients fluid status and body composition was assessed using results derived from bioimpedance measurements performed using Body Composition Monitor device.

Results: The 1xHD pts were younger (66,8±11,6 versus 67,4±10 years: P>0.05) and weighed less (74,4±14,7 versus 75,5±11,9 kg, p>0,05) with lower BMI. In both groups there were more males (60% versus 62,5%: P>0,05). The most common cause of ESRD in both groups was nephrosclerosis (45% in 1xHD versus 47,1% in 2xHD, p>0,05), followed by diabetic nephropathy (30% versus 20,8%, p>0,05), obstructive nephropathy (10% versus 8,3%, p>0,05), multiple myeloma (10% versus 8,3%, p>0,05), glomerulonephritis (5% versus 8,3%, p>0,05) and others in 2xHD group (12,5%; polycystic kidney disease and chronic interstitial nephritis).

The estimated glomerular filtration rate of all patients at the time of HD initiation was 7,5±2,2 ml/min/1.73m2 (8,2±2,8 in 1xHD group versus 6,9±1,48 ml/ min/1.73m2 in 2xHD group, p>0,05). Baseline daily urine output was similar, 1826,6±344,6 ml/day in 1xHD and 1772,2±343,8 ml/day in 2xHD group (p>0,05).

Patients in 1xHD concluded the study after mean period of 13,4 M (min 4 M, max 35 M). At the end of study period only three patients (15%) continued receiving dialysis once-weekly (mean 14,5 M, min 7 M, max 19 M), 12 pts (60%) transitioned to twice-weekly dialysis regime after 2 to 6 M (mean 3,1 M) and continued to receive this dialysis regime until the end of study period. Four pts (20%) transitioned to full-dose dialysis (mean 18,2 M, 11-24 M).

Most of the patients in 2xHD group (17; 70,8%) concluded study in the same dialysis regime (mean 20,4 M, 4-24 M), 7 pts (29%) transitioned to full-dose dialysis (mean 12,6 M, 5-21 M) and one patient transitioned to once-weekly HD (8M).

At the end of study daily urine output was 1463,1±317,5 in 1xHD versus 1321,1±309,1 ml/day in 2xHD group (p>0,05). Results of assessment of fluid status and body composition at the end of study are in Table 1. We evaluated nutritional status at the end of study: total protein 57,4±8,9 g/l in 1xHD versus 62,8±5,3 g/l in 2xHD, albumin 36,9±10,6 versus 37,6±4,4 g/l, total cholesterol 4,1±1,6 versus 4,4±1,3 mmol/l, triglycerides 1,3±0,8 versus 1,7±0,7 mmol/l (p>0,05 for all parameters).

At the end of the study 70% of patients treated with IHD maintained renal function that was sufficient to continue IHD regime with overall survival rate 90% in 1xHD group and 87,5% in 2xHD group.

Conclusion:IHD, in carefully selected patients with good compliance, provides preservation of UVO and RKF, thus delaying transition to full-dose dialysis and avoiding complications of dialysis, such as intradialytic hypotension and vascular access failure. This type of dialysis is individualized treatment that obtains easier adaptation to dialysis and better quality of life.

Assessment of fluid status	1xHD	2xHD	p
Overhydration before dialysis (l)	2,8±0,9	2,6±1,9	>0,05
Total body volume (l)	38,6±2,8	34,9±10,4	>0,05
Extracellular/Intracellular Water Ratio	0,97±0,1	1,02±0,1	>0,05
Systolic blood pressure (mmHg)	136±15	143±11	>0,05
Dyastolic blood pressure (mmHg)	74,5±12	73,5±7,8	>0,05
Oedema (%)	15	16,7	>0,05
Assessment of body composition	**1xHD**	**2xHD**	**p**
Body Mass Index (kg/m²)	24,4±4,6	25,5±1,9	>0,05
Lean tissue index (kg/m²)	14,3±2	14,2±2,7	>0,05
Fat tissue index (kg/m²)	8,7±4	14,8±2,7	>0,05
Lean tissue mass (kg)	43,2±11,7	41,2±12,3	>0,05
Fat mass (kg)	20±10,6	27,1±9,6	>0,05
Adipose tissue mass(kg)	27,4±14,2	29,6±9,6	>0,05
Body Cell Mass (kg)	24±5,6	29,6±4,8	>0,05

Figure:

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THE CHANGE OF PLASMA SCLEROSTIN AND OTHER BIOMARKERS IN HEMODIALYTIC PATIENTS USING DIALYZER WITH MEDIUM CUT-OFF MEMBRANE

Jong Hwan Jung[1], Seon-Ho Ahn[1], Ju Hung Song[1]

[1]*Wonkwang University School of Medicine and Hospital, Internal Medicine, Iksan, Korea, Rep. of South*

Background and Aims: Protein-bound toxins and uremic toxins with middle molecular weight usually develop uremic symptoms in patients with advanced chronic kidney disease (CKD) or end-stage renal disease (ESRD). Although the effect on uremic toxicity of the molecules is not proven yet, middle molecules or larger middle molecules is regarded with important substance concerning of development of uremic symptoms and cardiovascular complication, particularly in CKD patients. Hemodialysis (HD) or hemodiafiltration (HDF) using dialyzer with high flux membrane provided improved clearance for uremic toxins with middle molecular weights. However, uremic toxins with larger middle molecular weight could not be easily removed through above methods. Medium cut-off (MCO) membrane can remove larger middle molecules which can be not removed through high flux membrane and HDF. From this perspective, chronic use of MCO membrane lowering the plasma concentration of larger middle molecules associated with cardiovascular complications including vascular calcification may give beneficial effect, particularly in patients with ESRD.

Method: Twenty-five patients undergoing chronic hemodialysis were prospectively analyzed for 6 months. We randomly divided enrolled patients into two groups: control group and MCO group. Patients in the control group used dialyzer with high flux membrane and patients in MCO group used dialyzer with MCO membrane. The enrolled patients performed hemodialysis thrice a week during 6 months. We measured plasma levels of several biomarkers at baseline and 3-month and 6-month through the multiplexing using Luminex® technology. In this prospective study, we performed comparative analysis with larger middle molecules, such as CXCL16, sclerostin, and FGF-23, in both groups.

Results: The plasma levels of all biomarkers at baseline did not show significant difference between two groups (CXCL16: $p = 0.904$, Sclerostin: $p = 0.322$, FGF-23: $p = 0.065$, respectively). However, plasma sclerostin levels at 3-month and 6-month were significantly lower in MCO group ($p = 0.060$, $p < 0.005$, respectively). In addition, even after analysis of covariance through ANCOVA analysis, plasma sclerostin levels at 3-month and 6-month were significantly lower in MCO group compared with the control group ($p = 0.042$, $p = 0.001$, respectively). But, there was no a significant decrease of plasma sclerostin levels according to time, particularly in MCO group ($p = 0.157$, $p = 0.412$, respectively) (Figure 1).

Conclusion: This study showed the 6-month outcome for changes of the plasma levels of larger middle molecules, including CXCL16, sclerostin, and FGF-23, particularly in dialytic patients using dialyzer with MCO membrane. Plasma sclerostin associated with vascular calcification showed decreasing tendency during 6 months after application of MCO membrane, but, there was no statistical significance. However, plasma levels of sclerostin were significantly lower in dialytic patients using MCO membrane than those using high flux membrane at 3 and 6 months, respectively. Therefore, hemodialysis using dialyzer with MCO membrane may be an option to attenuate cardiovascular complications in ESRD patients.

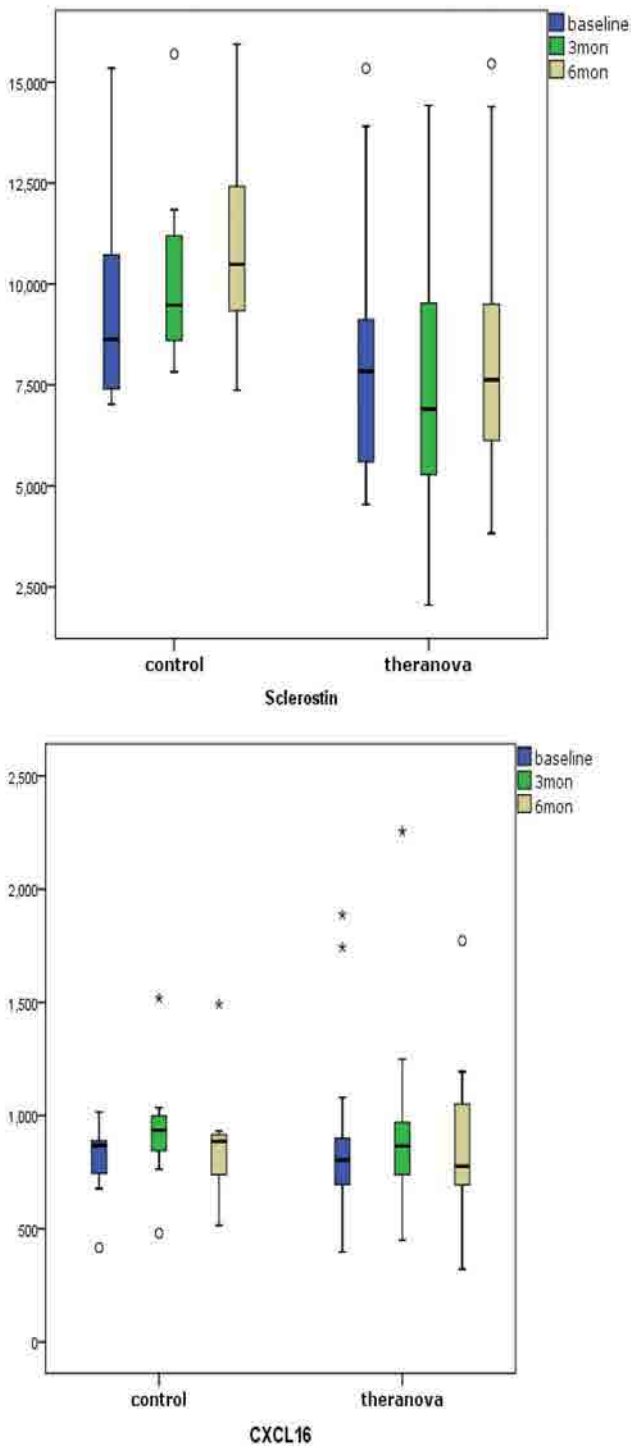


Figure:

P1099 **EVALUATION OF THE DEPURATION OF SOLUTES IN THE MIDDLE TO HIGH MOLECULAR WEIGHT RANGE WITH DIFFERENT TECHNIQUES OF HAEMODIALYSIS**

Barbara Cancho Castellano[1], Rosa Diaz Campillejo[1], Cristina López Arnaldo[1], Julián Valladares Alcobendas[1], Rosa María Ruiz Calero Cendrero[1], Maria Victoria Martín Hidalgo Barquero[1], Juan M López Gómez[2], Purificación García Yun[2], Lilia Olivera Azevedo[3], Elena García de Vinuesa Calvo[1], Nicolas-Roberto Robles-Perez[1]

[1]Infanta Cristina Hospital, Nephrology, Badajoz, Spain, [2]Infanta Cristina Hospital, Biochemistry and Clinical Analysis, Badajoz, Spain and [3]General Hospital Llerena, Nephrology, Llerena, Spain

Background and Aims: Haemodialysis is the most commoly used replacement therapy for chronic kidney disease. We are looking for new solutions to remove solutes in the middle to high molecular weight range. Our objective is to evaluate and compare the purification of small and middle to high molecular weight between 15-45 KDa with Haemodyafiltration On Line postdilutional (HDF-OL-post) technique, Haemodialysis High-Flux (HD-HF) and Haemodialysis Expanded (HDx) using specific high permeability membranes: in the first two techniques polyphenylene membranes (1.7m^2) and in the HDx technique cut point membranes PAEs/PVP (1.7 m^2).

Method: 10 chronic prevalent patients on haemodialysis, older than 18 years, without diuresis and stable, 60% males. Mean age 65.3±17.47 years. Time in HD, mean 49.5 months. Etiologies: 20% NAE, 30% ND, 10 % Glomerulopathies, 40% unaffiliated. Vascular Accesses: 50% FAVn, 20% FAVp, 30% CVC-T. They were evaluated for three consecutive weeks with analytics in the intermediate session, modifying the technique and the membrane, keeping the dialysis patient stable. Post-dialysis concentrations of solutes in the middle to high molecular weight range were corrected in relation to haemoconcentration. A comparison of the reduction percentages (RP%) of various molecules was performed. The possible normal distribution was studied in the continuous variables with the Shapiro-Wilk test and the comparison of means using the t-Student or Wilconson test as the most appropriate. SPSS statistical program 17.0.

Results: No serious adverse events or allergies were recorded. The comparative results between the three techniques are shown in the figure 1.

Conclusion: The mean reduction of medium molecules (β2-microglobulin, cystatin-C) was not lower in HDx compared to HDF-OL-post. From 20 KDa there is no greater capacity to reduce solutes in HDx in our sample than in the other techniques. Between the three techniques, the HDF-Ol-post is the one that shows a higher percentage of mean reduction of α1-acid glycoprotein and albumin.

	HDF-OL-POST Polyphenylene 1.7 m^2	HD-HF Polyphenylene 1.7 m^2	HDxPAES/PVP 1.7 m^2	HDF-OL-POST vs HD-HF	HDF-OL-POST vs HDx	HD-HFvsHDx
Qb (ml/min)	335	342,5	340	n.s	n.s	n.s
KT (l)	44,97±2,48	45,29±2,26	49,35±2,57	n.s	p=0,001	p=0,001
KT//V	1,57±0,24	1,52±0,19	1,74±0,26	n.s	p=0,009	p=0,003
URP %	73,23±5,31	72,09±4,34	76,61±4,58	p<0.05	p=0,003	p< 0,001
Vol. inf post (l)	21±2,47(21- 27,3)	-	-	-	-	-
Creatinine(RP%)	66,00±5,37	63,46±5,09	67,03±4,41	n.s	n.s	p=0,002
Phosforus (RP%)	48,18±17,71	53,61±8,43	55,98±8,30	n.s	n.s	n.s
Vitamin B_{12}(RP%)	1,53±10,19	6,17±5,27	5,13±7,03	n.s	n.s	n.s
ß 2 microglobulin (RP%)	76,14±10,51	78,33±1,44	81,26±3,05	n.s	n.s	p=0,01
CystatinC(RP%)	77,44±6,95	72,39±7,57	76,08±6,08	p<0,001	n.s	p=0,01
Prolactin(RP%)	71,36±14,11	66,69±5,54	62,58±8,9	n.s	n.s (p=0,055)	p=0,03
Alfa 1 acid glycoprotein(RP%)	42,50±9,96	15,37±4,35	8,79±7,2	p<0,001	p=0,008	p<0,001
Albumin(RP%)	14,44±8,47	8,62±5,93	8,1±4,69	p=0,014	n.s (p=0,069)	n.s

P1100

IMPACT OF THE RELATIONSHIP BETWEEN LOW MOLECULAR WEIGHT PROTEINS REMOVAL EFFICIENCIES AND THE VOLUME OF ALBUMIN LEAKAGE IN HEMODIAFILTRATION THERAPY

Kenji Sakurai[1], Takeshi Saito[1], Hiromi Hosoya[1], Yoshitaka Kurihara[1], Kaori Kurosawa[1], Ayumi Suzuki[1], Ruka Kishihara[1], Kazunari Yoshida[2], Akihiro Yamashita[3], Kokubo Kenichi[4], Toru Hyodo[5]

[1]Hashimoto Clinic, Dialysis Center, Sagamihara, Japan, [2]Kitasato University Shool of Medicine, Organ Transplant Medicine, Sagamihara, Japan, [3]Hosei University, Clinical Science and Technology, Tokyo, Japan, [4]Kitasato University School of Allied Health Sciences, Chemical Science and Technology, Sagamihara, Japan and [5]Eijin Clinic, Dialysis Center, Hiratsuka,

Background and Aims: The purpose of hemodiafiltration (HDF) is to remove small- to large molecular weight solutes in order to prevent and treat complications and to improve the prognosis of dialysis patients. Especially, larger low molecular weight proteins (LMWPs) must be removed efficiently. β_2-microglobulin (MG) (molecular weight [MW], 11.8 kDa: Stokes radius, 15.6A), is considered as an important marker of dialysis efficiency. However, MW of β2-MG is too small as a marker in HDF. Conversely, α1-MG (MW, 33 kDa: Stokes radius, 28.4A) is the most appropriate marker for evaluation of solute removal efficiency of HDF because of the following reasons: (1) optical molecular size; (2) not very low physiological blood concentration; (3) stable production rate; (4) removal by convection; and (5) accumulation in ESRD. Efficient removal of α1-MG without losing albumin (Alb) (MW,66 kDa: Stokes radius, 35.5A) is impossible even by HDF. In this study, we investigated the relationship between LMWP removal efficiencies and the volume of Alb leakage by analyzing the results of patients undergoing HDF. And we also evaluated the trend of the serum levels of patients who had received high-efficiency HDF for more than three years

Method: Eighty-seven patients who had received HDF in 2018–2019 were included. The results of HDF (a total of 435 sessions) were analyzed (blood flow rate, 261.5±28.5 mL/min; replacement fluid volume, 48.7 L/s pre-dilution on-line HDF and 14.2 L/s post-dilution on-line HDF). The removal efficiencies of β2-MG, prolactin (PRL), and α1-MG, and the volume of Alb leakage were examined. In addition, the relationship between the removal efficiency of each solute and the volume of Alb leakage was investigated. Changes in serum Alb level were analyzed in 13 patients who continued to receive high-efficiency HDF (the removal rate of α1-MG was 30% or more) for more than three years.

Results: Analysis of the results (mean ± SD) obtained from a total of 435 sessions (87 patients) showed that the removal rates of β2-MG, PRL, and α1-MG were 80.7 ± 4.5%, 75.8±9.4 and 33.8 ± 9.4%, respectively, and the Alb leakage was 3.9 ± 1.8 g/s. The equations of the approximate curve between Alb leakage and β2-MG, PRL, and α1-MG removal rates were expressed as follows: ï$^1/_2^{TM}$= 1.4197ln(x) + 78.972 (R^2 = 0.0426), y = 9.7185ln(x) + 64.134 (R^2 =0.4632), and ï$^1/_2^{TMTM}$= 11.225ln(x) + 20.282 (R^2 = 0.6191), respectively. These results indicate that the dynamics between Alb leakage and α1-MG removal are very similar. That is, although the molecular weight of Alb is twice as that of α1-MG, the difference in their Stokes radius is 20%; therefore, separate removal of Alb and α1-MG is impossible. The mean serum Alb level in 13 patients who received high-efficiency HDF for 3 years or longer was 3.59 ± 0.23 g/dL in January 2017 and 3.69 ± 0.28 g/dL in December 2019, revealing no changes.

Conclusion: The efficient removal of larger LMWPs leads to the leakage of Alb. However, an Alb leakage of 3 to 6 g/s has little influence on the serum Alb level of patients. Thus, α1-MG is the most appropriate marker of the solute removal efficiency of HDF.

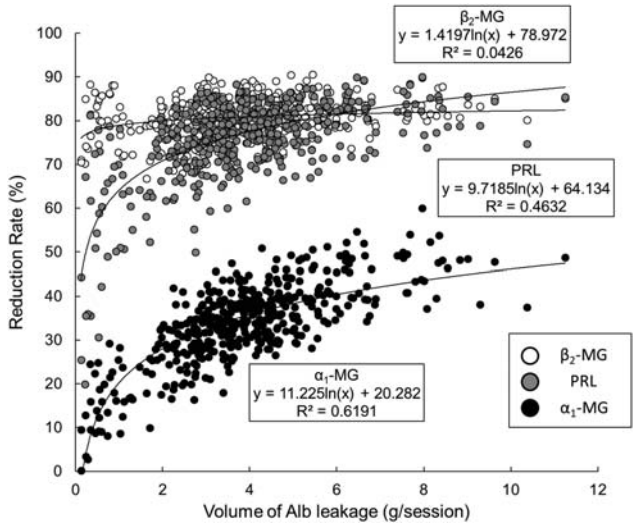


Figure:

P1101

A BIFUNCTIONAL ADSORBER PARTICLE FOR THE REMOVAL OF HYDROPHOBIC UREMIC TOXINS FROM WHOLE BLOOD OF RENAL FAILURE PATIENTS

Marieke Sternkopf[1], Thimoteus Speer[2], Claudia Göttsch[3], Vera Jankowski[1], Joachim Jankowski[1], Heidi Noels[1]

[1]Institute for molecular cardiovascular research (IMCAR), Germany, [2]Department of Internal Medicine - Nephrology and Hypertension, Germany and [3]Department of Internal Medicine I, Germany

Background and Aims: Hydrophobic uremic toxins accumulate in patients with chronic kidney disease, contributing to a highly increased cardiovascular risk. The clearance of these uremic toxins using current hemodialysis techniques is limited due to their hydrophobicity and their high binding affinity to plasma proteins. Adsorber techniques may be an appropriate alternative to increase hydrophobic uremic toxin removal.

Method: We developed an extracorporeal, whole-blood bifunctional adsorber particle consisting of a porous, activated charcoal core with a hydrophilic polyvinylpyrrolidone surface coating. The adsorption capacity was quantified using analytical chromatography after perfusion of the particles with an albumin solution or blood, each containing mixtures of hydrophobic uremic toxins.

Results: A time-dependent increase in hydrophobic uremic toxin adsorption was depicted and all toxins showed a high binding affinity to the adsorber particles. Further, the particle showed a sufficient hemocompatibility without significant effects on complement component 5a, thrombin-antithrombin III complex, or thrombocyte concentration in blood in vitro, although leukocyte counts were slightly reduced.

Conclusion: In conclusion, the bifunctional adsorber particle with cross-linked polyvinylpyrrolidone coating showed a high adsorption capacity without adverse effects on hemocompatibility in vitro. Thus, it may be an interesting candidate for further in vivo studies with the aim to increase the efficiency of conventional dialysis techniques.

P1102

EVALUATION THE EFFICACY OF MEDIUM CUT- OFF MEMBRANE DIALYZERS AND COMPARISON WITH HIGH FLUX DIALYZERS IN CONVENTIONAL HEMODIALYSIS

Irena Rambabova Bushljetikj[1], Lada Trajcheska[1], Vladimir Pushevski[2], Sefedin Biljali[3], Trajan Balkanov[4]

[1]University Clinic of Nephrology, Skopje, Republic Of North Macedonia, [2]University Clinic of Nephrology, Skopje, , [3]University Clinic of Clinical Biochemistry, Skopje, and [4]Institute of Pharmacology, Skopje, Republic Of North Macedonia

Background and Aims: Hemodialysis (HD) is the most widely used modality of renal replacement therapy. The high-flux dialyzers in standard hemodialysis offer numerous benefits for ESRD patients, such as, increasing the uremic toxins removal and improving patients survival, reduced patients admission and morbidity. A new class of membranes, medium cut-off (MCO) membranes, has been designed to achieve better removal capacities for middle and large middle molecules, as well as to ensure the retention of albumin in hemodialysis (HD) treatments. We evaluated the removal efficacy of Theranova® in standard HD in comparison with standard high- flux HD.

Method: Four stable HD patients (M/F 1/4) were included in 12-weeks small observational pilot study in HD with Theranova® 400 (sup. 1.7 m2) and Theranova® 500 (sup. 2.0 m2) dialyzers. Each patient was assessed four times, T0 with standard high flux dialyzers, T1 at 1 month, T2 at second month and T3 at third month, by measuring pre and post-HD samples of: urea, creatinine, beta2-microglobilin (B2M), myoglobin, albumin and FLC-k, FLC-λ . Data are reported as mean ± standard deviation (SD). The removal rates of uremic toxins are expressed as percentages.

Results: The average removal rates for the uremic toxins with standard high-flux membranes were 18.4% for B2M, 14.3% for Myoglobin, 19.8 % for FLC-k and 17.4 % for FLC-λ. The data showed a higher average removal rate for all the uremic toxins with Theranova® dialyzers for B2M, Myoglobin, FLC-k and FLC-λ (62.7%, 56.9%, 63.5%, 54.6%, respectively) during the 3 months of follow up. The using of Theranova® dialyzers in standard HD was enough to significantly decrease the pre-dialysis value of Urea (17.72 ± 2.26 vs 13.75 ± 3.75, p=0.001), Creatinine (700.50 ± 315.07 vs 570.00 ± 206.64, p=0.021), B2M (40.90 ± 11.00 vs 29.00 ± 4.64, p=0.005), FLC-k (267.25 ± 113.28 vs 225.25 ± 100.62, p=0.018), FLC-λ (324.25 ± 116.12 vs 215.23 ± 64.44, p=0.011), Myoglobin (199.96 ± 124.41 vs 137.00 ± 83.14, p= 0.049). Finally, albumin retention was observed with Theranova® dialyzers, between T_0 and T_3 it increased significantly (40.50 ± 4.79 vs 42.25 ± 4.50, p=0.0001).

Conclusion: Compared to high-flux dialysis membranes, novel medium cut-off (MCO) membranes show greater permeability for larger middle molecules in mid - term report. But the long term analysis and larger number of patients is necessary to evaluate a clinical significance of this innovative therapy.

P1103

A RANDOMIZED CONTROLLED STUDY ON THE DIALYZERS WITH CELLULOSE TRIACETATE MEMBRANE AND WITH POLYSULFONE MEMBRANE FOR MAINTENANCE HEMODIALYSIS PATIENTS

Zhang Chen[1], Yang Yun[2], Nai-quan Liu[2], Guang-yu Zhou[2], De-tian Li[2]

[1], Department of Nephrology, shenyang, P.R. China and [2]Department of Nephrology, shenyang, P.R. China

Background and Aims: With the continuous development and optimization of dialysis membrane materials, polysulfone (PS) as the third generation of dialysis membrane has replaced cellulose triacetate (CTA) and dominated the market because of its better biocompatibility. However, we found that the hypersensitivity to PS could be remitted by the application of CTA in clinical practice. Objective to compare the differences in toxin removal, hematological change and biocompatibility in maintenance hemodialysis (MHD) patients using CTA dialyzer and PS dialyzer.

Method: A total of 20 MHD patients treated in the Second Blood Purification Center of Shengjing Hospital from June 2017 to September 2017 were enrolled in this study. They were randomly divided into group CTA and group PS (n=10/each group). They were treated with regular hemodialysis of 4 hours/time and 3 times/week for one month. The clearances of creatinine (CR), blood urea nitrogen (BUN) and serum phosphorus (P), the changes of hemoglobin (Hb), platelet (PLT) and white blood cell (WBC), and the differences of C-reactive protein (CRP), IgE, complement 3 (C3), vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) were compared between group CTA and group PS.

Results: Age (t=-0.735, P=0.465), gender (c2 =2.410, P=0.120), dialysis age (t=0.336, P=0.738) and primary diseases (c2 =3.817, P=0.701) had no statistical differences between the two groups. Before the hemodialysis with CTA dialyzer and PS dialyzer, there were no statistical differences in all of the parameters between the two groups (P>0.05). After application of CTA dialyzer and PS dialyzer for one month, ①there were no statistical differences in CR, BUN and P, nor in the changes of the above indicators between the two groups (P>0.05); ② there was a statistical difference in Hb change between the two groups (t=-2.282, P=0.027), with better improvement of anemia in group CTA; ③ there was a statistical difference in PLT (t=2.947, P=0.005) between the two groups, with slighter change in group CTA than in group PS (t= 2.219, P=0.031); ④there were no statistical significances in WBC, VCAM-1, ICAM-1, IgE, CRP and C3 between the two groups (P>0.05).

Conclusion: ①There were no significant difference in the clearances of small molecule toxins between CTA dialyzer and PS dialyzer. ② CTA was better than PS in the improvement of anemia. ③ The effect on PLT was less in group CTA than in group PS. ④ There were no significant differences in biocompatibility between CTA dialyzer and PS dialyzer.

P1104 **THE ROLE OF THERAPEUTIC PLASMA EXCHANGE COMBINED WITH HEMODIALYSIS IN MANAGEMENT OF POISONING AND INTOXICATION**

Judith VanSickle[1]

[1]*Children's Mercy Adele Hall Campus, Division of Pediatric Nephrology, Kansas City, United States of America*

Background and Aims: Background: Poisonings, intoxications, and drug overdoses are common occurrences and rapid lowering of the toxin level is key of all effective therapies. Therapeutic plasma exchange (TPE) has several unique characteristics that allow it to be a potentially effective therapy in rapidly achieving this goal with large molecular weight, protein-bound molecules that have a small volume of distribution. Ibuprofen is a commonly used anti-inflammatory, antipyretic, and analgesic drug. The number of reported ibuprofen overdoses (IO) has increased. Although the vast majority of IOs are not consequential, large ingestion can cause severe metabolic acidosis (MA) resulting in multi-organ failure and death. TPE has been reported as solo intervention in IO, however frequently with remaining renal dysfunction. We report two cases of massive IO that responded well to prompt combined TPE with continuous renal replacement therapy (CRRT).

Method: Literature and chart review of cases of IO in our institute treated with TPE+CRRT.

Results: Case 1: A 17 year old male presented to the Emergency Department (ED) following intentional IO in coma with serum pH of 7.09, cardiorespiratory failure and acute kidney injury (AKI). Urine drug screen was positive for only ibuprofen. He reportedly took 1381 mg/kg. Supportive care was unsuccessful, therefore TPE+CRRT was soon initiated. After two days of treatment the patient was able to be extubated, maintained normal cardiovascular status and renal function. The patient fully recovered.

Case 2: A 17 year old female presented to the ED following intentional IO with serum pH of 6.9, cardiorespiratory failure, AKI, arrhythmia and bilateral leg compartment syndrome. Urine drug screen was positive for ibuprofen. The estimated ibuprofen exposure was above 2000 mg/kg. The initial ibuprofen serum plasma level was 330 µg/mL (therapeutic range is 10-50 µg/mL). Initial Supportive care was unsuccessful and TPE+CRRT was immediately started. Plasma ibuprofen level was normal after the 3rd TPE+CRRT. The patient fully recovered.

Conclusion: Intentional IO may result in major morbidity and mortality. TPE is more efficient in removing drugs with a high protein binding and/or a low volume of distribution, such as ibuprofen. In settings of massive overdose, hemodialysis may provide additional removal of unbound portion, as well corrects acidosis and allows provision of optimal nutrition. Combined TPE+CRRT is beneficial and may facilitate recovery. To our knowledge this is the first pediatric report of severe IO successfully treated with combined therapy.

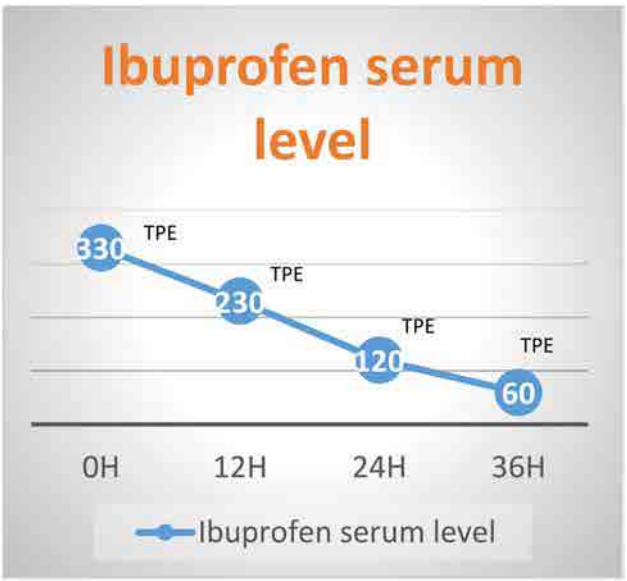


Figure 1: Change in ibuprofen serum level after each TPE.

The patients remained on CRRT as well.

P1105

CAN BETTER EFFICACY OF MIDDLE WEIGHT MOLECULES REMOVAL IN DIALYSIS PATIENTS TREATED WITH MEDIUM CUT-OFF MEMBRANES PREDICT SUPERIORITY OVER CONVENTIONAL HIGH FLUX DIALYSERS?

Ana Ostojic[1], Rodoljub Markovic[2]

[1]*Clinical Hospital Center Zemun, Clinic of Internal medicine, Department of Nephrology, Belgrade, Serbia*

Background and Aims: During last two decades there was a significant improvement in dialysis field, especially with introducement of high flux haemodialysis and on-line haemodiafiltration. In recent years, expanded haemodialysis has emerged as a new attempt to imrove effectiveness of dialysis. These so called medium cut-off membranes (MCO), allow removal of wider range of uremic toxins, especially middle weight molecules, most of which have important role in chronic inflammation and mortality. The aim of this prospective pilot study was to evaluate the effectiveness of middle molecules and other uremic toxins removal in patients treated with medium cut-off membrane (Theranova 500^{tm}, Baxter), compared with patients on conventional high flux dialysis programme.

Method: We examined 10 patients on chronic haemodialysis programme, five of them dialyzed with Theranova 500tm dialyser for one year, and other five patients dialyzed with high flux membranes (polysulfone membrane, 1.8m2) during the same period. Patients were matched according to their age, sex, main disease, and the beginning of dialysis. Analyzed laboratory parameters were urea, creatinine, calcium, phosphorus, PTH, and hemoglobin, on the beginning of the study and after one year follow up, while hepcidin and β2 microglobulin levels were measured only in the end of follow up period. We used descriptive and analytic statistical methods (T test for independent and dependent means).

Results: Patients were divided in two groups, Group 1 - dialyzed with Theranova, and Group 2- patients on high flux haemodialysis, both followed during one year period (Group 1: 63.2±7.01 years, 3 males and 2 women, one of them with polycystic kidney disease (PCKD), the other four with hypertension as main disease, median dialysis time 54.6±8.32 months, Group 2: 63±6 years, 3 males, 2 women, main disease in one was PCKD, in other four hypertension, median dialysis time 53.6±17.98months). Our patients didn't differ statistically in basic examined laboratory parameters on the beginning of examination (mean urea 21.38±2.15 vs. 27.44±3.93 mmol/ ($p>0.05$), mean creatinine 936±88.5 vs. 927.6±98.8μmol/L, mean albumin 40±2.54 vs 39.8±2.77g/L ($p>0.05$), mean calcium 2,24±0.16 vs 2.21±0.17mmol/L ($p>0.05$), mean phosphorus level 1,84±0.39 vs 1.67±0.56mmol/L ($p>0.05$), mean parathyroid hormone level 266.16±279.64 vs 236.14±43.99pg/mL ($p>0.05$), and mean hemoglobin 122.2±5.72 vs 106.4±8.62g/L ($p>0.05$). In patients on high flux haemodialysis programme there was no significant change in examined parameters during one year follow-up (for all examined parameters p value was >0.05). After switching the first group on Theranova dialysers for one year there was small but statistically significant rise in urea (23.26±2.02mmol/L, $p<0.05$), and also statistically significant decrease in serum creatinine level (840.2±75.34μmol/L, $p<0.05$) in this group, while other parameters were not statistically significant. Comparing two groups after one year follow up, there was statistically significant higher level of hemoglobin in the first group (112.2±7.46 vs. 102g/L ±4.47, $p<0.05$), and statistically significant decrease of beta-2 microglobuline (27.41±2.58 vs. 33.82± 2.47ng/mL, $p<0.05$) and hepcidin (75.64±32.2 vs 100.26±10.58ng/mL, $p<0.05$), while other parameters didn't show statistical significance.

Conclusion: Our results implicate better clearance of middle weight molecules (B2M, hepcidin) in patients treated with Theranova 500 tm membrane, which could suggest anti-inflammatory effect of medium cut-off membranes, additionaly with the higher hemoglobin level after one year treatment, comparing to conventional high flux dialysis. Our results are promising, but need to be confirmed in larger randomized trials.

P1106 DETERMINANTS OF SERUM POTASSIUM IN HEMODIALYSIS PATIENTS. DOES JUST ONE COUNT?

Giuseppe Sileno[1], Silvia Brazzo[2], Paola Baiardi[2], Massimo Torreggiani[3], Vittoria Esposito[2], Marco Colucci[2], Ettore Pasquinucci[4], Giuseppe Locatelli[4], Chiara Morelli[4], Ciro Esposito[1]

[1]Via Salvatore Maugeri, Nefrologia e dialisi, Pavia, Italy, [2]Via Salvatore Maugeri, Pavia, Italy, [3]ICS Maugeri, Nefrologia e dialisi, Pavia, Italy and [4]The University of Pavia, Pavia, Italy

Background and Aims: Potassium (K) is mostly an intracellular ion, with a complex homeostasis that is deeply modified in ESRD patients undergoing hemodialysis (HD). Several factors (diet, insulin, acid-base balance, aldosterone, etc) may contribute to determine the level of serum extracellular K, but it is not clear which factor contributes the most. We aimed to evaluate the importance of several factors in inducing hyperkalemia in HD patients.

Methods: Chronic tri-weekly HD patients were evaluated. Patients on diuretics or on potassium binders were excluded. For every patient we recorded age, sex, Kt/V and we measured the post-HD kalemia on the day before the long interHD interval. On the day after the long interHD interval we evaluated: pre-HD K, glucose, creatinine, aldosterone, LDH, CPK, arterial blood gases, ECG, overhydration by bioelectrical impedance analysis, body weight increase after the long interHD interval and daily urinary output. K amount introduced by diet was calculated by a dietitian from each patient's daily food diary. Treatment with ARB, ACE-inhibitors, beta-blockers, insulin or heparin was recorded. Data are presented as mean±SD for each variable analyzed. Correlations between the serum K values and change in serum K (delta K) and the other patient medical data were determined through the two-tailed Pearson's test or Spearman test according to data distribution.

Results: We enrolled 56 patients (male 53.6%), aged 72±13, with a mean Kt/V 1.44±0.25. Mean post-HD kalemia was 3.65±0.4 mmol/L, mean pre-HD kalemia was 5.23±0.72 mmol/L, with a mean delta 1.58±0.64 mmol/L. Medium pH was 7.37±0.01, with serum bicarbonate 20.15±4.0 mmol/L. Overhydration estimated by bioelectrical impedance analysis was 2.3±0.6 L, while mean daily intake of K was 1697.13±711.13 mg. We found a strong positive correlation between delta K and pre-HD kalemia ($r=0.79$, $p<0.0001$). Surprisingly, a positive correlation was found between delta K and serum bicarbonate ($r=0.27$, $p=0.04$), while no correlations were present between delta K, mean pre-HD kalemia and dietary intake of K (p=ns). No difference in delta K was found between anuric and not anuric patients. No other statistically significant differences were found.

Conclusion: Potassium homeostasis is markedly altered in ESRD and several factors contribute to determine the serum K values. In this study we found that delta potassium correlates to pre-HD kalemia. We did not study the temporal kinetic of K increase, but it is reasonable to infer that a significant post-HD rebound may contribute to increase kalemia, as dietary intake of K was not found to correlate to delta K or to serum K after the long interdialytic interval. The positive correlation between delta K and serum bicarbonate is unexpected and difficult to explain. However, since we did not measure serum bicarbonate post-HD, we may speculate that patients with high delta K and serum bicarbonate might have even higher levels of bicarbonate after HD. In conclusion, our study shows that none of the examined factors prevales in determining high serum potassium in HD patients.

P1107 CENTRALIZED CONTROL OF HEMODIALYSIS PROCEDURES AND CORRECTION OF CKD COMPLICATIONS WITH BI TOOLS

Aleksei Galchenkov[1,2], Andrey Malkoch[1,3,4], Vladimir Novitskiy[1,5], Vadim Parfenov[1,2]

[1]Nephrology Expert Council, Moskva, Russia, [2]Moscow State University of Food Production, Moskva, Russia, [3]Moscow State University of Food Production, Therapy and children diseases, Moskva, Russia, [4]Russian Medical Academy of Continuous Professional Education, Nephrology and Hemodialysis, Moskva, Russia and [5]Moscow State University of Food Production, Informatics and computing technology of food production, Moskva, Russia

Background and Aims: Life expectancy of patients with terminal stage of chronic kidney disease depends on the quality of dialysis therapy and timely and adequate correction of dialysis complications. The goal of this work is to improve the treatment quality for dialysis patients in a setting of multi-facility hospital by employing of Business intelligence (BI) tools for centralized control of diagnostic and treatment process.

Method: We have created a system for centralized control of patients' condition, using Microsoft Power BI platform. This system allows to analyze the process of hemodialysis procedure as well as treatment of hypertension, anemia and mineral bone disorder. The system generates various reports that may include parameters of a specific patient, single clinic, or multi-facility hospital for the period from arbitrary date to the day, previous to the report generation date.

The effect of system usage was assessed on 288 patients from 30 hemodialysis facilities of "Nefrosovet" private organization, for the period of 6 month.

Results: Before deployment of the system, target value of Kt/V (1.4) was reached or exceeded in 49% of hemodialysis procedures, median duration of hemodialysis procedure was 227±18 minutes (mean total duration per week - 683 minutes). As the result of usage of centralized control and prescription correction system, target values of Kt/V was reached or exceeded in 65% of hemodialysis procedures, median duration of hemodialysis procedure increased to 238±11 minutes (mean total duration per week - 714 minutes). Before the start of the study, hypotensive episodes were registered in 34% of hemodialysis procedures, and hypertensive episodes were registered in 22% of hemodialysis procedures. As the result of centralized control of hemodialysis procedures, number of procedures with hypotensive episodes reduced to 28%, and number of procedures with hypertensive episodes reduced to 17%. Number of patients with blood hemoglobin value in target range of 100-120 g/l, increased from 1617 patients (56%) to 2051 patients (71%). Number of patients with blood ferritin value in target range of values, increased from 1013 patients (35%) to 1386 patients (48%). Number of patients with TSAT value in target range of values, increased from 873 patients (30%) to 1097 patients (38%). We have also noticed an increase in number of patients with target values of calcium and phosphorus metabolism parameters: calcium corrected for albumin – from 1992 (69%) to 2165 (75%) patients, phosphorus – from 693 (24%) to 982 (34%) patients, intact parathyroid hormone (iPTH) – from 635 (22%) to 837 (29%) patients.

Conclusion: The usage of BI based centralized patients' condition control system allows to improve adequacy of dialysis therapy and quality of CKD complications correction in dialysis patients.

P1108 **FLUID DYNAMIC ASSESSMENT OF THERANOVA DIALYZER THROUGH CT IMAGING TECHNIQUE**

Anna Lorenzin[1], Gianlorenzo Golino[1,2], Llaria Godi[1,2], Massimo De Cal[1,3], Claudio Ronco[1,2,3]

[1]International Renal Research Institute of Vicenza, San Bortolo Hospital, Vicenza, Italy, [2]University of Padova, Medicine, Padova, Italy and [3]San Bortolo Hospital, Nephrology, Dialysis and Transplantation, Vicenza, Italy

Background and Aims: Inadequate removal of molecules between 5and50KDa, due to their restriction in diffusibility, may cause long-term complication in chronic hemodialysis patients. Medium Cut-off(MCO) is a new class of membranes with enhanced sieving properties and negligible albumin loss, thanks to its high molecular weight(MW) retention onset and MW cut-off value lower than albumin MW. MCO membrane used in HD allows to perform expanded hemodialysis (HDx), a technique based on high internal filtration(IF). Our previous study quantified the IF of Theranova dialyzer leveraging a nuclear imaging technique. In order to characterize the local distribution of the IF, an in vitro study assessing the fluid dynamics inside Theranova dialyzer was conducted through CT imaging technique.

Method: Dialyzers Theranova 400 and 500(Baxter, Deerfield, USA) were placed in vertical position in the CT gantry. Blood and dialysate were circulated in countercurrent at 300ml/min and 500 ml/min, respectively. The two compartments were analyzed separately, injecting the dye solution, for both filters. Longitudinal sections, 0.5cm thick, were recorded for 60seconds.

Results: In blood compartment, dye solution immediately after its entrance in the dialyzer demonstrates homogeneous progression, while different velocity profiles were observed among the fibers proceeding to the outlet port (Fig b). In dialysate compartment, dye solution is distributed in the periphery first (Fig d), then seeps in the fibers bundle and reaches the complete compartment filling.

Conclusion: The homogeneous dye profile immediately after its entrance in blood compartment demonstrated a good design of the inlet port; the optimal dye distribution reached in both blood and dialysate compartments ensure that IF phenomenon is equally achieved in both central and peripheral regions of the dialyzer.

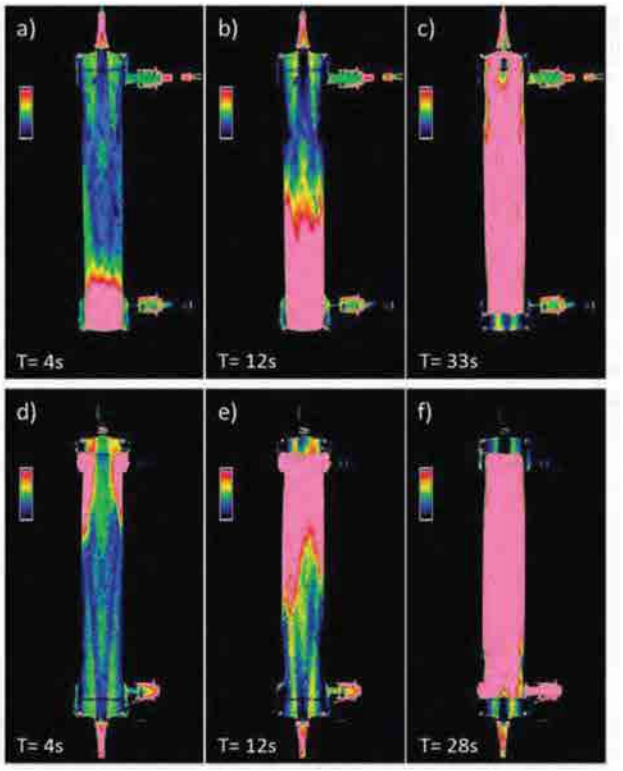


Figure: Dye progression in blood (a,b,c) and dialysate (d,e,f) compartment of Theranova 400 after 4, 12 and at total filling.

P1109 HDX: IS IT A BETTER WAY TO DIALYSE?

Nageen Anwar[1], Noshaba Naz[1], Anna Reynolds[1], Ruby Chumber[1]

[1]*Wirral University Teaching Hospital NHS Foundation Trust (WUTH)., Birkenhead, United Kingdom*

Background and Aims: Inadequate dialysis has been linked to reduced quality of life, increased symptom burden and increased risk of cardiovascular illness in patients with chronic kidney disease. This is especially significant in long-term haemodialysis patients who have little to no residual urine output and are thus almost entirely dependent on good quality dialysis to remove toxins and fluid.

In most conventional haemodialysis modes middle molecule clearance is inadequate. This in turn plays an important part in causing multiple complications.

HDx is a new type of haemodialysis being introduced using Theranova® dialyzer. This claims to have medium cut-off membranes, functioning similar to a kidney, hence providing better clearance of middle molecules, whilst selectively preventing loss of proteins from the body.

In order to test the safety and efficacy of HDx using Theranova® we tried it in a cohort of our patients in the form of an audit.

Our primary objective was to find out the effect of HDx on quality of life.

Secondary objective was to determine whether HDx improves blood biochemistry, with a reduction in medication & transfusion needs.

Method: Thirty seven Haemodialysis patients were switched from hemodiafiltration to HDx, out of these 3 patients were transplanted, 2 patients died, 1 patient switched back and 7 patients were transferred to satellite units. Audit was continued with the remaining 24 patients.

All patients completed an Integrated Palliative Care Outcome Score (IPOS) prior to commencing on HDx and then at six months.

Blood parameters including phosphorous, calcium, haemoglobin, Ferritin and CRP were measured monthly and mean values of 6 months before and after HDx initiation were compared.

Comparison of erythropoietin, intravenous iron and packed red blood cell transfusion requirements pre and post HDx commencement were also undertaken.

Results: No obvious adverse effects were noted with use of HDx dialysis.

All patients had an improvement in overall IPOS scores after being on HDx for 6 months. Shorter post dialysis symptom recovery times were also noted.

13 patients had a decrease in their erythropoietin requirements, in 2 patients requirement remained the same, 9 patients had increase in their requirement however 3 of these patients had been requiring packed red blood cell transfusion prior to HDx commencement, no longer required transfusion.

We found an overall improvement in patients iron infusion need. 11 patients had a dose reduction, with 4 of these patients no longer requiring iron. 9 patients continued to have the same requirements. 4 patients had an increase in iron dose, but 3 of these patients previously being transfusion dependant no longer required regular transfusions.

We also noted that with use of HDx clotting risk was reduced and patients who were switched from Evodial (heparin coated dialyzer membranes) to HDx did not have increased circuit clotting.

With regards to inflammation we noted no significant changes in CRP, ferritin levels and other blood parameters.

Conclusion: Looking at our cohort of patients we concluded that HDx is safe to use with no obvious adverse effects.

It seems that use of HDx is particularly helpful in improving quality of life in dialysis patients as indicated by improvement in IPOS scores. IPOS is a validated questionnaire to measure symptoms and concerns in patients with advanced illnesses. As life quality is a major concern in dialysis patients, this outcome is of particular significance.

HDx was also helpful in reducing the overall burden of transfusions, iron and erythropoietin requirements. This is beneficial in overall patient health and cost burden.

Based on the above we found out that HDX was safe and effective in our patient cohort, however large-scale studies will be required for more conclusive evidence.

P1110 IN VITRO CYTOKINE REMOVAL - COMPARISM OF CONVENTIONAL HDF AND HDX (MIDDLE-CUT-OFF-DIALYZER, BAXTER THERANOVA)

Sebastian Koball[1], Andreas Koertge[2], Benjamin Heskamp[2], Silvius Frimmel[1], Michael Hinz[1], Steffen Mitzner[1]

[1]University of Rostock, Department of Internal Medicine - Nephrology and Dialysis, Rostock, Germany and [2]Fraunhofer-Institut für Zelltherapie und Immunologie, Rostock, Germany

Background and Aims: The removal of inflammatory mediators and cytokines is of great importance in the treatment of patients with acute or chronic renal failure. In patients with acute renal failure and sepsis, an attempt is made to achieve removal through the use of high-volume treatments or adsorbers in order to achieve better circulatory stability. In chronic dialysis patients, this has so far not been sufficiently addressed, but is important for mortality and cardiovascular events (MIA syndrome). Some studies show a superiority of HDF over conventional HD. By using new MCO filters in HD mode such as the Baxter Theranova (HDx), an improvement of cytokine status seems to be possible in both areas (chronic and acute).

The effectiveness of MCO filters (HDx) compared to high flux hemodiafiltration in the removal of interleukins (interleukin 6, interleukin 10 and TNF (tumor necrosis factor) alpha will be assessed.

Method: The efficacy of HDx was compared with that of conventional high-flux dialysis filters (Fresenius FX80, HDF) in HDF mode. Based on real world conditions the ultrafiltration/substitution rate was set to 50 ml/min. (blood flow 200 ml/min., dialysate flow 500 ml/min.) No effective ultrafiltration was used. The measurements were performed in vitro in a 3l pool of fresh frozen plasma (citrate anticoagulated, with additional heparin during dialysis treatment). IL6 (24.5 kDa) IL10 (18.6 kDa, dimer)) and TNFalpha (17.4 kDa, trimer) were added to the plasma pool in concentrations of 1.5 µg/l each. This results in very high cytokine levels, as for example in severe sepsis. Samples were taken before and after the dialyzer for 180 minutes (after 5, 15, 30, 60, 120 and 180 minutes).For HDF the measured cytokine concentration was corrected for ultrafiltration rates. In addition to cytokines, albumin and total protein concentration were measured (ELISA Kit LEGEND MAX Human IL-6 / IL-10 / TNF-α; Biolegend and Cobas Mira Plus; Roche Kit LT-AB 0103 and LT-TP 0253). Every test was repeat 5 times.

Results: Theranova HDx showed higher removal rates of all tested cytokines over a period of 180 minutes. A comparison of the concentrations at the beginning and end of the measurements showed:

IL-6 reduction - HDx about 77% / HDF about 63%.

IL-10 reduction - HDx about 53% and HDF about 22%.

TNF-α Reduction - HDx about 26%; HDF about 18%

The concentration of albumin and total serum protein was not significant different during the treatments in both groups.

Conclusion: Hemodialysis therapy with Theranova HDx appears to be a superior or equal therapy option for the removal of cytokines. This opens up new treatment options for both acute renal failure and chronic dialysis patients, especially if citrate anticoagulation is necessary. The ultrafiltration rate in HDF was lower than recommended for high volume diafiltration,but as high as in our real world experience. Therefore the effect of HDF could be underestimated. Clinical studies with clinically relevant blood flow and ultrafiltration rates are still necessary.

P1111

MULTI ORGAN SUPPORT WITH EXTRACORPOREAL CARBON DIOXIDE REMOVAL (ECCO2R) AND CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT) WITH CITRATE ANTICOAGULATION IN THE CLINICAL SETTING OF DIFFICULT WEANING FROM MECHANICAL VENTILATION

Davide Ricci[1], Alessandra Sagliocchi[1], Antonio Siniscalchi[2], Marco Ranieri[2], Elena Mancini[1]

[1]Policlinico Sant'Orsola-Malpighi, Nephrology, Dialysis, Hypertension, Bologna, Italy and [2]Policlinico Sant'Orsola-Malpighi, Anesthesiology, Intensive Care and Transplantation, Bologna, Italy

Background and Aims: Prolonged mechanical ventilation is associated with the risk of difficult weaning due to the onset of muscle weakness. A disproportion occurs between the respiratory workload and the muscular force, which leads to failure of the ventilatory pump and hypercapnia. Some early experiences suggest that $ECCO_2R$ facilitates weaning from the ventilator in patients with a high risk of failure.

Method: Clinical case: a 49 year-old man with a) recent orthotopic liver transplantation (cryptogenic cirrhosis), b) acute renal injury (AKI) on continuous veno-venous hemofiltration (CVVH) and c) acute respiratory distress syndrome (ARDS) requiring prolonged mechanical ventilation. After unsuccessful attempts at weaning from the ventilator, a lung membrane was inserted in series, before the hemofilter, on the CRRT circuit in order to remove CO2 and so reduce the workload of the respiratory muscles (Fig. 1). The patient was then extubated. We used citrate anticoagulation due to the presence of contraindications to systemic heparin (high bleeding risk, thrombocytopenia).

Results: ECCO2R + CRRT treatment requires a relatively high blood flow (300-350 ml / min) in order to extract a significant amount of CO2, but, the more the blood flow increases, the more citrate must be infused, and the more the metabolic load increases. The patient developed mild alkalosis as an initial sign of citrate accumulation (Table 1), but it was self-limiting. During ECCO2R we actually obtained the desired decrease in respiratory muscle effort (decrease in respiratory rate from 24 to 18 per minute and a maximum negative value of esophageal pressure from -8 to -4 cmH2O) and the treatment was interrupted after 36 hours. Mechanical ventilation was restored due to a complication independent of ECCO2R (massive pneumothorax). The patient tolerated the treatment for 36 hours.

Conclusion: ECCO2R proved an efficient and relatively simple technology helping respiratory function recovery. Due to the very frequent association of AKI and ARDS, leading to a high mortality rate, nephrological care in intensive care units should include this new treatment. Moreover, reduction of the inflammatory pathway secondary to mechanical ventilation could also benefit the evolution of AKI.

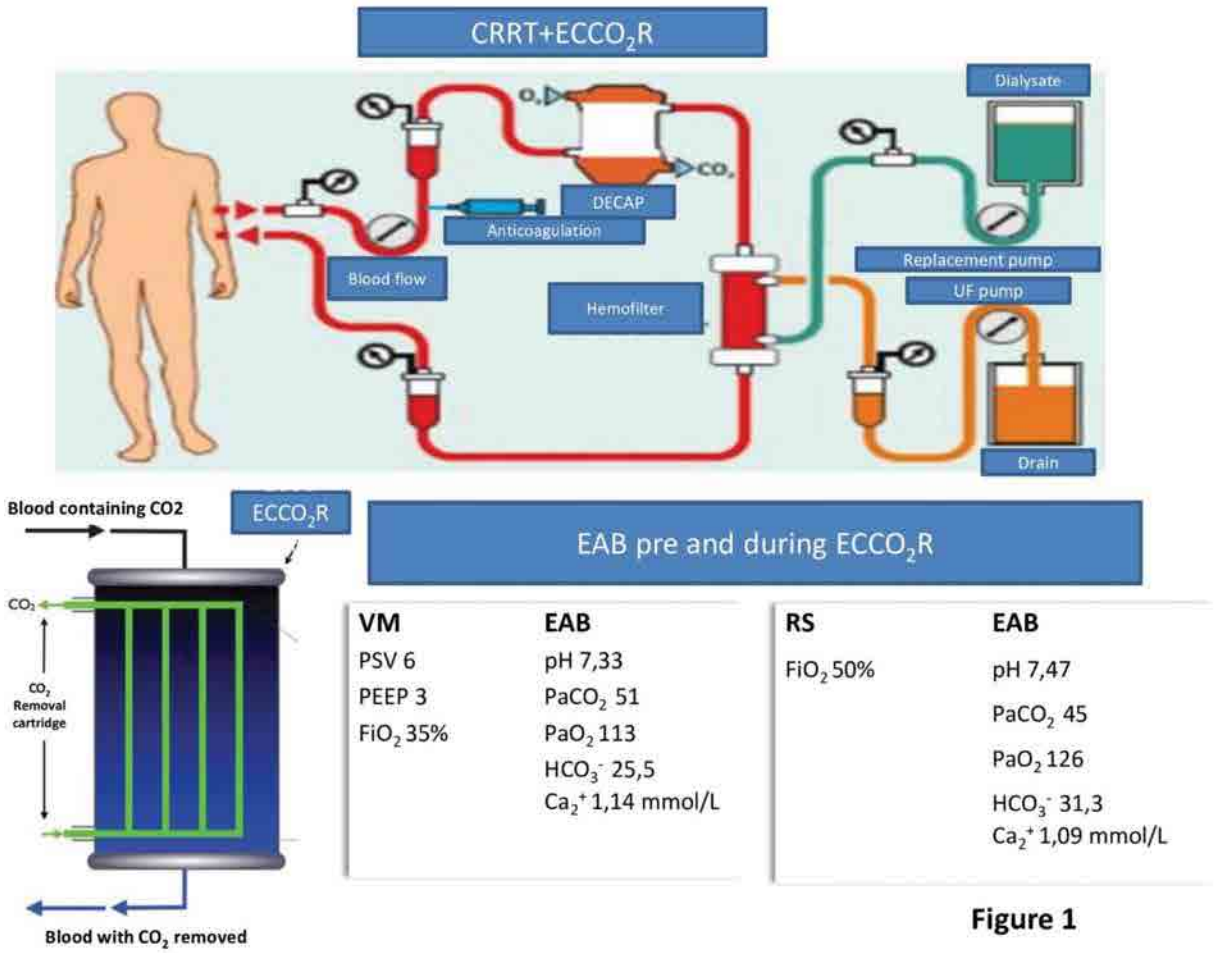


Figure 1

Figure:

P1112

COMPARISON OF EFFICACY BETWEEN MAINTENANCE HEMODIALYSIS AND THEIR COMBINATION WITH HEMOPERFUSION IN PATIENTS UNDERGOING CHRONIC HEMODIALYSIS TREATMENT

Amela Beciragic[1], Alma Mutevelic-Turkovic[1], Badema Äœengiä† Roljiä†[1], Fahrudin Masnic[1], Aida Coric[1], Selma Ajanovic[1], Nejra Prohic[1]

[1] *University Clinical Centre Sarajevo , Clinic for Hemodialysis, Sarajevo, Bosnia and Herzegovina*

Background and Aims: The occurance of mid- and longterm uremic complications is related to the low clearance rate of middle and large molecule uremic toxins when hemodialysis (HD) alone is adopted. As the uremic toxins and their corresponding biological effects become increasingly clear, blood purification treatment that aims to remove these toxins, has developed from a stage of life-sustaining to improving the quality of life.

The objective of this study was to evaluated demographic, clinical and laboratory data in patients who underwent the combination of maintenance hemodialysis with hemoperfusion (HP) and in those who recieved HD alone and to investigate whether this combination could improve the clearance rate of middle and large molecule uremic toxins.

Method: A total of 26 patients, who underwent routine hemodialysis, were assessed in this study. Those patients were randomly divided into three groups: Group 1 (7 patients) received combined treatment of HD with HP biweekly (HD 2 times a week with HD+HP once a week), whereas Group 2 (10 patients) was given HD with high flux dialyzer and Group 3 (9 patients) was given HD with low flux dialyzer 3 times a week. This study was followed for 4 months. Before and after the observational period demographic and clinical data were taken from the medical history and blood samples were taken for hemoglobin (Hb), iron (Fe), total iron binding capacity (TIBC), albumin (Alb), calcium (Ca), phosphorus (P04) and parathyroid hormone (PTH).

Results: This study included 13 female and 13 male patients with a mean age of 41, 62 $\pm$ 11.12 and a mean dialysis duration of 62, 78$\pm$53, 33 months. When it comes to baseline characteristics, patients of the group 3 were significantly older than patients in other groups (p=0.001). At the end of the four months observation period, the same difference according to age was noticed (p=0.01). Also, HD+HP group had significantly higher values of TIBC (p=0.006) and significantly lower serum levels of P04 (p=0.001). EPO doses were very similar in group 1 and 2, but in group 3 there were noticeably lower than in those two groups but without a significant difference. The serum levels of albumin were higher in group 3 compared to the other two groups but also without statistical difference. No statistical difference between groups after the follow up period was observed in terms of Hb, Fe, PTH, Ca, BMI, duration of dialysis treatment and vascular access. When groups are viewed individually, in the HD+HP group serum P04 levels were significantly lower after the 4 months off the follow up period than it was at the beginning (p=0.031) and also TIBC was significantly higher (p=0.018). In group 2 the values of TIBC were significantly lower after the follow up period than it was at the beginning (p=0.025). No significant difference was noticed in group 3 but serum PTH levels tends to decrease after 4 months compared to baseline measurement.

Conclusion: This combination treatment of HD with HP was superior to HD in reducing levels of phosphorus. These findings suggests a potential role of reducing the risk of cardiovascular events in this population especially when it is known that hyperphosphatemia has been pointed out as the primary culprit in the process of cardiovascular calcification. Also, patients who underwent the combined treatment showed higher values of TIBC but unfortunately no difference was noticed between Hb levels and EPO doses. These results eventually demonstrates their role in the improvement of renal disease anemia, which opens up the possibility of further research on a larger sample and over a longer period of time.

P1113 **TREATMENT OF ACUTE LITHIUM INTOXICATION WITH SUSTAINED LOW-EFFICIENCY DIALYSIS (SLED)**

Tommaso Di motta[1], Francesca Di Mario[1], Rosa Giunta[2], Cristina Zambrano[1], Caterina Maccari[1], Elisabetta Parenti[1], Giuseppe Regolisti[1], Enrico Fiaccadori[1], Paolo Greco[1]

[1]UO Nefrologia, Azienda ospedaliero universitaria di Parma, Parma, Italy and [2]UOC Nefrologia, policlinico Catania, catania,

Background and Aims: Lithium salts are widely used in psychiatry for prophylaxis and treatment of bipolar affective disorders. Given its narrow therapeutic range, drug overdosage is not infrequent, and lithium intoxication has potentially fatal neurologic and cardiac side effects. Owing to its low molecular weight (7 Da), relatively small volume of distribution, and its negligible protein binding, lithium can be efficiently removed by any extracorporeal modality of renal replacement therapy (RRT). Although conventional intermittent haemodialysis (IHD) is effective in promptly cleating lithium, post-dialysis rebound is common. The use of sustained low-efficiency dialysis (SLED) in lithium intoxication seems to be a valid therapeutic strategy, but strong evidence is still lacking in the literature. We present here two cases of lithium intoxication, in one case acute (naïve patient) and in the other case acute-on-chronic (a deliberate overdose in a patient previously on lithium therapy), successfully treated with SLED.

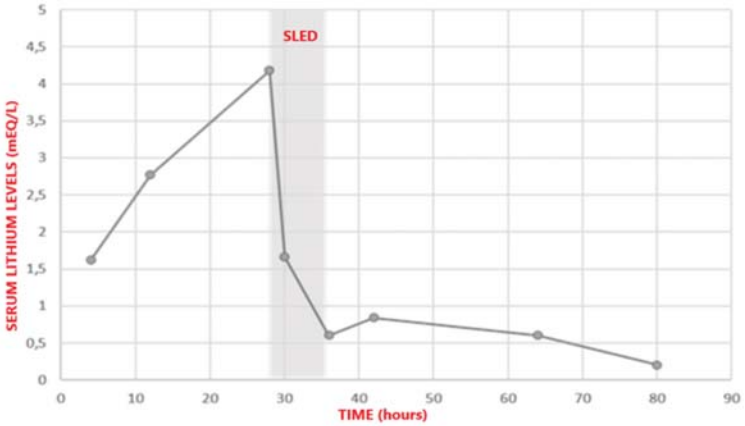
Method: Patient A - A 47 years-old woman without history of lithium consumption was admitted to the ER. after a voluntary acute lithium ingestion of 40 tablets of lithium carbonate (8.12 mEq lithium each). Notwithstanding treatment with intravenous crystalloids and gastric lavage, lithium concentration increased up to 4.18 mEq/l at about 24 h after admission. She developed mental status changes, oliguria, hypotension and bradycardia.

Patient B – A 58 years-old man on lithium therapy for bipolar syndrome was admitted to ER after a voluntary acute lithium ingestion of an unknown quantity of lithium carbonate tablets. Lithium concentration, after an initial level of 0.4 mEq/L, increased up to 4.35 mEq/l about 15 h from admission, despite irst-line therapies with intravenous crystalloids and gastric lavage were promptly started. His mental status worsened, together with oliguria, bradycardia and hypotension.

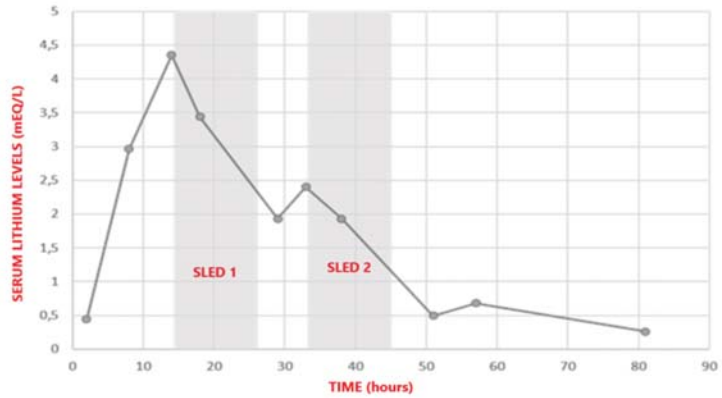
Results: Patient A - A 8-hour SLED session with regional citrate anticoagulation (RCA) was planned [blood flow rate (Qb) 200 mL/min; dialysis fluid rate (Qd) 300 mL/min; countercurrent flow direction]. Lithium serum levels decreased by 87% during treatment (0.55 mEq/L), and the patient fully awoke recovering a normal mental status within the first 4 h of treatment. SLED was completed safely within the prescribed time. After the end of treatment, lithium rebound was unremarkable and renal function completely recovered and the patients was discharged after 3 days.

Patient B - A 12-hour SLED session with RCA was planned (Qb 200 mL/min; Qd 500 mL/min; countercurrent flow direction). Serum lithium levels decreased by 55% (2.10 mEq/L) during treatment, and the patient awoke, recovering a normal mental status. At the end of treatment, rebound of lithium concentration was observed at 4 hours from SLED end detected (from 2.1 to 2.5 mEq/L), with initial signs of mental deterioration. A second SLED (12 h) was performed, with the same operative parameters and, by the end of the second treatment, lithium concentration was 0.49 mEq/L. Afterward, mental status and renal function fully recovered and no rebound rebound was observed. The patient was discharged after 6 days.

Conclusion: SLED could represent a good therapeutic strategy to treat acute lithium intoxication, providing an initial rapid clearance with resolution of symptoms, and limiting major rebound.



Patient A – monitoring of serum lithium levels before, during and after renal replacement therapy with a single session of Sustained Low efficiency dialysis (SLED) of 8 hours (grey box).



Patient B – monitoring of serum lithium levels before, during and after renal replacement therapy with two session of Sustained Low efficiency dialysis (SLED), both of 12 hours (grey boxes).

Figure:

P1114

HA-130 HEMOPERFUSION CARTRIDGE IN THE TREATMENT OF CAST NEPHROPATHY IN A 58-YEAR-OLD MALE WITH MULTIPLE MYELOMA: A CASE REPORT

Joanna Margarita Santos[1], Maria Kristina L. Alolod[1]

[1]St. Luke's Medical Center, Section of Nephrology, Quezon City, Philippines, The

Background and Aims: Multiple myeloma is a plasma cell neoplasm that results in the production of monoclonal immunoglobulin. Renal failure is a common complication of multiple myeloma, occurring in approximately one-half of patients on initial presentation and is associated with increased mortality. Cast nephropathy in particular, is considered to be one of the major mechanisms of renal failure in multiple myeloma, and is characterized by precipitation of free light chains in the distal nephron, leading to intratubular obstruction, inflammation and fibrosis. Recent studies have demonstrated the use of extracorporeal methods such as plasmapheresis and high-cutoff membrane dialysis as an adjunctive therapy to chemotherapy in the management of cast nephropathy, however currently there are no existing guidelines in the use of extracorporeal therapies in the management of complications of multiple myeloma. Hemoperfusion is an extracorporeal treatment technique which utilizes adsorption in the removal of specific toxins. The HA 130 cartridge in particular has a resin pore size distribution of 500Da- 40 KDa and is able to remove molecules at 5-30kDa. In this case report we describe the use of HA 130 hemoperfusion cartridge in the treatment of cast nephropathy in Multiple Myeloma.

Method: A 58-year-old male, diabetic, non-hypertensive came in for 5-day history of generalized body weakness, associated with myalgia, lumbar pain and undocumented fever, with 1-day history of loose stools and vomiting. Upon admission blood tests done revealed anemia with a hemoglobin of 7.8g/dl, creatinine of 9.97mg/dL and potassium of 5.5mmol/L. He was diagnosed with acute renal failure and underwent hemodialysis on the second hospital day. On workup he had lytic bone lesions in the spine, pelvis and cranium on CT scan and x-ray. Serum Protein Electrophoresis (SPEP) and Serum Free Light Chain (sFLC) tests showed a monoclonal gammopathy. Serum beta 2 microglobulin was elevated at 12,618ng/ml. Free kappa and lambda light chains were also elevated at 19,250mg/L and 25.7mg/L, respectively. Bone marrow biopsy was done, with findings of markedly hypercellular marrow with 80% plasma cells confirming the diagnosis of Multiple Myeloma. Combined hemodialysis with hemoperfusion were done using HA 130 filter and hi flux dialyzer for 2.5 hours then hemodialysis for three times a week. Patient was also started on chemotherapy using Bortezomib with Dexamethasone for 2 cycles.

Results: Patient had a total of 14 sessions of combined hemoperfusion with hemodialysis. On repeat free kappa light chains decreased to 212.5mg/L. Patient was maintained on hemodialysis three times a week and was discharged after 55 hospital days. Outpatient hemodialysis was continued three times a week, and after 2 weeks, patient showed signs of renal recovery with a repeat creatinine of 2.1mg/dL. Four weeks after discharge, patient was independent of hemodialysis with a repeat creatinine of 1.3mg/dL.

Conclusion: This report highlights the use of hemoperfusion using HA 130 cartridge in combination with chemotherapy using Bortezomib in reducing free light chain levels in a 58-year-old male that developed renal failure secondary to cast nephropathy. Patient was able to achieve reduction in free light chain levels, improvement in renal function and eventually independence from hemodialysis four weeks after the last hemoperfusion treatment. Further studies using a randomized control trial on the use of hemoperfusion in directly reducing serum free light chain levels is recommended. The value of hemoperfusion on the rate of independence from hemodialysis, as well as survival rates among patients with renal failure secondary to multiple myeloma may also be worth investigating using larger studies.

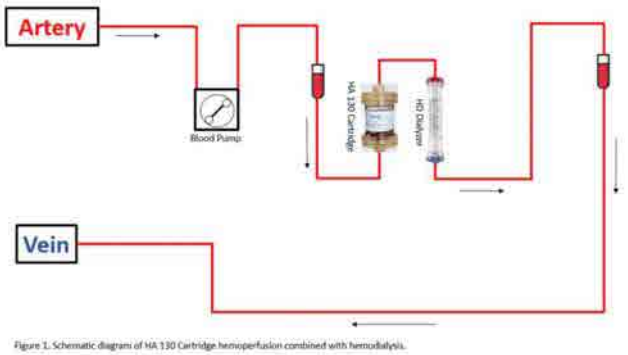


Figure 1. Schematic diagram of HA 130 Cartridge hemoperfusion combined with hemodialysis.

Figure:

P1115 MEDICAL WASTE MANAGEMENT - HOW INDUSTRY CAN HELP US TO PROTECT ENVIRONMENT AND MONEY

Jacek Zawierucha[1], Tomasz Prystacki[2], Wojciech Marcinkowski[2], Jolanta Malyszko[3]

[1]Fresenius Medical Care Polska S.A., Poznań, Poland, [2]Fresenius Nephrocare Polska sp. z o.o., Poznań, Poland and [3]Medical University of Warsaw, Deparment of Nephrology, Dialysis and Internal Medicine, Warszawa, Poland

Background and Aims: The global climate change and its consequences force us to remodel our processes and rethink current model of providing the HD treatments. One of the crucial point, which have massive impact on the environment and the economy is the waste management. Every HD session produces above 1 kg of medical waste, which should be properly stored and destroyed. Well thought out processes and our choices can improve dialysis unit budget as well as decrease CO_2 emission produced during the waste incineration.

The aim of the study was was assessment of weight the different dialysers used during HD treatments and consequences of choice different types of filters.

Method: The weight of dialyser is the most crucial component of the medical waste produced during dialysis session. The authors checked the weight of different dialysers regularly used in dialysis centers in Poland. The Kern CM 320-IN scale was used for the measurement. The measurement accuracy was 0,1 g.

Also the filling volume of each dialyser has been taken into consideration.

Results: The dialysers were divided into four groups depending on the surface. 1,4m^2 in group one, 1,5-1,6m^2 in group two, 1.7-1,8m^2 in group three and finally 2,0-2,2m^2 in the group four. FX class dialysers were lightest in every group. The heaviest ones were Polyflux dialysers. Difference between the lightest and heaviest dialysers was about 95 g. Also the filling volume was lowest in FX class dialysers and the highest in case of Elisio dialysers. The difference was 20 ml.

Conclusion: The weight of different dialysis sets available on the market significantly differs. The decision-makers should take into account this fact as the additional quality feature. In extreme cases the weight difference reaches 95 g. In yearly perspective, the usage of the lighter dialysis set can cause the 17 millions kilograms decrease of medical waste and significant savings.

On the other hand modern HD machines like Fresenius 6008 machine, due to the dialysis set emptying function additionally decrease the mass of the medical waste about 150 g per one HD session, independently on the dialyser used.

P1116 IS DIALYSIS ADEQUACY AMELIORATED AFTER INCREASING DIALYSATE FLOW RATE IN CHRONIC HEMODIALYSIS? - ONE YEAR FOLLOW-UP

Aggeliki Barbatsi[1], Eugenia Karakou[2], Theodoros Chiras[1], Jacob Skarakis[3], Nikolaos Trakas[2], Makrouhi Sonikian[4]

[1]Sismanoglio General Hospital, Nephrology, Athens, Greece, [2]Sismanoglio General Hospital, Biochemistry, Athens, Greece, [3]DEMO S.A. Pharmaceutical Industry, Research and Development, Athens, Greece and [4]Sismanoglio General Hospital, Nephrology, Greece

Background and Aims: Hemodialysis (HD) adequacy, as measured by single pool (sp) Kt/V and urea reduction rate (URR), has been reported to be ameliorated after increasing dialysate flow rate (DFR). However, this is a matter of controversy as no benefit has been observed with dialyzers incorporating features to enhance dialysate flow distribution. We investigated the effect of increasing DFR on dialysis adequacy and on various laboratory parameters.

Method: Twenty-three patients, M/F=20/3, aged 65(44-89) years, dialyzed thrice weekly for 50(6-274) months, using polysulfone low flux dialyzers, participated in an annual randomized cross-over study. Patients were dialyzed with DFR of 500 ml/min and 700 ml/min for 6 consecutive months respectively, according to their usual dialysis prescription and with ultrafiltration volumes according to clinical need. Blood was sampled before and at the end of midweek sessions at the beginning of the first, 7th and 13rd month for urea, creatinine, potassium, sodium, albumin, total Ca and phosphate (sP). URR, spKt/V, corrected for albumin Ca(sCa) and sCa x sP product (CaxP) values were calculated.

Results: Under both 500 and 700 ml/min DFRs used, the expected post-dialysis alterations were found: decreased values in serum urea (respectively 161,5±38,0 to 49,9±20.1-p<0,001 and 140,3±30 to 56,0±20.4 mg/dl-p<0,001), creatinine (respectively 10,2±2 to 3.9±1,2-p<0,001 and 10,2±3,3 to 4,1±1,6 mg/dl-p<0,001), potassium (respectively 5,2±0,7 to 3,7±0,3 mM-p<0,001 and 5,3±0,6 to 3,9±0,3mM-p<0,001) and phosphate (respectively 5,4±1,7 to 2,9±0,6-p<0,001 and 5,7±1,6 to 2,6±0,6 mg/dl-p<0,001); increased values in serum albumin (respectively 4,3±0,4 to 4,7±0,4 g/dl-p=0,001 and 4,2±0,3 to 4,7±0,4 g/dl-p<0,001) and sCa (9,1±0,7 to 11,3±0,9 mg/dl-p<0,001 and 8,7±0,6 to 9,9±0,7 mg/dl-p<0,001). After increasing DFR from 500 to 700 ml/min we observed no reductions in pre-dialysis serum urea and creatinine levels or URR (68,6±8,1% to 69,9±7,9%-p=NS) and Kt/V (1,41±0,4 to 1,42±0,3-p=NS) values. However, under DFR of 700ml/min post-dialysis sCa, sP and sCa x sP product values were always lower compared with those under DFR of 500 ml/min (respectively 9,9±0.7 vs 10,8±0.8 mg/dl-p<0,001, 2,6±0,6 vs 2,9±0,6 mg/dl-p=0,02 and 25,6±6,2 vs 30,9±6,7 mg^2/dl^2-p<0,001).

Conclusion: DFR increase from 500 to 700 ml/min did not lead to favorable effects on dialysis adequacy but resulted in post-dialysis amelioration of serum calcium and phosphate levels and may be useful in cases of hypercalcemia, hyperphosphatemia and calcifications. DFR increase utility needs further investigation in patients with disorders of calcium-phosphate metabolism.

P1117 **EXPLORATORY COMPARISON OF DIALYSIS EFFICIENCY AT DIFFERENT DIALYSATE FLOW (QD) IN EXPANDED HEMODIALYSIS IN TWO CENTERS IN COLOMBIA**

Alejandra Molano Trivino[1,2,3], Eduardo Zúñiga[1,2], Mauricio Sanabria[4], Jasmin Vesga[4], Carolina Ramos[5], Juan Felipe Gutiérrez[5], Ha Tran[6], Claudio Ronco[3], Angela Rivera[6]

[1]Fundacion Cardio Infantil Instituto De Cardiologia, Nephrology, Bogotá, Colombia, [2]RTS Cardioinfantil, Nephrology, Bogotá, Colombia, [3]International Renal Research Institute of Vicenza IRRIV, Dialysis and Transplantation, Vicenza, Italy, [4]Baxter Health Services Latin America, Clinical research, Bogotá, Colombia, [5]Universidad del Rosario, Nephrology, Bogotá, Colombia and [6]Baxter Healthcare, Miami, United States of America

Background and Aims: Dialysate flow rate (Qd) has minimal effect in removal of molecules in hemodialysis, allowing to use lower amounts of dialysate with no effect in clearance of molecules. According to recent literature, Expanded hemodialysis (HDx) improves the clearance of middle size molecules, diminishing the effect of Qd in adequacy. We found no data about clearance at different dialysate flow rates in HDx.

Our aim is to evaluate the clearance of middle molecules (beta 2 microglobuline [Mβ2], interleukin-6 [IL-6], interleukin-10 [IL-10 light chains (CLL-κ -λ) with HDx at different Qd using membranes Theranova^{MR} in patients with body weight less than 70 Kg.

Method: We performed an observational retrospective analysis of clearance of Mβ2, IL-6, IL-10, CLL-κ; CLL-λ in HDx using Theranova^{MR} filters with Qd 400 mL/min and 500 mL/min. We performed variance analysis, T student test and Wilcoxon test. Data were extracted from an HDx multicentric trial performed in Bogotá, Colombia in 2018.

Results: 11 (47%) patients received Qd 400 mL/min and 12 (52.1%) patients with Qd 500ml/min. Demographic data are included in table 1. We found no differences in reduction rate of mid-molecules. (Table 2) We found that lower water consume in the Qd 400 mL/min group, with water savings of 24 Liters/patient (13824 L in 12 weeks of follow up). (Table 3)

Conclusion: Expanded hemodialysis seems to allow diminishing Qd rate without changes in mid-size molecules clearance.

Table 1. Demographic data

	Qd 400 (n 11)	*Qd 500 (n 12)*	*p*
Age (Median; SD) years old	64.92 +-13.20	55.93 +- 12.81	0.0364 *
Male gender (N; %)	54.55 (6)	50.00 (6)	0.579 **
ESRD aetiology (N; %)			
Hypertension	63.64 (7)	75.00 (9)	0.438**
Diabetes	9.09 (1)	25.00 (3)	
Autoimmune disease	9.09 (1)	.	
Obstructive disease	9.09 (1)	.	
Idiopatic (unknown)	9.09 (1)	.	
Time on therapy (Months)	130.94 +-89.17	72.56 +- 62.98	0.0564*
Urine Output			
< 100 ml/d	90.91 (10)	75.00 (9)	1**
100 to 400 ml/d	.	8.33 (1)	
> 400 ml/d	9.09 (1)	16.67 (2)	
Dry weight (Median; SD) Kg	53.36 +-7.60	60.41 +- 6.72	0.0266*
Vascular access (N; %)			
AV Fistula	72.73 (8)	91.67 (11)	0.261**
HD Catheter	27.27 (3)	8.33 (1)	
Ultrafiltration (Median; SD) Lts	2.00 +- 0.84	1.63 +- 0.76	0.242*
Urea distribution volume (Median; SD) Lts	32.41 +- 5.19	32.77 +- 4.3	0.7818*

*U Mann Whitney;
**Fisher test

Table 2. Middle size molecules clearance

Molecule	**Qd 400 (n11)**	**Qd 500 (n12)**	***p*- Value***
Beta-2 microglobuline pre mg/L (Media; SD)	24.26 +- 9.28	21.69 +- 8.52	0,497
Beta-2 microglobuline post mg/L (Media;SD)	9.42 +- 11.56	7.19 +- 3.02	0,527
Aclaramiento Beta-2 microglobuline (Media;SD)	14.84 +- 16.62	14.50 +- 7.20	0,949
Interleukin 6 pre pg/mL (Media; SD)	5.49 +- 2.29	9.44 +- 3.96	0,009
Interleukin 6 post pg/mL (Media; SD)	8.66 +- 11.11	9.93 +- 4.11	0,715
Interleukin 6 clearance (Media;SD)	1.91 +- 0.89	1.61 +- 0 .76	0,410
Lambda pre mg/L (Media; SD)	183.5 +- 144.44	157.00 +- 55.12	0,561
Lambda post mg/L (Media; SD)	115.93 +- 106.94	97.28 +- 38.24	0,577
Lambda Clearance (Media; SD)	2.77 +- 1.15	2.10 +- 0.95	0,142
Kappa pre mg/L (Media; SD)	378.04 +- 343.94	222.26 +- 106.63	0,150
Kappa post mg/L (Media; SD)	78.42 +- 49.55	77.44 +- 36.74	0,957
Kappa clearance (Media; SD)	2.17 +- 0.81	1.85 +- 0.85	0,367

*Student Test

Table 3. water consumption according to Qd

	n 11	n 12
	400 mL/min	500 mL/min
	Water consumption (L)	
1 HD session per patient	96	120
Monthly water consumption* (L)	12672	17280
Water use in 12 weeks **(L)	38016	51840
Water saving in 12 weeks (L)	**13824**	

Figure:

P1118 PATIENT SAFETY PROGRAM IN DIALYSIS UNIT: THREE YEARS FOLLOW UP

Sergio Sloboda[1], Andre Felipe Sloboda[2], Sheila Pinto[3], Claudia Monteiro[3]

[1]Renalduc Instituto de Terapia Renal, hemodialysis, Duque de Caxias, Brazil, [2]Renalduc Instituto de Terapia Renal, hemodialysis, Rio de Janeiro, Brazil and [3]Renalduc Instituto de Terapia Renal, Duque de Caxias, Brazil

Background and Aims: In January 2016 we initiated in our dialysis unit a Patient Safety Program (PSP) with the following goals: risk management, improvements in patient care and quality of hemodialysis. The program was based on four pillars: 1 - Individualized care through a Singular Therapeutic Plan (STP); 2 -Practices of processes surveillance and monitoring; 3 - Effective communication program (ECP), valuing the intensive and continuous education of the whole team and 4 –Technological management. The first results in the year of implementation were presented at the 54th ERA-ADTA Congress, Madrid 2017 (MP524). We analysed these established indicators results through three years of the program, comparing them to those found in 2015. The aim of this study is to verify the degree of response of the proposed model over time, and achieve the objectives set monthly (M), quarterly (Q) and annually (A): Hospitalization rate <5% (M); Seroconversion Rate of Viral Hepatitis, 0% (A); Mortality rate, < 5% (A); Patient with hemoglobin values> 10 g/dl, 80% (M); Patient with serum albumin>3 mg%, 90% (Q); SpKt/V $\geq$ 1.4, 80% (M); Patients with normal serum values of P^{3+}, 60% (M); Rate of infections related to health care, < 5% (A).

Method: We conducted a longitudinal study in the period 2016-18, where we analysed the indicators stipulated. We systematically and continuously apply policies, procedures and conducts in the assessment of risks and events. We compared the results found to those collected in 2015. In the statistical analysis, we used in the indicators collected monthly the median $\pm$ standard error, as a measure of central trend and Wilcoxon-Mann-Whitney Test for analysis of the samples. In the annual indicators, we used linear correlation coefficient.

Results: Among the 240 patients studied in a chronic dialysis program in the studied period, there was no exclusion of patients due to the etiology of kidney disease, presence of comorbidities, gender or age. The percentage of patients with Hemoglobin levels >10g/dl was 68$\pm$2.0 in 2015, and 71$\pm$1.8, 72$\pm$2.4, 76$\pm$1.4 from 2016 to 2018, respectively, with statistical significance only in 2018 when compared to 2015, p=0.01. The percentage of SpKt/V $\geq$ 1.4 in 2015 was 72$\pm$2.5, with an increase in 2016, 74$\pm$2.5, without statistical significance, in 2017 it was 80$\pm$2.4 with p=0.01 and in 2018 82$\pm$1.9, p=0.002. In the Patients with normal serum values of P^{3+} index, we observed in 2015 the percentage of 55$\pm$2.9, 2016 63$\pm$2.4, 2017, 68$\pm$2.0, and 2018 73$\pm$1.9 statistical significance in the last two years, p<0.05 and p=0.001, respectively.. There was no seroconversion to Hepatitis C in the whole period. Patient with serum albumin rate >3 mg% was achieved in the three years of the 2016-18 program, 92%, 91% and 95%, respectively, with statistical significance only in 2018, p=0.01, when compared to 2015, 85%. The Hospitalization rate was achieved in the three years of the study, 5% in 2016, and 4% in the following two years, r=0.92. Mortality rate decreased over the PSP, reaching the target in 2018, r=0.69. Finally, the Rate of infection related to healthcare we observed a progressive drop during the program, 8% in 2015, 6% in 2016 and 2017 and reached the target in 2018, 5%, r=0.85.

Conclusion: The Patient Safety Program brings good results in the quality of treatment and consequently decreases comorbidities, hospitalizations and mortality. The results become more evident over time because the improvement of many indicators depends on the direct and continuous work with each patient, and with incessant training of all professionals involved. We strongly believe this program will keep improving all those indicators, especially mortality rate, as patients will benefit clinically, in a cardiovascular standpoint, from P^{3+}, albumin and haemoglobin normal levels over time.

P1119

ASSOCIATION OF VARIOUS RISK FACTORS WITH HEMODIALYZER SET CLOT INCIDENCES WHEN USING LOW DOSE UF- HEPARIN OF 400 IU BOLUS AND 400 IU INFUSION IN MAINTENANCE DIALYSIS SESSION : A CASE CONTROL STUDY.

Farrukh Umair[1], Azib Aftab[1], Safia Awan[1], Imrana Amin[2]

[1]Aga Khan University Hospital, Nephrology, Karachi, Pakistan and [2]Patel Hospital, Medicine, Karachi, Pakistan

Background and Aims: Efforts were made in the past to reduce the use of heparin as anticoagulation to escape from the its Sid effects like Bleeding and HIT among others. We use Low dose UF -heparin use with bolus of 400 IU and 400 IU/hour infusion as an anticoagulation in hemodialysis patients. Set clot incidences were comparable to other studies. The objectives of this study is to see aassociations of different risk factors with hemodialyzer set clot incidences using Low dose heparin Infusion protocol in maintenance haemodialysis session.

Method: Data were obtained from the outpatient haemodialysis unit at tertiary care Hospital in Karachi, Pakistan. UF-low dose heparin 400 I.U bolus and 400 I.U maintenance infusion protocol were given to all patient. Case to control ratio was approximately 1:4. 300 cases of set clot were taken and 1200 control sessions without set clot outcome were matched for heparin use taken from the dialysis unit. The crude odds ratios (OR's) and adjusted ORs (aORs) for various risk factors were obtained using conditional logistic regression.

Results: In a prelimary part of the study the incidence of set clot was 7% (309/4000 sessions) Age, dialysis vintage, hemoglobin level, Blood flow rate and type of anti-platelet therapy were significantly associated to the incidence of set clot. Among patients having **age > 40 yrs**. the odds of set clot were 2.8 (95% CI= 1.8-4.3) as compare to the patients with age $\leq$ 40 yrs. The odds of set clot were 0.268(95% CI=0.081-.88) among patients with **hemodialysis vintage** less than 1 year as compare to those who have more than 1 year. **Blood flow rate** <350 ml/min have an odds of 1.03(95%CI=0.76-1.40) of set clot incident as compare to BFR>350 ml/min. Those patients with **Hemoglobin < 9 gm/dl** have odds of set clot of 0.67(95%CI =0.48-0.92) as compare to hemoglobin > 9 gm/dl. Off all patients ,60.36% patients were either on aspirin or clopidogrel while around 9.58% were on combine antiplatelets therapy. The odds of set clot were 4.6 (95% CI =1.9-10.8) among patients on **Combine antiplatelet therapy** as compare to no antiplatelet therapy.

Conclusion: Age, low Blood flow rate and combine antiplatelet therapy (aspirin and clopidogrel) are positively associated with set clot accidents in dialysis sessions. Dual anti platelet therapy patients are given in ischemic heart disease patients hence Blood flow pumps are kept at lower speed which can increase the risk of set clot. Lesser duration on Hemodialysis (i.e. less than 1 year) and low hemoglobin levels are protective for incidence of set clot in our study population.

P1120 QUANTIFICATION OF ACID-BASE TRANSPORT IN HEMODIALYZERS

Pietribiasi Mauro[1], Jacek Waniewski[1], John (Ken) Leypoldt[1]

[1]*Institute of Biocybernetics and Biomedical Engineering, Modeling and Supporting of Internal Organs Functions, Warszawa, Poland*

Background and Aims: Quantification of bicarbonate and dissolved carbon dioxide (CO_2) transport in hemodialyzers can be described by the product of a dialysance (D) and their respective concentration differences between dialysate and plasma. It is typically assumed that D values are constant for a given hemodialyzer and flow conditions; however, this approach neglects the chemical interconversion of bicarbonate and dissolved CO_2 within blood. We assessed the validity of this approach by developing a comprehensive mathematical model of acid-base transport in hemodialyzers.

Method: Mass balance relationships in a hemodialyzer were defined using a one-dimensional model with counter-current flows of blood and dialysate. The molecular biochemistry of bicarbonate, dissolved CO_2, and non-bicarbonate buffer in both plasma and erythrocytes, together with carbaminohemoglobins within erythrocytes, was assumed to be in equilibrium as described by Rees and Andreassen (Crit Rev Biomed Eng 2005). The model equations were solved numerically, and optimal mass transfer-area coefficients for bicarbonate and dissolved CO_2 were determined by comparing model predictions with the data from Sombolos et al (Artif Organs 2005). The latter data included measured concentrations of bicarbonate and dissolved CO_2 in plasma and dialysate inlet and outlet flows at a blood flow rate of 300 mL/min, dialysate flow rate of 700 mL/min, and dialysate bicarbonate concentration of 32.5 mEq/L. Base excess of blood was assumed as -5 mEq/L. Model simulations then evaluated the effect of the plasma bicarbonate concentration at the blood inlet (assuming constant mass transfer-area coefficients and flow rates) on D for both bicarbonate (Dbic) and dissolved CO_2 (DCO_2). D values were calculated as the loss of the molecule from the dialysate divided by the difference in inlet concentrations of dialysate and plasma.

Results: Optimal mass transfer-area coefficients for bicarbonate and dissolved CO_2 were 396 and 1360 mL/min, respectively. Simulation results at different plasma bicarbonate concentrations at the blood inlet ([Bicarbonate]) as expected during a typical hemodialysis treatment are tabulated:

[Bicarbonate] (mEq/L)	Dbic (mLmin)	DCO_2 (mL/min)
20.4	177	450
22.4	171	482
24.4	162	512
26.4	146	540

DCO_2 exceeded the blood flow rate as previously reported by Sombolos et al (Artif Organs 2005) due to the conversion of bicarbonate into dissolved CO_2 after its transport into blood within the hemodialyzer.

Conclusion: Quantification of acid-base transport in hemodialyzers requires dialysance values for bicarbonate and dissolved CO_2 that are not constant but instead are dependent on the plasma bicarbonate concentration at the blood inlet for a given hemodialyzer at fixed blood and dialysate flow rates.

P1121

TOTAL PLASMA EXCHANGE (TPE) AND CITRATE CRRT IN A LOW-WEIGHT PEDIATRIC PATIENT WITH MACROPHAGE ACTIVATION SYNDROME (MAS): FEASIBILITY AND COMPLEXITIES OF BOTH TREATMENTS

Alessandra Sagliocchi[1], Davide Ricci[1], Fabio Caramelli[2], Elena Mancini[1]

[1]Policlinico Sant'Orsola-Malpighi, Nephrology, Dialysis, Hypertension, Bologna, Italy and [2]Policlinico Sant'Orsola-Malpighi, Pediatric Intensive Care Unit, Department of Woman, Child and Urological Diseases, Bologna, Italy

Background and Aims: Low-weight extracorporeal pediatric dialysis treatments remain a challenge due to their clinical and technical complexity.

Apart from some metabolic congenital disorders, the usual indications for CRRT in early pediatric patients and newborns are the same as for adults with acute kidney injury (AKI). But the implementation of TPE is still in the anecdotal stage.

Method: Clinical case: a 7-month female infant, weighing 5.7kg, in the neonatal intensive care unit with fever, lymphadenopathy, hepatosplenomegaly, pancytopenia, hyperferritinemia, hypertriglyceridemia, was diagnosed as having macrophage activation syndrome (MAS). She developed AKI and acute respiratory distress syndrome (ARDS), due to sepsis. Because of oliguria, ruling out administration of drugs and parental nutrition, and fluid overload (more than 20% of her body-weight), CRRT was started.

Results: CRRT lasted 22 days in continuous venovenous hemodiafiltration (CVVHDF), with regional citrate anticoagulation (Table 1). Mean filter patency: 26±17h. 43% of treatments were interrupted after CVC failure, 21% after clinical procedures, 7% after filter coagulation. There was in this case no citrate accumulation and satisfactory metabolic and electrolyte control were obtained (Figure 1).

After treatment of MAS failed with both i.v. immunoglobulins and corticosteroids, we considered TPE as a rescue therapy for the disease, even though we could not find a similar experience reported in the literature in such a small infant. We performed 3 TPE sessions, with heparin anticoagulation (Table 1), non-consecutively, with CRRT in between.

Conclusion: The treatments were well tolerated, resulting in a large decrease in triglycerides and ferritin (MAS index, Figure 2).

Despite the death of the patient after ARDS worsened, we showed that even in a small critically ill infant, complex depurative treatments such as total plasma exchange are feasible. Highly skilled nephrologists and dialysis nurses are mandatory for treatment management.

P1122 VIRAL INFECTIONS :VHC, VHB AND VIH IN HEMODIALYSIS .

Ali MADIOU[1]

[1]Tizi Ouzou, Nephrology, TIZI OUZOU, Algeria

Background and Aims: Viral infections, especially those caused by hepatitis B and C viruses are common in chronic hemodialysis patients. The hepatitis C virus is the main cause of post-transfusion hepatitis. The main objective of this study is to determine the prevalence of hepatitis B and C and HIV in chronic hemodialysis patients at the TIZI OUZOU University Hospital Center, as well as the main risk factors for contamination, in chronic hemodialysis patients treated at the from our center.

Method: This retrospective study carried out on 149 chronic hemodialysis patients consisted in searching for anti-HCV, anti-HIV antibodies and the HBs antigen and in determining the possible causes of contamination, in particular the age of the hemodialysis and history of blood transfusion. The characteristics studied for all patients are: demographic characteristics, initial nephropathy, seniority on hemodialysis, the concept of hemodialysis outside our center at the time of dialysis or for a limited period during follow-up (vacation. . .), the notion of transfusion; patients are considered to be multi-transfused when they have received more than four transfusions, the search for hepatitis B and C virus infection by ELISA, the concept of hepatic cytolysis: a transaminase level that exceeds 1.5 times normal, vaccine status, HIV serology

Results: The average age of our 149 patients varies between 19 and 82 years with a male predominance (92 men and 57 women) and an average duration of dialysis of 90 months. The predominant etiology of IRCT is vascular nephropathy. We also note other causes including glomerular, diabetic and tubulointerstitial nephropathies. The etiology was largely undetermined. Hepatic serology C is positive in 5% of patients. None of our patients tested positive for HBS. No case of HIV infection has been noted.

The prevalence of hepatitis B and C in hemodialysis patients varies from country to country but remains higher than in the general population (HCV: 2.7-22.2% in the DOPPS register). In our series the prevalence is around 5% lower than that reported in other regional and international studies.

Conclusion: In hemodialysis, the risk of infection is very high, on the one hand due to access to regular blood and on the other hand due to the alteration of the immune defenses induced by chronic renal failure. Nosocomial transmission plays a very important role. It is strongly linked to the age of dialysis. Compliance with hygiene measures is a very essential element; isolation of the infected patient is no longer recommended

P1123

HEMOPERFUSION COMBINED WITH CRRT IN SEPTIC SHOCK AKI PATIENTS CAUSED BY OSTEOFASCIAL COMPARTMENT SYNDROME

Xiaohua Sheng[1], Niansong Wang[1], Weifeng Huang[2], Gang Yu[1], Hongda Bao[1], Yumei Liu[3], Yang Fei[1]

[1]Shanghai Jiaotong University Affiliated Sixth People's Hospital, Department of Nephrology, Shanghai, P.R. China, [2]Shanghai Jiaotong University Affiliated Sixth People's Hospital, Department of Critical Care Medicine, Shanghai, P.R. China and [3]Shanghai Jiaotong University Affiliated Sixth People's Hospital, Department of Nephrology,, Shanghai, P.R. China

Background and Aims: Although Osteofascial compartment syndrome is rare, it can cause severe complications, including septic shock and acute kidney injury. Most commonly found on the palmar side of the forearm and lower leg. This article reported two cases of septic shock with acute kidney injury caused by osteofascial compartment syndrome, and explored the application of hemoperfusion combined with continuous renal replacement therapy in these two severe patients.

Method: Two young men, patient A was 38 years old and patient B was 44 years old. Hospitalized in June 2016 and February 2018, respectively. Previous healthy, after questioning, patient A had a history of type 1 diabetes and patient B had a history of gout. Patient A had a history of being beaten by his wife, patient B has no clear history of injury. Patient A showed swelling and pain in the right forearm and patient B showed swelling and pain in the right lower leg. After admission, they quickly developed shock, oliguria, acute kidney injury, multiple organ dysfunction. They were received fluid resuscitation, vasopressors, anti-infectives, respiratory support, nutritional support, and vital signs monitoring. Blood culture of patient A showed a case of group A hemolytic streptococcus, patient B showed streptococcus pyogenes and staphylococcus hemolytic. Patient A was performed CRRT for 3 days, combined with two hours hemoperfusion (HA-330, Jafron, Zhuhai City, China) on the first day of CRRT, once every 24 hours for two days. Patient B was performed CRRT for 16 days. combined with two hours hemoperfusion (HA-330, Jafron, Zhuhai City, China) on the first day of CRRT, once every 24 hours for two days. Both patients underwent multiple orthopaedic surgeries. Patient A underwent right upper limb amputation and patient B underwent right thigh amputation.

Results: After hemoperfusion, the amount of norepinephrine was significantly reduced, and the circulation became stable. Finally, two patients improved and were discharged from the hospital, and their renal function returned to normal.

Conclusion: Once the osteofascial compartment syndrome is diagnosed, the fascia should be decompressed immediately. After local incision and decompression, blood circulation is improved, and a large number of toxins from necrotic tissue enter the blood circulation, which can lead to serious complications such as sepsis, shock, acute kidney injury, and multiple organ failure. Renal replacement therapy and amputation surgery may save lives. Hemoperfusion can reduce the amount of norepinephrine, improve circulation and win surgical opportunities.

P1124 A NOVEL ALGORITHM TO IDENTIFY PRESUMABLY FLUID OVERLOADED HEMODIALYSIS PATIENTS

Priscila Preciado Rojas[1], Hanjie Zhang[1], Peter Kotanko[1,2]

[1]Renal Research Institute, New York, United States of America and [2]Icahn School of Medicine, Nephrology, New York, United States of America

Background and Aims: Adequate volume control is a major challenge in hemodialysis (HD) patients, as both fluid overload and depletion are associated with increased morbidity and mortality. In many cases, fluid overloaded patients may require further interventions, e.g. increasing ultrafiltration volume, treatment time or additional HD sessions to achieve their prescribed target weight. Relative blood volume (RBV) monitoring is widely used in HD patients, and past evidence suggests that flat RBV slopes indicate fluid overload [1,2]. The goal of this study was to develop an algorithm that would allow clinicians to identify presumably fluid overloaded HD patients based on a small number of consecutive RBV recordings.

Method: We based our analysis on the 842 prevalent HD patients enrolled in our previously published multicenter study [1], where RBV (Crit-Line®, Fresenius Medical Care, Waltham, MA) was assessed over a 6-month baseline period and all-cause mortality recorded during a median follow-up of 30.8 months; we found in this study that attainment of a RBV between 86 and 92% three hours into the HD session was associated with significantly better patient survival.

The goal of our current research was to develop an algorithm that would require an observation period much shorter than 6 months yet yield clinically meaningful sensitivity and specificity to identify (presumably fluid overloaded) patients with flat RBV profiles ("flat" being defined as RBV $>$ 92% at 3 hours.) We categorized patients in study [1] as either "positive" (their mean RBV at 3 hours was $>$92%) or "negative". We computed sensitivities and specificities relative to the "positive" and "negative" cases for 1 to 15 HD sessions and various rates of treatments with flat RBV curves (30, 40, 50 and 60%).

Results: Sensitivities, specificities, and Youden's indices (= sensitivity + specificity – 1) for 1 to 15 treatments and across the different rates of "positive" RBV curves are shown (Figure 1). We found a sensitivity of 92%, a specificity of 80%, and a Youden's index of 73% when $>$=50% of 10 preceding treatments were "positive". Based on these results we propose an RBV based algorithm to identify "positive" cases (i.e. patients with a flat RBV profile) (Figure 2).

Conclusion: Our algorithm requires only a small number (10) of RBV readings to identify presumably fluid overloaded patients with a clinically acceptable sensitivity (92%) and specificity (80%). It would be of interest to compare the performance of this algorithm with volume status as determined by bioimpedance; however, bioimpedance has not yet been approved for use in HD patients in the U.S.

Figure 1. Sensitivity, specificity and Youden's index as a function of HD treatments (1 to 15) and rate of treatments with flat RBV curves (30, 40, 50 and 60%).

Figure 2. Proposed RBV based decision tree

P1125 IS THE SURPRISE QUESTION USEFUL AS A PREDICTOR OF MORTALITY IN HEMODIALYSIS PATIENTS?

Jorge Estifan Kasabji[1], Cristina Lucas[2], Arancha Sastre[2], Benjamin De León[2], Carmen Barnes[2], Elena Monfa[2], Veronica Barcia[2]

[1]*Complejo Universitario asistencial de León, Servicio de Nefrología, Leon, Spain and* [2]*Complejo Universitario asistencial de León, Servicio de Nefrología, León, Spain*

Background and Aims: among the predictors of hemodialysis mortality, the "surprise" question (SQ) (Would you be surprised if this patient died within the next 6 or 12 months?) is a subjective variable, based on the patient's medical history, experience and knowledge. Recognized as a useful tool to identify a patient with a high risk of early mortality in Hemodialysis.

Objective: to assess a prognostic model of early mortality, based on clinical - biochemical parameters and the prediction of the clinician attending the patient.

Method: SQ is performed on 4 nurses and 4 nephrologists of the hospital hemodialysis unit, the Karnofsky Performance Scale Index of the patients is collected (KPSI 0: normal activity, KPSI 1: Unable to work, frequent medical attention, KPSI 2 : Unable to self-care, requires special care), and prospectively analyzed mortality at 6 and 12 months.

Results: The prevalent population studied in Hemodialysis is 180 patients, average age 69 years ± 14.1 (R 27-94), According to sex (Male 69%-Female 31%), the follow-up of the study was 1 year, we had 11 deaths 6 months and 17 deaths at 12 months, total 28 patients (15.7%).

The distribution of patients according to nurses and nephrologists staff (table 1) and patients characteristics (Table 2)

Table 1

Group would not surprise 6 months	According Nursing 32%	According to nephrologist 9%
Group would not surprise 12 months	41%	32%
Group would Yes surprise 6 months	68%	91%
Group would Yes surprise 12 months	59%	68%

Table 2

Age (yr, mean)	Group "NO" 75	Group "Yes" 66	P <0.05 0.002
Population 12 months (n[%])	73 (41%)	105 (59%)	
Deceased (n[%])	20 (27%)	8 (7.6%)	0,002
Karnofsky scale 0 (n[%])	25 (44%)	85 (70%)	0,007
Karnofsky scale 1 (n[%])	23(40%)	25 (21%)	0,011
Karnofsky scale 2 (n[%])	9 (16%)	11 (9%)	0,039
Phosphorous (mean)	4.1	4.42	0,28
Albumin (mean)	3.44	3.87	0,001

In our study, SQ sensitivity is 71%. 64% specificity, and Positive Predictive Value: 27%, negative predictive value: 92%.

Conclusion: T he surprise question is a specific and sensitive instrument to predict sort-term survival in dialysis population especially in those with older age, more comorbid illnesses, lower functional status and hypoalbuminemia. of the analyzed factors; Karnofsky Index, age, surprise question and albumin have significant predictive value for mortality at 6 and 12 months.

We observed that the surprise question for nephrologists Staff is closer to prediction than nursing, and with a high negative predictive value for the "group of NO surprise"

P1126 PLASMAPHERESIS TREATMENT FOR SEVERE PEMPHIGUS: 10 YEARS' EXPERIENCE OF A SINGLE CENTER IN CHINA.

Yan Liu[1], Jie Ma[1], Haiyun Wang[1], Xiaohong Fan[1], Ke Zheng[1], Limeng Chen[1], Xuemei Li[1], Xuewang Li[1], Yan Qin[1]

[1]*Peking Union Medical College Hospital, Nephrology, Beijing, P.R. China*

Background and Aims: Pemphigus is a potentially life-threatening autoimmune bullous disorder. The pathogenesis involves with IgG antibodies against desmogleins (Dsg) (Dsg 1 and Dsg 3) on epithelial cell surface. Systemic corticosteroid is considered as the basis of the treatment for pemphigus. As an interventional treatment, plasmapheresis was introduced for treating severe or refractory pemphigus. The literature in this field is limited. This study aimed to review our 10 years' experience in a single center.

Method: We retrospectively analyzed 17 patients with severe pemphigus who were unresponsive to high-dose prednisone and received double-filtration plasmapheresis (DFPP) treatment between January 2010 and January 2020. The information on demographic characteristics, clinical and laboratory data, treatment regimens, and clinical outcomes were collected.

Results: 1. Clinical characteristics: Among 17 patients, 11 patients had pemphigus vulgaris (PV), 3 patients had pemphigus foliaceus (PF), 2 patients had paraneoplastic pemphigus (PNP) and 1 patient had pemphigus herpetiform (PH). The mean age of patients was 47.8±10.0 years; 8 male patients and 9 female patients. All seventeen patients were suffering from severe pemphigus and had a period of at least one week of high-dose prednisone (1∼1.5mg/kg/d), but they were unresponsive to corticosteroid and immunosuppressants treatment. 2. As an adjuvant therapy, they received DFPP treatment with 1 to 4 sessions for each patient. Most of the patients (7 patients) received 2 sessions every other day, 5 patients received 3 sessions, 4 patients just received 1 session and only one patient received 4 sessions. For each session, the exchange volume was 1∼1.5 plasma equivalent. After DFPP treatment, the titers of Dsg antibodies significantly decreased ($p<0.001$, Figure 1), Nikolsky's sign became negative and no new blisters appeared. The erosions showed reepithelialization and started healing gradually. The dosage of corticosteroid could begin to taper down rapidly in 1 to 2 weeks. On discharge, the dosage of prednisone was 0.8-1mg/kg/d. 3. As to adverse events, 4 patients had transient hypotension during the procedure, but they could recover spontaneously after parameter adjustment. No major adverse events happened.

Conclusion: Plasmapheresis is an effective and relatively safe treatment for severe pemphigus. Plasmapheresis can also contribute to the dosage reduction of steroid to avoid more drug-related side effect.

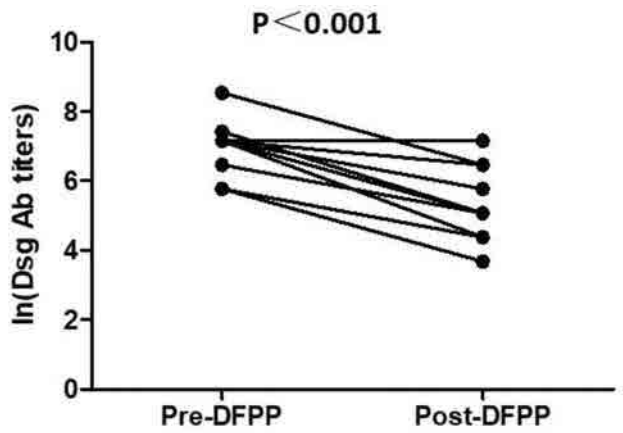


Figure 1. The titers of Dsg antibodies decreased significantly after DFPP treatment.

P1127 BIOELECTRIC IMPEDANCE IN ESTIMATION OF DRY WEIGHT IN CHRONIC DIALYSIS PATIENTS

Safa Fattoum[1], Hela Jebali[1], Braiek Nessrine[1], Badr Ben Kaab[1], Ikram Mami[1], Wided Smaoui[1], Soumaya Beji[1], Ben Hmida Fathi[2], Lamia Raies[1], Mohamed Karim Zouaghi[1]

[1]La Rabta Hospital, Nephrology, Tunis, Tunisia and [2]Charles Nicolles Hospital, Kidney pathology laboratory lrsp001, Tunis, Tunisia

Background and Aims: Fluid status evaluation is essential to adjust the dry weight(DW) in chronic hemodialysis (HD) patients. Bioelectric impedance is a non invasive technique. Its contribution in HD population is well demonatrated. The aim of this study is to compare evaluation of fluid status clinically and by bioimpedance analysis.

Method: It's a transversal study conducted in December 2018.We included chronic dialysis patients(for more 3 months) having 3 dialysis sessions(DS) a week. Bioimpedance analysis (BIA) was performed before and after DS.

Results: There were 26 patients with an average age of 51,4 years. Sex ratio was 3,33 . Average period spent in HD was 73,7 months. Vascular access was a native arteriovenous fistula in 24 patients, and a catheter in 2 patients. Seven patients had residual diuresis. Average ultrafiltration rate was 2,82 L (10 mL/Kg/h).

Before DS, 20 patients had no clinical signs of fluid overload. Unconformity with BIA was noted in 12 patients, with a subclinical overload in all cases. Six patients had clinical signs of fluid overload (including hypertension (HT) in 5 cases), which was concordant with BIA.

After DS, 22 patients reached their DW with a correct hydration status, 2 patients still had clinical signs of fluid overload, and 2 had isolated HTA. BIA revealed the persistence of fluid overload in 10 patients contrasting with the absence of clinical signs of hypervolemia in 8 patients. Patients who kept only HT had a normal hydration status.

Conclusion: Fluid status is an important adequacy issue in the treatment of renal failure. It's a modifiable risk factor associated to mortality. Bioimpedance analysis is a great help to precise dry weight that must be integrated into our daily practice.

P1128 INTERMITTENT SALINE FLUSH VS CONTINUOUS SALINE INFUSION IN HEPARIN FREE DIALYSIS, A COMPARATIVE ANALYSIS

Pratim Sengupta[1], Sumanta Biswas[1], Tarpan Sasmal[1]

[1]*ILS Hospital, Nephrology, Kolkata, India*

Background and Aims: Proper anticoagulation during dialysis for the patients with bleeding risk or contraindication for heparin is a challenge. Regional anticoagulation with heparin and protamine or citrate and calcium though accepted has well known complications and has logistic and monitoring problem. Intermittent saline flush is another well accepted techniques. But it is labour intensive and often leads to fiber loss or coagulation of the dialyser. Keeping these in mind we hypothesised continuous pre-pump saline infusion may be another alternative technique in these situations. In this study We compared the outcome between intermittent saline flush versus continuous saline infusion while dialysing patients without heparine.

Method: Patients >18 year of age, on mHD @3/wk atleast for 3 months, having mature Avfistula and Hb between 8.5-11.5gm/dl with standard EPO and decided for heparin free dialysis were included for the study. Exclusion criteria were Intradialytic weight gain more than 3kg receiving any blood component transfusion or albumin,parenteral nutritional product infusion, any need for UF /Na/HCO3 profiling. Patients on anti-platelet drug or P-time prolonged > 6sec, APTT > 2 times normal, and platelet count less than 80,000 were also excluded. After inclusion, for each patient 8 session were studied systematically as per the preset protocol. Session 1,3,5,7 was subjected to intermittent saline flush(ISF) where as session 2,4,6,8 were subjected to continuous saline infusion(CSIF). The blood flow during dialysis was kept in the range of 250ml/min to 300ml/min and dialysate flow was kept fixed at 500ml/min. and UF goal was kept between 2.5 to 3.5lit and treatment duration was fixed at 4hrs.In ISF, every 15min 80ml (=priming volume of the dialyser, F6, Polysulphone, Fresenius)0.9%NS was flushed in the dialyser clamping the arterial line where as in CSIF 0.9%NS bottle is connected to the prepump arterial line and saline is infused through saline infusion pump @320ml/hr. The each dialysis session outcome were recorded and analysed. Potential clotting in the bubble trap was visually observed in each hour and graded on a 4 point scale. 1=normal, 2= fibrinous ring,3=clot formation and 4= coagulated system. In either group the total saline infusion volume added in the net UF goal. The dialyser was inspected visually at the end of each session 1= normal,2= a few blood stripes affecting less than 10% of the surface area,3= many blood stripes more than 10% of surface area, 4= coagulated dialyser. URR(as per KDOQI guideline) and kt/v(by diascan software of Gambro AK96 machine) was calculated in each session. Data were analysed with spss v23.

Results: Total 8 patients(5men 3 women) were included for the study. After exclusion total 54 session of dialysis were finally analysed. The incidence of the of blood clot in the whole dialysis system leading to stopping of dialysis was 3 in ISF and 1 in CSIF (p=0.001).The multiple linear regression analysis with repeated measurememt for the time and UF rate adjusted clot incidence of different grade in bubble trap was significantly low in the CSIF group than the ISF group.(p=0.0001). When adjusted for total body water,net UF,PreHD Urea, blood flow the difference in URR and Kt/v both the group was not significantly different (p=0.8). Among the two group the operational comfort for nurses were significantly better(p=0.3) in the CSIF group than the ISF group.

Conclusion: While considering heparine free dialysis Continuous saline infusion @320ml/hr is easy less labourintensive method than intermittent saline flush technique with significantly less clotting incidence and without any adverse effect on the dialyser clearance.

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DIALYSIS. PERITONEAL DIALYSIS

P1133 XYLITOL-BASED PERITONEAL DIALYSIS SOLUTIONS MITIGATED IN VITRO MESOTHELIAL AND ENDOTHELIAL TO MESENCHYMAL TRANSITION

Valentina Masola[1], Arduino Arduini[2], Mario Bonomini[3], Giovanni Gambaro[1], Gianluigi Zaza[1]

[1]Division of Nephrology and Dialysis, Department of Medicine, Verona, Italy, [2]CoreQuest Sagl, R&D Department, Manno, Switzerland and [3]Section of Nephrology and Dialysis, G. d'Annunzio University, SS. Annunziata Hospital, Department of Medicine, Chieti, Italy

Background and Aims: Fibrosis, angiogenesis and microvascular alteration are main pathogenetic mechanisms involved in the progressive loss of the peritoneal ultrafiltration capacity in patients undergoing peritoneal dialysis (PD). Main cause of this condition is the continuous peritoneal exposure to hyperosmotic and hyperglycaemic agents. High glucose level activates the Mesothelial to Mesenchymal Transition (MMT) and the Endothelial-to-Mesenchymal (EndMT) program, which are responsible for the development of fibrosis/chronic peritoneal damage. Moreover, the high glucose content of PD solution may induce the VEGF production with consequent neo-angiogenesis. Therefore, the introduction of more biocompatible solutions in clinical practice is necessary for preserving the long-term peritoneal membrane. To this purpose we tested the *in vitro* effects of a new commercially available PD solutions containing xylitol, carnitine and reduced glucose, at comparable osmotic strength (XyloCore).

Method: Human vein microvascular endothelial cells (HMVEC) were cultured in EGM^{TM}-2MV medium (Lonza) and Human peritoneal mesothelial cell line (HMrSV5) were cultured in Dulbecco's Modified Eagle Medium (DMEM; Gibco) containing 10% fetal bovine serum. Cells were cultured to confluence and then treated for 3 hours with serum free medium, XyloCore 0.7 (0.5% Glucose, 0.7% Xylitol and 0.02% L-carnitine), XyloCore 1.5 (0.5% Glucose, 1.5% Xylitol and 0.02% L-carnitine) and commercially available glucose-based solutions (Fixioneal) 1.36% and 2.27% Glucose. Gene expression of MMT/EndMT, apoptosis, inflammation, extracellular remodeling and angiogenesis markers was evaluated by real-time PCR. Cell viability was assayed by MTS assay.

Results: Our *in vitro* results demonstrated that XyloCore solutions, by influencing only partially the mesothelial and endothelial cells viability, demonstrated a good biocompatible profile. Then, gene expression analysis of HMVEC and HMrSV5 treated with XyloCore solutions revealed a significant down-regulation of transcripts encoding for MMT and EndMT biomarkers (Zinc finger protein SNAI1, TGF-beta, alpha-SMA and vimentin), and pivotal biological elements involved in apoptosis (Bcl-2), extracellular matrix remodeling (matrix metallopeptidases), inflammation (IL-1beta, IL-6) and angiogenesis (Vascular endothelial growth factor) compared to glucose-based solutions with comparable osmotic strength.

Conclusion: These *in vitro* results demonstrated, for the first time, that XyloCore solutions have a better biocompatible impact and less pro-fibrotic potentials compared to conventional glucose-based solutions. These effects, if confirmed in *in vivo* studies, could have interesting clinical potentials.

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P1134 **HIGH PREVALENCE OF SLEEP-DISODERED BREATHING AND ITS ASSOCIATION WITH RENAL FUNCTION AMONG CHRONIC KIDNEY DISEASE PATIENTS (CKD1-5,HD AND PD) : A CROSS-SECTIONAL STUDY.**

Kanji Ota[1], Yosuke Nakayama[1], Yokota Yunosuke[1], Goh Kodama[1], Sakuya Itou[1], Kei Fukami[1]

[1]*Division of Nephrology, Department of Medicine, Kurume university, Kurume, Fukuoka, Japan*

Background and Aims: Sleep-disordered breathing (SDB) is known as a novel risk factor for cardiovascular disease, and one of five adults suffer from SDB in general population. In non-dialysis chronic kidney disease (CKD) and hemodialysis (HD) patients, a high prevalence of SDB has been reported due to the excess accumulation of extracellular fluid. However, precise prevalence and associated factors of SDB in patients with peritoneal dialysis (PD) has not been known. This cross-sectional study aimed to investigate the prevalence and determinant factors associated with SDB in patients with CKD.

Method: This was a single-center retrospective cohort study recruited 334 patients with CKD stages 1-3a, 3b-5, HD, and PD enrolled from 2018 to 2020. All patients were hospitalized and received our CKD educational program, and did not have sleep complaints. The diagnosis and assessment of the severity of SDB were evaluated using PULSOX-Me300 and SAS2100 systems. The 3% oxygen desaturation index and SpO_2 were measured during sleep. SDB was defined as 3% oxygen desaturation index (ODI)>15.0 and SpO_2<92% in this study.

Results: Proportion of the patients with CKD1-3a, CKD3b-5, HD, and PD were 28%, 53%, 11%, and 8%, respectively. Thirty-one% of the patients were diagnosed with SBD in all CKD patients. In a generalized linear model, 3% ODI>15.0 and SpO_2<92% were significantly correlated with apnea hypopnea index ($p<0.05$, $r=0.87$ and $p<0.05$, $r=-0.45$, respectively). Further, it became clear that the proportion of 3%ODI>15 and SpO_2<92% was significantly higher in PD patients (50%) than in other CKD patients. Furthermore, 3% ODI was significantly correlated with BMI and HDL cholesterol levels in PD patients ($p<0.05$, $r=0.67$ and $p<0.05$, $r=-0.54$, respectively).

Conclusion: We reported for the first time that the prevalence of SDB was very high and that the severity of SDB was significantly associated with BMI in patients with PD. These findings suggest that the extracellular fluid overload and excess glucose exposure due to PD fluid might accelerate SDB in patients with PD. Further clinical studies are needed to determine whether PD-associated SDB might influence the development of cardiovascular disease in CKD patients.

P1135 WHETHER USPD PATIENTS ARE SUITABLE FOR INCREMENTAL PERITONEAL DIALYSIS:YES OR NO?

Wenjing Zhang[1], Jia LV[1], Lan Li[1], Zhigang Wang[1], Dapeng Hao[1], Jiping Sun[1]

[1]*The First Affiliated Hospital of Xi'an Jiaotong University, Nephrology Department, Xi'an, P.R. China*

Background and Aims: Incremental Peritoneal Dialysis (IPD) is the practice of initiating PD exchange less than four times a day in consideration of residual renal function (RRF). More clinical studies have confirmed the feasibility and effectiveness of IPD, especially in the protection of residual renal function, which is obviously superior to full-dose PD. Urgent-start peritoneal dialysis (USPD) is a popular PD method. Due to lack of pre-dialysis education, most of patients who were newly diagnosed with ESRD in China chose USPD. Well, can incremental peritoneal dialysis be used for USPD patients when starting dialysis? Compared to full-dose PD, whether incremental PD affects the residual renal function in USPD patients? Here we report the first study of incremental peritoneal dialysis's effect on residual renal function.

Method: A retrospective analysis of medical records was performed on 169 patients who received USPD from August 2008 to March 2017. Patients were divided into 2 groups according to dialysis dose: incremental PD(i-PD) group (dialysis dose were less than or equal to 6000ml or 3 exchanges per day) and full-dose PD(f-PD) group (dialysis dose were great than or equal to 8000ml or 4 exchanges per day). The demographics, clinical biochemical indexes, dialysis dose, urine volume, dialysis ultrafiltration volume, RRF, dialysis adequacy, peritoneal dialysis infection complications, mechanical complications and survival rates were compared between two groups in 1 year follow-up.

Results: **(1).**A total of 169 patients were enrolled, including 111 patients (average age 45.01±12.84 years) in i-PD group and 58 patients (average age 43.5±15.62 years) in f-PD group. The demographics and clinical biochemical indexes in the two groups before peritoneal dialysis were similar ($P>0.05$). **(2).**During the follow-up period, the dialysis dose in f-PD group(8034.48±262.61ml/d, 8080.00±395.80ml/d, 8155.17±523.21ml/d, 8051.72±906.55ml/d) were more than those in i-PD group(5891.89±528.31ml/d, 6159.57±1185.06ml/d, 6468.47±1588.71ml/d, 6900.90±1543.05ml/d), $P<0.05$. And the dialysis adequacy in both groups were up to standard: the total Kt/V (i-PD group: 1.96±0.56, 2.01±0.70, 2.02±0.55, 1.90±0.52; f-PD group: 2.18±0.47, 2.22±0.55, 2.05±0.44, 2.03±0.42) were greater than 1.7 and the total Ccr (i-PD group: 79.39±29.75, 79.02±25.11, 78.26±30.00, 73.09±29.14; f-PD group: 89.78±29.89, 91.54±35.56, 82.38±29.27, 72.96±23.75) were greater than 60L. **(3).**During the whole follow-up period, the residual renal function between two groups had no statistically significant(i-PD group: 3.96±2.52ml/min, 3.46±1.95ml/min, 3.58±2.85ml/min, 2.91±2.33ml/min; f-PD group: 4.31±4.83ml/min, 3.45±2.36ml/min, 3.16±2.15ml/min, 2.36±1.65ml/min), $P>0.05$. **(4).**During the whole follow-up period, the blood pressure control, correction of anemia, and correction of calcium and phosphorus abnormalities were also similar in both groups, $P>0.05$. **(5).**At 1-month and 6-month, the urine volume were higher in i-PD group(1024.33±492.91ml/d, 1017.03±571.66ml/d) than those in f-PD group(782.93±415.89ml/d, 788.27±491.02ml/d), $P<0.05$. The dialysis ultrafiltration volume in f-PD group (481.67±723.69ml/d, 632.77±687.89ml/d, 338.87±963.14ml/d, 750.43±849.69ml/d) were higher than those in i-PD group(343.30±520.00ml/d, 495.70±916.76ml/d, 341.78±925.57ml/d, 439.65±1297.13ml/d) during the whole follow-up period, but the differences were not statistically significant ($P>0.05$). **(6).**The exit-site infection, peritonitis, mechanical complications and technical survival were similar between the two groups ($P>0.05$).

Conclusion: Incremental peritoneal dialysis will not cause rapid decline of residual renal function in USPD patients, and the dialysis effect and complications are similar to full-dose peritoneal dialysis. Therefore, we recommend that USPD patients can be treated by incremental peritoneal dialysis.

P1136 **STUDY DESIGN OF ELIXIR, A MULTICENTER EUROPEAN PHASE III CLINICAL TRIAL AIMED TO TEST A GLUCOSE-SPARING PD SOLUTION WHERE GLUCOSE IS MOSTLY REPLACED WITH OSMO-METABOLIC AGENTS.**

Werner Kleophas[1], Mario Bonomini[2], Jose Carolino Divino[3], Gianpaolo Reboldi[4], Massimo Iacobelli[5], Arduino Arduini[6]

[1]Clinic for Nephrology, Heinrich-Heine-University, Dusseldorf, Germany, [2]Nephrology and Dialysis Unit, "G. d'Annunzio" University, Chieti, Italy, [3]Division of Renal Medicine, CLINTEC, Karolinska Institutet, Campus Flemingsberg, Stockholm, Sweden, [4]Department of Medicine - Nephrology, University of Perugia, Perugia, , [5]Iperboreal Pharma, Pescara, and [6]Iperboreal Pharma, Pescara, Italy

Background and Aims: Peritoneal dialysis (PD) faces particular challenges that include multiple barriers to the therapy and unsatisfactory and poorly defined technique survival as well as limitations relating to peritoneal membrane longevity and metabolic alterations. Glucose is the most used osmotic agent for PD. However, the peritoneal membrane is not impermeable to glucose, so that a rapid reduction of the osmotic gradient and an increase of serum carbohydrates are seen in CAPD patients. Increased glucose absorption may result in metabolic abnormalities like hyperglycemia, hyperinsulinemia, obesity and hyperlipidemia. Therefore, a more satisfactory composition of PD solution (PDS) is urgently needed.

XyloCore PDS (Iperboreal Pharma, Pescara, Italy) has been formulated to significantly reduce glucose exposure by replacing most of it with two crystalloid agents, D-xylitol and L-carnitine.

A randomized controlled trial to evaluate the safety and efficacy of a newly introduced PDS is needed to provide the necessary clinical evidence to guide policy decision-making. The randomized controlled study designs in small populations are challenging because it is very difficult to adequately assess changes between variable groups.

The aim of this program was to develop an adequate clinical trial protocol and validate it by reaching agreement with regulatory authorities.

Method: Pre-approval trials include a study protocol and test the drug in a highly selected patient population designed to provide the most robust evidence on the drug's benefits and risks.

The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design, including the primary and secondary endpoints, minimization of bias (including randomization and blinding), "discontinuation criteria" for individual subjects, statistical analysis of primary end-point, and the strategy to handle missing data.

An international steering committee of clinical experts and statistician has been set for this study to discuss and develop an adequate study protocol to produce evidence to support regulatory submissions. The proposed protocol has been discussed with the regulatory agency in Germany BfArM in order to reach agreement on the study design for this Phase 3 pre-approval trial.

Results: BfArM agreed with the proposed study design for the planned pivotal phase III study NCT03994471.The study will be a randomized, controlled parallel groups, open, multicenter study, comparing the effects of the low glucose PD solution, XyloCore, to glucose regimen only, in ESRD patients receiving CAPD. All patients will receive 7.5% Icodextrin for nocturnal (long-dwell) exchange. Randomization will be performed centrally and the study will be stratified for diabetic/non-diabetic patients. The primary objective is to demonstrate the non-inferiority of XyloCore compared to the glucose PDS with regards to safety and efficacy. The primary outcome measure is total weekly Kt/V urea after a 24-week period using the assigned PD solution, assessed using a peritoneal function test. The non-inferiority margin of -0.25 with a 1-sided level of significance of 2.5% and 80% power has been agreed (Kt/V will not be less than 1.7 at any time). Consequently, a sample size of 170 patients has been defined. The Agency agreed that the study cannot be blinded and recommended a blinded and independent assessment of the end-point Kt/V urea. A Feasibility Study is in progress to identify the centers in several countries.

Conclusion: A well written and complete protocol is essential for a high-quality study. Many clinical studies have problems with incompleteness, ambiguity and inconsistency. Many of these problems are avoidable by careful planning during the protocol writing process. Involving regulatory authorities early in the discussion of the protocol should ensure acceptability of study design of pre-approval clinical trials.

P1137

FACTORS DETERMINING CHOICE OF DIALYSISI MODALITY AMONG PATIENTS INITIATING DIALYSIS. RESULTS OF THE PERIDIALYSIS STUDY

James G. Heaf[1], Maija Heiro[2], Aivars Petersons[3], Baiba Vernere[3], Johan Vestergaard Povlsen[4], Anette Bagger Sørensen[4], Naomi Clyne[5], Inge Bumblyte[6], Alanta Zilinskiene[6], Else Randers[7], Niels Løkkegaard[8], Mai Ots-Rosenberg[9], Stig Arne Kjellevold[10], Jan Dominik Kampmann[11], Björn Rogland[12], Inger Karin Laegreid[13], Olof Heimbürger[14], Bengt Lindholm[14]

[1]Zealand University Hospital, Roskilde, Denmark, [2]Turku University Hospital, Turku, Finland, [3]P. Stradins University Hospital, Riga, Latvia, [4]Aarhus Univeristy Hospital, Aarhus, Denmark, [5]Lund University and Skåne University Hospital, Lund, Sweden, [6]Lithuanian University of Health Sciencs, Kaunas, Lithuania, [7]Viborg Hospital, Viborg, Denmark, [8]Holbaek Hospital, Holbaek, Denmark, [9]University Hospital of Tartu, Tartu, Estonia, [10]Vestfold Hospital, Tønsberg, Norway, [11]Hospital of Southern Jutland, Sønderborg, Denmark, [12]Kristianstad Hospital, Kristianstad, Sweden, [13]St. Olav University Hospital, Trondheim, Norway and [14]Karolinska Hospital, Clinical Science, Intervention and Technology, Stockolm, Sweden

Background and Aims: Home dialysis with peritoneal dialysis (PD) or home hemodialysis (HD) has medical and socioeconomic benefits but home dialysis is generally underutilized. While many factors determine choice of initial dialysis modality, starting patients on home dialysis requires timely planning, educational activities and an active program to promote home dialysis. Here we investigated factors including patient suitability, pre-dialysis preparations and institutional factors determining choice of dialysis modality among patients initiating dialysis.

Method: Choice of dialysis modality was investigated in 1588 consecutive patients (age 63.8 ±15.3 years. 35.8% female; diabetic nephropathy 24.4%) participating in the Peridialysis study, a multinational multi-centre prospective study of causes and timing of planned and unplanned dialysis initiation (DI) over a 3-year period in 15 Nordic and Baltic nephrology departments. All dialysis modalities were available and free of charge to patients. All centres offered pre-dialysis education programs to patients with timely referral. Clinical and biochemical data during the pre-dialytic period, centre data, and reasons for DI and choice of dialysis modality were registered.

Results: 516 (32.4%) patients were not offered home dialysis because they were judged to be unsuitable (**384**; 24%): PD was contraindicated in 338 (21.2%) patients - for physical (142; 8.9%), mental (80, 5.0%) or abdominal (116; 7.3%) reasons and HD was contraindicated in 46 (2.9%) patients. In addition, **106** (6.7%) were not offered home dialysis for various reasons; and deaths before modality choice occurred in **26** (1.6%) patients. Factors associated with unsuitability were high age, comorbidity, late referral (risk ratio, RR, 1.9), inflammation (C-reactive protein >50 mg/L (RR 2.6) and rapid loss of renal function (RR 2.0). Patients who were not assessed for home dialysis comprised mainly patients with late referral (RR 5.8) and/or unplanned DI (RR 9.6). Of the remaining **1072** (67.6%) patients, who had a free choice of modality, **700** (65.3%) chose home dialysis, either PD (**661**; 61.7%) or home HD (**39**: 3.6%) while **372** (34.7%) patients chose centre HD. Factors associated with choice of centre dialysis were late referral (RR 1.8), suboptimal DI (RR 2.0), symptomatic uraemia (RR 1.6) and p-urea >30 mM (2.6). Somatic differences between patients choosing home dialysis and centre dialysis were minor. Independent institutional factors reducing information about home dialysis were treatment at a university hospital (RR 4.3) and absence of an active preference for home dialysis, "home dialysis first" policy (RR 3.0).

Conclusion: The results of the Peridialysis study indicate that the incidence of home dialysis could be increased by a "home dialysis first" department policy and by efforts to reduce the incidence of late referrals and unplanned DI. Acutely ill patients and patients with unplanned DI may be candidates for home dialysis if assessment of home dialysis suitability and dialysis educational program are performed after their clinical condition has improved. Given a free choice, most patients (65%) choose home dialysis.

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FLOW CYTOMETRIC ANALYSIS ON LYMPHOCYTE SUBSETS APPEARED IN PERITONEAL DIALYSIS EFFLUENT IN RELATION WITH PERITONEAL FUNCTION

Atsuki Ohashi[1], Madoka Kondo[1], Fumitaka Ihara[1], Noriyuki Toshima[1], Yoshitatsu Ohara[1], Tomomi Tanaka[1], Yoshitaka Maeda[1]

[1]*JA toride medical center, nephrology, toride-shi, Japan*

Background and Aims: We previously reported that an increase of lymphocytes in peritoneal dialysis (PD) effluent was correlated with risk of encapsulating peritoneal sclerosis (EPS). In the present study, we analyzed subsets of lymphocytes in PD effluent by flow cytometry and evaluated their changes every six month to elucidate the etiological background of peritoneal dysfunction.

Method: We enrolled patients who started PD between 2006 and 2017, and of whom the data for PET and flow cytometric analysis was available at least for three consecutive times with an interval of six months. We excluded the patients who experienced PD peritonitis during the observation period. Consequently, the levels and changes of lymphocyte subset, such as $CD4^+/CD8^+$ naïve T cell ($CCR7^+/CD45RA^+$), $CD4^+/CD8^+$ central memory T cell ($CCR7^+/CD45RA^-$), $CD4^+/CD8^+$ effector memory T cell ($CCR7^-/CD45RA^-$), $CD4^+/CD8^+$ terminally differentiated effector memory T cell ($CCR7^-/CD45RA^+$), D/P creatinine ratio, FSC ratio of mesothelial cells and lymphocytes (a possible indicator for mesothelial cell size) were analysed in 23 patients over one year.

Results: We evaluated whether the observed variables on the first evaluation (six months after initiation of PD) affected the changes of D/P creatinine and FSC ratio over one year by a simple linear regression analysis. In the examined variables, only a fraction of $CD8^+$ central memory T cell was significantly correlated with the change rate of D/P creatinine ratio (β=1.47, p=0.001, adjusted R^2=0.379). We also evaluated whether the change rate of observed variables was correlated with the change rate of D/P creatinine and FSC ratio by a simple linear regression analysis. A fraction of $CD8^+$ naïve T cell or $CD8^+$ central memory cell was negatively correlated with the change rate of D/P creatinine ratio (naïve T cell; β=-0.058, p=0.022, adjusted R^2=0.188, central memory T cell; β=-0.096, p=0.046, adjusted R^2=0.137). The change rate of $CD8^+$ effector memory T cell was not significantly correlated with the change rate of D/P creatinine ratio (β=0.172, p=0.096, adjusted R^2=0.085). However, the change rate of D/P creatinine ratio tends to be higher in accordance with the increased change rate of $CD8^+$ effector memory T cell by One way ANOVA, where the change rate was divided into three groups in descending order (p=0.0796) (Fig.1). Besides, the change rate of $CD8^+$ effector memory T cell tends to be higher in accordance with the increased fraction of $CD8^+$ central memory T cell at the first evaluation by Kruskall-Wallis test, where the change rate was divided into three groups in descending order (p=0.169) (Fig.2).

Conclusion: A decrease in the fraction of $CD8^+$ naïve or central memory T cell was significantly correlated with the increase of D/P creatinine ratio. An Increase in the fraction of $CD8^+$ effector memory T cell was also possibly correlated with the increase of D/P creatinine ratio, although it was not statistically significant (p=0.096). An initial fraction of $CD8^+$ central memory T cell was significantly correlated with the change rate of D/P creatinine ratio. From these results, central memory T cells and naïve T cells at an initial stage may be transformed into effector memory T cells by repeated exposure to unknown antigens derived from PD solution and these effector memory T cells may damage the peritoneum to increase D/P creatinine ratio. An initial higher fraction of $CD8^+$ central memory T cell suggested an acceleration in the transformation into $CD8^+$ effector memory T cell.

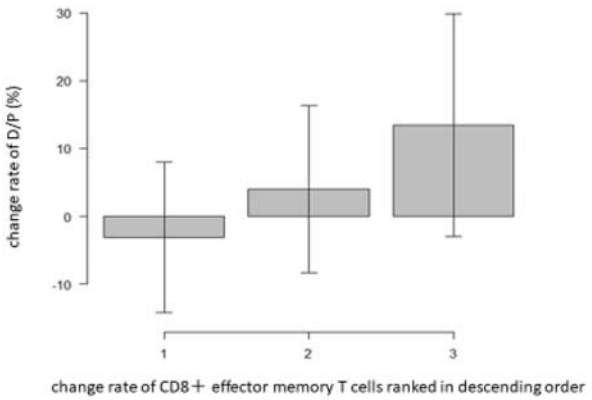


Fig. 1

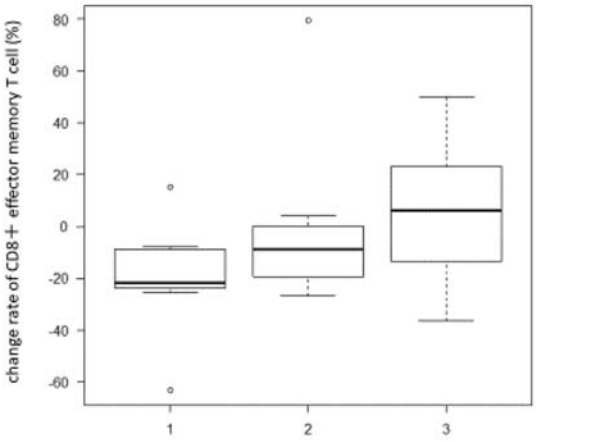


Fig. 2

Figure:

P1139 EXPRESSION OF TOLL LIKE RECEPTORS, CELL ADHESION MOLECULES AND PRO-INFLAMMATORY CYTOKINES IN ESRD PATIENTS

Mantabya Singh[1], Narayan Prasad[1], Nida Fatima[2], Amit Gupta[1], Chinmoy Sahu[2]

[1]SGPGIMS, Nephrology, lucknow, India and [2]SGPGIMS, Microbiology, lucknow, India

Background and Aims: CAPD is well established modality of treatment for patients with end stage renal disease (ESRD). Peritonitis is a leading cause of technique failure and death in patients on CAPD. Studies on expressions of host factors like TLRs, CAMs and their relationship with inflammatory cytokines (IL-6, IL-12, TNF-alpha and IL-1 beta) involved in peritonitis and other co-morbidity and functional status are lacking throughout the world. Hence the present study has to be done to determine the expressions of TLR2 and TLR4, and CAMs in ESRD patients.

To compare the expression of TLR2, TLR4, ICAM 1 and Pro-inflammatory cytokines (IL-6, IL-12, TNF-alpha and IL-1-beta) in Peritonitis, CAPD and CRF group patients.

Method: A total of 85 ESRD patients recruited and sub-divided into 3 groups. Group1- CAPD patient (n=25), Group 2- Peritonitis patient (n=30), and Group 3- CRF (n=30 patients). mRNA expression of TLR-2, TLR-4 were examined at gene levels by RT PCR and cell adhesion molecule (ICAM-1) were examined at gene and protein levels by RT PCR and ELISA respectively in Serum and Pro-inflammatory cytokines level were also examined by ELISA in serum. We performed microbiological culture for bacterial and fungal pathogens using automated BACTEC culture system. Cell counts were routinely done on every dialysate.

Results: Out of 30 samples of peritonitis group 15 were culture positive and 15 were culture negative. We found that in peritonitis group the mRNA expression of TLR-2 and TLR-4 was higher as compared to CRF (4.183±2.857vs 3.633±2.41) (p=0.049), (4.314±2.91vs 4.14±1.99) (p=0.015) and CAPD (4.183±2.857vs3.683±2.85) (p=0.041), (4.314±2.91vs 3.88±1.91) (p=0.009) respectively. At gene and protein level ICAM-1 was higher in peritonitis patient compared to CAPD (mRNA expression 4.76±2.64vs 4.36±3.48) (level in sera 660±201.2vs 514±157) (p=0.003). The IL-6 and IL-12 expression was higher in Peritonitis group as compared to CAPD (66.87±64.51vs214.35±220.05) (p=0.04) and (230.17±153.45vs417.04±302.96) (p=0.028) respectively. The TNF-alpha and IL-1-beta expression was not significant among the groups.

Conclusion: TLRs activation by bacterial molecules leads to the induction of cytokines (IL-6 and IL-12) and chemokine through the activation of NF-kB pathway and may be responsible for atherosclerosis, morbidity and mortality in ESRD patients. Elevated level of ICAM-1, IL-6 and IL-12 may be responsible for chronic inflammation in Peritonitis group patients.

P1140

THE REDUCTION OF THE SIEVING OF SODIUM IS THE FIRST AND EARLY FUNCTIONAL CHANGE OF PERITONEAL MEMBRANE IN A LARGE PATIENT POPULATION ON PERITONEAL DIALYSIS

Vincenzo La Milia[1], Gianfranca Cabiddu[2], Valerio Vizzardi[3], Andrea Cavalli[1]

[1]A. Manzoni Hospital, Nephrology and Dialysis, Lecco, Italy, [2]G. Brotzu Hospital, Nephrology and Dialysis Department, Cagliari, Italy and [3]Spedali Civili, Nephrology and dialysis, Brescia, Italy

Background and Aims: The reduction whit time of peritoneal removal of salt and water is an important cause of reduced patient and technique survival in peritoneal (PD) patients. Solute transport increase after the start of PD and continue to increase throughout the course of treatment. Fast peritoneal transport results in ultrafiltration (UF) failure (UFF). UFF is due to the more rapid absorption on glucose, with a loss of the osmotic driving force for UF, and to reduction in osmotic conductance of the peritoneal membrane. The free water transport (FWT), through the aquaporin-1 channels, is about 45% of the total peritoneal UF during a dwell with a hypertonic glucose solution. It has suggested that the reduction of the FWT is due to the peritoneal fibrosis. The peritoneal sieving of sodium (Na) is a decrease (Δ) of the dialysate Na concentration during a peritoneal dwell with a hypertonic solution due to FWT. ΔNa, an indirect measure of the FWT, is maximum after 1 hour of a peritoneal equilibration test (PET) with a 3.86% glucose solution (3.86%-PET).

The aim of this study was to evaluate the functional changes of the peritoneal membrane, assessed by the PET-3.86%, in a large patient population on peritoneal dialysis (PD) followed for a long period of time.

Method: We evaluated the PET-3.86% in a large population of incident PD patients attending 27 Italian dialysis centres. During the 3.86%-PET we calculated the ratio of the concentrations of creatinine in dialysate/plasma (D/P_{Creat}), the ratio between the concentrations of glucose at the end/beginning of the test (D/D_0), the UF, uncorrected and corrected for bag overfill, and ΔNa.

The 3.86%-PET was repeated each year in each patient.

Results: We evaluated the results of 758 PET-3.86% in 758 incident PD patients (one test per patient) at the start of the PD therapy and then we evaluated the results of the 3.86%-PET (one test per patient and one test per year of treatment) in 382, 211 and 109 PD patients with at least two, three and four 3.86%-PET, respectively. The mean duration of PD was 5 ± 3 months, 17 ± 3 months, 30 ± 3 months and 41 ± 3 months in PD patients with at least one, two, three and four 3.86%-PET, respectively. ΔNa changed significantly after the second 3.86%-PET (8.8 ± 3.8 to 7.9 ± 4.1 mmol/L, $p<0.001$), about after 17 months of the start of PD therapy, and its value has continued to decline significantly after 30 months (9.0 ± 3.5 to 8.3 ± 3.6 to 7.6 ± 4.1 mmol/L, $p=0.001$), in the cohort of PD patients with at least three 3.86%-PET, and after 41 months (9.3 ± 3.2 to 9.0 ± 3.8 to 8.2 ± 4.0 to 7.7 ± 4.0 mmol/L, $p=0.02$) of PD treatment, in the cohort of PD patients with at least four 3.86%-PET. D/P_{Creat}, D/D_0 and UF, uncorrected and corrected for bag overfill, changed significantly only during the fourth 3.86%-PET, about after 41 months of PD treatment.

Conclusion: The results of this study indicate that the reduction of the ΔNa is the first and an early functional alteration of the peritoneal membrane and may mean that fibrosis of the peritoneal membrane is a process that begins early after the initiation of PD. The ΔNa could be used to evaluate the effect of new solutions and/or new drugs on the functions of the peritoneal membrane since the beginning of the PD therapy.

P1141 CT IMAGING FEATURES AND INFLUENCE FACTORS IN PEROTONEAL DIALYSIS RELATED PERITONEAL INJURY

Jie Yang[1], Jia Chen[1], Yani He[1]
[1]Daping Hospital, Army medical university, Nephrology, Chongqing, P.R. China

Background and Aims: Peritoneal dialysis (PD) is one of the most important renal replacement methods for end-stage renal disease. CT scan found some patients have peritoneal thickening, omental structure change. However, the underlying regularity of change still unknown. This study aim to investigate the regularity of change and influencing factors of CT peritoneal imaging features in PD patients.

Method: A 173 total routinely follow-up patients on CAPD are evaluated by the abdominal CT scans. A total of 109 patients were enrolled for analysis according to the inclusion criteria. The 109 patients who meet the criteria were evaluated by the semi-quantitative scoring system, including the thickness of the parietal peritoneum, the calcification of parietal peritoneum and omentum, abdominal compartment and encapsulated effusion, bowel dilatation and intestinal obstruction, and the correlation between CT imaging evaluation index and age, dialysis age, primary disease, type of peritoneal transport, glucose exposure, and the incidence of peritonitis were analyzed. Logistic regress was used to analyze the influence factors of peritoneal thickening and abnormal omental structure and the risk incidence of peritoneal thickening and abnormal omental structure.

Results: 70 patients with parietal peritoneum thickness, 63 patients with abnormal omental structure, 4 patients with the calcification of parietal peritoneum and omentum, 11 patients with abdominal compartment and encapsulated effusion, 24 patients with bowel dilatation and intestinal obstruction. The peritoneal thickening and abnormal omental structure in patients with dialysis age $>$ 5 years was significantly higher than that of age $<$ 1 year. The peritoneal thickening and abnormal omental structure in patients with peritonitis more than once was significantly higher than that in patients without peritonitis. The abnormal omental structure in patients with total glucose exposure $>$ 165kg was significantly higher than that with total glucose exposure $<$60 kg. The abnormal omental structure in patients with high-average peritoneal transport was significantly higher than that with low-average peritoneal transport. The risk factors of abnormal omental structure including dialysis age, the peritonitis occurrences, the cumulative score of peritonitis, the total glucose exposure, and the high-average peritoneal transport. The independent risk factors are the occurrence and the cumulative score of peritonitis. The incidence risk of peritoneal thickening and abnormal omental structure will increase 4.364 and 5.393 times separately with the occurrence of peritonitis, and increase 2.191 and 2.072 times separately with the cumulative score of peritonitis increased by 1 point.

Conclusion: The main imaging features of peritoneal dialysis patients with progressive peritoneal injury are thickness of the parietal peritoneum and the structure change of omentum. The major risk factor of progressive peritoneal injury is peritonitis. The abdominal CT scan can comprehensively investigate the characteristics and extent of peritoneal dialysis and injury, which is benefit for the early diagnosis of peritoneal injury.

Table 3. Logistic regress analysis the relationship between the cumulative score of peritonitis and the risk of peritoneal thickening and abnormal omental structure.

	peritoneal thickening		abnormal omental structure	
	OR(95%CI)	P	OR(95%CI)	P
Model1	2.191(1.536∼3.124)	<0.001	2.072(1.498∼2.866)	<0.001
Model2	2.333(1.577∼3.449)	<0.001	2.127(1.509∼2.996)	<0.001
Model3	2.340(1.559∼3.511)	<0.001	2.071(1.456∼2.947)	<0.001
Model4	2.388(1.581∼3.608)	<0.001	2.066(1.452∼2.939)	<0.001
Model1: unadjusted				
Model2: adjusted age,gender,Diabetes				
Model3: adjusted PD duration on Model2				
Model4: adjusted total glucose exposure on Model3				

Figure:

P1142 DICHLOROACETATE AND L-CARNITINE REDUCED TGF-BETA-INDUCED MESOTHELIAL-TO-MESENCHYMAL TRANSITION

Valentina Masola[1], Arduino Arduini[2], Mario Bonomini[3], Giovanni Gambaro[1], Gianluigi Zaza[1]

[1]Division of Nephrology and Dialysis, Department of Medicine, Verona, Italy, [2]CoreQuest Sagl, R&D Department, Manno, Switzerland and [3]Section of Nephrology and Dialysis, G. d'Annunzio University, SS. Annunziata Hospital, Department of Medicine, Chieti, Italy

Background and Aims: Mesothelial to Mesenchymal Transition (MMT) plays a main role in the induction of peritoneal fibrosis in long term peritoneal dialysis. Mesothelial cells exposed to high glucose produce great amount of TGF-beta that plays a pivotal role in MMT. Recent findings suggest that TGF-beta controls mesothelial fibrosis via the activation of hyperglycolysis, thus we suppose that coupling glycolysis with Krebs cycle may improve mesothelial cells tolerance to TGF-beta.

Method: To test this hypothesis, we assessed the effects of Dichloroacetate (DCA), a pyruvate dehydrogenase kinase inhibitor, and L-carnitine (which sustains the production of Acetyl-CoA in multiple ways) on mesothelial cells treated with TGF-beta. Recent findings, in fact, highlight the potential anti-fibrotic effects of DCA and L-carnitine (through energy metabolic balancing) in different organs. Particularly, human peritoneal mesothelial cells (HMrSV5) were cultured in Dulbecco's Modified Eagle Medium (DMEM; Gibco) containing 10% fetal bovine serum. Then, cells, cultured to confluence, were pre-treated for one hour with or without 10mM DCA, 1 or 5 mM L-Carnitine and then with 10ng/ml TGF-beta for 4 hours. Gene expression of alpha-SMA and vimentin (markers of MMT) and IL1-beta and IL-6 (inflammatory markers) was evaluated by real-time PCR.

Results: Our results revealed that TGF-beta significantly increased the gene expression level of alpha-SMA (2.04 ± 0.3, $p<0.05$ versus control) and vimentin (1.61 ± 0.23, $p<0.05$ versus control) as well as the expression level of the pro-inflammatory cytokines IL1-beta (3.44 ± 0.87, $p<0.05$ versus control) and IL-6 (2.56 ± 0.51, $p<0.05$ versus control). Pre-treatment with DCA and L-carnitine (at 1 or 5 mM) significantly reduced these effects. In detail, pre-treatment with DCA reduced alpha-SMA expression (0.97 ± 0.24, $p<0.05$), vimentin (1.03 ± 0.1, $p<0.05$), IL1-beta (1.47 ± 0.16, $p<0.05$) and IL-6 (0.88 ± 0.28, $p<0.05$) respect to TGF-beta treated cells. Pre-treatment with 1 and 5 mM L-carnitine reduced respectively alpha-SMA expression at 0.96 ± 0.09 ($p<0.05$) and 0.98 ± 0.06 ($p<0.05$), vimentin 1.01 ± 0.12 ($p<0.05$) and 1.02 ± 0.1 ($p<0.34$), IL1-beta 1.02 ± 0.15 ($p<0.05$) and 1.68 ± 0.33 ($p<0.05$), and IL-6 0.72 ± 0.04 ($p<0.05$) and 0.85 ± 0.01 ($p<0.05$) respect to TGF-beta treated cells.

Conclusion: These preliminary results suggest, for the first time, that the use of both Dichloroacetate and L-carnitine, coupling glycolysis with Krebs cycle and oxidative phosphorylation, could restore physiological energy metabolism in mesothelial cells and control fibrosis.

P1143 REDOX PROFILING IN MESOTHELIAL CELLS IN EXPERIMENTAL PERITONEAL DIALYSIS

Rebecca Herzog[1,2], Anja Wagner[1], Klaus Kratochwill[1,2]

[1]Medical University of Vienna, Christian Doppler Laboratory for Molecular Stress Research in Peritoneal Dialysis, Vienna, Austria and [2]Medical University of Vienna, Department of Pediatrics, Pediatric Nephrology and Gastroenterology, Comprehensive Center for Pediatrics, Vienna, Austria

Background and Aims: PD-fluids lead to generation of reactive oxygen species (ROS) in the peritoneal cavity. The caused oxidative stress, defined as a cellular oxidant-antioxidant imbalance impairs not only peritoneal cell viability but also contributes to progression of local and systemic PD-related pathomechanisms. We aim to analyze the impact and specific targets of ROS during PD and the anti-oxidative mechanism of supplementation of PD-fluid with alanyl-glutamine (AlaGln) on a global proteome-wide level.

Method: To establish a redox-proteomics workflow for studying oxidative stress in peritoneal mesothelial cells we used a gold-standard model of redox-stress (H_2O_2) and PD-fluid induced stress. Levels of oxidative stress were first validated by increased intracellular ROS and superoxide dismutase activity with PD-fluid and H_2O_2 treatment and a reduction of these parameters by the addition of AlaGln. To detect alterations of the redox proteome, cysteine residues were either directly or indirectly labeled with fluorescent dyes (redox-2D-DiGE) or isobaric tags (iodo-TMT).

Results: The gel-based approach allowed global visualization of the reduced and oxidized cysteines and revealed redox profiles of 540 protein spots. Compared to control, we found an increase in oxidized and decrease in reduced cysteines in all PD treatments. The development of a highly sensitive LC/MS-based redox proteomics workflow allowed identification of ~950 proteins affected by redox-stress in mesothelial cells and confirmed the quantitative levels seen on cysteine oxidation. The addition of AlaGln reduced the overall redox status (intracellular ROS and superoxide dismutase activity) but further showed different proteins to be affected by redox modifications.

Conclusion: Redox proteomics of peritoneal cells could represent a novel approach for the identification of mediators of PD-induced pathomechanisms, but also to evaluate effects of novel anti-oxidant therapeutical or pharmacological interventions.

P1144 ODORIBACTER AND ANAEROTRUNCUS: GUT MICROBIOME SIGNATURE MIGHT BE RELATED TO COGNITIVE IMPAIRMENT IN PATIENTS ON PERITONEAL DIALYSIS.

Fabiola Martin del Campo[1], Natali Vega Magaña[2], Noe A Salazar-Félix[1], Marcela Peña Rodríguez[3], María de Lourdes Romo-Flores[4], Laura Cortés Sanabria[1], Enrique Rojas Campos[1], Alfonso Martín Cueto Manzano[1]

[1]Mexican Institute of Social Security, Biomedical Research Unit 02, Guadalajara, Mexico, [2]University of Guadalajara, Department of Microbiology and Pathology, Guadalajara, Mexico, [3]University of Guadalajara, Department of Molecular Biology and Genomics, Guadalajara, Mexico and [4]Mexican Institute of Social Security, Nephrology Department, Regional General Hospital 46, Guadalajara, Mexico

Background and Aims: Cognitive impairment is very common in dialysis patients, with negative effects on quality of life and mortality. In neurodegenerative conditions (Alzheimer, Parkinson) a gut-brain axis has been identified; however, there is no information about the relationship of gut microbiota alterations and presence of cognitive impairment in chronic kidney disease. The aim was to associate the gut microbiota profile with the cognitive function in patients on automated peritoneal dialysis (APD).

Method: Cross-sectional study in 39 APD patients; those with visual or mental disabilities, psychiatric or neurodegenerative diseases, inflammatory causes of ESRD, with active infections (including peritonitis), on anti-inflammatory drugs or antibiotics, were excluded. All patients had a clinical, biochemical, nutritional and dialysis adequacy evaluation, and were classified according to the presence of cognitive impairment using the Montreal Cognitive Assessment (MoCA) test. Fecal samples were collected and immediately stored at -80 °C. DNA extraction was performed with Quick-DNA Fecal/Soil Microbe Miniprep Kit (Zymo Research). Subsequently, V3 and V4 regions of 16S rRNA were sequenced using illumina platform. Statistical analysis: Student *t* test and χ^2 were used to compare quantitative and qualitative variables, respectively. Quantitative Insights Into Microbial Ecology (QIIME) pipeline and Linear Discriminant Analysis Effect Size (LEfSe) were employed for bioinformatic analysis.

Results: Eighty-two percent of subjects were male, mean age 47 ± 24 years, and dialysis vintage 11 (7-48) months. Sixty-four percent of patients had cognitive impairment. Patients with cognitive impairment were significantly older (53 ± 16 *vs* 38 ± 14, p=0.006), had higher frequency of diabetes mellitus (56% *vs* 21%, p=0.04), and had lower creatinine concentrations (11.3 ± 3.7 *vs* 14.9 ± 5.4, p=0.02) compared to patients with normal cognitive function. No differences were found in other biochemical, nutritional or dialysis adequacy variables.

A total of 38,083 sequences per patient were obtained after the microbiome analysis. LEfSe analysis showed a preponderance of S24_7, Rikenellaceae, Odoribacteraceae, *Odoribacter*, and *Anaerotruncus* in patients with cognitive impairment. In contrast, patients without cognitive impairment were characterized by *Dorea*, *Ruminococcus*, *Sutterella* and *Fusobacteria* (LDA score (Log_{10}) > 2.5; $p < 0.05$).

Conclusion: Cognitive impairment was present in two-thirds of these APD patients. *Odoribacter* and *Anaerotruncus* were significantly more abundant in patients with cognitive impairment than in those with normal function. Such gut bacteria might enhance cognitive impairment as have been described to increase the uremic toxin production and activation of inflammatory pathways in the central nervous system. This is the first study providing evidence than brain and behavior might be influenced by the gut-brain axis in dialysis patients.

P1145 **ADEQUACY AND SURVIVAL IN PERITONEAL DIALYSIS: TEN YEARS EXPERIENCE.**

Vincenzo Terlizzi[1], Elena Pezzini[1], Roberta Cortinovis[1], Diana Bertoni[1], Alessandra Pola[2], Valerio Vizzardi[2], Massimo Sandrini[2], Ezio Movilli[2], Francesco Scolari[1,2]

[1]Università degli Studi di Brescia - Facoltà di Medicina e Chirurgia - and [2]U.O. Nefrologia - ASST Spedali Civili di Brescia

Background and Aims: in Italy only a minority of uremic patients perform peritoneal dialysis (PD). In dialysis centers where PD is practiced and proposed the prevalence is no more than 23%. Proposed advantages of PD over HD are a more preserved Residual renal function (RRF), that has been associated with better survival, and better Quality of life (Qol) due to possible more preservation of previous lifestyle, independence, possibility of traveling, and flexibility. Incremental peritoneal dialysis is a promising way to further improve Qol and to preserve RRF. Lastly, PD is less expensive than HD. Aim of this study has been to retrospectively evaluate our ten-years experience of PD treatment

	All	*CAPD*	*APD*	*p*
Age (years)	*65±16*	*66.5±15.1*	*64.8±16.9*	*0.41*
wKt/V	*1,75±0,36*	*1.69±0.35*	*1.80±0.36*	*<0.05*
wClCr (l/sett)	*65,7±19,8*	*71.1±17.1*	*62.1±20.6*	*<0.05*
Diuresis (ml/die)	*1054±654*	*1290 (845;1633)*	*850 (448;1397)*	*<0.05*
RRF (ml/min)	*3,7±2,5*	*4.6±2.3*	*3.2±2.6*	*<0.05*
PNA (g/kg/die)	*0,99±0,16*	*1.01±0.15*	*0.99±0.17*	*0.34*
BMI (Kg/m²)	*24±4*	*23.5±4.2*	*24.3±3.8*	*0.11*

Figure 1.

	Incremental	*Standard*	*p*
Age (years)	*67.0±13.0*	*64.8±17.4*	*0.32*
wKt/V	*1.75±0.37*	*1.75±0.35*	*0.98*
wClCr (l/sett)	*76.6±17.6*	*60.8±18.7*	*<0.05*
Diuresis (ml/die)	*1509 (1217;1740)*	*798 (373;1277)*	*<0.05*
RRF (ml/min)	*5.4±2.1*	*3.0±2.3*	*<0.05*
PNA (g/kg/die)	*1.02±0.15*	*0.99±0.17*	*0.12*
BMI (Kg/m²)	*23.4±3.8*	*24.3±4.1*	*0.07*

Figure 2.

	Incremental	*Standard*	*p*
Age (years)	*67.0±13.0*	*64.8±17.4*	*0.32*
wKt/V	*1.75±0.37*	*1.75±0.35*	*0.98*
wClCr (l/sett)	*76.6±17.6*	*60.8±18.7*	*<0.05*
Diuresis (ml/die)	*1509 (1217;1740)*	*798 (373;1277)*	*<0.05*
RRF (ml/min)	*5.4±2.1*	*3.0±2.3*	*<0.05*
PNA (g/kg/die)	*1.02±0.15*	*0.99±0.17*	*0.12*
BMI (Kg/m²)	*23.4±3.8*	*24.3±4.1*	*0.07*

Figure 2.

Figure:

on survival, dialysis adequacy, preservation of RRF and nutrition in uremic patients followed at our Dialysis Center.

Method: We retrospectively evaluated all the incident patients that started PD treatment due to uremia from 01-01-2008 to 31-12-2018 at the U.O. Nephrology ASST Spedali Civili of Brescia. The exclusion criteria were time of dialysis treatment less than 3 months and absence of previous dialytic treatment or kidney transplantation. For each patient anthropometric, clinical-anamnestic data and comorbidities at dialysis start were recorded.

Data on dialysis adequacy, nutrition, RRF and PD dialysis modality performed were also recorded.

Results: During the observation period 329 patients started PD. 60 were excluded due to follow-up of less than 3 months. Therefore, 269 patients (males 160, 59%) were studied. The average age was 65 ± 16 years, BMI 24 ± 4 kg/m^2. Comorbidities were: hypertension (87%), diabetes mellitus (32%), cerebral vascular disease (26%) and ischemic heart disease (25%). The mean duration of dialysis treatment was 2.1 ± 1.5 years. At the end of ten-years follow-up 24% of patients have had a kidney transplant, 18% were on PD treatment, 17% have had a shift towards HD, 39% had died. The main causes of death were: infection (39%) and cardiovascular disease (31%). The most common dialysis modality performed was APD (61%); CAPD was performed in 39% of pts. Dialysis modality (CAPD; APD), nutrition parameters (PNA; BMI), as well as RRF, expressed as an average value during follow-up, are shown in Figure 1. 81 patients (30%) were treated with incremental PD; 85% of them with manual exchanges. The comparison of dialysis parameters between incremental PD and standard PD are shown in Figure 2.

Multivariate analysis with survival as dependent variable (Figure 3), showed that age, diabetes mellitus, and low wKt/V were independently associated with an increased risk of mortality. Diuresis volume and male gender were protective factors. No independent influence on mortality of the dialysis treatment modality was found.

Conclusion: In this ten-years experience of patients undergoing PD at our Center, incremental PD seems to be a protective factor for the maintenance of a preserved diuresis and better dialysis adequacy, and these factors are associated with better survival of the patients.

P1146 **ENHANCED EXPRESSION OF THIOREDOXIN-INTERACTING-PROTEIN (TXNIP) MAY REGULATE OXIDATIVE DAMAGE IN PERITONEAL DIALYSIS PATIENTS**

Tina Oberacker[1], Severin Schricker[1], Moritz Schanz[1], Dominik M. Alscher[1], Markus Ketteler[1]

[1]*Robert-Bosch-Hospital, Department of Internal Medicine, Stuttgart, Germany*

Background and Aims: Glucose-based solutions used as peritoneal dialysis fluids influence the peritoneal membrane. Exposure to high glucose-based peritoneal dialysis solutions induces reactive oxygen species (ROS) production due to upregulation of TXNIP as shown by several studies in rats as well as in human primary cells. Enhanced expression of TXINP also regulates oxidative damage. Therefore the aim of this study was to investigate the expression of TXNIP and the extent of oxidative damage in human peritoneal biopsies.

Method: Human peritoneal biopsies of healthy controls, PD patients and patients with EPS were collected. TXNIP and thioredoxin-1 (TRX) mRNA expression was determined by qPCR. Protein expression and the extent of oxidative damage were examined by immunohistochemistry.

Results: Biopsies from the peritoneum of 7 healthy controls, 36 patients on PD without signs of EPS as well as of 12 patients with EPS were collected. The age of the healthy controls was higher (median 64.00 years, IQR: 53.00-70.00) than in the other subgroups (PD: median 60.50 years, IQR: 46.00-69.00 and EPS: median 51.00 years, IQR: 38.00-58.75). Furthermore, compared to the PD- (39 %) and EPS-group (33 %), there were more female participants in the control-group (86 %). Time on PD was longer in EPS patients (median 70.00 months) than in PD patients (median 33.50 months).

In a preliminary study, exposure to high glucose-based peritoneal dialysis solutions did not markedly influence the mRNA expression of TXNIP and TRX.

However, on protein level a significant glucose-related upregulation of TXNIP could be observed especially in PD patients. Interestingly, there was no glucose-related change in protein expression of its interacting partner and cellular anti-oxidant TRX.

To study the effect of TXNIP expression on the generation of oxidative damage, pH2AX positive nuclei were counted on peritoneal membrane sections. A slight increase of pH2AX positive nuclei upon exposure to dialysis solutions could be observed in the cohort analysed.

Conclusion: Here, we show for the first time a clear tendency for upregulation TXNIP in human peritoneal tissue after exposure to high glucose-based peritoneal dialysis solutions especially in PD patients. This increase in TXNIP expression may correlate with the accumulation of oxidative damage of macromolecules. Therefore, manipulation of TXNIP expression may be a promising therapeutic target to improve peritoneal membrane function.

P1147

SEQUENTIAL ULTRASOUND BASED APPROACH IN PERITONEAL CATHETER MALFUNCTION: THE COMBINATION OF B-MODE AND DOPPLER ULTRASOUND.

Matthias Zeiler[1], Antonio Federico[1], PAOLO LENTINI[2], Roberto Dell'Aquila[2], Antonio Granata[3], Stefano Santarelli[1]

[1]"Carlo Urbani" Hospital, Nephrology and Dialysis Unit, Jesi, Italy, [2]"San Bassiano" Hospital, Nephrology and Dialysis Unit, Bassano del Grappa, Italy and [3]"Cannizzaro" Hospital, Nephrology and Dialysis Unit, Catania, Italy

Background and Aims: The clinical approach to peritoneal catheter malfunction consists usually in laxative prescription, abdominal radiography, brushing of the catheter lumen, guide-wire manipulation or catheter fluoroscopy. Only specialized centers apply videolaparoscopy for catheter rescue interventions. Up to now, limited experience is present regarding the evaluation of the intraperitoneal tract of the peritoneal catheter in adult patients. The aim of the study was to evaluate the diagnostic capability of B-mode ultrasound (US) followed by colour Doppler US (Doppler US) in persistent peritoneal catheter malfunction.

Method: US followed by Doppler US of the intraperitoneal part of the catheter was performed prior to videolaparoscopy intervention in 40 adult patients presenting persistent peritoneal catheter malfunction despite non-invasive therapy such as laxative prescription and brushing of the catheter lumen. US and Doppler US diagnosis were compared to the corresponding at videolaparoscopy intervention, and the causes of mismatch analyzed. In all patients US was performed after filling of the abdominal cavity with peritoneal dialysis solution of at least one liter. Doppler US along the intraperitoneal segment of the catheter was performed by flushing with dialysis fluid.

Results: In US, causes of persistent malfunction were catheter dislocation combined with omental wrapping in 21 cases, omental wrapping without dislocation in 11 cases, dislocation only in 4 cases, adherences to non-omental structures in 3 cases and entrapment in the lateral inguinal fossa in one case. The correspondence of US and videolaparoscopy diagnosis was 90%, respectively in 36 of 40 cases. The discrepancies were due to improper visualization of the catheter caused by constipation and embedding of the catheter between intestinal loops, resulting in an erroneous US diagnosis of omental wrapping, whereas videolaparoscopy showed encasement of the catheter between intestinal loops in three cases and presence of adherences to tubal structures in one case. Doppler US clarified the functional aspects of the catheter, thus increasing the correspondence to videolaparoscopy up to 39 out of 40 cases (97.5%)

Conclusion: US combined with Doppler US is helpful in making a correct pre-operative diagnosis of persistent peritoneal catheter malfunction and in planning of the videolaparoscopy rescue intervention.

P1148

THE ASSOCIATION WITH LOWER SYSTOLIC BLOOD PRESSURE AND ALL-CAUSE MORTALITY IN PATIENTS UNDERGOING PERITONEAL DIALYSIS

Motoyasu Kurahashi[1], Kenji Harada[1], Hidetoshi Kanai[1]

[1]*Kokura memorial hosipital, Nephrology, Kitakyusyu, Japan*

Background and Aims: Previous observational studies have been reported that a U-shaped association between systolic blood pressure (SBP) and mortality in patients undergoing hemodialysis. However, the optimal blood pressure in patients undergoing peritoneal dialysis (PD) remains unclear.

Method: The present study is observational and conducted in a single center. Four hundred and sixteen patients undergoing PD managed in our hospital from April 2010 to December 2017 were participated in this study. The patients were divided into four groups depended on office SBPs, as follows; group1: SBP $<$110 mmHg (n=60), group2: SBP 110-139 mmHg (n=187), group3: SBP 140-159 mmHg (n=113) and group4: SBP $\geqq$160 mmHg (n=56). When using the Cox proportional hazards model, group 2 was regarded as a reference. Hypertension was defined as SBP $\geqq$140 mmHg, diastolic blood pressure $\geqq$90 mmHg, or use of any anti-hypertensive drugs. The association between SBP with several outcomes such as the risk of all-cause deaths, cardiovascular events and these composite events were estimated using cox proportional hazards model. Adjusted factors were age, sex, comorbidities, laboratory covariates, left ventricle ejection fraction and medications such as renin-angiotensin system blockades and statins.

Results: The mean follow-up period was 29.2 months. The prevalence of hypertension was 90.4% (n=376) of all patients. The risk of all-cause deaths with multivariate cox proportional hazards regression analysis was significantly higher in the group 1 (hazard ratio 2.08, 95% CI 1.23-3.51, p=0.006). While the risk of CV events with univariate analysis tended to be higher in group 4, there was no significant association between SBP and the risk of CV events with multivariate analysis. The risk of the composite events with multivariate analysis was significantly higher in group 4 (hazard ratio 1.61, 95% CI 1.01-2.57, p=0.047).

Conclusion: This study indicated that lower SBP was independently associated with all-cause mortality in patients undergoing PD. Moreover, higher SBP might be involved with composite events.

P1149 PERITONEAL MEMBRANE CHARACTERISTICS OVER TIME: A LONGITUDINAL STUDY

Olga Balafa[1], ANILA DUNI[1], Paraskevi Tseke[2], Karolos Pavlos Rapsomanikis[1], Margarita Oikonomou[1], Haralambos Pappas[1], Ioanna Theodorou[1], Evangelia Ntounousi[1]

[1]*University Hospital of Ioannina, Department of Nephrology, Ioannina, Greece and* [2]*General Hospital Alexandra, Department of Nephrology, Athens, Greece*

Background and Aims: Modified PET (use of 3.86% glucose dialysate instead of 2.27%) and temporal drainage at one hour allows a more complete study of peritoneal membrane transport, as it provides information about sodium sieving, free water transport (FWT) and ultrafiltration failure (UFF). Longitudinal data using this PET are sporadic. Aims of our study were a) longitudinal follow-up of the membrane function using modified PET b) evaluation of UFF and association with clinical and membrane characteristics.

Method: We analyzed all modified PET tests performed in our unit during the last 9 years. Patients who underwent the first test during the first year of treatment and then once a year were included. We estimated classic peritoneal transport parameters like D/P creatinine, D/D0 glucose and ultrafiltration (UF) at 4 hours. Moreover we calculated sodium seiving expressed as Dip/DPNa= (Dialysate sodium time 0/plasma sodium)-(Dialysate sodium time 1 hour/plasma sodium)], sodium removal (in one hour) and FWT. We collected clinical and lab data of the patients too.

Results: A total of 219 PETs were performed in 85 PD patients, (median age 64 years (range 18-45). The baseline membrane characteristics of the patients were: DP creatinine=0.74±0.11, D/D0glucose=0.28±0.08, DipDPNa=0.05±0.04, sodium removal=29,804 ±26,894 (mmol/L), FWT=214.9±194.7 ml and UF =655.1±265.5 ml. On multivariate regression analysis D/P creatinine, FWT and sodium removal were significant independent covariates accounting for 50% of the variability of ultrafiltration . The patients were followed-up for a median of 36 months (range 2.4-143).For the repeated measurements, the analysis showed that the observed values of D/Pcre,D/D0, Dip/DPNa, FWT and UF remained rather stable across the different time measurements. During the study, 23 out of 85 pts developed peritoneal UF failure (UFF). Analysis was performed using univariate random effects logistic time-series models and only D/D0 (OR=0.84, P=0.001), D/P Cre (OR=1.15, p<0.001), urine volume (OR=1.26, p=0.027) and sodium removal (OR=0.99, p=0.003) were significantly associated with relative risk of UFF development.

Conclusion: Surprisingly, our patients present a stable membrane function over time. Possible explanations could be the low peritonitis rate and strict use of hypertonic glucose dialysates. Ultrafiltration failure was correlated with higher D/P creatinine and lower D/D0 glucose values, higher baseline urine volume and lower sodium sieving.

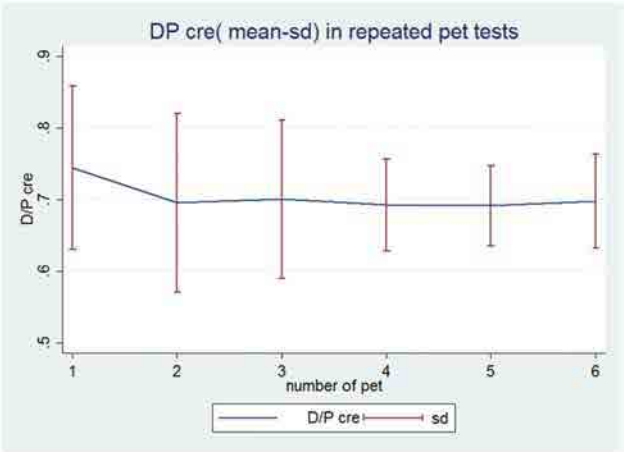


Figure:

P1150 BURDEN OF SYMPTOMS EVALUATION AND DETERMINANTS IN PERITONEAL DIALYSIS PATIENTS USING ESAS-R AND IPOS RENAL SCORE

Eunice Cacheira[1], Luís Leite de Sousa[1], Ana Rita Martins[1], Patricia Matias[1], Patricia Branco[1]

[1]*Hospital Santa Cruz, Nephrology, Carnaxide, Portugal*

Background and Aims: CKD patients are known to have a substantial burden of symptoms. Effort towards treatment modifications aiming to improve the quality of life in ESRD patients is growing among clinicians. ESAS-r and IPOS renal score are well known among conservative and palliative care physicians, used to evaluate the burden of symptoms in their renal patients. However, there are few studies including patients in chronic peritoneal dialysis. Using these tools, we aim to evaluate the symptoms and determine patient and treatment-related conditions associated with their burden in a PD population.

Method: We have conducted 73 phone interviews to the prevalent PD population in our centre. ESAS-r and IPOS renal (3-days patient version) questionnaires were answered by each patient/family caregiver. The population was then characterized according to gender, race, age, PD technique and duration, number of daily exchanges, patient autonomy, diabetes mellitus and cancer status, Charlson score and number of cardiac events and hospitalizations since PD beginning. Statistical analysis of data was carried out using SPSS®.

Results: We obtained a total of 63 answers to both questionnaires. Three were answered by a family caregiver. 60.3% of the patients were male, mean age 53 (±14.9) years. 15.9% were on automated PD, with mean number of daily exchanges of 3.45 (±0.7) and mean PD duration of 25.7 (±33.5) months. 38,1% were diabetic, six (9.5%) patients had cancer and mean Charlson score was 4.24 (±1.8). Only 3 patients were caregiver dependent for treatment. 31.3% had at least one hospitalization since PD beginning. Each patient reported a mean 3.1 (±2) number of symptoms on ESASr: renal. Mean IPOS-renal score was 9.5 (±6.4). In univariate analysis (t-student test), greater IPOS-renal score was associated with female gender only ($p = 0.056$; CI -0.07-6.1). In multivariate analysis (linear regression) the number of symptoms reported by each patient on ESASr renal was associated with number of hospitalizations during PD time ($B = 0.46$; CI(95%) 0.18-0.75; $p = 0.02$) in model adjusted to time of PD.

Conclusion: The majority of variables analysed do not have an association with IPOS renal score. The number of hospitalizations was associated with greater burden of symptoms, adjusted to PD time. Oddly, Charlson score, diabetes mellitus and cancer status had no relation to the symptoms reported or IPOS renal score. More modifiable patient and treatment-related variables can be studied to better characterize which interventions may ease the burden of symptoms in PD patients. Patients can answer these questionnaires periodically to help clinicians understand weather treatment modifications have a positive impact on their well-being.

P1151 **CLINICAL OUTCOMES IN REMOTE PATIENT MONITORING IN AUTOMATED PERITONEAL DIALYSIS : A COLOMBIAN EXPERIENCE**

Leyder Corzo[1], Jasmin Vesga[2], Mauricio Sanabria[3], Angela Rivera[4]

[1]Renal Therapy Services (RTS) Colombia, Medical, Bogota, Colombia, [2]Renal Therapy Services (RTS) Colombia, Clinical Research, Bogota, Colombia, [3]Baxter Renal Care Services (BRCS) Latin America, Clinical Research, Bogota, Colombia and [4]Baxter Healthcare Corporation, RCS Medical & Quality, Deerfield, United States of America

Background and Aims: Patients with remote monitoring are followed-up daily by clinical teams, allowing early detection and correction of problems, which could result in improvements in therapy outcomes.

Aims: To evaluate the association between Remoted Patient Monitoring (RPM) program and clinical outcomes (technique failure and peritonitis rates).

Method: A historical, multicenter, observational cohort study in Automatized Peritoneal Dialysis (APD) prevalent patients, included between October 1, 2016, and June 30, 2017 with follow-up until June 30, 2018, at Renal Therapy Services (RTS) network. Patients were older than 18 years, divided into two cohorts based on the RPM use: 1) APD-RPM cohort: patients using the HomeChoice Claria® device with Sharesource® technology (Baxter Healthcare, Deerfield, USA) and 2) APD-Without RPM cohort: patients using APD systems HomeChoice Legacy® without RPM. Sociodemographic and clinical characteristics of all patient were summarized descriptively. Propensity score matching 1:1 was used.

Results: 558 patients met the inclusion criteria for data analysis. The mean age was 54 years, 40% were female, 26% had APD RPM, see **Table 1.** After propensity score matching, APD therapy with RPM (n=148) as compared to APD-Without RPM (n=148) was associated with significant reduction in technique failure, IRR= 0.46 95% CI: [0.24 - 0 .89], and a trend in peritonitis rate reduction, IRR= 0.87 [0.41 - 1.00], P= 0.051, **see table 2**. Main reasons of technique failure are presented **in table 3.**

Conclusion: The use of RPM program in APD patients is associated with lower technique failure rate, supporting the role of this technology as performance enhancer.

Table 1. Baseline demographic and clinical characteristics

Characteristics	n=148 APD-RPM	n= 410 APD-Without RPM	Standardized differences
Age, year	53.93	53.83	0.01
Sex: Female	37.84	40.98	-0.06
Caregiver: Yes	36.48	35.60	0.02
Social level			
Low	31.08	53.66	Reference
Medium	66.22	43.66	0.46
High	2.70	2.68	0.00
School level			
Elementary or none	30.41	48.05	Reference
High school	52.03	40.98	0.22
University degree	17.57	10.98	0.19
Hypertension history	87.84	85.37	0.07
Diabetes history	37.16	39.51	-0.05
Cardiovascular disease history	24.32	24.39	0.00
Hemoglobin, g/dL	11.89	11.72	0.09
Phosphorus, mg/dL	5.31	5.26	0.04
Potasium, mEq/L	4.77	4.78	-0.01
Albumin, g/dL	3.62	3.82	0.34
Vintage dialysis			
< 1 year	23.65	32.44	Reference
1 to 3 years	38.51	30.24	0.17
> 3 years	37.84	37.32	0.01
Follow-up time, years	0.93	1.22	-0.56

Table 2. Clinical outcomes associated with RPM in matched sample

Outcomes	n=148 APD-RPM	n= 148 APD-Without RPM	IRR[b] [95%CI]	P value
Technique failure rate [95% CI] (Episodes per patient-year)	0.07 [0.03 - 0.12]	0.15 [0.10 - 0.19]	0.46 [0.24 - 0 .89]	0.023
Peritonitis rate [95% CI] (Episodes per patient-year)	0.21 [0.14 - 0.30]	0.24 [0.17 - 033]	0.87 [0.41 - 1.00]	0.051

[b]IRR: Incidence Rate Ratio is defined as APD-RPM/APD-Without RPM

Table 3. Main reasons by technique failure in matched sample

Main reasons for technique failure	APD-RPM N= 148		APD-Without RPM N=148	
	n	%	n	%
Peritonitis/ Infection	7	63.64	4	18.18
Loss of Dialysis Adequacy	1	9.09	5	22.73
Catheter Problems	1	9.09	4	18.18
Psychological/Medical	2	18.18	7	31.82
Patient desire	0	0.00	2	9.09
Total	**11**	**100**	**22**	**100**

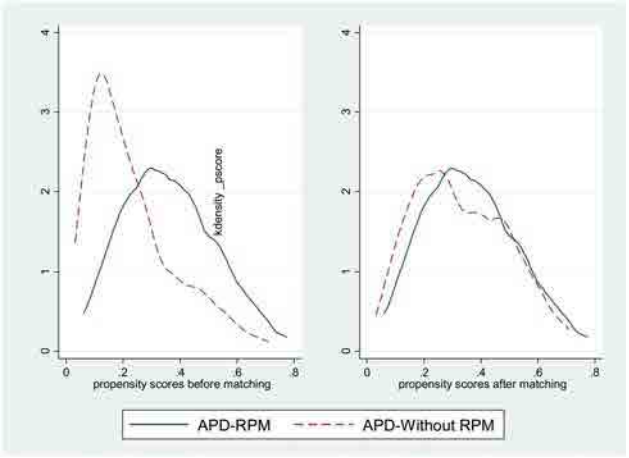


Figure: Distribution of propensity scores for the two cohorts before and after the matching

P1152 **USE OF URGENT START PERITONEAL DIALYSIS IN END STAGE RENAL DISEASE PATIENTS: A RETROSPECTIVE ANALYSIS IN A NORTH-INDIAN POPULATION**

Manzoor Parry[1], MASTAKIM AHMED MAZUMDER[2], Shahzad Alam[2], Hamad Jeelani[2]

[1]Sher-I-Kashmir Institute of Medical Sciences, Nephrology, Srinagar, India and [2]Gauhati Medical College and hospital, Nephrology, Guwahati, India

Background and Aims: End-stage renal diseases (ESRD) that are referred late to dialysis usually need hemodialysis via central vein catheter (CVC). Urgent start peritoneal dialysis (PD) can be used in these patients to avoid need of CVC. Catheter patency and other complications related to urgent-start PD have not been thoroughly clarified. We evaluated the clinical outcomes of urgent-start PD in a North-Indian cohort.

Method: In this retrospective study, we enrolled ESRD patients who were started on urgent-start PD (starting PD within 14 days after catheter insertion) in our center from January 1, 2008 to December 31, 2017, and followed them up to 10 years. Catheter failure was primary outcome of study while as secondary outcomes included short-term and long-term complications related to urgent-start PD.

Results: In this study882 patients (60.3% male, mean age 47.28 ± 14.1years) were enrolled. There were few peri-operative complications with significant hemorrhage seen in 2 patients. Early peritonitis occurred in 8 (0.9%) patients. Within the first month of catheter insertion, abdominal wall complications (hernia, hydrothorax, hydrocele, and leakage) occurred in 24 (2.7%) patients while as functional catheter malfunction developed in 36 (4.1%) patients. On follow-up of the patients (median 35.7 months), 32 (3.6%) patients experienced catheter failure, and 141 (15.9%) had death-censoring technique failure. Catheter patency rate at the end of 1-month, 1 -year, 3-year, and 5-year, was 98.2, 94.9, 93.1,92.4%; and technique survival rate was 99.2, 96.9, 90.2, 82.8%, respectively. Every 5-year increase in age was associated with 17% decrease of risk for catheter failure (hazard ratio [HR]: 0.83, 95%confidence interval [CI]: 0.73–0.89). Risk factors for abdominal wall complications included male sex (HR: 1.45, 95% CI: 1.03–2.1), low hemoglobin levels (HR: 0.88, 95% CI: 0.79–0.98) and diabetic nephropathy (HR: 1.65, 95% CI:1.13–2.35).

Conclusion: Urgent-start PD is a safe option for ESRD who need urgent dialysis to avoid CVC insertion for HD. For a successful urgent start PD programs, a well-trained PD team, catheter insertion procedure by experienced personnel, and a well-designed PD prescription and a good follow-up care is needed.

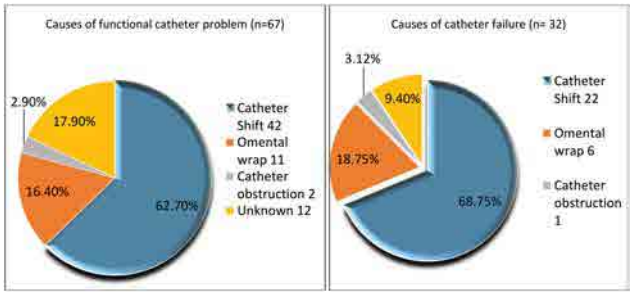


Figure 1. The distributions of the onset time and the causes of functional catheter problems and catheter failure

P1153 ARE LONG-TERM PERITONEAL DIALYSIS PATIENTS SLEEPING WELL?

Luisa Pereira[1], Anabela Malho Guedes[1], Ana Rita Martins[2], Patricia Matias[2], Patricia Branco[2]

[1]Hospital de Faro, Centro Hospitalar Universitário do Algarve, Nephrology, Faro, Portugal and [2]Hospital de Santa Cruz, Centro Hospitalar Lisboa Ocidental, Nephrology, Lisboa, Portugal

Background and Aims: Sleep quality is an important and determining factor in the quality of life (QoL) during dialysis. The prevalence of sleep disorders in the general population varies between 10 and 40%; this figure increases to 50% in dialysis patients.

This study was conducted to determine which factors influence sleep quality in end stage renal disease patients on automated (APD) and continuous (CAPD) ambulatory peritoneal dialysis.

Methods: This was a cross-sectional study which included stable patients from two Peritoneal Dialysis Units. We excluded patients who weren't able to understand the questionnaires, the language and the ones who had hospitalar admissions in the previous 3 months. Pittsburg Sleep Quality Index (PSQI) was used for assessing sleep quality (the higher the score, the lower the sleep quality), while quality of life parameters were assessed by self-administered EuroQol questionnaire (EQ-5D-5L). The presence of depressive symptoms was made with Patient Health Questionnaire (PHQ-9). In all patients, demographic variables, Charlson Comorbidity Index (CCI), clinical and laboratory parameters were recorded and analyzed. Descriptive statistics was performed. Two groups were created according to Pittsburg Sleep Quality score: G1 (n=42) - "poor" sleep quality and G2 (n=28) - "good" sleep quality. Groups were compared using independent t-test for comparison of continuous variables and Chi square test for categorical variables. In order to evaluate relationship between sleep quality and the other variables multivariate logistic regression and Pearson bivariate analysis were used.

Results: The study enrolled 70 patients (male/female 44/26; mean age 55.3±14.6 years; APD/CAPD 25/45; PD duration 28±24.2months). One third (31.4%) of the patients was diabetic, 12.9% presented cardiac insufficiency and 20% had cardiovascular disease. 50% of our population had a sleep disorder, although the majority of the problems were slight to moderate.

We found that PD patients who sleep better (G2) had significant better life quality ($p<0.001$), lower CCI ($p<0.001$) and were less depressed ($p<0.001$). 77.3% of the patients with worst sleep quality (G1) were diabetic ($p=0.04$), regardless glycemic control and hemoglobin A1c.

There were no significant differences between the two modalities of peritoneal dialysis (APD and CAPD patients), between genders or in patients who were PD first. We found no significant association between sleep quality and dialysis efficacy (weekly kt/v).

Multivariate analysis (linear regression) showed a significant association between sleep quality and EuroQol (ExpB=0.000; IC 95% 0.000 to 0.054; $p=0.002$) and, depression (ExpB=1.274; IC 95% 1.045 to 1.552; $p=0.017$) in a model adjusted to age, PD duration and diabetes.

Conclusion: Our results show that poor sleep quality seems to be linked to life quality, comorbidity burden and depression. A better understanding of risk factors associated with poor sleep quality may help to signalize the patients who may benefit of specific treatment. The PSQI survey is a simple tool offering very complete information on sleep quality. The implementation of actions aimed at improving the hygiene of sleep may be an excellent way to improve the patients' quality of life in an efficient and effective manner.

P1154 EFFECTS OF SHORT-TERM HEMODIALYSIS WITH CENTRAL VENOUS CATHETER(HD-CVC) ON PATIENTS WITH URGENT-START PERITONEAL DIALYSIS(USPD)

Wenjing Zhang[1], Jia LV[1], Zhigang Wang[1], Lan Li[1], Jiping Sun[1]

[1]*The First Affiliated Hospital of Xi'an Jiaotong University, Nephrology Department, Xi'an, P.R. China*

Background and Aims: Urgent-start peritoneal dialysis (USPD) has gained increasing worldwide attention. Studies have suggested that USPD has many advantages concerning the early complications, survival rates and medical expenses. Due to the lack of predialysis education, most patients newly diagnosed with ESRD in China have less knowledge about the dialysis methods, whether HD or PD. So, some patients choose to receive the short-term hemodialysis with central venous catheter (HD-CVC) before USPD. Whether the HD-CVC affected USPD, and whether it was necessary for ESRD patients without indications of emergency dialysis to undergo HD-CVC transition before USPD, were addressed. So we investigate the effects of the HD-CVC on urgent-start peritoneal dialysis.

Method: Retrospective analysis was performed on patients who received USPD from August 2008 to March 2017 in the first affiliated hospital of Xi'an Jiaotong University. According to whether hemodialysis and central venous catheterization were performed before PD, these patients were divided into two groups: USPD group (HD-CVC was not performed before PD) and HD-PD group (HD-CVC was given after admission, and then the PD catheterization was performed within 2 weeks). The follow-up time was 1 year. The differences in clinical biochemical indexes, dialysis dose, urine volume, residual renal function, dialysis adequacy, peritoneal dialysis complications and technical survival rate between the two groups were observed.

Results: 1.A total of 482 patients were enrolled in this study, including 315 in the USPD group (average age 48.56±14.92 years) and 167 in the HD-PD group (average age 48.87±14.49 years). The demographics and clinical biochemical indexes (including creatinine, glomerular filtration rate, and blood potassium before admission) were similar between the two groups, and the differences were not statistically significant($P>0.05$).2. After PD for 1month, residual renal function, UKt/V and TKt/V in the USPD group were significantly higher than those in the HD-PD group, blood urea nitrogen and creatinine were significantly lower than those in the HD-PD group (USPD group: 4.41±4.0ml/min, 0.79±0.44, 2.17±1.39, 17.79±4.96mmol/L, 663.15±182.03umol/L; HD-PD group: 3.67±2.39ml/min, 0.64±0.42, 1.92±0.55, 19.08±8.21 mmol/L, 711.02±280.3umol/L), and the differences were statistically significant ($P<0.05$, respectively).After PD for 6months, the urine volume in the USPD group were significantly higher than those in the HD-PD group(USPD group:964.84±539.95ml/d; HD-PD group 794.39±569.17ml/d), and the difference was statistically significant ($P=0.002$). 3. During the whole follow-up period, the exit-site infection rate, peritonitis infection rate, mechanical complications and technical survival rate were similar between the two groups, with no statistically significant difference ($P>0.05$,respectively).

Conclusion: Hemodialysis with central venous catheter before USPD affected the residual renal function and dialysis adequacy. HD-CVC as a pretreatment is not recommended to the end-stage renal disease patients who required PD but without the indication of emergency dialysis.

P1155 REMOVAL OF PHOSPHATE AND CREATININE DURING PD WITH DIFFERENT GLUCOSE CONCENTRATIONS

Joanna Stachowska-Pietka[1], Josep Teixido-Planas[2,3], Maria-Isabel Troya[2,3], John (Ken) Leypoldt[1]

[1]Nalecz Institute of Biocybernetics and Biomedical Engineering, Warsaw, Poland, [2]Hospital Universitari, Nephrology Department, Barcelona, Spain and [3]Fundacio Institut d'Investigacio en Ciencies de la Salut, Barcelona, Spain

Background and Aims: Adequate removal of creatinine and phosphate is one of the key objectives in peritoneal dialysis (PD). Whereas the mechanism of creatinine removal is well known, there are gaps in understanding regulation of phosphate removal. Clinical studies show that although the size of both molecules is similar, their removal might behave differently (Badve et al CJASN 2008). Several, but not all, studies have suggested that peritoneal phosphate clearance is larger when using CAPD than APD prescriptions, suggesting the dwell time or duration is an important determinant of phosphate clearance. The aim of the study was to investigate specifically the effect of dwell duration at the level of single PD exchange with different glucose concentrations on peritoneal phosphate clearance.

Method: A prolonged 8-hour PET was carried out in 32 clinically stable PD patients with each of three glucose-based solutions: 1.36% (G1), 2.27% (G2), and 3.86% (G3) with temporary drainage at 1 and 4 hours of peritoneal dwell. Dialysate and blood samples were taken to measure infused and drained volume and concentration of phosphate and creatinine in dialysate and blood. Clearances were calculated for a single exchange for each solution and for 4-hour (4H) and 8-hour (8H) dwell periods. For each patient, the 4-hour creatinine D/P ratio for G3 was calculated. The clearance ratio, ClR, defined as the ratio of solute clearance for particular solution to its clearance for the G1 solution, was calculated for both solutes and each solution and dwell durations.

Results: The obtained values of 4H creatinine D/P ratio for G3 solution were 0.67 ± 0.11 (mean $\pm$ SD). The values of solute clearances per single exchange expressed in mL/min, are presented in table below.

Solute	Dwell time, h	Glucose 1.36%	Glucose 2.27%	Glucose 3.86%
Creatinine	4	5.54	6.34	7.84
	8	3.16	3.61	4.29
Phosphate	4	4.86	5.37	6.86
	8	2.86	3.23	3.93

Creatinine and phosphate clearances were found to be solution and dwell duration dependent with $p<0.001$. The clearances of both solutes were correlated for the same dwell duration or solution (not for creatinine G2 for 4H vs 8H) with $p<0.05$. Moreover, solute clearances were also correlated with creatinine D/P for 4H but not for 8H. The clearances of phosphate were also correlated with that for creatinine each solution at both dwell durations with $p<0.001$. Both calculated ClR were found to be dependent on the solution ($p<0.001$) but not dwell duration. Similar dependence on solution and correlations are valid in one analyze solute mass removal.

Conclusion: Phosphate and creatinine clearances were found to be well correlated during a long, 8-hour PET proving similarities in their transport. Interestingly, the dependence of both clearances and ClR on solution glucose concentration suggest that the removal of phosphate as well as creatinine depends on the ultrafiltration induced by glucose concentration in dialysis solution.

P1156 **TWO YEAR FOLLOW UP QUALITY INDICATORS COMPLIANCE IN A LARGE INTERNATIONAL PERITONEAL DIALYSIS INSTITUTION**

Belén Marrón[1], Suzanne Pearce[2], Claudia Martín[3], Dan Munteanu[4], Michael Roesch[5], Janusz Ostrowski[6], Marietta Torok[7], Daniel Pérez[8], Attila Orosz[9], Pawel Kochman[6], Charlotta Wollheim[10], Carlos Lucas[11], Fernando Macário[12]

[1]Diaverum Renal Services, Corporate Home Therapies & Patient Safety Director. Medical Office, Mälmo, Sweden, [2]Diaverum Renal Services, Corporate Nursing Director. Medical Office, Mälmo, Sweden, [3]Diaverum Renal Services, Barracas Clinic, Buenos Aires, Argentina, [4]Diaverum Renal Services, Fundeni Clinic, Bucharest, Romania, [5]Diaverum Renal Services, Schlankreye Clinic, Hamburgo, Germany, [6]Diaverum Renal Services, Wloclawek Clinic, Wloclawek, Poland, [7]Diaverum Renal Services, Corporate Medical Integration Director. Medical Office, Mälmo, Sweden, [8]Diaverum Renal Services, SEINE Clinic, Montevideo, Uruguay, [9]Diaverum Renal Services, Bajcsy Clinic, Budapest, Hungary, [10]Diaverum Renal Services, Corporate Data Management Director. Medical Office, Mälmo, Sweden, [11]Diaverum Renal Services, Corporate Medical Protocols & Standarization, Mälmo, Sweden and [12]Diaverum Renal Services, VP Medical Office, Mälmo, Sweden

Background and Aims: Peritoneal dialysis (PD) practice is not universally homogeneous, best clinical practices are not completely understood as reference values are often obtained from small sized populations and/or frequently based on chronic kidney disease (CKD) and/or hemodialysis data.

To evaluate two years of follow up of compliance with PD-related quality indicators (QIs) following definition of new targets in an international PD network.

Method: All English and Spanish language CKD and PD guidelines were reviewed. Twelve Qis were considered being of significant relevance and targets for these QIs were defined (see table). Retrospective data analysis.

Results: Achievement of QI targets for years 2017-2018 is shown in table. Variability among countries not shown.

Conclusion: There was a significant increase in QIs achievement in 2018 vs. 2017. ≥75% of patients met the target for the following variables: total weekly Kt/Vurea, 24 h fluid removal, mean arterial blood pressure and serum albumin. Peritonitis rates are clearly over International objectives and were improving. Due to the lack of referral source data, these series may help to understand PD practice and outcomes in a global setting.

2017 vs. 2018	2017	2018	
Total PD patients (pt., n)	1200	1207	
Total PD pt. - data on registry (n)	879	857	
Pt. by Regions (Eu/LA/Others)	532/339/8	508/342/7	
Age (y.)	53.8	54	
DM (%)	18.3	18,4	
Charlson index (Last quarter)	4.3	4.4	
CAPD use (Last quarter, %)	76.2	74.5	
Mean time on PD (months)	34,2	36.1	
QIs achievement (%)	**2017**	**2018**	**p<0.001**
Total weekly Kt/V ≥ 1.7 (including anurics)	79.2	79.5	
24 h fluid removal [24 h residual diuresis +24 h ultrafiltration]: ≥750 ml/day (including anurics)	96.9	96.7	
Albumin ≥35 g/L	74.0	76.6	
nPNA ≥ 0.8 g/kg/day	68.6	68.0	
Serum K: 3.5-5.5 mEq/L	74.9	72.3	
Serum bicarbonate: 24-28 mEq/L	40.9	41.7	
Serum phosphorus: 2.5-5.5 mg/dl	65.5	63.5	
Serum calcium: 8.6-10 mg/dl	67.1	65.8	
Intact parathyroid hormone: 100-600 pg/ml	64,4	65.9	
Hb: 10-12 g/dl (all patients)	58.0	58.8	
Serum ferritin: 100-500 ng/ml	50.6	51.1	
Mean arterial blood pressure < 105 mm Hg	79.2	80.2	
Total score	**819.3**	**820.1**	
Others			
Hb: 10-12 g/dl (ESA treated)	65.5	65	
Hb: >12 g/dl (non- ESA treated)	57.6	52,7	
Peritonitis rates (episodes/pt-year at risk)	**0.25**	**0,18**	

P1157 **IMPACT OF MODE OF DIALYSIS ON COMPLICATIONS AFTER SIMULTANEOUS PANCREAS- KIDNEY TRANSPLANTATION**

Adoración Martinez[1], Manuel Lanuza[1], Diana Manzano[2], Francisca Lopez[1], Eulalia Carceles[1], M. Teresa Valda de Miguel[1], Julian Navarro[3], Julio Domingo[4], Juan Bernardo Cabezuelo[1]

[1]Hospital Clínico Universitario Virgen de la Arrixaca, Nephrology, El Palmar, Spain, [2]Hospital General Universitario Santa Lucía, Nephrology, Cartagena, Spain, [3]Rafael Méndez Hospital, Intensive care unit, Lorca, Spain and [4]Hospital Clínico Universitario Virgen de la Arrixaca, Transplant Coordination, El Palmar, Spain

Background and Aims: Simultaneous pancreas-Kidney transplantation (SPKT) has established its position in treating patients with type 1diabetes and end-stage renal disease. Infections in the early post-transplantation period are one of the most significant causes of the high morbidity and mortality rates associated with SPKT. Pre-transplant dialysis modality may affect evolution and it has suspected that peritoneal dialysis (PD) is associated whit more surgical complications, especially intra-abdominal infections.

The aim: evaluate whether pretransplant dialysis modality affects the risk for postoperative complications in SPKT transplant recipients

Method: retrospective and descriptive study of a series of patients who underwent SPKT from 2000 to 2018 in our hospital. We studied complication occurring during the first 3 months after transplantation

Results: From 2000 to 2019 we performed 38 SPKT in 22 men and 16 women. The mean age of the patients was 35.3(28-44) years. Of the 38 SPKT patients, 44.7% on hemodialysis before transplantation, 26.3% were on peritoneal dialysis and 28.9% had not received any substitutive renal therapy. Were similar regarding baseline characteristics.

The complications of the post-transplant period are shown in graph 1. The most frequent complications were infectious in almost 2/3 of the patients and within them the intra-abdominal infections affected almost half, 18, of the patients. Were 3 thrombosis of the pancreas that caused the loss of the graft but none of the kidney.

All early postoperative complications are compared in table 1.Whit no significant difference between groups of intraabdominal infection (p. 0.5) and graft thrombosis (p 0.7). There were also no differences in relaparotomy, acute rejection and delayed graft function

During the follow-up 4 patients died, one case due to a heart attack while the other 3 in relation to intraabdominal infectious processes and need for reintervention

Conclusion: Despite improvements in the outcomes of STKP infectious complications remain a significant cause of morbidity and mortality

Peritoneal dialysis is not a risk factor postoperative complication after STPK

Table 1:

N	no dialysis 11	HD 17	DP 10	p ns
Intra-abdominal infection	**6(54%)**	**9(53%)**	**3(30%)**	**ns**
Thrombosis	**1(9%)**	**1(6%)**	**1(10%)**	**ns**
Relaparotomy	**2(18%)**	**6(35%)**	**2(20%)**	**ns**
Acute rejection	**3(27 %)**	**6(35%)**	**22(20%)**	**Ns**
Delayed graft function	**3(27%)**	**2(11.8%)**	**2(20%)**	**ns**

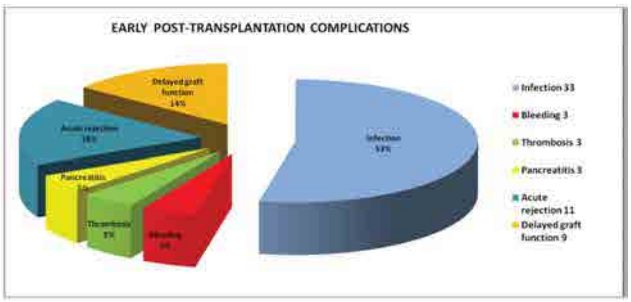


Figure: 1

P1158 DOES THE PERITONEUM SWELLS OR SHRINK DURING PERITONEAL DIALYSIS?

Jacek Waniewski[1], Joanna Stachowska-Pietka[1], Roman Cherniha[2], Bengt Lindholm[3]

[1]Nalecz Institute of Biocybernetics and Biomedical Engineering, Laboratory of Modelling of Biomedical Systems, Warszawa, Poland, [2]Institute of Mathematics NASU, Kyiv, Ukraine and [3]Karolinska Institutet, Division of Renal Medicine and Baxter Novum, Stockholm, Sweden

Background and Aims: The width of the peritoneum (composed mainly of connective tissue and relatively free of vasculature) is increased in patients on peritoneal dialysis compared to healthy subjects. We investigated to what extent increased intraperitoneal (ip) hydrostatic and osmotic pressures following the infusion of dialysis fluid will change hydration status and width of the peritoneum.

Method: Using linear theory of poroelasticty, clinical data on transport parameters and experimental data on elastic characteristics of the interstitium, the relative change of the width of the poroelastic layer subject to the combined effect of external hydrostatic and effective osmotic pressures (that is, ideal osmotic pressure multiplied by reflection coefficient for osmotic agent) can be described as a function of effective pressure and elastic modulus of the layer: Lmod/L0 = 1/(1-deltaP*/lambda*), where L0 is initial thickness of the tissue, Lmod is modified thickness of the layer, deltaP* is change in effective combined pressure, and lambda* is the elastic modulus of the poroelastic material. The same formula describes also the change in fractional free fluid volume ratio, thetaF. The elastic modulus of the connective tissue was assumed to be 110 mmHg, as measured for the subcutaneous layer of the tip of mouse tail by Swartz et al (J Biomech, 1999), and reflection coefficient for glucose in the interstitium of 0.0035 as estimated by Stachowska-Pietka et al (NDT, 2019) from clinical data for patients on peritoneal dialysis.

Results: The ip hydrostatic pressure increases by 2-3 mmHg to 15 mmHg at rest depending on infused volume of dialysis fluid (and posture, body weight and location in abdominal cavity), and may increase to 100 mmHg during activities as coughing, whereas the osmotic pressure of glucose 3.86% dialysis fluid is around 400 mmHg above the osmotic pressure of plasma and interstitial fluid (in equilibrium with plasma). However, due to the low reflection coefficient of interstitium, the effective osmotic pressure of dialysis fluid minus the physiological value of interstitial osmotic pressure is only 1.4 mmHg, and is quickly decreasing with dwell time. Therefore, hydrostatic pressure is the dominant factor for interstitial hydration. Assuming ip pressure of 15 mmHg, the stretch of the peritoneum increases its equilibrium width (at 0 mmHg and isotonic interstitial fluid) by 15%. During physical activities peritoneum may transiently thicken even more.

Conclusion: The peritoneum becomes overhydrated after infusion of dialysis fluid, which increases interstitial hydrostatic pressure; the thickness and fractional free fluid volume of the peritoneum increase by 15% although transiently higher increases may occur following activities that increase intraperitoneal pressure. The mechanical changes in the peritoneum may contribute to the biological changes in cells present there, as fibroblasts and mesothelial cells. The swelling of the peritoneum is in agreement with the increase in the fractional free fluid volume of the intramuscular interstitium behind the peritoneum as reported by Zakaria et al (Am J Physiol Heart Circ Physiol, 1999).

P1159 **MILD BLOOD PRESSURE VARIABILITY IS ASSOCIATED WITH BETTER SURVIVAL IN PATIENTS WITH END STAGE RENAL DISEASE AND PERITONEAL DIALYSIS.**

Hanri Afghahi[1,1], Salmir Nasic[2], Khaled Alhomsi[1], Henrik Hadimeri[1], Helena Rydell[3], Johan Svensson[2]

[1]Skaraborg Hospital, Department of Nephrology, Skövde, Sweden, [2]Skaraborg Central Hospital, Department of research and development, Skövde, Sweden and [3]Karolinska University Hospital, Department of Nephrology, Stockholm, Sweden

Background and Aims: Recently, variability in blood pressure (BP) has been recognized as a risk factor for mortality and cardiovascular events in the general population. However, most studies included patients with normal or near normal kidney function.

Aim: To study the association between BP variability and the risk of all-cause mortality in patients with end stage renal disease (ESRD) and peritoneal dialysis (PD) treatment.

Method: From 2008 until the end of 2017, 2329 patients with ESRD and at least three months of PD (mean age: 63.8 years, men: 67.5%) were followed for 16 months in median (interquartile range: 11-28 months). Data were extracted from the Swedish Renal Register (SNR).

The coefficient variation (CV = the ratio of the standard deviation (SD) to the mean value) was defined as BP variability in terms of systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) [SBP(SD)/SBP(mean), DBP(SD)/ DBP(mean), and MAP(SD)/MAP(mean), respectively].

The relationships between BP variability and mortality were examined by time-dependent Cox models to estimate hazard ratios (HR) and 95% confidence intervals (CI) in univariate and multivariate analyses, with adjustment for demographics, laboratory findings and comorbidity.

Results: During the follow-up period, 1054 (45%) deaths occurred. The mean level of BP variability was CV=0.10$\pm$ 0.1.

The highest rate of mortality was observed in the patients with the highest variability in SBP (CV>0.25; 64% of those patients died).

In the multivariate model, for each of the BP variables, we compared the risk of mortality in the lowest variability group (CV$\leq$ 0.05) with that in the CV=0.10-0.15 group (reference):

SBP: (HR 1.74, 95% CI 1.44- 2.09; p<0.001); DBP: (HR 1.91, 95% CI 1.59- 2.23; p<0.001); and MAP: (HR 1.73, 95% CI 1.44- 2.06; p<0.001). Thus, for all BP variables, the lowest variability was associated with increased mortality risk.

We then compared the highest variability group (CV>0.25) with the CV=0.10-0.15 group (reference):

SBP: (HR 1.60, 95% CI 1.14- 2.25; p<0.001); DPB: (HR 1.74, 95% CI 1.44- 2.09; p<0.001); and MAP: (HR 1.98, 95% CI 1.21- 3.27; p<0.001). Thus, for all BP variables, the highest variability was related to increased mortality risk.

Conclusion: In this study, the association between BP variability and the risk of mortality was U-shaped in patients with ESRD and PD. Thus, both very low and high levels of BP variability were related to higher risk of mortality. Mild BP variability was associated with the lowest risk of mortality, which could suggest that, non-intensive and long duration of ultrafiltration (UF) with PD was probably beneficial in terms of survival

P1160 **INCREASED REMOVAL RATES OF FLUID AND SODIUM DURING STEADY CONCENTRATION PERITONEAL DIALYSIS COMPARED TO ICODEXTRIN AND PERITONEAL EQUILIBRATION TEST**

Ola Carlsson[1], Olof Heimbürger[2], Ann-Cathrine Johansson[3], Giedre Martus[4], Martin Wilkie[5], Jörgen Hegbrant[6], Ann Johansson[1], Charlotte De Leon[1]

[1]Triomed AB, Lund, Sweden, [2]Karolinska Institute, CLINTEC, Solna, Sweden, [3]Skåne University Hospital, Department of Nephrology, Malmö, Sweden, [4]Skåne University Hospital, Department of Nephrology, Lund, Sweden, [5]Sheffield Teaching Hospital National Health Service Foundation Trust, Department of Nephrology, Sheffield, United Kingdom and [6]Lund University, Department of Nephrology, Lund, Sweden

Background and Aims: Removal of fluid and sodium may be a major challenge in PD, which can be addressed using icodextrin for the long dwells. Steady concentration PD (SCPD) with Carry Life® UF is a novel treatment modality where the intraperitoneal glucose concentration can be kept stable throughout the treatment maintaining ultrafiltration and sodium removal. This is performed by transferring a small volume of the dialysate into the device, where glucose is added and the dialysate returned to the patient. The present study was performed to compare the effect of SCPD with icodextrin and peritoneal equilibration test (PET) on ultrafiltration and sodium removal.

Method: Eight stable PD patients (high or high average transporters) were included in the study. Subjects were treated with three 5-hour Carry Life UF treatments using three different glucose doses (11, 14, 20 g/h). An initial fill with 1500 ml, 1.36% glucose PD solution was used. A small volume of dialysate was drained hourly to avoid overfill. An icodextrin 11-hour dwell (2000 ml, 7.5% Extraneal®), and a 4-hour PET (2000 ml, 2.27% glucose PD solution), were used as controls. Data expressed as mean ± SD, statistical analysis using one-way ANOVA, $^{**}p<0.01$, $^{***}p<0.001$.

Results: The treatment time for icodextrin was 11.4±1.5 hours, for PET 4.1±0.1 hours, and for the Carry Life UF treatments 5.2±0.3 hours. Carry Life UF treatments generated increased ultrafiltration rates compared to icodextrin and PET (Figure a). The sodium removal rates with Carry Life UF treatments were also significantly increased compared to icodextrin and PET (Figure b). However, the total ultrafiltration volumes during Carry Life UF treatments were not significantly different compared to the icodextrin dwell (646±256, 739±312, 863±380, 595±239, ml/treatment for 11 g/h, 14 g/h, 20 g/h, and icodextrin, respectively). The ultrafiltration volume during PET was significantly lower than all other treatments (162±242 ml, $p<0.001$). Peritoneal sodium removal did not differ between Carry Life UF treatments and the icodextrin dwells (86±27, 92±33, 110±37, 88±34 mmol/treatment for 11 g/h, 14 g/h, 20 g/h, and icodextrin, respectively). Peritoneal sodium removal during PET was significantly lower than during the other treatments (22±33 mmol/treatment, $p<0.01$).

Conclusion: Treatments performed with Carry Life UF maintain a stable intraperitoneal glucose concentration during the entire dwell, resulting in higher ultrafiltration and sodium removal rates than for controls (PET and icodextrin). The fluid and sodium was removed during the 5-hour Carry Life UF treatments was comparable to the 11-hour icodextrin dwells.

In summary, the increased removal rates of fluid and sodium during SCPD result in a more efficient treatment than conventional CAPD or icodextrin.

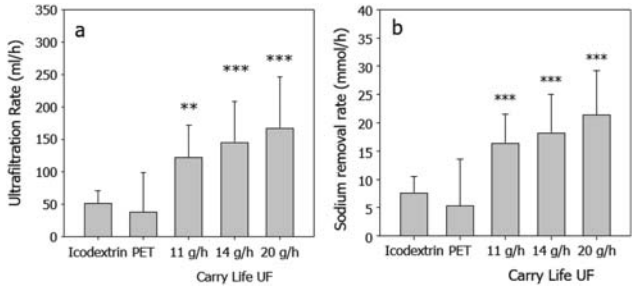


Figure: Ultrafiltration rate in ml/hour during icodextrin, PET, and Carry Life UF treatments (a). Sodium removal rate in mmol/h during icodextrin, PET, and Carry Life UF treatments (b).

P1161 CUTANEOUS MICROCIRCULATORY DYSFUNCTION IN PERITONEAL DIALYSIS PATIENTS

Jennifer Williams[1], Mark Gilchrist[1], Donald Fraser[2], David Strain[1], Angela Shore[1]
[1]*University of Exeter, United Kingdom and* [2]*Cardiff University, United Kingdom*

Background and Aims: Microvascular impairment is an early step in cardiovascular disease (CVD), the major cause of morbidity and mortality in patients with CKD. Changes in skin microvascular reactivity have been shown to reflect more widespread changes in the systemic and coronary microcirculation. Microvascular function is attenuated by advancing age and conditions that commonly coexist with CKD such as diabetes and hypertension. We investigated whether skin microvascular reactivity is impaired in peritoneal dialysis (PD) patients compared with healthy controls and whether this impairment is independent of comorbidity.

Method: Forearm skin vasculature was examined in 27 healthy controls, 27 patients on PD and 27 controls matched to the PD patients for age, gender, diabetes and previous CV events. Microvascular function was assessed using laser Doppler flowmetry in combination with post-occlusive reactive hyperaemia (a test of generalised microvascular function) and iontophoretic application of acetylcholine (ACh) and sodium nitroprusside (SNP) to investigate endothelium dependant and non-endothelium dependant vasodilation respectively.

Results: Peak post-occlusive flow was lower in the PD patients than in both the healthy controls and the co-morbidity matched group; 90.45 AU (60.9-128.35) in healthy controls, 73AU (58.8-134.4) in matched controls and 56.95AU (45.1-89.8) in PD patients ($p=0.0239$ healthy controls versus patients, $p=0.0373$ matched controls versus patients). SNP-mediated vasodilatation was statistically lower in the PD group compared with healthy controls ($p= 0.016$), ACh response was lower but did not reach statistical significance ($p= 0.076$). ACh and SNP-mediated vasodilatation trended towards being lower in PD patients than matched controls but did not reach statistical significance.

Conclusion: The PD patients were characterised by a generalised dysfunction of the skin microcirculation compared with healthy controls and controls matched for factors known to affect the microcirculation. This appears to be the result of impaired endothelium dependant and independent vasodilatory mechanisms.

P1162 **RED BLOOD CELL DISTRIBUTION WIDTH AND PERITONEAL DIALYSIS-ASSOCIATED PERITONITIS PROGNOSIS**

Peng He[1], Jinping Hu[1], Chen Huang[1]

[1]*Xijing Hospital, Department of Nephrology, Xi'an,*

Background and Aims: The red blood cell distribution width (RDW) is a parameter of the heterogeneity of circulating erythrocyte size. Recent researches have pointed out a link among RDW, chronic kidney disease and inflammation. We sought to investigate the prognostic value of baseline RDW in patients with peritoneal dialysis-associated peritonitis (PDAP), which remains unknown.

Method: Our study included 337 peritonitis episodes experienced by 202 patients who were undergoing continuous ambulatory peritoneal dialysis (CAPD) at a single center from 2013 to 2018. Episodes were categorized according to the tertiles of baseline RDW levels (T1, <13.2%; T2, 13.2 - 14.3%; T3, >14.3%). Routine logistic regression, generalized estimating equation and restricted cubic spline were used to estimate the association between RDW and treatment failure, which was defined as relapse or recurrent episodes, catheter removal, or death during peritonitis therapy. The predictive performance of multivariate models including RDW and other potential predictors were also evaluated.

Results: After adjusting for other potential predictors, RDW exhibited an incremental relationship with the risk of treatment failure. The baseline RDW of >14.3% (T3) indicated a 43% and 52% increased venture of treatment failure in logistic and GEE analyses, respectively, compared with < 13.2% (T1). As a continuous variable, the fitting curve based on restricted cubic spiline showed that the relationship was nolinearly but positively correlated. The multivariate model A (combined RDW with age, duration on PD, albumin and ferritin) showed an area under the curve (AUC) of 0.671 (95% CI, 0.592 to 0.749) for the prediction of treatment failure. In sensitive analyses, the predictive performances for other unfavourable outcomes were also reliable (AUC for catheter removal, 0.72, 0.62 to 0.81; for relapse or recurrence, 0.61, 0.48 to 0.74).

Conclusion: Higher levels of baseline RDW was significantly associated with greater rates of treatment failure among peritonitis episodes independent of other potential predictors.

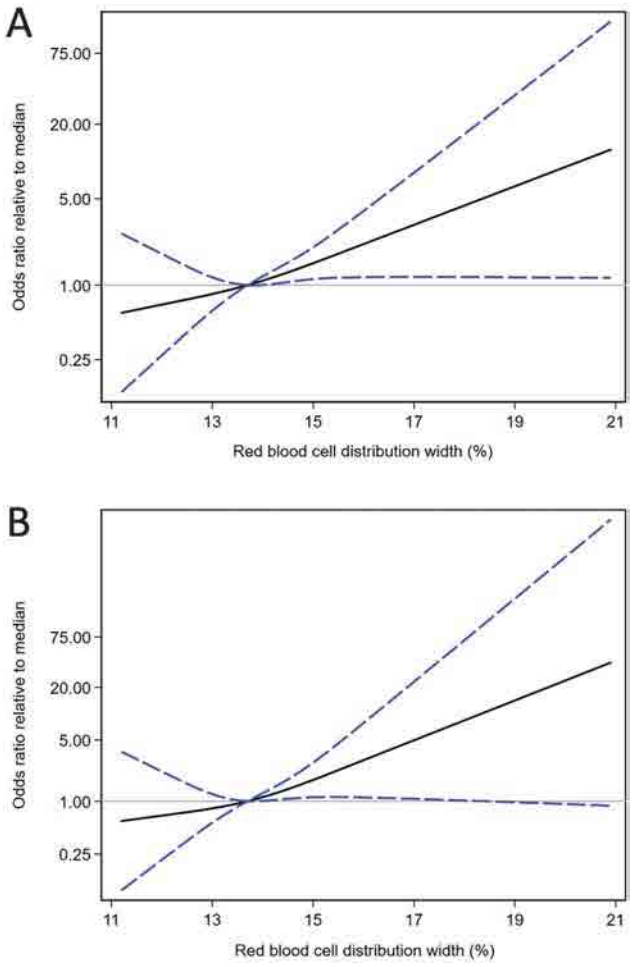


Figure 1. Associations betweem baseline RDW and treatment failure. Logistic regression (**A**) and generalized estimation equation (**B**) models were conducted through restricted cubic splines with knots at the 25th (12.2%), 50th (13.7%), and 75th (15.62%) percentiles.The reference value (the gray lines) was set at the medians.The solid line indicated the trend of estimated odds ratios, the area between 2 dashed line indicated the 95% confidence intervals. The odds ratios of baseline red blood cell distribution width (RDW) in 2 models were adjusted for age, duration on peritoneal dialysis, white blood cell count (WBC), albumin, ferritin, dialysate WBC on day 3 and infection type (gram-positive, gram-negative or culture negative peritonitis).

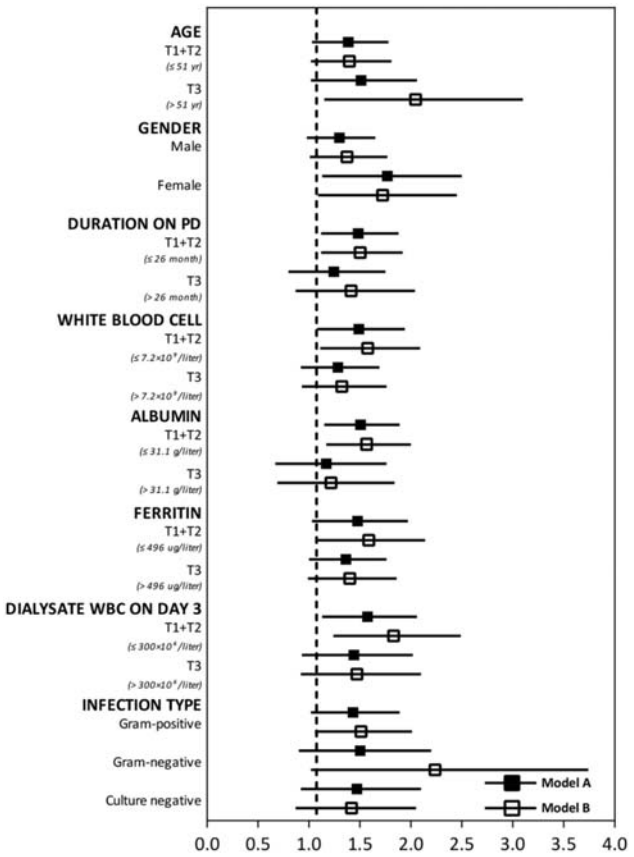


Figure 2. Stratified analyses for the adjusted odds ratios of baseline RDW in model A and model B. The stratified analyses were performed according to gender (male or female), infection type (gram-positive, gram-negative or culture negative peritonitis), and binary variablesdefined by the highest tertile (T3) of other clinical parameters (age, duration on peritoneal dialysis (PD), white blood cell count (WBC), albumin, ferritin and dialysate WBC on day 3) and the combined 2 lower tertiles (T1 + T2). The odds ratio of red blood cell distribution width (RDW) in model A was adjusted for age, duration on peritonieal dialysis (PD), albumin, and ferritin. The odds ratios in model B was adjusted for age, duration on PD, albumin, ferritin and dialysate WBC on day 3.

P1163

IMPACTS OF IRON-BASED PHOSPHATE BINDER ON ANEMIA AND IRON METABOLISM IN PERITONEAL DIALYSIS PATIENTS: A CROSS-SECTIONAL, LONGITUDINAL MULTICENTER STUDY IN KANAGAWA, JAPAN.

KIYOTO KOIBUCHI[1,2], Masahito Amagasa[2,3], Tomoyuki Otsuka[2,4], Kenichiro Koitabashi[2,5], Hiroo Kawarazaki[2,6], Daisuke Komukai[2,7], Masaru Murasawa[2,8], Yasuhiro Taki[2,9], Togo Aoyama[2,10], Hiroki Nishiwaki[2,3], Tsutomu Sakurada[2,5]

[1]Saiseikai Yokohama City Tobu Hospital, Department of Nephrology and dialysis, Yokohama, Japan, [2]PD OASIS Group, Kanagawa, Japan, [3]Showa University Fujigaoka Hospital, Division of Nephrology, Department of Internal Medicine, Yokohama, Japan, [4]Nippon Medical School Musashikosugi Hospital, Division of Nephrology, Department of Internal Medicine, Kawasaki, Japan, [5]St. Marianna University School of Medicine, Division of Nephrology and Hypertension, Department of Internal Medicine, Kawasaki, Japan, [6]Inagi Municipal Hospital, Department of Nephrology, Inagi, Japan, [7]Kawasaki Saiwai Hospital, Department of Nephrology, Kawasaki, Japan, [8]St. Marianna University School of Medicine, Yokohama City Seibu Hospital, Department of Nephrology, Yokohama, Japan, [9]Kawasaki Municipal Tama Hospital, Department of Nephrology, Kawasaki, Japan and [10]Kitasato University School of Medicine, Department of Nephrology, Sagamihara, Japan

Background and Aims: Iron-based phosphate binder (IPB) is a noncalcium phosphate binder that demonstrated sustained serum phosphorus control, good tolerability and lower pill burden compared with sevelamer carbonate in a Phase 3 study conducted in dialysis patients. These efficacy of IPB has been demonstrated for hemodialysis (HD) patients, but few studies have focused on patients undergoing peritoneal dialysis (PD). We evaluated efficacy of IPB and focused on effects for anemia and iron metabolism in patients on PD.

Method: This study was a cross-sectional, longitudinal multicenter study conducted by PD OASIS, organized committee in Kanagawa Japan. We analyzed the effects of IPB during a 6 months observation period in chronic kidney disease patients on PD who had administrated IPB, Ferric citrate hydrate and Sucroferric oxyhydroxide, between 2017 and 2019. The primary endpoint was the changes of phosphate, and several secondary endpoints were assessed: calcium, intact PTH, RBC, hemoglobin, MCH, RDW-VC, Fe, TSAT, Ferritin, albumin, CRP, monthly dosage of Erythropoietin stimulating agents (ESA) and ESA resistance index (ERI).

In addition, we assessed the association between these markers and iron metabolism utilizing multivariate logistic regression analysis.

Results: A total of 102 patients were registered in the study who had received IPB.

The initial doses of Ferric citrate hydrate and Sucroferric oxyhydroxide were 1010.9 ±400.9 mg and 941.7 ±502.9 mg daily, finally increased to 1213.6 ±559.9 mg and 1310.0 ±521.8 mg respectively at the end of the observation.

We observed a significant reduction of serum phosphate to 5.27 ± 0.98 mg/dL from 6.56 ± 1.52 mg/dL with follow-up of six months ($p < 0.01$). At the end of the study, 76.4% of participants had achieved the target of less than 6 mg/dL. The hemoglobin, TSAT and Ferritin increased significantly from 10.47 ±1.26 g/dl, 27.95 ±11.05 % and 139.0 ±147.6 ng/mL to 11.17 ±1.16 g/dl, 40.46 ±15.00 % and 305.9 ±232.0 ng/mL respectively in six months ($p < 0.01$).

No significant changes of serum calcium, intact parathyroid hormone (PTH) and CRP occurred over the study period.

The monthly dosage of ESA was significantly decreased after administration with IPB and ERI significantly improved to 0.11±0.12 (μg/month/kg/g Hb) from 0.21±0.16 (μg/month/kg/g Hb) ($p<0.01$). Hemoglobin overshoot, an increase of more than 12 g/dl, was observed in 27.5% patients. This related low MCH and high RDW-VC at baseline which was proven by multivariate logistic regression.

Additionally, we assessed the factors of ferritin increase because it was remarkable in follow-up six months compared to HD patients. In multivariate analysis, phosphate (Odds ratio 5.85, 95%CI 1.18-91.77, p=0.027), intact PTH (0.99, 0.97-1.15, p=0.015), hemoglobin (Odds ratio 0.10, 95%CI 0.05-0.59, p=0.025), RBC (Odds ratio 1.16, 95%CI 1.04-1.41, p=0.003), and RDW-CV (Odds ratio 0.44, 95%CI 0.10-0.99, p=0.046) were significantly associated with ferritin increase more than 300 ng/ml ,after adjusted.

Conclusion: This study confirmed the efficacy of Iron-based phosphate binder, Ferric citrate hydrate and Sucroferric oxyhydroxide, in the treatment of hyperphosphatemia in PD patients. In addition, IBP caused secondary effects of anemia improvement and ESA dosage reduction resulting in ERI improvement. However, in this study, the increase in ferritin levels was remarkable. It may be because PD does not lose iron by treatment compared to HD. Therefore, we should check iron metabolism more frequently for PD patients taking IPB than HD patients. It is necessary to further investigate the effects of IPB on anemia and iron metabolism in PD patients.

P1164 **INTERVENTIONAL NEPHROLOGY SERVICE ENHANCES PERITONEAL DIALYSIS UTILISATION AND UPTAKE: EXPERIENCE FROM A SINGLE CENTRE IN SINGAPORE**

Yan Lun Allen Liu[1]

[1]*Khoo Teck Puat Hospital, Singapore, Singapore*

Background and Aims: Interventional nephrology (IN) is not having a well-defined role in peritoneal dialysis (PD) service provision. Impact to PD catheter outcomes, PD utilisation and uptake on integrated care approach under IN service was not known. Here we report the experience and outcomes of IN practice in PD service from a single centre in Singapore.

Method: We postulated an IN-led, multidisciplinary collaborative model of care for end stage renal failure patients, who transited through a seamless care pathway from pre-dialysis counselling to insertion of PD catheter, could improve utilisation and increase uptake of PD as dialysis modality of choice. This approach was based on: 1. Interventional nephrologist-led PD catheter insertion service, 2. coordination of care (figure 1) and 3. early start of PD. Outcomes of IN involvement in PD access management and coordination of care were included in this study.

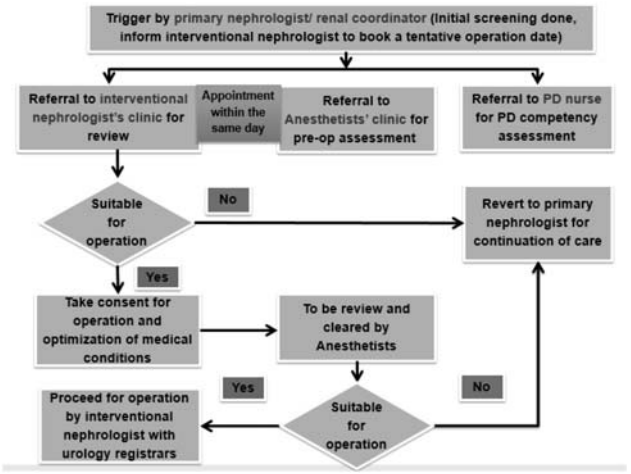


Figure 1. Workflow for IN service in PD

Results: From January 2015 to May 2019, a total of 140 PD catheter insertions were performed by interventional nephrologist (table 1). The prevalence of PD patients in our program was increased by 217% after initiation of IN service (figure 2). Annually, incident ESRF patients who chose PD as dialysis modality increased from 10% to 28% (figure 3). We had a very low PD catheter-related complication rate in reference to international standards (table 2). Catheter adjustment-free survival was 94% and 83% at 12 months and 36 months respectively (figure 4).

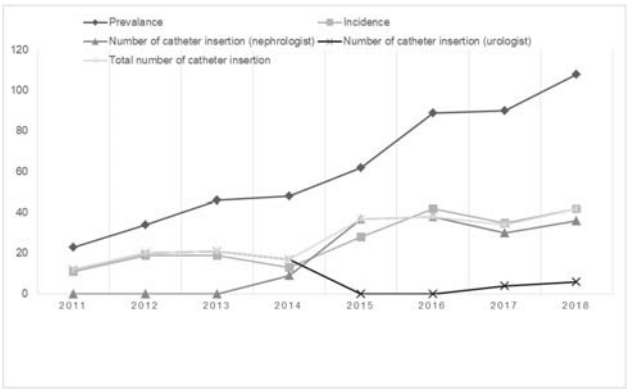


Figure 2. Number of PD catheter insertion between 2011 and 2018*

*Interventional nephrologist started to perform PD catheter insertion independently since January 2015.

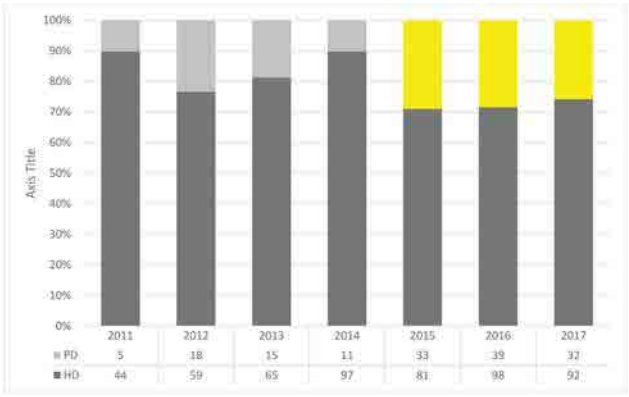


Figure 3. Percentage of dialysis modality for incident ESRF patients, 2011-2017

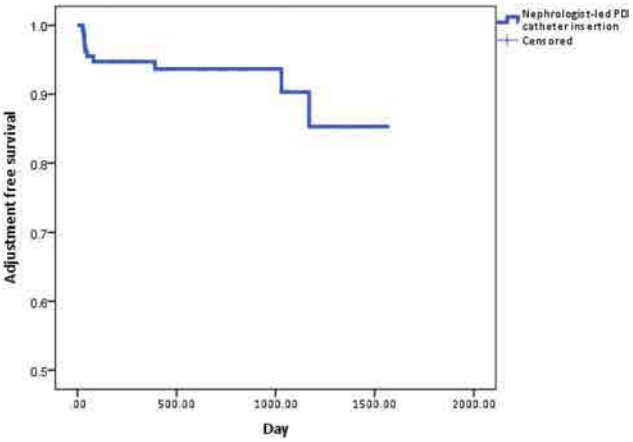


Figure 4. Kaplan-Meier survival analysis for catheter survival (between 2015 and 2018)

Table 1. Patient characteristics

Total number	PD catheter by nephrologists 140
Age, year (mean +/- SD)	61.7 +/- 12.1
Gender, n(%)Male	78 (55.7)
Ethnicity, n(%)	
Chinese	89 (63.6)
Malay	43 (30.7)
Indian	6 (4.3)
Others	2 (1.4)
Diabetes mellitus, n(%)	103 (73.6)
Hypetension, n(%)	126 (90)
Ischaemic heart disease, n(%)	39 (27.9)
Amputee, n(%)	4 (2.9)
Total Kt/V (mean +/- SD)	2.08 +/- 0.49
Modality, n(%)APD	68 (48.6)

Table 2. Peritoneal dialysis catheter-related complication rate from 2011 to 2018

	ISPD guidelines [16]	PD catheter by nephrologists, n(%)	PD catheter by urologists, n(%)	P value
Number of insertion		140	80	
Bowel perforation:	<1%	0 (0)	0 (0)	-
Significant haemorrhage:	<1%	2 (1.4)	1 (1.3)	0.91
Exit-site infection within 2 weeks of catheter insertion	<5%	5 (3.5)	5 (6.3)	0.36
Peritonitis within 2 weeks of catheter insertion	<5%	0 (0%)	1 (1.3)	-
Functional catheter problem requiring manipulationor replacement or leading to technique failure	<20%	14(9.9)	13 (16.3)	0.17

Conclusion: The multifaceted and holistic role of IN in PD translated into remarkable outcomes on PD utilisation and uptake. It also confirms the safety and efficacy of IN procedures in PD when performed by appropriately trained nephrologists.

P1165 **PERITONEAL DIALYSIS OR HAEMODIALYSIS FOR POLYCYSTIC KIDNEY DISEASE? TEN YEARS' EXPERIENCE IN A SINGLE CENTRE**

Zi Chan[1], Ka Lok Chan[1], Chi Kwan Lam[1], Way Ping Law[1], Wai Lun Will Pak[1], Yick Hei Wong[1], Sze Ho Sunny Wong[1]

[1]*United Christian Hospital, Medicine and Geriatrics, Hong Kong, Hong Kong, P.R. China*

Background and Aims: When polycystic kidney disease (PKD) progresses into end-stage renal disease (ESRD), the choice of dialysis modality is often not straight forward. It is believed that PKD may increase risk of complications and technique failure (TF) in peritoneal dialysis (PD) due to enlarged kidneys and/or liver. In this study, we looked at the long-term outcomes of PKD patients put on either PD or haemodialysis (HD).

Method: New cases of ESRD due to PKD that entered into the dialysis program of United Christian Hospital, Hong Kong from 1st December 2009 to 30th November 2019 were identified. Their baseline demographics, mean kidney size (mean size of right and left kidneys) and clinical outcomes were recorded. Hong Kong has a 'PD first' policy. But for PKD patients, the decision to start PD or HD is by the attending nephrologists' clinical judgment. For the statistical analysis, chi-square test was used for comparison of categorical variables, while t-test was used for continuous variables. Kaplan-Meier curve was used to analyse survival.

Results: A total of 45 patients were identified. Thirty-one patients were put on PD, while fourteen were put on HD. Their baseline characteristics were shown in Table 1. HD patients had significantly higher mean kidney size to body weight ratio (0.32 ± 0.12 cm/kg) compared to PD patients (0.25 ± 0.08 cm/kg). The median survival between PD patient (7.1 years) and HD patients (7.2 years) was not significantly different.

For those PKD patients on PD, the 5-year TF rate was 0.22, which was similar to overall PD patients in our centre. Four patients had early TF (mean time 1.6 years) due to possible PKD related reasons. Two of them had significant pressure symptoms, the other two had inadequate dialysis. Further analysis showed that for those with TF, both the mean kidney size (20.0 ± 5.3 cm) and mean kidney size to body weight ratio (0.32 ± 0.08 cm/kg) were significantly higher than those without TF (15.0 ± 4.1 cm and 0.24 ± 0.07 cm/kg respectively) (Table 2).

Conclusion: This study showed that for PKD patients with moderate enlarged kidneys, PD could be a reasonable choice. However, for patients with very large kidneys, the early TF rate with PD was high, HD would be a better choice for these patients.

Table 1

	PD	HD	p-value
Patient number	31	14	
Age	54.9 ± 8.5	53.0 ± 10.0	0.513
Gender (male)	45.2%	35.7%	0.553
Diabetes Mellitus	22.6%	0.0%	0.053
Hypertension	54.8%	57.1%	0.885
Previous abdominal surgery	12.9%	14.3%	0.899
Mean kidney size (cm)	15.7 ± 4.5	17.7 ± 7.3	0.266
Mean kidney size to body weight ratio (cm/kg)	0.25 ± 0.08	0.32 ± 0.12	0.029
Liver involvement	61.3%	50.0%	0.674

Table 2

	Early TF	No early TF	p-value
Patient number	4	27	
age	53.0 ± 7.7	55.2 ± 8.7	0.638
Gender (male)	50.0%	44.0%	0.835
Diabetes Mellitus	0%	25.9%	0.247
Hypertension	50.0%	55.6%	0.835
Previous abdominal surgery	0.0%	14.8%	0.409
Mean kidney size (cm)	20.0 ± 5.3	15.0 ± 4.1	0.036
Mean kidney size to body weight ratio (cm/kg)	0.32 ± 0.08	0.24 ± 0.07	0.048
Liver involvement	75.0%	59.3%	0.546

P1166 DOES PERITONEAL PROTEIN LOSS AFFECT CARDIOVASCULAR MORTALITY OF PERITONEAL DIALYSIS PATIENTS ?

Marios Theodoridis[1], Stylianos Panagoutsos[1], Ioannis Neofytou[1], Konstantia Kantartzi[1], Efthimia Mourvati[1], Triantafyllia Bounta[1], Pelagia Kriki[1], Ploumis Passadakis[1], Elias Thodis[1]

[1]*University Hospital of Alexandroupolis, Department of Nephrology, Alexandroupolis, Greece*

Background and Aims: Peritoneal protein loss (PPL) through peritoneal effluent has been a well-recognized detrimental result of peritoneal dialysis (PD). The amount of protein lost will depend on dialysis time, protein size, its serum concentration and other factors including patients' clinical status. Peritoneal protein loss may be a manifestation of endothelial dysfunction, as with another type of capillary protein leakage, microalbuminuria, a recognized endothelial dysfunction marker. The aim of this study was to retrospectively evaluate the influence of PPL on cardiovascular mortality of peritoneal dialysis patients

Method: This is a single center retrospective study of 84 PD patients (m=54, f=30) with mean age of 65.2±17 years, mean PD duration of 43.2±24.9 months conducted for the time period from 2006 to 2019 (13 years). The patients were divided into two groups according to the amount of protein excreted during the modified Peritoneal Equilibration Test (PET) procedure using PD solution of 3.86% DW, 2 Lt infusion volume for total time of 4 hours. The total amount of proteins excreted was calculate from PET by multiplying the concentration of proteins at the end of the test with the total volume of PD fluid at the same time. Group A excreted a total amount of proteins $<$ 1.55 gr (median value) at the end of PET test and Group B $>$ 1.55 gr. The cumulative all-cause and cardiovascular survival of the PD patients was calculated by Kaplan Meier while the possible effect of any parameter in survival rates was evaluated by using Cox Regression analysis

Results: There was not any statistically significant difference between the two groups according to PD duration, age, dialysis adequacy targets, Residual Renal Function(RRF), BMI, ultrafiltration volume during PET and their transport status. The cumulative all-cause survival using Kaplan-Meier analysis revealed no statistically significant deference between the two groups (Log Rank p=0.55) even though mortality risk was adjusted for several factors (Cox Regression). When cardiovascular survival, using Cox Regression analysis, was adjusted for age, sex, Diabetes, PD modality, dialysis Kt/V and RRF we found that Group A (with protein excretion $<$ 1.55 gr) had statistically significant better cardiovascular survival (p=0.029) compared to Group B. We confirm these results while trying to find among the total of our patients the possible risk factors for cardiovascular mortality. Using Cox Regression analysis, the amount of protein excreted during PET procedure and the type of PD solutions (high or low in GDPs) used were statistically significant (p=0.019 and p=0.04 respectively) independent risk factors for cardiovascular survival in our patients.

Conclusion: These results indicate that protein loss during peritoneal dialysis procedure has negative impact on cardiovascular mortality and survival of PD patients. Additionally, the use of PD solutions with low Glucose Degradation Products (GDPs) and AGEs may improve PD patient's cardiovascular survival. Randomized interventional studies are encouraged to address the pathological concern of PPL in the future, namely its effects on cardiovascular conditions or its role as marker and effort to reduce PPL using ACE inhibitors or vit D should be considered only if it diminishes cardiovascular morbidity or mortality.

P1167 **SERUM MAGNESIUM IS INVERSELY CORRELATED WITH MEAN PLATELET VOLUME IN PERITONEAL DIALYSIS PATIENTS**

Eleutheria-Kleio Dermitzaki[1], Panagiotis Giannakopoulos[2], Anastasia Georgoulidou[3], Ourania Tsotsorou[2], Petros Nikolopoulos[2], Olga Balafa[4], Evangelia Ntounousi[4], Kostas Stylianou[1], Spyros Katsoudas[2], Periklis Kyriazis[5], Dimitra Bacharaki[2], Demetrios Vlahakos[2]

[1]University Hospital of Heraklion, Greece, [2]Attikon University Hospital, Nephrology, Chaidari, Greece, [3]General Hospital of Komotini, Greece, [4]University Hospital of Ioannina, Greece and [5]University of Massachusetts, Internal Medicine, United States of America

Background and Aims: Higher Mean Platelet Volume (MPV), as an indicator of larger and hyper-reactive platelets and low serum Mg levels (sMg) have emerged as cardiovascular risk markers, in the general and dialysis population. Magnesium deficiency is linked to platelet hyper-reactivity. Since HypoMagnesemia is common and associated to increased mortality among Peritoneal Dialysis (PD) patients, we aimed to investigate the association of sMg with MVP in PD patients.

Method: We studied 95 stable PD patients, 51 men 44 women, with a mean age of 63 ±14 year**s.** Data analyzed included patients demographics, clinical and biochemical data. Univariate and multivariate regression analysis were used to test the associations of variables related to MPV.

Results: . The mean platelet (PLT) volume was 9.4 ±1.5 (median: 9.2) fl. The mean platelet (PLT) count was 235 ± 69 (median: 233) [x10^3μ/L]. The mean sMg was 2.25 ± 0.47 (median: 2.2) mg/dl. MPV was associated positively ($p=0.303$; $p<0.01$) with C-reactive protein (CRP) and negatively with sMg ($r= -0.246$; $p<0.05$), use of Renin Angiotensin System (RAS) Inhibitors ($r=-0.273$; $p<0.05$), PLT count ($r=-0.360$; $p<0.001$) and white blood cell (WBC) count ($r=-0.254$; $p<0.05$). The results of our multiple regression model (Table) showed that all the above mentioned factors that were included in the model, except WBC, were independent determinants of MPV.

Conclusion: Our results show a significant inverse correlation of serum Magnesium with Mean Platelet Volume in Peritoneal Dialysis patients. Given the emerging role of Mg in platelet reactivity, sustaining higher sMg levels, along with minimizing inflammation and using RAS inhibitors may improve cardiovascular outcomes in PD patients via modulation of MPV.

Table

Parameter	B	Std Error	Beta	P
sMg	-0,577	0,288	-0,183	0,049
PLT count	-0,007	0,002	-0,311	0,001
CRP	0,147	0,049	0,267	0,003
RAS Inhibitors	-0,789	0,272	-0,260	0,005
WBC	0.000	0.000	-0,155	0,082

P1168

ABDOMINAL AORTIC CALCIFICATION SCORE MODIFIES THE PROGNOSTIC VALUE OF SERUM MAGNESIUM LEVELS ON ALL CAUSE MORTALITY IN PERITONEAL DIALYSIS PATIENTS

Panagiotis Giannakopoulos[1], Stavros Fokas[2], Eleni Drosataki[3], Ourania Tsotsorou[1], ANILA DUNI[4], Marios Theodoridis[5], Kostas Stylianou[6], Evangelia Ntounousi[4], Ploumis Passadakis[5], Spyros Katsoudas[1], Periklis Kyriazis[7], Dimitra Bacharaki[1], Demetrios Vlahakos[1]

[1]Attikon University Hospital, Nephrology, Chaidari, Greece, [2]Gennimata General Hospital, Nephrology, Greece, [3]University Hospital of Heraklion, Greece, [4]University Hospital of Ioannina, Greece, [5]University Hospital of Alexandroupolis, Greece, [6]University Hospital of Heraklion, Nephrology, Greece and [7]University of Massachusetts, Internal Medicine, United States of America

Background and Aims: Low serum Mg (s-Mg) concentration has been associated with an increased risk of death in both the general and dialysis populations. In peritoneal dialysis (PD) patients, an inverse correlation between s-Mg and abdominal aortic calcification (AAC), estimated by plain lateral lumbar x-rays, as Leena Kauppila (LK) score (range 0-24), is well documented. LK score of 0-4 has been associated with the best event free survival (CORD study CJASN 2011). Here, we explored the possibility whether AAC could modify the relationship between s-Mg and all-cause mortality in PD patients.

Method: We studied 95 stable PD patients, 51 men 44 women, with a mean age of 63 ±14 years. The degree of AAC was evaluated with on plain lateral abdominal radiographs, as LK score. After completion of baseline assessment, including s-Mg measurements, patients were followed up for all-cause mortality.

Results: The mean of s-Mg and AAC in the whole group were 2.25±0.47 mg/dl and 6.65 ± 5.94 respectively. There was an strong inverse correlation (rho = -0.225; p=0.029) between s-Mg and AAC. During a median follow-up period of 23 months, 16 (17%) deaths occurred. There was a 78% reduction of all-cause mortality for every 1 mg/dl of increase in s-Mg {crude HR: 0.22 (95% CI, 0.06 - 0.78)}. An interacting effect between s-Mg and AAC was significant (p=0.005) after controlling for main effects. Then, the association between s-Mg and all-cause mortality by subgroups of AAC: higher tertile vs all lower, was examined (cut-offs of the tertiles for AAC were 3 and 9). In patients grouped in the lower tertiles, s-Mg was a significant predictor of all-cause mortality, even after adjustment for univariate significant predictors of all-cause mortality: age, cardiovascular disease, PD vintage and malnutrition-inflammation score (MIS) {adjusted HR: 0.14 (95% CI, 0.02-0.0.98)}. On the contrary, patients with AAC in the higher tertile of the baseline distribution, s-Mg levels were not predictive of outcome in either crude or the adjusted models.

Conclusion: The predictive value of s-Mg in all-cause mortality in PD patients appears to be critically dependent on AAC score. Thus, sustaining higher sMg levels, as by using higher Mg dialysate concentration, may have beneficial effects on clinical outcomes only in patients without AAC or at least in those with early lesion development.

P1169 **NUTRITIONAL STATUS OF PATIENTS IN PERITONEAL DIALYSIS: TWO METHODS COMPARED**

Giuseppe Paribello[1], Oto Di Gruttola[1], Immacolata Gaia Paduano[1], Silvia Migliaccio[1], Gennaro Argentino[2], Giuseppina Sannino[1], Domenico Russo[1]

[1]AOU FEDERICO II NAPOLI, NEPHROLOGY, NAPLES, Italy and [2]ASL NA1CENTRO "OSPEDALE DEL MARE", NEPHROLOGY, NAPLES, Italy

Background and Aims: Nutritional status and survival are closely related: a state of undernutrition favors the onset of fatal and non-fatal events. This association becomes even more important in the dialysis patient in which a vicious circle is generated in which undernutrition worsens the basic condition. The issue of our study is to evaluate the nutritional status of patients on peritoneal dialysis (PD) comparing the two methods (CAPD-APD).

Method: We evaluated 36 PD patients whose characteristics are reassumed in Tab1. In these patients, dialysis adequacy was assessed by Kt/v and nutritional status through biochemical parameters and the following scores (Tab.2):

- PCR (Protein catabolic rate)
- PEW (Protein energy waste)
- GNRI (Geriatric nutritional risk index)
- CONUT (Controlling nutritional status score)

Results: The data collected shows that 29 patients have a dialysis adequacy compliant with that proposed by the international guidelines (Kt/v $\geq$ 1.7), of the 7 patients who do not achieve this adequacy 4 are in CAPD and 3 in APD. From a nutritional point of view we consider the ideal PCR of about 1.2 g/kg weight, but this value is difficult to reach by many patients; therefore, a value of at least 0.8 g/Kg/day is considered acceptable. This target is reached by 26 patients; of the 10 patients who do not reach it, 3 are in CAPD and 7 in APD. Analyzing the two methods separately, we can observe that in the CAPD patients the PCR is significantly higher ($p < 0.002$). As regards GNRI, a score <92 is considered as an indicator of an unfavorable prognosis; in this case we can observe that only 3 patients have a score <92, all in APD without however a significant difference between the two methods ($p < 0.36$). Taking into account the reference values for PEW (Tab2) we can highlight the difference between the two methods in the number of patients with a moderate/severe undernutrition status: 13 in APD vs 6 in CAPD. The same can be said for CONUT where an important state of undernutrition is observed in 4 patients in APD vs 1 single patient in CAPD.

Conclusion: The study shows how the combined use of multiple parameters is fundamental in managing of patients nutritional status in peritoneal dialysis. The overall analysis of the scores used has shown a greater risk of malnutrition in APD patients in which is necessary to monitor carefully nutritional status, eating habits and lifestyle.

TAB.1 Clinical characteristics of study population

MAN/WOMAN	18/18
MIDDLE AGE (years)	60,6 ± 12,5
DIALYSIS TIME (months)	54,9 ± 31,0
DIALYSIS METHOD (CAPD/APD)	18/18

CAPD: CONTINUOUS AMBULATORY PD
APD: AUTOMATED PD

Tab 2. Nutritional evaluation indices

		APD	CAPD	TOTAL
Kt/v		2,6 ± 0,9	1,9 ± 0,4	2,2 ± 0,8
PCR (g/kg/die)		0,8 ± 0,2	1,1 ± 0,3	0,9 ± 0,3
PEW		3 (17%)	6 (33%)	
0/3	Normal			9 (25%)
1/3	Medium	2 (11%)	6 (33%)	8 (22%)
2/3	Moderate	9 (50%)	5 (28%)	14 (39%)
3/3	Severe	4 (22%)	1 (6%)	5 (14%)
GNRI		104,5 ± 14,7	108,3 ± 9,1	106,4 ± 12,2
CONUT		4 (22%)	4 (22%)	8 (22%)
0-1	Normal			
2-4	Medium	10 (55%)	13 (72%)	23 (64%)
5-8	Moderate	3 (17%)	1 (6%)	4 (11%)
9-12	Severe	1 (6%)	0 (0%)	1 (3%)
TOTAL PROTEINS (g/dl)		6,6±0,6	6,5±0,6	6,6±0,6
ALBUMINEMIA (g/dl)		3,7±0,3	3,7±0,3	3,7±0,3
TOTAL CHOLESTEROL (mg/dl)		159,2±34,7	142,1±30,8	150,7±33,5
TRIGLYCERIDES (mg/dl)		153,8±78,6	142,1±54,4	153±67,5
Hb (g/dl)		11,4±1,4	11,1±1	11,2±1,2
Vit. D (ng/ml)		16±6	15,3±6,3	15,6±6,1
SERUM CALCIUM (mg/dl)		9±0,8	8,8±0,6	8,9±0,7
PHOSPHOREMIA (mg/dl)		5,5±1,1	4,7±0,8	5,1±1
BMI (Kg/m^2)		26,4±5,8	29,5±4,3	28±5,3

Figure:

P1170

ENCAPSULATING PERITONEAL SCLEROSIS: ARE CALCINEURIN INHIBITORS A RISK FOR PERITONEAL DIALYSIS PATIENTS UNDERGOING RENAL TRANSPLANTATION?

Valerio Vizzardi[1], Diana Bertoni[2], Vincenzo Terlizzi[2], Alessandra Pola[3], MAttia Tonoli[2], Marianna Moscato[2], Francesco Scolari[2,3]

[1]OU of Nephrology. ASST Civil Hospital of Brescia, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health. University of Brescia, Brescia, Italy, [2]University of Brescia, Postgraduate School in Nephrology, Brescia, Italy and [3]OU of Nephrology. ASST Civil Hospital of Brescia, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health., Brescia, Italy

Background and Aims: Encapsulating peritoneal sclerosis (EPS) is a rare but severe complication of peritoneal dialysis (PD). Its prevalence, ranging from 0.7 to 3.3%, and its reported mortality is 25-55%. Post-transplantation encapsulating peritoneal sclerosis (PT-EPS) usually occurs within two years from PD interruption due to kidney transplantation. Calcineurin inhibitors are thought to be involved in the pathogenesis of PT-EPS.

Method: This is a retrospective, single-center study: all the patients who received PD for 2 or more months before kidney transplantation between 1979 and 2018 in our unit were enrolled. All PD patients diagnosed with EPS after transplantation were identified, and their data were compared with those of non-transplanted PD patients (NT-PD).

Results: Data from a total of 1014 PD patients were examined; 215 underwent kidney transplantation and 799 remained on PD. PT-EPS occurred in 5/215 patients (2.3%), a prevalence not significantly different from that of NT-PD (21/799= 2.6%; P = 0.39) (Table 1). Calcineurin inhibitors were administered to 178/215 (83%) patients without EPS and all 5 patients with PT-EPS (P = 0.68). Calcineurin inhibitors were associated with corticosteroids (41%), mycophenolate mofetil (34%), or both (42%). Inhibitors of mammalian targets of rapamycin were used in association with calcineurin inhibitors in 25%, with calcineurin inhibitors and steroids in 24% and steroids alone in 7%. Mortality due to PT-EPS was 4.3% *vs* 1.2% in NT-PD (P = 0.38) (Figure 1).

Conclusion: The prevalence of PT-EPS was similar to that of EPS in NT-PD. Therapy with calcineurin inhibitors did not appear to be a crucial risk key in the development of PT-EPS.

Table 1. Encapsulating peritoneal sclerosis (C-EPS) vs those with post-transplantation encapsulating Comparison of characteristics between the non-transplanted PD patients (NT-PD) vs those transplanted (KT-PD) and between the patients with classic peritoneal sclerosis (PT-EPS)

	NT-PD	KT-PD	p
Number of patients (%)	799 (78.9)	215 (21.2)	–
Male/female	444/355	125/90	0.56
Total time on PD* (months) (median, IQR)	26 (10-44)	27 (16-46)	0.38
Deceased for all causes (%)	662 (82.8)	47 (21.9)	<0.001
Deceased for EPS (%)	8 (1.2)	2 (4.3)	0.38
	C-EPS	PT-EPS	P
Cases of EPS (%)	21 (2.6)	5 (2.3)	0.39
Age at EPS diagnosis (M±SD)	64±12	55±7	0.08
Months spent on PD at diagnosis* (median, IQR)	103 (42-156)	79 (54-97)	0.33
Months from diagnosis to the end of observation# (median, IQR)	22 (5-75)	62 (46-114)	0.13
Deceased due to EPS (%)	8 (38.1)	2 (40.0)	0.94

**For all treatments. #Dead or lost to follow-up*

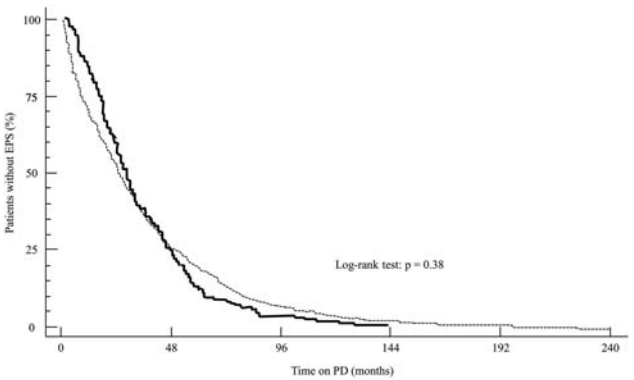


Figure 1. Comparative cumulative survival from EPS in the 215 KT-PD patients (continuous line) vs the 799 NT-PD patients (dotted line) (log-rank test: p=0.38).

P1171

DIALYSIS PRESCRIPTION FOR THE SPREAD OF PERITONEAL DIALYSIS IN THE ELDERLY PATIENTS CLARIFIED BY THE EXAMINATION OF RELATIONSHIP BETWEEN KT/V AND NURSING CARE LEVEL

Makoto Hiramatsu[1,2], Keisuke Maruyama[2], Akifumi Ohnishi[2], Noriya Momoki[2], Keisuke Nonaka[4], Yuri Nakashima[5]

[1], Okayama City, Japan, [2]Center for Kidney and Diabetic Diseases, Okayama Saiseikai General Hospital, Okayama City, Japan, [4]Center for Kidney and Diabetic Diseases, OKayama Saiseikai General Hospital, Okayama City, Japan and [5], Okayama University Medical School, Okayama City, Japan

Background and Aims: Recently, more elderly patients who are independent or able to live at home with support of family are opting for peritoneal dialysis (PD). And assisted PD becomes the useful cure in the super-aging society. Japanese nursing-care insurance system which began in 2000 is useful for the spread of PD in the elderly.

A purpose of this study is to check the current situation of the PD therapy in the elderly needing care. And it is to plan the spread of assisted PD in the elderly patients.

Method: Of the 789 elderly patients controlled by dialysis at our hospital between 2000 and 2018, 265 patients (33.6%) selected PD. 106 patients (30.1%) of young-old group (65-74 years, n=352), 108 patients (32.6%) of old group (75-84 years, n=331), and 51 patients (48.1%) of oldest old (≧85 years, n=106) started PD.

We studied total Kt/V, total Ccr, volume of urine, volume of dialysate, the bag exchange number and dialysate retention time in 90 PD patients.

We estimated total Kt/V and relations of the nursing care level in elderly PD patients.

The data of patients divided into 4 groups: young group (≦64 years, n=30), young-old group (65-74 years, n=19), old group (75-84 years, n=27) and oldest-old group (≧85 years, n=14). Total Kt/V and relations of the nursing care level between 1 and 5 based on assessment of care requirements in PD patients with or without assisted PD were studied.

Results: The nursing-care insurance acquisition rate of each age group was 3.3%, 18.8%, 51.9%, 78.6% and assisted PD rate was 0%, 21.1%, 55.6%, 92.9%, respectively.

Total urine volume was 759±506 L/day in the independent elderly patients and was 603±433 in the elderly patients with assisted PD.

Dialysate volume was 5.5±2.0L/day in the independent elderly patients and was 4.0±2.1 in the elderly patients with assisted PD ($p<0.05$).

The daily bag exchange number of times was 3.6±1.0 in the independent elderly patients and was 2.9±1.1 in the elderly patients with assisted PD ($p<0.05$). The volume of dialysate was 5.5 ±2.0 L/day in the independent elderly patients and was 4.0±2.1 L/day in the elderly patients with assisted PD ($p<0.05$).

Though total Kt/V did not have the difference in each age group, total Kt/V was 1.74±0.36 in the non-need of nursing care elderly patients and was 1.37±0.30 ($p<0.05$) in the need of nursing care elderly patients.

Total Kt/V was 1.72±0.30 in the independent elderly PD patients and was 1.53±0.44 in the elderly patients with assisted PD.

Total Kt/V and the nursing care level were significantly inversely correlated ($p = 0.011$). Total Kt/V and the life independence degree of patients with dementia were significantly inversely correlated ($p = 0.001$)

Conclusion: Elderly PD patients can achieve improved levels of well-being with low volume peritoneal dialysates. The application of dialysis prescriptions using APD and and/or icodextorin decrease the burden of changing PD bags for elderly patients, nurses and families who support them (assisted PD).

PD for elderly patients will create a paradigm shift of dialysis therapy in the super aging society.

P1172 IS PERITONEAL PROTEIN LOSS A CONSEQUENCE OF OVERHIDRATATION?

Anabela Malho Guedes[1,2], Ana Domingos[1], Roberto Calças[1], Ana Silva[1], Idalécio Bernardo[1], Pedro Neves[1], Anabela Rodrigues[2,3]

[1]Centro Hospitalar Universitario Algarve, Portugal, [2]Instituto de Ciências Biomédicas Abel Salazar, Portugal and [3]Centro Hospitalar Universitário do Porto, Portugal

Background and Aims: Peritoneal protein loss (PPL) in peritoneal effluent is a well-recognised detrimental result of peritoneal dialysis treatment since its inception. Hydrostatic convection is a major drive for peritoneal protein transport; therefore venous congestion may have a role in peritoneal protein loss (Krediet RT et al Perit Dial Int. 2019). The aim of this study was to explore the importance of overhydration on the magnitude of peritoneal protein clearance in incident PD patients.

Method: A total of 97 adult incident PD patients were included. A standard peritoneal equilibration test, 24-hour urine and dialysate collection, and multifrequency bioimpedance analysis were performed. Independent-samples t test and Pearson correlation coefficient were performed to evaluate relevant clinical associations and linear multivariable regression was done.

Results: Statistically significant univariable relationships for 24h PPL were found for continuous ambulatory PD technique (CAPD) and, with a correlation coefficient >0.20, for age, pulse pressure, 4-hour dialysate/plasma creatinine and extracellular water/total body water. On multivariable analysis, type of PD technique ($\beta=0.327$, $p=0.011$), 4-hour dialysate/plasma creatinine ($\beta=0.247$, $p=0.037$), and extracellular water/total body water ($\beta=0.304$, $p=0.016$) were significant independent predictors of peritoneal protein loss.

Conclusion: Overhydration revealed the most important connection with peritoneal protein loss. Mortality has been associated with PPL in some studies, but not others. This could be a result of this relationship, as volume overload has been strongly related with lower survival.

P1173 **PERITONEAL DIALYSIS INFECTIONS IN MALTA - TRENDS OVER ELEVEN YEARS**

Angela Borg Cauchi[1], Maria Angela Gauci[1], Theresia Dalli[2], James Gauci[3], James Farrugia[4], Emanuel Farrugia[1], Michael A. Borg[5]

[1]Mater Dei Hospital, Nephrology Department, Malta, [2]Mater Dei Hospital, General Medicine, Malta, [3]Mater Dei Hospital, Gastroenterology Department, Malta, [4]Mater Dei Hospital, Infectious Diseases Department, Malta and [5]Mater Dei Hospital, Infection Control & Sterile Services, Malta

Background and Aims: Infections related to peritoneal dialysis (PD) are still a cause of morbidity and mortality. We describe an overview of PD peritonitis and catheter-related infections (CRI) in Malta over a period of eleven years. We also describe trends in dialysis modality over the years.

Method: All patients undergoing PD in Malta during 2008 and 2018 were analysed. Data from 2008-2012 was retrospective, shown as mean, that from 2013-2018 prospective. International Society for Peritoneal Dialysis (ISPD) definitions were used.

Results for categorical responses were summarized using absolute numbers and percentages. Medians (range) were used to describe continuous non-normally distributed data.

Results: The total number of patients undergoing PD from 2008 till 2018 were 137 (2008-2012), 91, 80, 126, 117, 102, 103 respectively. There was an overall male predominance of 63.5% (61-67). Patient years at risk were 85.80, 85.25, 89.71, 83.70, 79.69, 72.88 since 2013 respectively.

The overall incidence of diabetes mellitus was 45.3% (41.8-50), cardiovascular disease 34.2% (33.8-35), hypertension 79.3% (73.8-84.6).

PD was used in 50% of dialysis modality prior to 2012, 39% in 2018. Initially 51% used Automated PD (APD), with 21% assisted PD, in 2018 39% used APD, with 6% assisted PD.

PD peritonitis rates from 2008 were 0.38, 0.31, 0.35, 0.46, 0.43, 0.57, 0.54, 0.43, 0.39, 0.40, 0.46 episodes/patient year respectively

There was marked dominance of Gram-positive peritonitis, mainly *Staphylococcal*, with a reduction of coagulase-negative-*Staphylococcus* from 0.26 episodes/patient in 2013 to 0.03 in 2017, 0.11 in 2018. Methicillin-resistant *S. aureus* (MRSA) peritonitis decreased from 0.03 episodes/patient to nil in 2016, 2017, 0.01 episodes/patient in 2018.

Amongst Gram-negative peritonitis, *Pseudomonas* rates decreased from 0.06 to 0.03 episodes/patient in 2018, nil in 2016. *Escherichia coli* rates decreased from 0.02 episodes/patient to nil in the last three years. Fungal rates from 0.03 to 0.01 episodes/patient/year, with nil in 2016, 2017.

Catheter-related infection rates were 0.39 (2008-2012), 0.35, 0.91, 0.37, 0.38, 0.25, 0.50 episodes/patient/year respectively. There was a higher incidence of recurrent infections in 2014, none in 2015 and 2016. Gram-negative organisms accounted for 57% of all CRI, predominantly *Pseudomonas* at 0.12 (2008-2012), 0.06, 0.09, 0.09, 0.14, 0.03, 017 episodes/patient/year respectively. Gram-positive CRI were mostly *Staphylococcus aureus,* peaking in 2014 at 0.38 episodes/patient/year. MRSA rates declined from 0.15 to 0.01 episodes/patient/year in 2018.

Conclusion: PD peritonitis rates in Malta between 2008 and 2018 were below the ISPD recommended threshold. There were no episodes of MRSA in 2016, 2017, no *Pseudomonas* in *2016,* no *E coli* in the last three years and no fungal PD peritonitis in 2016, 2017.

CRI rates also declined, with an overall predominance of Gram-negative infections.

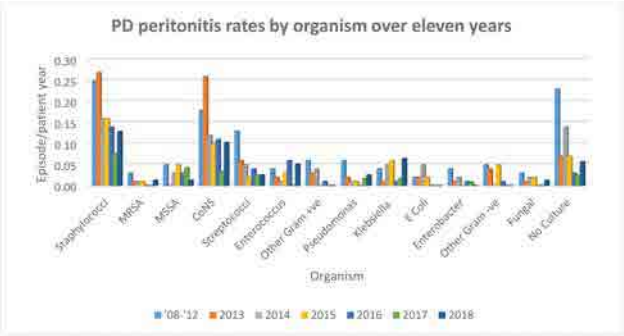


Figure:

P1174 **STUDY ON THE RELATIONSHIP BETWEEN HYPOCHLOREMIA AND ALL-CAUSE DEATH IN PATIENTS RECEIVING CONTINUOUS AMBULATORY PERITONEAL DIALYSIS**

Tao Xu[1], Niansong Wang[1], Cheng Qiao[1]

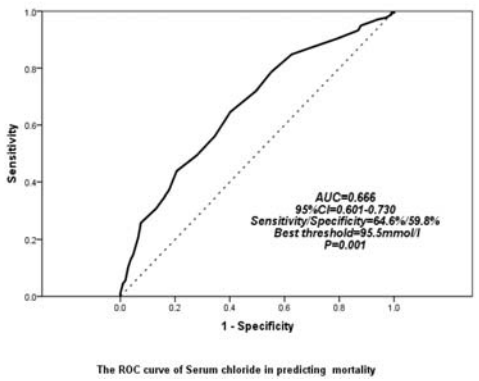
[1]*Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai, Nephrology, Shanghai, P.R. China*

Background and Aims: To investigate the relationship between hypochloremia on all-cause death in patients receiving continuous ambulatory peritoneal dialysis (CAPD).

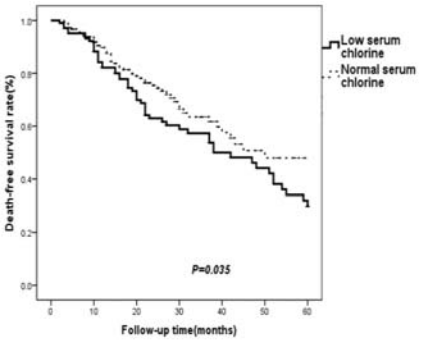
Method: 300 CAPD patients from January 2013 to December 2019 in the Sixth People's Hospital affiliated to Shanghai Jiaotong University. According to the serum chloride level, the patients were divided into two groups: hypochloremia group (serum chlorine $\leq$ 96mmol / L, n = 135) and normal chloride group (106mmol / L $<$ serum chlorine $>$ 96mmol / L, n = 165). The endpoint was all-cause death. We used the receiver-operating characteristic (ROC) curve to analysis the diagnostic value and logistic regression to assess the predictive value in relation to serum chloride with all-cause death in CAPD patients. Kaplan Meier curve was used to evaluate the effect of serum chloride on all-cause death survival analysis. All statistics were analyzed by SPSS 20.0 software, P $<$ 0.05, indicating significant difference.

Results: 114 cases of all-cause death occurred in CAPD patients during follow-up (62.1 $\pm$ 11.1 months). The results of correlation analysis showed that serum chloride was positively correlated with serum sodium and potassium (r=0.721,0.199, P=0.001) and the negative correlation between serum chloride and dialysis age and serum phosphorus (r=-0.321, - 0.300, P=0.001). ROC curve analysis showed that serum chloride was statistically significant in predicting all-cause death in CAPD patients (AUC = 0.666, 95% Cl = 0.601-0.730, sensitivity / specificity = 64.6% / 59.8%, best threshold = 95.5mmol/l). Kaplan Meier analysis of all-cause death risk curve shows that the incidence of all-cause death in the low chloride group is higher than that in the normal serum chloride group. Logistic regression analysis showed that low chloride level was an independent risk factor for all-cause death in CAPD patients.

Conclusion: Hypochloremia is an independent risk factor for all-cause death in CAPD patients.



The ROC curve of Serum chloride in predicting mortality



Kaplan-Meier curves of freedom from mortalityin patients between Low serum chlorine and Normal serum chlorine levels.

Figure:

P1175 **INTESTINAL MICROBIOME, METABOLOME AND BACTERIALLY-DERIVED UREMIC TOXINS IN PD-PATIENTS - DISPARITIES IN CHRONIC KIDNEY DISEASE AND ACUTE KIDNEY INJURY**

Lisa Daniel-Fischer[1,2], Rebecca Herzog[1,2], Christoph Aufricht[2], Klaus Kratochwill[1,2]

[1]Medical University of Vienna, Christian Doppler Laboratory for Molecular Stress Research in Peritoneal Dialysis, Department of Pediatrics and Adolescent Medicine, Vienna, Austria and [2]Medical University of Vienna, Department of Pediatrics and Adolescent Medicine, Division of Pediatric Nephrology and Gastroenterology, Competence Center for Pediatrics, Vienna, Austria

Background and Aims: Recent evidence suggests a bidirectional relationship between the intestinal microbiome and CKD. CKD and concomitant uremia lead to loss of integrity of the intestinal barrier, causing increased intestinal permeability and potentially contributing to systemic inflammation. Uremia itself has been speculated to cause a selection of certain microorganisms, known as dysbiosis. The alteration of the intestinal microbiome may favor the formation of specific uremic toxins. We hypothesized that the composition of the microbiome is altered between patients with CKD and AKI. The aim was to investigate the effect of CKD (with already established uremic dysbiosis) and AKI (without established uremic dysbiosis) and the exposure to PD-fluids on the intestinal microbiome and on a local (peritoneal) and systemic metabolome level of patients treated with PD.

Method: Patients on PD therapy with CKD and AKI were included. Stool samples were analyzed by 16S rRNA sequencing, 188 systemic (serum) and local (PD-effluent) metabolites as well as 10 uremic toxins (including p-cresyl sulfate and indoxyl sulfate) were analyzed using a mass spectrometric approach. Clinical standard parameters in serum and PD-effluent were measured by routine laboratory techniques.

Results: Changes in relative abundances of intestinal bacteria and differences in gut microbiome composition at the phylum level were associated with chronic disease. Patients with CKD and AKI had significantly increased levels of uremic toxins and revealed a distinct metabolomic pattern. Cross-omics correlation between bacterial phyla and metabolites was performed to obtain functional information on differentially abundant species and molecules.

Conclusion: Patients with CKD on PD are characterized by an altered intestinal microbiome, local and systemic metabolome changes in contrast to patients with AKI. PD-patients with CKD and AKI have increased serum levels of bacterially-derived uremic toxins. Further investigations are required to obtain deeper understanding of reciprocal influences of the uremic status and intestinal microbiome.

P1176

DECLINING PERITONEAL HOST DEFENCES REVEALED BY EX-VIVO CYTOKINE RELEASE ASSAY OF PERITONEAL DIALYSIS EFFLUENT CELLS

Rebecca Herzog[1,2], Andreas Vychytil[3], Christoph Aufricht[2], Klaus Kratochwill[1,2]

[1]Medical University of Vienna, Christian Doppler Laboratory for Molecular Stress Research in Peritoneal Dialysis, Vienna, Austria, [2]Medical University of Vienna, Department of Pediatrics, Pediatric Nephrology and Gastroenterology, Comprehensive Center for Pediatrics, Vienna, Austria and [3]Medical University of Vienna, Department of Medicine III, Nephrology and Dialysis, Vienna, Austria

Background and Aims: Infectious complications occur in a significant proportion of patients treated with peritoneal dialysis (PD), limiting its long-term applicability. Reduced peritoneal immune-competence, caused by the continuous exposure to PD-fluids, has been described as a therapy-related pathomechanisms, prompting the need for a tool to assess the functional peritoneal immune status. We established an ex-vivo stimulation assay to test host defence mechanisms in only 9ml of crude PD-effluent. The assay was used in two randomized clinical trials investigating immune-modulatory effects of a novel additive (alanyl-glutamine) to PD-fluid. Here we aimed to evaluate the assay as a method to assess peritoneal immune-competence in the general PD-population and linking it to PD vintage and outcome parameters.

Method: 462 PD-effluent samples, originating from 148 adult and paediatric PD patients, were stimulated ex-vivo (24h, 37°C) with toll-like receptor (TLR)-agonists lipopolysaccharide (LPS) and Pam_3Cys. Unstimulated samples of each effluent were used as controls. Interleukin 6 (IL-6) and tumor necrosis factor α (TNF-α) concentrations and the predictive value of the assay for clinical outcome parameters were analyzed using Wilcoxon matched-pairs signed rank test and a mixed model logistic regression analysis.

Results: Ex-vivo stimulation of peritoneal cells resulted in a dwell-time dependent increase of cytokine release, with a significant lower cytokine released at the 1h PET time point (normalized to unstimulated controls). Ratios between stimulated PDE-samples and unstimulated controls, accounting for a potential increase in basal inflammation, significantly declined with PD therapy duration. Correlation of the cytokine levels with the predefined clinical parameters revealed predictive potential of the assay for the occurrence of infectious complications, as well as of ultrafiltration and technique failure.

Conclusion: In summary, the current study provides evidence of a correlation of declining local host defence and duration of PD-therapy. These data support the hypothesis of PD-duration dependent progressive impairment of the ability of the peritoneal immune cells to secrete cytokines in response to a pathogenic stimulus and thereby dampening the global peritoneal immuno-competence. The results suggest the utility of this clinically feasible ex-vivo induced cytokine-release assay in crude peritoneal effluent as a surrogate of the functional peritoneal immune competence. Future analyses will have to evaluate the assay as a tool to predict common clinical outcomes and define reference values to facilitate stratification of patient populations, clinical staging and to guide novel therapeutic interventions.

P1177

THE INFLUENCE OF PERITONEAL GLUCOSE LOAD ON LEAN AND ADIPOSE TISSUE MASS IN PERITONEAL DIALYSIS PATIENTS USING A NOVEL AND QUANTITATIVE INDEX

Kamal Hassan[1], Nihal Khatib[2], Fadi Hassan[3]

[1]Galilee Medical Center, Nephrology and Hypertension, Nahariya, Israel, [2]Clalit Health Services, Haifa, Israel and [3]Galilee Medical Center, Nahariya, Israel

Background and Aims: There is now widespread consensus among nephrologists to increase the number of patients on peritoneal dialysis (PD). Most of the PD dialysis solutions are based on glucose as an osmotic agent. The peritoneal glucose load can damage the peritoneal membrane, increases its permeability to water, glucose and electrolytes leading to the development of fluid overload, hypertension, stimulation of the inflammatory process and metabolic disturbances. This study aims to verify the influence of glucose exposure load on lean and adipose tissue mass in PD patients using a novel and quantitative index.

Method: This is a retrospective and analytical study based on the medical records. The study examined the entire population of PD patients who were treated at the Peritoneal Dialysis Unit at the Galilee Medical Center in north of Israel during the last eight years (from January 1, 2010 through December 31, 2017). The clinical and laboratory data of these patients were collected from their medical records and analyzed. The main variables examined included peritoneal glucose load index (PGLI), lean tissue index (LTI) and Fat Tissue Index (FTI).

LTI was calculated as the quotient of LTM/Height?(kg/m? and FTI was defined as the quotient of ATM/Height?(kg/m?. LTI and FTI were assessed using the Fresenius Medical Care Body Composition Monitor (BCM) device, based on Bio-impedance technology

Results: 187 assessments of the nutritional status in PD patients, using the BCM device, were evaluated. Among PD patients, 52.4% were men, 54% were treated with continuous ambulatory peritoneal dialysis (CAPD) and 46% had diabetes mellitus as primary renal disease. The average age was 57.8 ± 11.3 years, peritoneal dialysis vintage 31.36 ± 16.69 months, body mass index (BMI) 28.1 ± 4.4 kg/m^2, daily urinary output 1040.0 ± 649.8 ml/day, hemoglobin 10.84 ± 1.02 g/dl, HbA1c 7.05 ± 1.09 %, Kt/V 1.89 ± 0.17, PGLI 3.11 ± 1.13 g/kg/day, residual renal function 6.68 ± 2.46 ml/min/1.73m^2. A significant and positive correlation between the PGLI and FTI (r=0.28, p<0.001) and, a significant and negative association between PGLI and LTI (r=-0.24, p<0.001) were found.

Conclusion: Peritoneal glucose load may adversely influence the nutritional status of PD patients by increasing the adipose tissue mass and decreasing lean tissue mass.

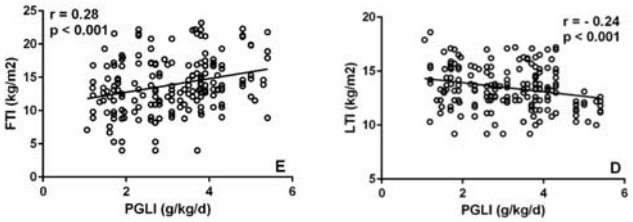


Figure:

P1178 FEASIBILITY OF UNPLANNED START IN PERITONEAL DIALYSIS (PD)

Eva López Melero[1], R. Haridian Sosa Barrios[1], Víctor Burguera Vion[1], Sofía Ortego Pérez[1], Milagros Fernandez Lucas[1,2], Maite Rivera[1,2,3]

[1]Hospital Ramón y Cajal, Nephrology, Madrid, Spain, [2]Universidad De Alcalá De Henares, Alcalá de Henares, Spain and [3]Biobanco RedInRen, Alcalá de Henares, Spain

Background and Aims: Chronic kidney disease (CKD) is increasing worldwide and there is a rising need for renal replacement therapies (RRT). PD has multiple advantages over hemodialysis (HD), but in most patients requiring an unplanned start HD is the selected RRT.

Method: We retrospectively analyzed all patients started on unplanned PD in our unit from January 2006 until April 2019. Demographics, blood test parameters and complications were collected. Unplanned start on PD was defined as initiating PD less than 4 weeks after PD catheter implantation.

Results: Of 14 patients, 8 were referred from ACKD clinic, 3 were failing renal transplants and 3 previous PD patients that required catheter replacement due to severe peritonitis. Fluid overload with rapid decline in kidney function was the acute trigger for RRT in 4 patients and 1 had a nephrectomy. Late referral with uremic symptoms was the reason for unplanned start in 5 patients. Two patients (14.2%) had mechanical complications that did not require surgical intervention. None had infections related to technique. PD was performed by our PD unit nursing staff in all cases and technique was well tolerated. Results are summarized in table 1.

Conclusion: PD is a safe and valid option even when an unplanned start on RRT is required. It did not show higher morbidity nor mortality in our series, allowing avoidance of central lines in our patients and preserving vascular capital. Furthermore, PD is a less expensive technique than HD. Nursing staff support is key to develop it.

Table 1.

AGE (years)	57.7 ± 14.4*
ORIGIN	ACKD clinic: 57.2% PD :21.4% Failed transplant: 21.4%
GENDER (male)	71.4%
MEDIAN TIME TO START (days)	7.5 (range 0-26)
REASON TO URGENT START	Late referral:35.7% Acute trigger: 35.7% PD Catheter replacement :28.6%
MODALITY OF URGENT PD	Outpatient APD 78.6% Inpatient setting CAPD 21.4%
COMPLICATIONS	1 inguinal hernia 1 pericatheter leak

**Mean + standard deviation.*

ACKD: Advanced CKD; APD: automated PD; CAPD: continuous ambulatory PD.

P1179

PREDICTIVE FACTORS OF PERITONITIS IN PERITONEAL DIALYSIS PATIENTS AFTER TENCKHOFF CATHETER IMPLANTATION : A META-ANALYSIS

Firdian Makrufardi[1], Erri Larene Safika[2], Aulia Sigra Galayudha[1], Rachmat Aldhi Wijayanto[1]

[1]*Universitas Gadjah Mada, Department of Surgery, Yogyakarta, Indonesia and*
[2]*Universitas Gadjah Mada, Department of Public Health, Yogyakarta, Indonesia*

Background and Aims: Chronic kidney disease is one of the leading cause of years living with disability. Peritoneal dialysis has been an effective treatment for end-stage renal disease (ESRD). Unfortunately, there are infectious and non-infectious complication after tenckhoff catheter implantation in patients. Peritonitis has been the most common major clinical problem and is often the cause for failure of peritoneal dialysis. Many researchers have studied the predictive factors of peritonitis in peritoneal dialysis patients after tenckhoff catheter implantation, but their conclusion were not always consistent. Therefore we performed a meta-analysis to make a more integrated and precise estimation.

Method: Multiple databases were searched for comparative studies without language or date restrictions. Gray literature was sought. The meta-analysis study was conducted using Revman 5.3, with $p < 0.05$ considered significant. Aspects investigated included age at implantation, diabetes mellitus, and gender. Two reviewers independently assessed study eligibility and the quality of included studies.

Results: A total of 7 studies were identified and analyzed, and 3 were multi-institutional. Reporting standards were highly variable. Overall, 7730 patients with ESRD were incorporated in this study. Meta-analysis demonstrated there was significant difference in the incidence of peritonitis with age at implantation, (OR= 1.98 [1.81, 2.17], p=0.00001). Significant difference was not seen in the incidence of peritonitis with diabetes mellitus, (OR= 1.03 [0.23, 4.55], p=0.97). Meta-analysis showed that there was no association between gender with incidence of peritonitis (OR= 1.57 [0.62, 3.97], p=0.35), while male had a higher peritonitis incidence (See figure). No publication bias was noted in this study

Conclusion: Peritonitis is still a major problem in patients with peritoneal dialysis. Age at implantation is the predictive factors that affect peritonitis incidence in peritoneal dialysis patients after tenckhoff catheter implantation, while gender and diabetes mellitus do not appear to be correlated with peritonitis incidence.

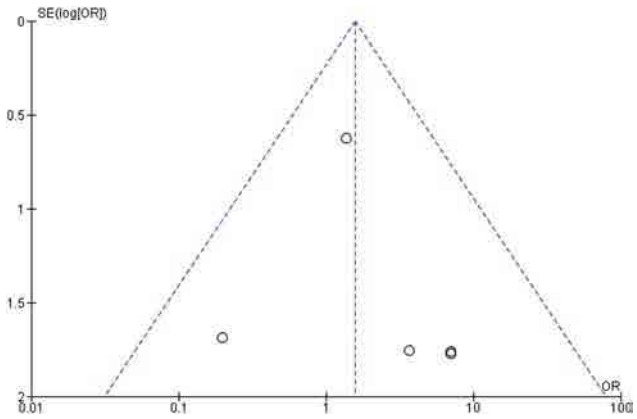


Figure 1. Funnel plot of peritonitis

P1180 EVOLUTION OF SERUM B2MICROGLOBULIN LEVELS IN INCIDENT PERITONEAL DIALYSIS PATIENTS

Diego Barbieri[1], ANDRÉS FELIPE DELGADO[1], Ana García-Prieto[1], Almudena Vega[1], Soraya Abad Esttebanez[1], Alejandra Muñoz de Morales[1], Javier Carbayo[1], Ángela González-Rojas[1], Adriana Acosta Barrios[1], Marian Goicoechea[1]

[1]*Gregorio Marañón Hospital, Nephrology, Madrid, Spain*

Background and Aims: Retention of ß2microglobulin (ß2M), an uremic toxin in the middle molecular range, has been associated with cardiovascular morbidity and mortality in dialysis patients. Although ß2M levels are usually measured in hemodialysis patients, this practice is not common among peritoneal dialysis (PD) patients. The aim of this study is to evaluate the evolution of serum ß2M levels in incident PD patients.

Method: Prospective, observational study including incident PD patients in our hospital from January 2015 to October 2019. Patients with cardiorrenal syndrome or patients coming from hemodialysis were excluded. Serum ß2M levels were collected before starting PD and during follow up. Weekly KtV, residual renal function and cardiovascular events were also collected during follow up.

Results: We included 30 patients with a mean age of 57 +/- 17 years. 56.3% were male and 15.6% were diabetic. Mean follow up was 19.8 +/- 16.9 months. 18 patients were on continous ambulatory PD and 12 in automated PD. Mean serum ß2M levels before starting PD were 12.8 +/- 6.6 mg/l and they remained stable during follow up (12.9 +/- 5.2 mg/l, 15 +/- 4.2 mg/l, 14.3 +/- 6.9 mg/l, 10.2+/- 4.5 mg/l at month 6, 12, 24 and 36, respectively; p NS). No differences in serum ß2M levels were observed between continous ambulatory PD and automated PD. Serum ß2M levels were inversely and significantly correlated with weekly KtV (r= -0.943; p 0.009) and residual renal function (r= -0.829; p 0.042). One cardiovascular event was recorded during follow up.

Conclusion: Serum ß2M levels remain stable during follow up in our cohort of incident PD patients and is significantly and inversely correlated with weekly KtV and residual renal function. Serum ß2M levels monitoring could be helpful in these patients and would yield important information in this population.

P1181 URGENT START OF PERITONEAL DIALYSIS: OUTCOMES AND EXPERIENCE FROM NORTHERN INDIA

Priti Meena[1], Vinant Bhargava[1], A K Bhalla[1], Ashwani Gupta[1], Manish Malik[1], Anurag Gupta[1], Devinder Singh Rana[1]

[1]*Sir Ganga Ram Hospital, Department of Nephrology, New Delhi, India*

Background and Aims: Peritoneal dialysis (PD) widely practiced as the first-line modality for renal replacement therapy in end-stage renal disease (ESRD) patients. Urgent-start PD (use of the PD catheter within 14 days of insertion) is an effective approach to prompt initiation of PD after catheter insertion. However, there is a paucity of data regarding complications of urgent-start PD. We investigated the outcomes of urgent-start PD in our subset (Indian population).

Method: All patients in whom PD was initiated between 01 January 2015 and 31 July 2019 (54 months) were included. Patients were grouped according to the initiation of PD (break-in period) as <8 days (PD1), 8 to 14 days (PD2), and >14 days (PD3).

Results: In 100 patients included in the study, 57.5% were males. Among them, 75%, 10%, and 15% patients were in the PD1, PD2, PD3 break-in groups respectively. The most common cause of ESRD was diabetes mellitus. Functional catheter malfunction was the most frequent complication in PD1. The incidence of mechanical complications during the first six months was similar in all three groups ($p = 0.06$). No significant differences with respect to the catheter dysfunction requiring surgical intervention ($p > 0.05$) were observed. In PD1 group, catheter patency rate at the end of the 1-month and 1-year was 98.6% and 95.4% respectively. No significant differences were found in the rate of peritonitis among the three groups. Female sex, low haemoglobin, and low albumin levels were independent risk factors for peritonitis.

Conclusion: Early break-in period of less than seven days is a feasible option for patients requiring urgent dialysis with no increased risk of mechanical or infectious complications. It offers a safe and efficacious option for unplanned ESRD patients.

P1182 PROGNOSTIC VALUE OF CHARLSON COMORBIDITY INDEX IN PERITONEAL DIALYSIS PATIENTS

Vincenzo Antonio Panuccio[1], Rocco Tripepi[2], Giovanni Luigi Tripepi[2], Giovanna Parlongo[1], Francesca Mallamaci[1]

[1]Grande Ospedale Metropolitano, Nephrology, Dialysis and Transplant Unit, Reggio Calabria, Italy and [2]National Research Council, Insitute of Clinical Physiology, Reggio Calabria, Italy

Background and Aims: Mortality risk is very high in the dialysis population and the Charlson Comorbidities Index (CCI) is considered as an useful risk stratification tool in these patients. The purpose of this study was to examine the accuracy of CCI for predicting mortality in peritoneal dialysis (PD) patients and to compare the prognostic power of CCI with that of a risk prediction model jointly including a clinical score of malnutrition and the NYHA classes.

Method: We analyzed this problem in a series of 66 consecutive PD patients on follow-up in our unit. Their mean age was 69±14 years, 64% were male, 36% were diabetic. The median dialysis vintage was 39 months (Interquartile range 23-67 months).

Results: During follow-up period, 37 patients died. On univariate Cox regression analysis, CCI largely failed to predict mortality [Hazard ratio (HR): 1.08, 95% CI: 0.94-1.24, P=0.30) and this relationship did not improve (HR: 0.93, 95% CI: 0.79-1.08, P=0.32) also after data adjustment for malnutrition and NYHA classes. In the same model, malnutrition (HR: 1.98, 95% CI 1.20-3.27, P=0.007) and NYHA classes (HR: 3.15, 95% CI 1.67-5.94, P<0.001) were strongly and significantly related to the risk of death. Of note, the prognostic accuracy of the model based on malnutrition and NYHA classes (ROC curve area: 74%) was higher than that provided by CCI alone (ROC curve area: 54%) and did not materially differ from that of an expanded model including CCI, malnutrition and NYHA classes (ROC curve area: 78%)

Conclusion: In this study, CCI did not predict survival in PD patients whereas malnutrition and NYHA score displayed a relevant prognostic accuracy for death in the same patient-population. These results generate the hypothesis, to be confirmed in a larger PD population, that CCI solely for risk stratification is unwarranted in PD patients.

P1183 **EFFECT OF DECREASE IN GLUCOSE GRADIENT ON CHANGE IN INTRAPERITONEAL VOLUME USING SEGMENTAL BIOIMPEDANCE DURING PET**

Fansan Zhu[1], Samer R Abbas[1], Roxana Bologa[3], Nathan W Levin[4], Peter Kotanko[1]

[1]Renal Research Institute, Research, New York, United States of America, [3]Rogosin Institute, PD Department, New York, United States of America and [4]Renal research Institute, Research, New York, United States of America

Background and Aims: The aim of this study was to investigate relationship of glucose gradient dynamics with change in intraperitoneal volume (IPV) measured by segmental bioimpedance analysis (SBIA).

Method: Ten PD patients (age 59±8.8 years, 7 females, 5 Blacks, weight 69.8±12.4 kg) were studied during standard peritoneal equilibrium test (PET). Dialysate glucose concentration (D) was measured hourly throughout the PET. IPV was monitoring continuously using SBIA (Hydra 4200; Zhu et al, Kidney Blood Press Res 2019). Hourly IPV was used to calculate (1) the difference between two conservative hours ($\Delta IPV_t = IPV_{t+1} - IPV_t$; t=0, 1, 2 and 3) and (2) the IPV_t / IPV_0 ratio vs. the concurrent D_t/D_0.

Results: IPVs were successfully measured in nine patients (1 high transporter, 6 high-average, 2 low-average). Ultrafiltration volume (UFV, 0.55±0.17 L) at the end of dwell was measured by SBIA. ΔIPV_1 (0.26±0.17 L) was positive during the first hour of dialysate dwell in 7 patients, their corresponding ΔD_1 (calculated as $D_1 - D_0$) was -902±278 mg/dL. However, 2 patients (1 high and 1 high-average transporter) showed negative ΔIPV_1 (-0.13±0.1 L) and a ΔD_1 of -861±367 mg/dL. The relationship between IPV_t/IPV_0 and D_t/D_0 is shown in Fig.1 (a) – (i). The figures indicate the dynamics of IPV and glucose concentration changes in all 9 patients.

Conclusion: Peak IPV appears at different time points and is associated with different glucose gradients. These findings may represent specific, individual characteristics of the peritoneal membrane. Since first hour ΔIPV represents almost half of total UFV at the end of dwell, it could emerge as an important indicator of peritoneal membrane characteristics. Monitoring IPV using SBIA provides a useful tool for further investigation.

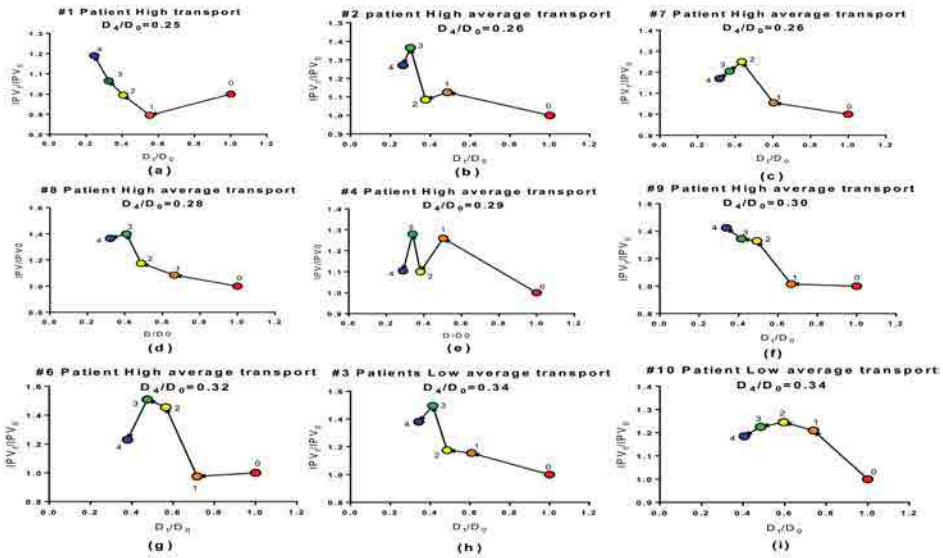


Fig.1 The colored dots indicate the dwell times (red, start; orange, 1 hr.; yellow, 2 hrs.; green, 3 hrs.; blue, 4 hrs.) .

Figure:

P1184 TRANSVERSUS ABDOMINIS PLAIN BLOCK RELIEVES PERIOPERATIVE PAIN ON PERITONEAL DIALYSIS CATHETER INSERTION: A RANDOMISED CONTROLLED STUDY

Kenji Harada[1], Hidetoshi Kanai[1]

[1]*Kokura memorial hospital, Nephrology, Kitakyusyu, Japan*

Background and Aims: The effectiveness of Transversus Abdominis Plain (TAP) block has been reported in the pain control at abdominal operation. However, its usefulness in pain management remains unclear in peritoneal dialysis (PD) patients undergoing catheter insertion. We investigated the effectiveness and safety of TAP block for perioperative on PD catheter insertion.

Method: The present study is a single-centred, prospective, randomised study of initiated PD patients between from October 2017 to January 2020. VAS (Visual Analogue Scale), which is often used around anesthesiology and pain management area, was measured as pain assessment. VAS was measured at five points, right after and 1, 3, 6, 24 hours after operation, using t-test with P values.

Results: Overall, 106 PD patients were included (mean age; 63.8 years old, male/female; 81/25, average eGFR 7.54±2.64). Patients were divided into two groups TAP block (n=50) and non-TAP block (n=56). There were significantly low VAS in TAP block group right after operation (1.39 vs 2.88, p=0.0035) and 1 hour after operation (1.86 vs 3.19, p=0.0078). Furthermore, total five points of VAS were significantly low VAS in TAP block group (10.59 vs 13.85, p=0.028). There were no cases needed for ventilation and anesthetic drug such as morphine. TAP block-related adverse events were not found.

Conclusion: TAP block technique was significantly associated with relief from postoperative pain in PD catheter insertion. This treatment procedure might be a minimally invasive and effective therapeutic option for perioperative pain management on PD catheter insertion.

P1185 LUNG COMETS AND EVALUATION OF HYDRATION STATUS IN PERITONEAL DIALYSIS PATIENTS

Robert Ekart[1,2], Lucijan Lucic Srajer[2], Katharina Marko[2], Nina Hojs[3], Sebastjan Bevc[2,3], Radovan Hojs[3]

[1]UNIVERSITY MEDICAL CENTRE MARIBOR, CLINIC FOR INTERNAL MEDICINE, DEPT. OF DIALYSIS, MARIBOR, Slovenia, [2]UNIVERSITY OF MARIBOR, FACULTY OF MEDICINE, MARIBOR, Slovenia and [3]UNIVERSITY MEDICAL CENTRE MARIBOR, CLINIC FOR INTERNAL MEDICINE, DEPT. OF NEPHROLOGY, MARIBOR, Slovenia

Background and Aims: Assessment of optimal hydration status in patients with end-stage renal disease (ESRD) on peritoneal dialysis (PD) is a challenge. Multiple diagnostic options to determine hydration status in PD patients are available. Multifrequency bioimpedance spectroscopy (MBIS) is a cheap, simple and non-invasive method of estimating body composition, including estimates of total body water (TBW), extracellular water (ECW), intracellular water (ICW) and the ratio between both spaces (ECW/ICW). Lung ultrasonography (LUS) and lung B-lines (lung comets) can be used for the evaluation of extravascular lung water. Ultrasound evaluation of inferior vena cava (UIVC) provides rapid, non-invasive assessment of a patient's hemodynamic and volume status. N-terminal pro-brain natriuretic peptide (NT-proBNP) is related to fluid status and fluid distribution. The aim of our study was to assess fluid status in PD patients comparing four different methods: MBIS, LUS, UIVC and NT-proBNP.

Method: We performed a single-centre cohort study in 19 PD patients. The body composition was measured using the portable whole-body MBIS device, Body Composition Monitor-BCM(®) (Fresenius Medical Care, Bad Homburg, Germany), LUS with portable US device (VScan, General Electrics Corporate), UIVC index with SonoSite US device. NT-proBNP was measured in a one-step sandwich chemiluminescent immunoassay (Dimension Vista® System 1500, Siemens Healthcare Diagnostics Inc., Newark, NJ, USA).

Results: The mean age of patients was 54 ± 10 years, mean dialysis vintage 53 (10-194) months, 63% were men. Thirteen (68.4%) patients had fluid overload (FO) > 1.1 L. Data of patients are presented in table 1. We found a statistically significant correlation between the number of lung comets and ECW/ICW ratio ($r = 0.496$, $P = 0.031$) and NT-proBNP ($r = 0.759$, $P < 0.0001$). In contrast, there was no significant correlation between the number of lung comets and UIVC ($r = 0.221$, $P < 0.364$).

Conclusion: According to our results, LUS with lung comets, MBIS with ECW/ICW ratio and NT-proBNP are useful and complementary methods for evaluation of fluid status in PD patients.

Table 1. Descriptive data of the patients included in the study (N=19)

Variable	*Mean ± SD*
Lung comets (number; mean ± *SD*)	1-87; 16± 21
UIVC (mm/m^2, mean ± *SD*)	8.11 ± 1.76
NT-proBNP (pmol/L)	1151 ±1077
MBIS: Total body water (L)	43.1 ± 10.3
MBIS: Extracellular water (ECW) (L)	20.3 ± 5
MBIS: Intracellular water (ICW) (L)	22.8 ± 6.1
MBIS: ECW/ICW	0.9 ± 0.14
MBIS: Overhydration (L)	2.45 ± 3.05

MBIS= multifrequency bioimpedance spectroscopy; UIVC = Ultrasound evaluation of the inferior vena cava;

P1186 PRELIMINARY RESULTS OF THE FIRST PHASE II CLINICAL TRIAL ON THE USE OF AN INNOVATIVE GLUCOSE-SPARING PD SOLUTION (FIRST)

Mario Bonomini[1], Teresa Lombardi[1], Giorgia Di Fulvio[1], Anna Gigante[1], Lorenzo Di Liberato[1], Roberto Russo[2], Loreto Gesualdo[2], Carmela Rago[3], Massimo Iacobelli[4], Arduino Arduini[4]

[1]Nephrology and Dialysis Unit, "G, d'Annunzio" University, Ospedale Clinicizzato SS. Annunziata, Chieti, Italy, [2]Nephrology, Dialysis and Transplantation Unit, "Aldo Moro" University, Azienda Ospedaliero-Universitaria Consorziale "Policlinico", Bari, Italy, [3]Post-graduate School of Nephrology, University of Foggia, Foggia, Italy and [4]Iperboreal Pharma, Pescara, Italy

Background and Aims: High amounts of glucose as the main osmotic agent for peritoneal dialysis (PD) could be harmful, as it may significantly increase cardiovascular morbidity and mortality. Glucose has long-term detrimental effects on the peritoneum, which ultimately may result in ultrafiltration failure, worsening fluid overload and cardiovascular disease. The absorption of glucose from the dialysate accentuates the disturbances of the carbohydrate metabolism, which is already impaired in the uremic state, leading to insulin resistance.

XyloCore (Iperboreal Pharma, Pescara, Italy), is a low glucose containing PD solution (PDS) proposed as an alternative to glucose PDS only regimen. It has been formulated replacing most of the glucose with two crystalloid agents, D-xylitol and L-carnitine.

PDS containing osmolar agents like xylitol and L-Carnitine added to glucose, used for the nocturnal exchange, may lead to a significant reduction of glucose level in PDS during the night dwell, while preserving or even improving the depurative efficacy of the standard PDS containing 2.5% glucose. The reduction of glucose level could be further enhanced if the PDS with xylitol and carnitine will be used for the diurnal exchanges and a PDS with icodextrin will substitute the standard PDS containing glucose 2.5% for the nocturnal dwell.

The aims of the study are to evaluate the effects of (I) the XyloCore PDS IPX15 [containing glucose (0.5%), xylitol (1.5%) and L-carnitine (0.02%) as osmotic agents, as compared to the standard 2.5% glucose PDS] for the nocturnal exchange, and (II) the XyloCore PDS IPX07 [containing glucose (0.5%), xylitol (0.7%) and L-carnitine (0.02%), as compared to the standard 1.5% glucose PDS] for the diurnal (short dwell) exchanges.

Method: Prospective, randomized, controlled clinical trial in stable ESRD patients treated by CAPD (study protocol registered as NCT 04001036). Key inclusion criteria are: ESRD treated for at least three months with CAPD, stable clinical condition within the four weeks before the screening, hemoglobin $\geq$ 9g/dL, absence of acute peritonitis and/or peritoneal catheter infection in the three months before. Key exclusion criteria are: androgen therapy, active infections, congestive heart failure stage III and IV NYHA; major cardiovascular events in the last 3 months, clinically relevant cardiac arrhythmia; clinically relevant abnormal hepatic tests; treatment with L-carnitine in the previous three months, pregnancy, life expectancy of less than one year, allergy to L-carnitine or xylitol. The sample size is 40 patients. Treatment duration is 4 weeks plus a 4 weeks safety follow up with no treatment. Primary end-point is the daily peritoneal ultrafiltration volume. Secondary end-points are the peritoneal equilibration test (D/P creatinine, D/P glucose), weekly total Kt/V urea, weekly total creatinine clearance, Adverse Events.

Results: Two centers participate in the study. One center has so far recruited 10 patients, 6 in the IPX15 group and 4 in the IXP07 group. The six patients in the IXP15 group were 4 males and 2 males, aged 69.5 $\pm$5.1 years. The four patients in the IXP07 were all male, mean age 56 $\pm$ 12 years. One patient already completed the study period. Results for Kt/V, creatinine clearance, D/P creatinine, D/P glucose, ultrafiltration volume, at time (T) 0 are 1.17, 85.6, 0.75, 0.18, 400 ml, respectively; at T28 (days) are 3.1, 80, 0.82, 0.23, 400 ml respectively, and at T56 are 3.5, 80, 0.77, 023, 450 ml, respectively. D/P glucose results indicate that this patient is a high transporter and D/P creatinine that the patient was an average/ high transporter.

There were no adverse events reported and tolerability has been excellent so far.

Conclusion: In the first 10 ESRD patients included in the study, XyloCore PDS used for 4 weeks has been well tolerated without significant adverse events. The study is in progress.

P1187 THE NUTRITIONAL STATUS IN PERITONEAL DIALYSIS PATIENTS: HOSPITALIZATION AND MORTALITY

Iryna Shifris[1], Anna Shymova[1], Iryna Dudar[1]

[1]SI "Institute of Nephrology Academy of Medical Science of Ukraine",, Efferent Technology Department, Kyiv, Ukraine

Background and Aims: The worldwide medical public attention focuses on the problems associated with decreasing morbidity frequency and improving of survival of patients with the end stage renal disease (ESRD). Peritoneal dialysis (PD), including continuous ambulatory peritoneal dialysis (CAPD), one of the known modality of renal replacement therapy (RRT). Several studies demonstrated that namely nutritional.

The aim of this study was to explore the relationship between the nutritional status in PD patients and their morbidity and mortality.

Method: This study was an observational, prospective, epidemiological tracking by clinical examination. The study included 105 patients with ESRD who started CAPD treated in single dialysis center of Ukraine (during 2012 - 2018). Fifty three (50.5%) patients were male, median age 60 (range 25–85 years) and the most common cause of ESRD was glomerulonephritis (63 patients, 60.0%). Median follow-up was 29 months (range 6- 132 months). Nutritional status (NS) indicators defined basing on the calculation of the subjective global assessment (SGA, points). Patients were classified into four groups according to their NS. Group 1 included 51 patients with normal NS, group 2- 30 patients with a light degree of malnutrition, group 3 (13 patients) and group 4 (11 patients) with moderate and severe degree of nutritional disorders, respectively. During follow-up, all hospital admissions and all causes of mortality were documented and compared for nutritional disorders versus normal NS**.**

Results: During follow up the 62 hospitalization cases (30 cardiovascular events, 15 PD-peritonitis, 13 other bacterial infections, 2 stroke and 2 - others) and 46 deaths among all patients were detected. The odds ratio for all-cause hospitalization in the group 3 (12/85.7% vs. 26/ 51.0%) were significantly higher than in the group 1 (OR = 5.7692, 95% CI: 1.1712 - 28.4178; p= 0.0312). A significant increasing of the hospitalization incidences both due infectious comorbidity (7/63.64% vs. 8/15.7%; χ^2= 8.880, p = 0.003) among patients with severe degree of malnutrition compared with patients group 1. At the same time, cardiovascular (CVD) hospitalization rate was significantly higher in patients group 3 (8/57.1% vs. 10/ 19.6%; χ^2= 5.968, p = 0.015) than in the group1.

Mortality rate was significantly higher in patients group with moderate (11/84.6% vs 16/31.37%, χ^2= 12.041, p <0.0001; OR =12.031; 95% CI: 2.3843 - 60.7105) and a light degree of nutritional disorders (11/84.6% vs 13/43.4%, χ^2= 6.267, p= 0.013; OR = 7.1923; 95% CI: 1.352- 38.2367) than with normal NS. Similarly, patients with a severe degree of malnutrition (group 4) showed a higher mortality rate versus patients group1: *8*/72.7%% vs. 16/31.37%,; χ^2= 6.522, p= 0.011 (OR = 5.8333, 95% CI: 1.3645-24.9376). Cardiovascular disease was the leading cause of death (22/47.8%).

Conclusion: Thus, the obtained findings suggest that nutritional disorders at PD initiation have a significant negative effect on prognosis. The results of our study demonstrated the predictive role of assessing nutritional status in all-cause mortality and hospital admissions in ESRD population.

P1188 ICODEXTRIN-INDUCED CHEMICAL PERITONITIS IN A PATIENT WITH CARDIORENAL SYNDROME

ATHANASIA KAPOTA[1], Katerina Damianaki[1], PANAGIOTA GIANNOU[1], AGLAIA CHALKIA[1], GEORGIOS MPOUGATSOS[1], DIMITRIOS PETRAS[1]

[1]*HIPPOKRATION GENERAL HOSPITAL OF ATHENS, NEPHROLOGY, ATHENS, Greece*

Background and Aims: The main cause of morbidity among patients who undergo peritoneal dialysis (PD) remains peritonitis. However there are rare references in published literature about the development of sterile peritonitis related to exposure to PD materials used to overcome the complications from glucose solutions.The objective of the present case report is to enhance clinical suspicion in order to avoid unnecessary antibiotic treatment or catheter removal.

Case description:A 56-year-old male became dialysis dependent from June 2017 due to cardiorenal syndrome type II, after multiple hospitalizations for pulmonary edema within a year. The patient was prescribed icodextrin 7,5% as a single 10-hour nocturnal dwell with dry day period in continuous ambulatory PD .At his scheduled appointment during drainage of the nighttime dialysate, slightly cloudy effluent with a lot of pale yellow substances "sesame" like, were observed without any signs of peritonitis or pathology from the Catheter exit site based on Twardowski classification.The dialysate contained 600 cells/ml. The floating yellow substances after laboratory and light microscopy examination accumulated epithilium cells with rare macrophages were found.Due to these findings,icodextrin was discontinued and empiric antibiotic therapy started including intraperitoneal administration of vancomycin and ceftazidime .After 3 days the floating substances disappeared and the number of cells in dialysate progressively decreased but not within the normal range so empirical antifungal therapy was decided. Daily repeated aerobic, anaerobic and fungal cultures of effluent and blood were negative as well the culture of exit site. ADA (*adenosine deaminase test) and β-koch culture were also negative.* Computed tomography scan of abdomen and colonoscopy showed no pathology.Due to fluid overload an additional long-term dwell of icodextrin solution was initiated.The re-exposure doubled the number of cells (310 cells/ml) and a second sample was sent for cytological examination which showed plenty of hyperplastic mesothelial cells in piles and isolated, abundant mature lymphocytes, few polymorphonuclear leukocytes as well as several mast cells. Based on these observations peritoneal cavity remained empty for 24 hours. Afterwards a 4-hour exchange of glucose-containing solution of 1,36%, 2,27%, 3,86% and finally of icodextrin was held once daily. The cells were 155, 120, 105 and 450/ml respectively with lymphocytes and mast cells being predominant.Based on these data, it was considered that the exposure to icodextrin produced hypersensitivity and the empiric antibiotic therapy was discontinued.The catheter was removed and sent for culturing which was negative.The biopsy of peritoneal membrane revealed mild fibrous sclerotic lesions, fibrous texture, partially collagenized membrane lacking mesothelial lining and exhibiting sparse chronic nonspecific inflammatory infiltration involving rare neutrophilic leukocytes. Plenty of small blood vessels were observed, with no immunomorphological features including IgG4 staining. These findings were attributed to chemical peritonitis from icodextrin solution ant the patient switched dialysis modality.

Discussion:the use of icodextrin in peritoneal dialysis patients has numerous advantages over glucose-based dialysates including improved ultrafiltration, better fluid control and less hypertension, especially in patients with cardiorenal syndrome. In the face of evident benefits, clinicians should, however, be aware of the potential of icodextrin to induce chemical sterile peritonitis.

P1189

OFFICE AND AMBULATORY RECORDING OF CENTRAL AORTIC PRESSURES, WAVE REFLECTION AND ARTERIAL STIFFNESS INDICES IN PERITONEAL DIALYSIS PATIENTS

Vasilios Vaios[1], Panagiotis Georgianos[1], Georgia Vareta[1], Evaggelia Geropoulou[1], Evangelia Ntounousi[2], Aikaterini Papagianni[3], Pantelis Zebekakis[1], Vassilios Liakopoulos[1]

[1]AHEPA Hospital, Aristotle University of Thessaloniki, Peritoneal Dialysis Unit, 1st Department of Medicine, Thessaloniki, Greece, [2]School of Medicine, University of Ioannina, Department of Nephrology, Ioannina, Greece and [3]Hippokration Hospital, Aristotle University of Thessaloniki, Department of Nephrology, Thessaloniki, Greece

Background and Aims: Among peritoneal dialysis (PD) patients, aortic blood pressure (BP) and arterial stiffness indices are independent predictors of cardiovascular morbidity and mortality. Previous studies in PD patients recorded these parameters only in the office. The present study provides comparisons between office and ambulatory recordings of these parameters and explores the association of demographic, clinical and hemodynamic variables with high arterial stiffness.

Method: In 81 stable PD patients (mean age: 61.3±16.3 years; male gender: 64.2%), brachial and aortic BP, heart rate-adjusted augmentation index (AIx75) and pulse wave velocity (PWV) were recorded after a 5-minute seated rest in the office using the oscillometric device Mobil-O-Graph (IEM, Stolberg, Germany). Subsequently, all patients underwent ambulatory recording of these parameters with the same device for 24 hours. Logistic regression analysis was performed to identify factors independently associated with high ambulatory PWV.

Results: As expected, office brachial systolic BP (SBP) was higher than 24-hour brachial SBP (134.2±22.7 vs. 129.0±18.0 mmHg, P<0.01). Similarly, office aortic SBP was higher than 24-hour aortic SBP (122.5±20.1 vs. 117.1±16.1 mmHg, P=0.001). By contrast, office AIx75 did not differ from 24-hour AIx75 (23.4%±11.7% vs. 23.9%±9.3%, P=0.602), whereas office PWV was only slightly higher than 24-hour PWV (9.2±2.3 vs. 9.0±2.2m/sec, P=0.001). Participants stratified in the high PWV tertile were older, had higher 24-hour mean BP (MBP) and had more commonly history of diabetes, dyslipidemia and coronary heart disease. In multivariate analysis, older age (OR: 4.23; 95% CI: 1.59-11.24) and higher 24-hour MBP (OR: 1.31; 95% CI: 1.03-1.67) were the only independent determinants of high PWV.

Conclusion: Among patients on PD, brachial and central aortic pressures recorded in the office were higher than 24-hour ambulatory pressures, whereas this variation between office and ambulatory recordings was diminished for AIx75 and PWV. Future studies are warranted to explore the prognostic significance of these parameters in the PD population.

P1190 OXIDATIVE STRESS AND INFLAMMATION IN PERITONEAL DIALYSIS: DANGEROUS AND TO BE SOLVED

Georgie Innico[1], Giovanni Bertoldi[1], Marianna Alessi[1], Elisa Pagnin[1], Monica Simeone[1], Gresa Baboci[1], Luciana Bonfante[1], Lorenzo Calò[1]

[1]University of Padova, Department of Medicine, Nephrology, Dialysis and Transplantation Unit, Padova, Italy

Background and Aims: Cardiovascular disease is the leading cause of excess mortality in chronic kidney disease (CKD) and dialysis patients with oxidative stress (OxSt) and inflammation playing a pivotal role, as non-traditional risk factors and OxSt and inflammation have been shown to increase in peritoneal dialysis. Rho kinase (ROCK) activation is deeply involved in the induction of OxSt and inflammation and is closely linked to cardiovascular-renal remodeling. We aimed to evaluate in peritoneal dialysis patients with a molecular biology approach OxSt, in terms of phosphorylation state of MYPT-1 (marker of ROCK activity), the protein expression of $p22^{phox}$ (subunit of NADPH oxidase, essential for the generation of ROS), and inflammation state, in terms of acute-phase proteins level (Interleukin 6 (IL-6), ultra-sensitive C-reactive protein (US-CRP), Ferritin, Albumin and Transferrin).

Method: 9 male ESRD patients (39-81 years old) were enrolled and analyzed before (baseline) and after three and six months of peritoneal dialysis treatment (CAPD 7 patients, APD 2 patients). Mononuclear cells (PBMCs) MYPT-1 phosphorylation state and $p22^{phox}$ protein expression were determined by Western Blot. Specific acute-phase proteins as IL-6, US-CRP, Ferritin, Albumin and Transferrin were assessed through blood chemistry tests.

Results: MYPT-1 phosphorylation was increased after six months of treatment with peritoneal dialysis compared with three months and predialysis (1.03 ± 0.07 vs 1.02 ± 0.04 vs 1.57 ± 0.16 d.u., $p<0.0001$). $p22^{phox}$ protein expression (0.72 ± 0.05 vs 0.73 ± 0.10 vs 1.28 ± 0.12 d.u., $p<0.0001$) and ferritin level (101.4 ± 15.3 vs 173.6 ± 11.5 vs 189.0 ± 20.3 µg/l, $p=0.002$) increased as well. Albumin was decreased after six months of peritoneal dialysis treatment compared with three months and predialysis (43.38 ± 0.10 vs 40.00 ± 1.59 vs 36.46 ± 1.43 g/l, $p=0.007$). IL-6 and US-CRP remained unchanged at a high level.

Conclusion: The increase of OxSt and inflammation during peritoneal dialysis is confirmed also at molecular biology level and may lead in the medium-long term to dangerous consequences. The necessary improvement of OxSt status in peritoneal dialysis needs a multitarget approach. It might include the use of neutral pH, low glucose degradation products, low lactate and iso-osmolar peritoneal dialysis solutions, strict glycemic control, optimal volume management and, likely, a supplementation with antioxidants as N-acetylcysteine.

P1191 PREDICTORS FOR QUALITY OF LIFE IN AUTOMATED AND CONTINOUS AMBULATORY PERITONEAL DIALYSIS

Luisa Pereira[1], Luís Leite de Sousa[2], Anabela Malho Guedes[1], Patricia Matias[2], Patricia Branco[2], Ana Rita Martins[2]

[1]Hospital de Faro, Centro Hospitalar Universitário do Algarve, Nephrology, Faro, Portugal and [2]Hospital de Santa Cruz, Centro Hospitalar Lisboa Ocidental, Nephrology, Lisboa, Portugal

Background and Aims: Quality of life (QoL) influences the morbidity and mortality in End-Stage Kidney Disease (ESKD) patients on dialysis and is increasingly well recognized as an important measure of treatment outcome. Identification of the factors that influence QoL in patients receiving peritoneal dialysis (PD) can help improving their management. This study was carried out to determine the clinical, biochemical and psychological predictors for QoL scores among ESKD patients on automated (APD) and continuous (CAPD) ambulatory peritoneal dialysis.

Methods: This was a cross-sectional study which included stable patients from two Peritoneal Dialysis Units. We excluded patients who weren't able to understand the questionnaires, the language and the ones who had hospitalar admissions in the previous 3 months. Quality of life parameters were assessed by self-administered EuroQol questionnaire (EQ-5D-5L) - higher scores indicate better QoL; Pittsburg Sleep Quality Index (PSQI) was used for assessing sleep quality and evaluation of each patient's depressive symptoms was made with Patient Health Questionnaire (PHQ-9). In all patients, demographic variables, Charlson Comorbidity Index (CCI), clinical and laboratory parameters were recorded and analyzed. Descriptive statistics was performed. Groups were compared using independent t-test for comparison of continuous variables and Chi square test for categorical variables. In order to evaluate relationship between QoL and the other variables multivariate logistic regression and Pearson bivariate analysis were used.

Results: The study included 70 patients (male/female 44/26; mean age 55.3±14.6 years; APD/CAPD 25/45; PD duration 28±24.2months). Mean CCI was 4.59±1.86; 31.4% of the patients were diabetic, 12.9% presented cardiac insufficiency and 20% had cardiovascular disease. We found that EuroQoL score was significantly associated with Pittsburg Sleep Quality Index (p=0.001), depression score (PHQ-9) ($p<0.001$), nPCR (p=0.006), duration of PD (p=0.017) and patients' perception of their own well-being (P=0.002). Comparing EuroQol Score between genders, males had a significant lower score (p=0.011). We found no association with N-terminal pro-brain natriuretic peptide (NTproBNP), overhydration, residual renal function, weekly KT/V and hospital admissions. There were no significant differences regarding EuroQol score between the two modalities of peritoneal dialysis (APD and CAPD patients) or in patients who were PD first.

We also found that the patients with lower EuroQol Score were significantly more depressed ($p<0.001$) and had poorer sleep quality ($p<0.001$). Sleep quality wasn't associated with hypertension or cardiovascular disease. There was no significant difference concerning to age and CCI between the group of patients with worst QoL (EuroQol<0.212) and better QoL (EuroQol Score>0.961).

Plus, there were no significant differences in the EuroQol score in patients with cardiovascular disease.

In a multivariate analysis (linear regression) there was a significant association between EuroQol and depression (B=-0.346; IC 95% -0.022 to -0.004; p=0.004), nPCR (B=-0.417; IC 95% -0.254 to -0.072; p=0.001) and duration of PD (B=-0.351; IC 95% -0.004 to-0.001; p=0,004).

Conclusion: Poor sleep quality, presence of depression and lower nPCR are associated with poorer quality of life. In order to improve life quality in PD patients, quality of sleep, depression and nutritional status should be serially evaluated and given appropriate treatment when required.

P1192 **METABOLIC SYNDROME IN PATIENTS UNDERGOING PERITONEAL DIALYSIS (PD): A SINGLE CENTER EXPERIENCE**

Oto Di Gruttola[1], Giuseppe Paribello[1], Immacolata Gaia Paduano[1], Silvia Migliaccio[1], Gennaro Argentino[2], Giuseppina Sannino[1], Domenico Russo[1]
[1]AOU FEDERICO II NAPOLI, NEPHROLOGY, NAPLES, Italy and [2]ASL NA1CENTRO "OSPEDALE DEL MARE", NEPHROLOGY, NAPLES, Italy

Background and Aims: Metabolic syndrome (MS) is a set of alterations represents a cluster of risk factors that increase the probability of causing cardiovascular (CV) events by three times. The aim of our study was to analyze the prevalence of MS in patients with Chronic Renal Failure undergoing replacement treatment by peritoneal dialysis afferent to our center.

Method: We retrospectively studied 117 patients in PD (2015-2019 census period). The characteristics are reassumed in tab1. We assessed the prevalence and impact of MS considering hard outcome: death for IMA and cerebral death. Patients with at least 3 of the following diagnostic criteria (CD) were considered affected by MS: waist circumference> 102 cm in men or > 88 cm in women, high blood pressure (PA> 130/85 mmHg or under pharmacological treatment), HDL levels <40 mg/dl in men or <50 mg/dl in women, triglycerides> 150 mg/dl and fasting glucose> 100 mg/dl or under pharmacological treatment.

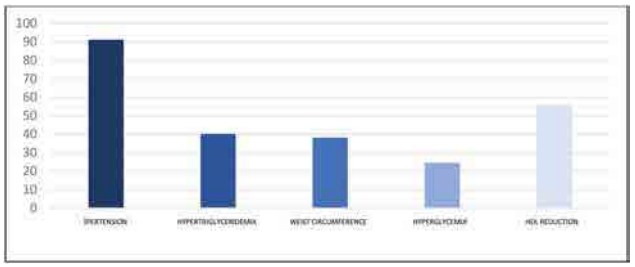
Results: The prevalence of MS in our cohort is 46% (54 patients), the patients who have 2 CD are 29% (34 patients), those with only 1 CD 25% (29 patients), no patient had 0 CD. Arterial hypertension represents the most represented risk factor (RF) (91.1%) in agreement with the literature and with the Framingham Offspring Study (non-dialysis patients). The others RF are distributed in this way: reduced HDL (55.8%), hypertriglyceridemia (40.2%), high waist circumference (38.2%), fasting hyperglycaemia (24.5%) (graph 1). Among the 54 patients with MS, 12 CV events occurred during the observation period, while among the 34 patients with two CD, 8 CV events occurred. Among the 29 patients with only 1 CD there was 1 death attributable to CV causes (graph 2). From these data it is clear that MS is a risk factor for CV events according to the literature. It is interesting to observe that comparing the group of patients with 2 CD and with 1 CD, it shows that the presence of 2 CD is a sufficient risk factor to increase the probability of CV events (OR = 8.6 & p <0.05).

Conclusion: The prevalence of MS in patients receiving peritoneal dialysis is elevated with a negative impact on the risk of CV events. At the same time, our data shows the importance of assessing each individual risk factor regardless of the presence of full-blown MS. In particular, we observed that the presence of 2 CD is sufficient to predispose CV events. This shows that timely treatment of RF, even in the absence of full-blown MS, could favor the reduction of the risk of CV events in patients in DP

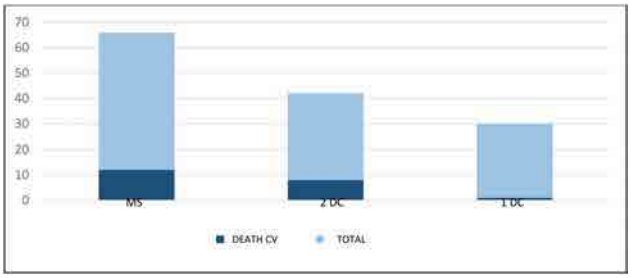
Tab.1 Clinical characteristics of study population

MAN/WOMAN	74/43 (63%/37%)
MIDDLE AGE (years)	59,4 ± 8,3
DIALYSIS TIME (months)	53,2 ± 28,4
DIALYSIS METHOD (CAPD/APD)	54/63 (46%/54%)

CAPD: continuous ambulary peritoneal dialysis
APD: automated peritoneal dialysis



Graf.1 – distribution of risk factors in our population (% population)



Graf.2 – number of patients and CV events in the three groups.

P1193 URGENT X EARLY START PERITONEAL DIALYSIS: PATIENTS´ PROFILE AND OUTCOMES

Viviane Calice-Siva[1,2], Helen Ferreira[1], Bruna Tonial[2], Izabel Ribeiro[2], Pedro Daudt[2], FABIANA NERBASS[1]

[1]Fundação Pró-Rim, JOINVILLE, and [2]UNIVILLE, School of Medicine, Joinville, Brazil

Background and Aims: In the last ten years, peritoneal dialysis (PD) has been considered a safe option to start renal replacement therapy (RRT) in end-stage renal disease patients in need to start dialysis urgently. The definition applied to the Urgent Start PD (US-PD) varies widely worldwide. Recently, it was proposed that US-PD definition should be according to patients' necessity of starting dialysis, considering "urgent start" when PD started up to 72 hours of catheter placement and "early start" PD when it is starts between 3 and 14 days after catheter placement. Considering this new definition, we aimed to compare demographical and clinical characteristics of patients´that started PD therapy as urgent and early starts as well as 30-day complications, 6-month hospitalization and dropout rate.

Method: All adult patients that started PD therapy up to 14 days after catheter insertion in our institution between October 2016 and February 2019 were included in the analyses. Patients were placed on urgent-start (US-PD) group if therapy started until 72-h after catheter insertion or early-start (ES-PD) group if PD initiated between 3 and 14 days. Dialysis records were reviewed to obtain clinical and demographic data, fill volume prescribed for the first PD session, 30-days complications (leakage, bleeding, catheter tip migration and peritonitis) and 6-month hospitalization and dropout rate.

Results: In our study, 72 patients were analyzed (US-PD=52, ES-PD=20), mean age was 53.2 ± 15.2 years old. No differences between US-PD and ES-PD regarding demographic characteristics, 30-day complications and 6-month hospitalization and dropout events were found. The most frequent short-term complication in patients who started PD urgently was leakage (US-PD 6 (11%) x ES-PD 2(10%) patients). The most common cause of patient's dropout was transfer to HD.Only patients from the US-PD group needed to switch to that modality (5 (10%)).

Conclusion: Almost three-quarters of our sample started PD less than 72 hours after catheter insertion. The lack of difference in the measured outcomes compared to patients that had therapy initiated after this period encourages the use of PD when urgent dialysis is needed.

P1194 RISK FACTORS FOR CARDIOVASCULAR DEATH IN NON-DIABETIC PERITONEAL DIALYSIS PATIENTS

Andreea Gabriella Andronesi[1,2], Luminita Iliuta[3], Cristina Cristache[1], Bogdan Marian Sorohan[2], Gabriela Elena Lupusoru[2], Danut Andronesi[4], Mircea Lupusoru[5], Bogdan Obrisca[2], Gener Ismail[1,2]

[1]Fundeni Clinical Institute, Nephrology Department, Bucharest, Romania, [2]Carol Davila University of Medicine and Pharmacy, Nephrology Department, Bucharest, Romania, [3]Carol Davila University of Medicine and Pharmacy, Department of Biostatistics, Marketing and Medical Technology, Bucharest, Romania, [4]Fundeni Clinical Institute, General Surgery and Liver Transplant Department, Bucharest, Romania and [5]Carol Davila University of Medicine and Pharmacy, Physiology department, Bucharest, Romania

Background and Aims: Chronic kidney disease and especially end stage renal disease are important public health issues with increasing incidence and significant economic burden. Despite advances in peritoneal dialysis (PD), mortality is still high mostly because of cardiovascular morbidity and mortality. The aim of the present study was to identify prognostic risk factors for cardiovascular death in non-diabetic PD patients.

Method: We performed a prospective study in which we included non-diabetic patients in stable PD programme for at least 6 months. Clinical, biological, heart and carotid ultrasound and arterial stiffness (evaluated through applanation tonometry) parameters were analysed. Independent risk factors for cardiovascular death were identified by logistic regression using *IBM SPSS ver. 20.0.*

Results: We included 246 consecutive non-diabetic patients (118F, 128M), mean age 56.3 + 15.7 years (20-85). Mean follow up was 6.5$\pm$1.1 years. 36 patients (14.6%) died because of cardiovascular reasons - sudden cardiac death 13 patients, acute coronary syndrome 8 patients, ischemic stroke 8 patients, and heart failure 7 patients. Individuals with cardiovascular death were significantly older (64.6$\pm$14.2 *vs* 54.7$\pm$15.5 years, p=0.01), with signs of malnutrition, inflammation and associated anemia - significantly lower total cholesterol (150.2$\pm$43.0 *vs* 194.3$\pm$58.2 mg/dl, p=0.002), serum albumin (2.9$\pm$0.4 *vs* 3.5$\pm$0.7 g/dl, p=0.002) and hemoglobin (9.7$\pm$1.1 *vs* 10.7$\pm$1.4 g/dl, p=0.007) and significantly higher serum fibrinogen (568.7$\pm$121.3 *vs* 509.8$\pm$115.0 mg/dl, p=0.04) and C-reactive protein (6.7$\pm$1.2 *vs* 9.5$\pm$0.9 mg/l, p=0.02). In univariate analysis risk for cardiovascular death was higher in patients with renal hypertensive disease (OR 4.0, 95%CI 1.4-11.5, p=0.01), iPTH serum level <150 pg/ml (OR 6.6, 95%CI: 2.3-18.9, p<0.001), left ventricular hypertrophy (OR 10.6, 95%CI 2.3-18.9, p=0.001) and diastolic dysfunction (OR 4.0, 95%CI 1.2-14.9, p=0.02). Compared to patients with an iPTH between 150-300 pg/ml, both patients with lower iPTH and also higher iPTH had an increased risk for cardiovascular death (OR=1.6, 95%CI: 1.2-2.0; p<0.001 for iPTH<150 pg/ml, and OR =1.2, 95%CI:1.04-1.34; p=0.01 for iPTH<300 pg/ml). Patients with cardiovascular death had signs of subclinic atherosclerosis- intima-media thickness at carotid level >0.9 mm (OR 4.3, 95%CI 1.1-16.3, p=0.02) and higher pulse wave velocity as a sign of increased arterial stiffness (11.9$\pm$2.5 *vs* 8.6$\pm$2.6 m/s, p=0.04). After adjusting for potential confounders, independent predictive factors for cardiovascular death were male gender, calcium-phosphate product>55 mg^2/dl^2, iPTH<150 pg/ml and peripheral arterial disease (Table 1).

Conclusion: We found an increased risk for cardiovascular death in non-diabetic PD patients, mostly because of sudden cardiac death. Malnutrition, inflammation, but especially abnormal mineral metabolism (both increased calcium-phosphate product and low bone turnover) were identified as risk factors for cardiovascular death and are potentially treatable risk factors to improve cardiovascular outcome in PD patients. A better understanding of pathogenesis and risk factors for cardiovascular death in PD may help improve patients' management and thus their long-term survival.

P1195

ASSESSMENT OF BODY FLUID VOLUME USING THE BIOIMPEDANCE METHOD IN PERITONEAL DIALYSIS PATIENTS

Misaki Moriishi[1], Hideki Kawanishi[2], Sadanori Shintaku[2], Shinichiro Tsuchiya[1]

[1]Tsuchiya general hospital, internal medicine, Hiroshima, Japan and [2]Tsuchiya general hospital, surgery, Hiroshima, Japan

Background and Aims: ppropriate maintenance of body fluid balance in peritoneal dialysis (PD) patients is important for the amelioration of cardiovascular complications and prognosis. In recent years, the usefulness of body fluid measurement with the bioimpedance method in PD patients has been reported. Meanwhile, peritoneal permeability plays an important role in maintaining body fluid balance in PD patients. In the present study, we examined the correlation between peritoneal permeability and body fluid volume in PD patients.

Method: A total of 58 patients who were undergoing PD at our hospital (42 men and 16 women; mean age, 68 $\pm$ 16.2 years; mean dialysis history, 63.5 $\pm$ 144.9 months; 25 DM and 35 non-DM patients). Overhydration (OH), total body water (TBW) volume, extracellular water (ECW) volume, and lean tissue mass (LTM) were measured using a body composition analyzer (BCM Fresenius Medical Care Japan). At the same time, peritoneal permeability was measured with fast peritoneal equilibration test to determine the dialysate-to-plasma ratio for creatinine (D/P-Cr), and its correlations with sex, age, age at the time of introduction of dialysis, dialysis history, diabetes history, brain natriuretic peptide (BNP) level, high-sensitivity troponin I (hsTnI) level, blood pressure, body weight, residual kidney function, and ultrafiltration were examined.

Results: The mean OH was 2.53 $\pm$ 2.44 L, and 8 patients (13.8%) had an OH of $\leq$1.1 L. The results of the multivariate analysis revealed that OH positively correlated with the presence or absence of diabetes, ultrafiltration, D/P-Cr, BNP level, hsTnI level, TBW, and ECW, but showed no correlation with sex, dialysis history, age, age at the time of introduction of dialysis, residual renal function, or LTM. Furthermore, the subjects were assigned to D/P-Cr $\geq$ 0.65 and $\leq$0.65 groups. In the former, OH correlated with diabetes and male sex by being negatively correlated with age and age at the time of introduction of dialysis and positively correlated with BNP level, hsTnI level, TBW, and ECW. However, in the D/P-Cr $\leq$ 0.65 group, OH positively correlated with BNP level and ECW.

Conclusion: Our results suggest that youth, complications of DM, and men are at risk for fluid overload in PD patients with increased peritoneal permeability.

P1196 AN INIHIBITOR OF KRUPPEL-LIKE FACTOR 5 SUPPRESSES PERITONEAL FIBROSIS IN MICE

Kumiko Muta[1], Yuka Nakazawa[2], Yoko Obata[1], Hiro Inoue[1], Kenta Torigoe[1], Tomoya Nishino[1]

[1]Nagasaki University Hospital, Department of Nephrology, Nagasaki city, Japan and [2]Hokusyo Central Hospital, Department of Nephrology, Sasebo city, Japan

Background and Aims: We presented previously that Am80, a synthetic retinoic acid receptor α specific agonist, inhibited the expression of Krüppel-like transcription factor 5 (KLF5) and reduced peritoneal fibrosis in mice. Now, we examined further detail about the mechanism to inhibit peritoneal fibrosis.

Method: Peritoneal fibrosis was induced by intraperitoneal injection of chlorhexidine gluconate (CG) into peritoneal cavity of ICR mice. Am80 was administered orally for every day from the start of CG injection. After 3 weeks of treatment, peritoneal tissues were examined using serial sections by immunohistochemistry to identify what kind of cells expressed KLF5. We also examined the effect of Am80 to inhibit peritoneal fibrosis in vitro.

Results: While KLF5 was expressed in the thickened submesothelial area of CG injected mice, Am80 treatment reduced KLF5 expression and remarkably attenuated peritoneal thickening. The numbers of transforming growth factor β positive cells, α-smooth muscle actin (αSMA) or F4/80 positive cells were significantly decreased in Am80 treated group. KLF5 was expressed in αSMA, F4/80 or CD31 positive cells.

Conclusion: These results indicate the KLF5 might not only associate phenotypical differentiation from fibroblasts to myofibroblasts but also regulate inflammatory responses and angiogenesis in peritoneal fibrosis model. Am80 can suppress peritoneal fibrosis through inhibiting these mechanisms. In vitro experiments are ongoing.

P1197 ASSISTED APD IN ITALY: TRENTO EXPERIENCE.

Elisabetta Devoti[1], Chiara Venturelli[1], Alessandro Laudon[1], Giuliano Brunori[1]

[1]*Azienda Provinciale per i Servizi Sanitari - Provincia Autonoma di Trento, Nefrologia, Trento, Italy*

Background and Aims: End-stage renal disease (ESRD) is common in elderly and fragile patients with several comorbidities. Dialysis (Hemodialysis-HD or Peritoneal Dialysis-PD) is often required. The choice between HD or PD is sometimes not easy. PD prevalence is significantly lower than HD prevalence in old and fragile patients because they are less likely to complete PD assessment, and due to stress over performing self-therapy. In the last years, in order to overcome these problems, assisted PD programs have spread out in several countries.

Method: Since 2008 in Trento Province (area of 541.399 people in the North East of Italy) we developed a program for elderly non-self sufficient patients requiring dialysis in nursing home. Admission criteria in nursing home were: age>65 years, living in the province, PD therapy, non-self patient, no acute complications, no home caregivers. This patient had a priority access to nursing home. We selected HomeChoice Baxter APD as PD technique. Our nurses gave specific training of 6 hours to nursing home nurses. The patients were on APD during the night. Every 45 days patients had a clinical visit by nephrologists and hospital PD nurses, with a particular emphasis on clinical data and dialysis performances.

Results: From 1.1.2008 to 12.31.2018 we enrolled 36 patients (16 male and 20 female) in a population of 226 PD incident patient, age (M±DS) at PD start was 78 ± 7.3 years (range 65-91); break-in was 27 ± 20.4 days and time in PD was 374 ± 347 days (range 15-1257). The cumulative incidence of peritonitis was 1/75-patient/month. During these eleven-year period we trained 19 nursing home nurses.

Conclusion: Assisted APD in nursing home could be an appropriate therapy choice for non-self sufficient elderly patients requiring renal replacement therapy. These option is safe for patients and could increase PD incidence.

P1198 CATHETER-RELATED INFECTIONS DUE TO SERRATIA SPECIES IN PATIENTS RECEIVING PERITONEAL DIALYSIS

Christy Au[1], Jasper Chan[2], Terence Yip[3], Desmond Yap[4], Daniel Tak Mao Chan[5]

[1]Pamela Youde Nethersole Eastern Hospital, Department of Medicine, Hong Kong, P.R. China, [2]Queen Mary Hospital, The University of Hong Kong, Hong Kong, Department of Microbiology, Hong Kong, P.R. China, [3]Tung Wah Hospital, Department of Medicine, Hong Kong, P.R. China, [4]Queen Mary Hospital, The University of Hong Kong, Department of Medicine, Hong Kong, P.R. China and [5] Queen Mary Hospital, The University of Hong Kong, Department of Medicine, Hong Kong, P.R. China

Background and Aims: *Serratia* species can cause catheter-related infections in peritoneal dialysis (PD) patients but data on this clinical entity remains limited. This study aims to investigate the clinical characteristics, antibiotics susceptibility/resistance profiles and treatment outcomes of *Serratia* catheter-related infections in PD patients.

Method: We retrospectively reviewed all PD patients who were followed up at Queen Mary Hospital and Tung Wah Hospital, Hong Kong between 2004 to 2017. Patients with *Serratia* exit site infection (ESI) or peritonitis were included for analysis.

Results: One hundred and seventy-three patients with *Serratia* catheter-related infections were included. 161 patients had ESI, of which 10 (6.2%) progressed to tunnel tract involvement and 11 (6.8%) developed PD peritonitis. Skin abnormalities surrounding the exit site were present in 58 patients (36%), and 40 patients (24.8%) were hospitalized within 1 month prior to *Serratia* ESI. 142 patients (88.2%) with ESI responded to medical therapy alone, and repeat ESI occurred in 56 patients (34.7%) at a median of 12 months. Twenty-two patients had *Serratia* peritonitis, which accounted for 1% of peritonitis during the study period. Concomitant intra-abdominal pathologies were detected in 12 patients (54.5%). Ten patients (45.5%) responded to medical treatment while the remaining 12 (54.5%) required catheter removal. Nine patients (36.4%) failed PD resumption and switched to chronic haemodialysis. Repeat peritonitis occurred in two patients at 2 months and 3 years after the initial episode respectively. While *Serratia* species in PD patients are generally susceptible to aminoglycosides, carboxy-/ureido-penicillins and carbapenems, they exhibit substantial rates of resistance to ampicillin, and 1st- and 2nd-generation cephalosporins.

Conclusion: *Serratia* ESI responds favourably to medical therapy and seldom progresses to tunnel tract infection or peritonitis. *Serratia* peritonitis is associated with considerable risk of catheter loss and peritoneal failure.

P1199 **THE IMPORTANCE OF DETERMINING ALPHA-2-MACROGLOBULIN CONCENTRATITON IN PATIENTS ON PERITONEAL DIALYSIS**

Marko Baralic[1], Ana Bontic[2], Jelena Pavlovic[2], Mirjana Lausevic[2], Selena Gajic[2], Milica Kravljaca[2], Voin Brkovic[2], Marija Milinkovic[3], Vidna Karadzic[3], Aleksandra Kezic[3], Milan Radovic'[3]

[1]Belgrade, Clinical centre of Serbia, Nephrology, Belgrade, Serbia and [2]Belgrade, Belgrade, Clinical centre of Serbia Nephrology, Belgrade, Serbia

Background and Aims: To determine the concentration of Alpha-2-macroglobulin (α2M) and its activity in patients treated with peritoneal dialysis (PD) and healthy subjects (H).

Method: a cross-sectional study included 50 PD and 30 H, in which the concentration of active α2M molecules was determined. The measurement is based on covalent binding of α2M and trypsin and zymography with gelatin incorporated into the electrophoretic gel.

Results: The intensity of proteolytic bands seen with native α2M was analyzed in relation to the concentration of α2M in patients with PD with less and / or more than three peritonitis. Linear dependence was only visible in the case of the upper range, which originates from the intact α2M-trypsin complex. The highest coefficient of variation is calculated for the smallest α2M concentration (4.2%). The signal intensities originating from α2M (H) were higher compared to PD, with the PD group being lower in patients with higher peritonitis, and the difference was more pronounced as concentration increased, resulting in a lower slope of dependence. The proposed method can reliably measure the amount of α2M originating in a group H, while the quantification of α2M in PD groups that may have structurally altered α2M can be seen more for condition estimation than for accurate measurements. The zymographic test in this experiment allows us to investigate the relationship of the concentration, structure and function of α2M in different pathological conditions, as well as in the presence of modifying agents that can accompany them.

Conclusion: A simple method for the determination of α2M concentration and function by zymography has been developed, which can be used to examine residual α2M activity after partial denaturation or structural modification due to disease.

P1200 PERITONEAL PROTEIN LOSSES: WHAT DO WE MEAN

Anabela Malho Guedes[1,2], Ana Domingos[1], Roberto Calças[1], Ana Silva[1], Idalécio Bernardo[1], Pedro Neves[1], Anabela Rodrigues[2,3]

[1]Centro Hospitalar Universitario do Algarve, Portugal, [2]Instituto de Ciencias Biomedicas Abel Salazar, Portugal and [3]Centro Hospitalar Universitário do Porto, Portugal

Background and Aims: The report of peritoneal protein loss should be related with a timely collection (24-hour measurement or 4-hour PET assessment) or concentration. Standardized and reproducible estimation of peritoneal protein transport is obtained during PET. The 24-hour measurements estimate the real amount of PPL, but may be affected by other factors unrelated to the prognosis of PD patients, as inconsistencies in collection and management of the samples. Overall, PET protein loss quantification may be a more specific marker of peritoneal large-pore dysfunction and is seemingly more convenient than 24-hour measurements. The aim of this study was to compare the results of both sampling methods.

Method: A total of 144 adult incident PD patients were included. A standard peritoneal equilibration test, 24-hour urine and dialysate collection, and multifrequency bioimpedance analysis were performed. Independent-samples t test and Pearson correlation coefficient were performed to evaluate relevant clinical associations.

Results: Statistically significant univariable relationships for 24h PPL were found for continuous ambulatory PD technique (CAPD) and, with a correlation coefficient >0.20, for pulse pressure, 4-hour dialysate/plasma creatinine and extracellular water/total body water. Studying 240 min PPL, only with 4-hour dialysate/plasma creatinine, creatinine clearance and bicarbonate levels were statistically significant. In both samples there was no significant association with age, gender, type of effluent (biocompatible solutions or lactate plus bicarbonate comparing with bicarbonate), comorbidity Charlson Index, or presence of diabetes. Correlation between 240 min PPL and 24h PPL ensues, but it is not strong ($p<0.001$; $r=0.365$).

Conclusion: The weak correlation between 24h and 240 minutes show that these two measurements should not be considered equivalent. Measurements of a 24h sample might be more close to patients' clinical status and prognosis, despite more frequent sampling errors. PET protein loss quantification should be regarded as a marker of peritoneal large-pore dysfunction.

P1201 **THE AGING OF THE IMMUNE SYSTEM AND FRAGILITY: TWO FEATURES IN PERITONEAL DIALYSIS AND END-STAGE RENAL DISEASE PATIENTS.**

Paula Jara Caro Espada[1], Noemi Ceprian Costoso[2], CLAUDIA YUSTE[1], Gemma Valero[2], Maria Fernandez-Vidal[1], Nadia Seroukh[2], Enrique Morales[1], Carmen Vida[3], Julia Carracedo[2]

[1]University Hospital 12 de Octubre, Nephrology, Madrid, Spain, [2]UCM School of Biological Sciences, Genetica, Fisiología y Microbiología, Madrid, Spain and [3]Facultad de Medicina, Biología de Sistemas, Alcalá de Henares, Spain

Background and Aims: Chronic kidney disease (CKD) is associated with premature immune aging and increased inflammatory activity leading into endothelial damage and macrophage senescence (CD14+CD16+).

Objective. To evaluate the influence of CKD in senescent immune cells, and its relationship with fragility in patients with nondialysis CKD (ND-CKD) and Peritoneal Dialysis (PD).

Method: A descriptive transversal study analysing lymphocyte absolute counts and subpopulations in 74 CKD patients (36 DP, 38 ND-CKD) compared with 10 healthy subjects (HS). We also assessed immunoglobulin levels, C3 and C4 fragment complement, Edmonton fragility score and the percentage of proinflammatory blood monocytes with the CD14+CD16+ phenotype.

Results: PD patients presented more absolute lymphopenia compared with LCC and HS (PD 1194,2, 1589 ND-CKD and 1802 HS; $p < 0{,}001$, respectively). This lymphopenia is also maintained in CD3, CD4, CD8 and NK cells. Lower CD4 lymphocytes levels were significantly correlated with higher fragility and incidence of peripheral vascular disease in uremic patients. Senescent macrophage was correlated with CD3 and CD4 lymphocytes all the cohorts (ND-CKD, PD and HS).

Conclusion: PD patients presented changes in immune system compared with healthy population, that could explain accelerated senescence. Accelerated senescence is associated with more fragility and endothelial damage. There are necessary more studies to identify the role premature aging in ND-CKD and to establish the differences between renal replacement modalities.

P1202 EPIDEMIOLOGICAL AND EVOLUTIONARY PROFILE OF MECHANICAL COMPLICATIONS IN PERITONEAL DIALYSIS

Safa Fattoum[1], Barbouch Samia[1], Hajji Mariem[1], Braiek Nessrine[1], Mesbahi Tasnim[1], Gorsane Imen[1], Harzallah Amel[1], Ben Hmida Fathi[1,1,2], Ounissi Mondher[1], Ben Abdallah Taieb[1]

[1]Charles Nicolles Hospital, Internal Medecine, Tunis, Tunisia and [2]Charles Nicolles Hospital, Kidney pathology laboratory lrsp001, Tunis, Tunisia

Background and Aims: The success of peritoneal dialysis (PD) depends on a functional and sustainable peritoneal access. The mechanical complications of PD (MCPD) are a major cause of technique failure. The aim of the study was to determine the different types of these complications and to define their prevalence.

Method: It's a retrospective study conducted in our PD unit in December 2019. We collected all data concerning clinical characteristics of all patients currently in PD, as well as incidence, type, outcome of MCPD.

Results: There were 90 patients with an average age of 45 years (extremes: 20.5 years and 80.6 years). The sex ratio is 1.25. Fourteen were diabetic (15.5%). All patients were on Automated PD (APD) except one on Continuous Ambulatory PD (CAPD). The average duration of PD was 40.5 months. The average body mass index (BMI) was 23,8 kg/m? All patients had a Tenckhoff 2 cuff catheter placed by a mini laparotomy.

Twenty six episodes of MCPD were noted in 17 patients (18,8%).The complications noted were early dialysate leakage in 2 patients(2,2%) spontaneously resolving before the beginning of the training, catheter obstruction in 8 patients(3 patients presented 3 episodes of obstruction each) (8,8%), umbilical hernia in 3 patients (3,3%), 2 patients had displaced repositioned catheter (2,2%). Five patients (5,5%) presented continued inflammation in the exit-site of the catheter: the outermost of the two Dacron cuffs spontaneously extruded in 2 patients, and was surgically extracted in 3 patients. Cuff externalization resolved the inflammation in all patients.

Conclusion: Successful access for PD placed by a trained operator is crucial in purpose to avoid MCPD. These complications must be treated on time to avoid technique failure.

P1203 **DEGREE OF FUNCTIONAL DEPENDENCE IN PATIENT IN SUBSTITUTE RENAL TREATMENT IN HGUCR**

MARIA PAZ CASTRO FERNÁNDEZ[1], LUIS GUILLERMO PICCONE SAPONARA[1], Agustin Carreno[1], Diego Siedel[1], NANCY GIOVANNA URIBE HEREDIA[2], CASIMIRO VALLE DOMINGUEZ[1], ELIANA OLAZO GUTIERREZ[1], PATRICIA SANCHEZ ESCUDERO[1], PAOLA VILLABON OCHOA[1], MARIA DEL CARMEN VOZMEDIANO POYATOS[1]

[1]Ciudad Real, Nephrology, Ciudad Real, Spain and [2]Guadalajara, Cardiology, Guadalajara, Spain

Background and Aims: Elderly patients and comorbidity present more frequently deterioration of their cognitive and / or functional capacity, and consequently worse quality of life related to health and the need for help to perform their basic activities. It has been described in the literature that peritoneal dialysis (PD) is a protective factor in the patient's survival against hemodialysis (HD). Quality of life is an important parameter in patients undergoing renal replacement therapy, which influences the choice of dialysis modality. We analyzed and compared the degree of functional dependence of patients on PD versus HD.

Method: Descriptive and cross-sectional study. A total of 84 patients belonging to the General University Hospital of Ciudad Real were included. Demographic variables (age, sex), associated comorbidity, etiology of CKD, among others, were collected. To assess the degree of dependence, the Barthel index and Lawton and Brody were performed. Statistical analysis with SPSS 25.0. Categorical variables are expressed as percentages and have been compared using the Chi2 test. Quantitative variables are expressed as mean +/- standard deviation, and the T-student was used to compare them. Statistical significance for a value of $p < 0.05$.

Results: Of the 84 patients, 40.5% received PD and 59.5% HD. 60.7% were male and 39.3% female, with an average age of 60.90 years. 75% were hypertensive, 38.1% diabetic, 61.9% dyslipidemic, 27.4% obese and 61.9% had peripheral vasculopathy. The most frequent causes of CKD were diabetic nephropathy (22.6%), glomerular etiology (21.4%), unfiltered (20.2%) and nephroangiosclerosis (14.3%), among others. The degree of functional dependence according to the Barthel index was 63.1.9% for total independence, 29.8% mild dependence, 4.8% moderate dependence and 1.2% total dependence; and for the Lawton and Brody index, 42.9% total independence, 14.3% mild dependence, 27.4% moderate dependence, 11.9% severe dependence and 3.6% total dependence. When comparing the degree of functional dependence between both dialysis techniques, we observed that patients in PD had a lower degree of functional dependence compared to patients in HD, these differences being statistically significant (Lawton and Brody 73.5% in PD vs. 22% in HD, $p < 0.001$ and Barthel index 85.3% in PD vs 48% in HD, $p = 00.4$).

Conclusion: In our experience, the degree of functional dependence in patients in PD is lower compared to patients in HD with less comorbidity, being able to condition the choice of the technique of renal replacement therapy.

P1204 PHROPHYLATIC GENTAMICIN - A THERAPEUTIC WEAPON IN THE COMBAT OF EXIT SITE INFECTIONS IN PERITONEAL DIALYSIS

Ana Abrantes[1], Francisco Ferrer[1], HernÂNi Ricardo Martins GonÇAlves[1], Ana Vila Lobos[1]

[1]*Centro Hospitalar Médio Tejo, Nephrology, Torres Novas, Portugal*

Background and Aims: Infection-related complications, such as exit-site infection (ESI) and peritonitis, are one of the main causes of technique failure and dropout in patients under peritoneal dialysis. Several studies have demonstrated the positive effect of daily topical antibiotics (AB) in preventing ESI. The aim of this study is to demonstrate the impact of topical gentamicin (TG) in preventing ESI, between 2009 and 2019, in a single-center of a medium-sized hospital in Portugal.

Method: Descriptive and retrospective analysis was performed. Demographic data, comorbidities, type of catheter placement and PD prescription were collected. For each patient, it was determined the time free of prophylactic AB (NTG) and under topical gentamicin (ophthalmic formula, once a day, applied on exit site). ESI cases were identify.

Results: Eighty-five patients were included, with a mean age of 53.2 ± 14.6 years; 69.5% were male. Cardiovascular comorbidities, like arterial hypertension and diabetes, were highly prevalent (88.2% and 76.5% respectively). Chronic glomerulonephritis and diabetes were the main causes of CKD (19; 22.4%; 15; 17.6%). More than 80% of the patients had previous Nephrology follow up. Percutaneous approach was the first option to catheter placement in 70.6% of the cases and DPA was performed in 53,0%. Every patient started the PD program free of prophylactic AB (n=85); 35 patients started TG at some point. Forty episodes of ESI were recorded, 39 (97.5%) in the NTG group. *Staphylococcus aureus* was the most frequently identified organism (16; 41.0%), followed by *Staphylococcus epidermis* (5; 12.5%) and *Corynebacterium* (5; 12.5%). The Kaplan-Meier analysis demonstrated that patients in TG were associated with better free-time of first peritonitis ((705 vs 985 days; p=0.001). The multivariate Cox regression model confirmed a 14 times higher risk of ESI in NTG group (HR 14.4; 95% CI 1.97-105.45; p=0.001).

Conclusion: Although mupirocin is still the first option in many centers, some studies have demonstrated a benefic role of gentamicin in reducing ESI, not only by *Pseudomonas species* but also *Staphylococcus aureus.* The results of our study confirmed that topical daily gentamicin is highly effective preventing ESI in PD patients. Despite of the concern with the gentamicin-resistant infections, just one patient developed ESI under gentamicin, and the identified microorganism was the *Staphylococcus epidermidis.*

P1205 ESTABLISHMENT OF HYPOCHLORITE-INDUCED PORCINE MODEL OF PERITONEAL FIBROSIS

Chun-Yuan Chao[1], Chin-Ho Wu[2], Yi-Ting Chen[1,3], SHUEI-LIONG LIN[1,3], Pei-Shiue Tsai[4]

[1]National Taiwan University, College of Medicine, Taipei, Taiwan, R.O.C., [2]National Taiwan University, Graduate Institute of Veterinary Clinical Science, Taipei, Taiwan, R.O.C., [3]National Taiwan University, Graduate Institute of Physiology, Taipei, Taiwan, R.O.C. and [4]National Taiwan University, School of Veterinary Medicine, Taipei, Taiwan, R.O.C.

Background and Aims: Patients with kidney failure rely on life-saving peritoneal dialysis to facilitate waste exchange and maintain homeostasis of physical conditions. However, peritoneal dialysis often results in peritoneal fibrosis and organ adhesion that subsequently compromise the efficiency of peritoneal dialysis and normal functions of visceral organs. Despite rodent models provide clues on the pathogenesis of peritoneal fibrosis, no current large animal model which shares high degree of physiological and anatomical similarities to human is available, limiting their applications on the evaluation of pre-clinical therapeutic efficacy.

Method: In this study, we established for the first time, porcine model of peritoneal fibrosis by the use of a bleach-like chemical, sodium hypochlorite. We demonstrated that intraperitoneal injection of 30ml/kg B.W., 0.1%-0.2% (0.1mM-0.2mM) hypochlorite induced peritoneal fibrosis and visceral organ adhesions in 5-week-old piglets.

Results: A dose- and time-dependent severity of peritoneal fibrosis characterized by mesothelium fragmentation, αSMA+ myofibroblasts accumulation, organ surface thickening and type I collagen deposition were observed. We also demonstrated that hypochlorite-induced overexpression of IL1β, CX3CL1 and TGFβ on the peritoneal mesothelium mimicked the mechanism of peritoneal dialysis-induced peritoneal fibrosis in human patients.

Conclusion: This pig model could not only be used as a platform for studying fibrosis/scar formation, but can also be used to evaluate the efficacy of potential candidates on the prevention (e.g. compounds) and treatments (e.g. stem cells) for regenerative medicine.

P1206 ARTERIAL STIFFNESS AND PERIODONTITIS IN PERITONEAL DIALYSIS PATIENTS: ARE THEY RELATED?

Josip Orešković[1], Katja Kovačević[1], Marijana Vučković[2], Hrvoje Raos[2], Marija Roguljić[1,3], Andrea Gelemanović[4], Josipa Radic[2,5]

[1]University of Split, School of Medicine, Study of Dental Medicine, Split, Croatia, [2]University of Split, School of Medicine, Split, Croatia, [3]University of Split, School of Medicine, Department of Oral Medicine and Periodontology, Split, Croatia, [4]MedILS - Mediterranean Institute for Life Sciences, Split, Croatia and [5]University Hospital Centre Split, Split, Croatia

Background and Aims: Arterial stiffness is an important risk factor for cardiovascular disease (CVD) in patients with end-stage renal disease (ESRD). However, little is known about risk factors that contribute to arterial rigidity in peritoneal dialysis (PD) patients. The periodontal diseases are highly prevalent among patients with ESRD. The aim of this study was to evaluate the dental status, incidence and severity of periodontitis among Dalmatian PD patients and to investigate possible correlations with arterial stiffness.

Method: 24 PD patients, 12 (50 %) men and 12 (50 %) women, aged 54.9 (range 21–79) years were included. Arterial stiffening was estimated by using pulse wave velocity (PWV). To measure PWV Agedio B900 device was used. Oral periodontal status included full mouth plaque score, full mouth bleeding score, periodontal probing depth and clinical attachment loss (CAL), all measured at six sites of each tooth. Also periodontitis stage was determined for each patient.

Results: Out of 24 PD patients 17 (70.1 %) was suffering from periodontitis. Among those with periodontitis 1 patient (5.9 %) was classified as periodontitis stage I (mild), 6 (35.3 %) as stage II (moderate), 10 (58.8%) as stage III and IV (severe). Significantly positive correlation between PWV, average interdental CAL and average total CAL, among all PD patients were found (R= 0.764, P=0.001), (R= 0.738, P=0.001), respectively, Also, in those PD patients statistically negative correlations between PWV and number of teeth were found (R= -0.565, P=0.012). Among those PD patients with periodontitis statistically positive correlation between PWV, periodontitis stage, interdental CAL, average total CAL and dental plaque were found (R= 0.73, P=0.002),(R= 0.731, P=0.00,5), (R= 0.72, P=0.005), (R= 0.558, P=0.047), respectively.

Conclusion: The incidence of peritonitis is high in Dalmatian PD patients and more than half of PD patients had severe stage of periodontitis. Despite small sample size, we showed that those PD patients with more severe periodontitis stage had significantly higher arterial stiffness. Routine dental examination should be suggested for all PD patients. A prospective cohort study needs to link the association of severe periodontitis and CVD and confirm desirable survival outcome on successful treatment of periodontal diseases.

P1207 ANALYSIS OF OUTCOME AND FACTORS ASSOCIATED WITH MAINTENANCE OF PERITONEAL DIALYSIS

Merita Rroji (Molla)[1], Saimir Seferi[1], Larisa Shehaj[1], Myftar Barbullushi[1]

[1]*University Hospital Center ' Mother Tereza", Tirana, Department of Nephrology, Tirana, Albania*

Background and Aims: Peritoneal dialysis (PD) is generally associated with a good survival rate and with great preservation of residual renal function (RRF). The various causes of technique failure are responsible for the relative short time staying in PD.

Objectives: This study aimed to analyze the outcome and factors correlated with maintenance peritoneal dialysis (PD) to guide for improving prognosis.

Method: In a retrospective way we examined our PD-cohort concerning mortality, technique survival, peritonitis rate, and other complications.

Results: From 2005 to 2019 the number of PD patients who have been treated in PD program for more than 3 months was around 199 patient, 29.1% diabetics, mean age 53.3±15.03 years old and meantime in therapy 32.39± 27.34 months. The PD was seen as an alternative for younger patients in the transplant list and elderly patients with comorbidity. Around 7.5% of the PD patients were transplanted and 8.5 % of patients were transferred from HD due to vascular access failure. Around 88.9% of patients were on PD for more than 1 year, 37.7% from 3 up to 5 years and 19.8% percent of the patients have stayed on PD for more than 5 years.

Cardiovascular mortality was the main cause of mortality with 53% of the cases. Higher comorbidity index, lower albumin levels, and lower residual renal function were the main risk factors for lower survival. The technical survival of patients was 92.3% during the first year, 79.5% and 69.6% in the second and the fifth year, respectively. There was not found a difference in technical survival between diabetics and nondiabetics patients. Ultrafiltration failure followed by peritonitis was the main reason for transfer patients with more than 24 months in therapy in hemodialysis probably linked with the no availability of icodextrin. Peritonitis rate was 1:41 patient months.

Conclusion: PD program in our center is organized based in the concept of integrated care in RRT. The outcome of our patients was at least comparable to those reported by larger registries Although we have done good progress in the prevention of infection the nonavailability of icodextrin is an important factor for a technical failure. RRF is an important factor and we need to be more focused to maintain it longer in the future.

P1208 **TREATMENT OUTCOMES IN PERITONEAL DIALYSIS PERITONITIS ARE NOT AFFECTED BY DEGREE OF RESIDUAL RENAL FUNCTION**

Sarah Gleeson[1], Arun Navaratnarajah[1], Nora Hisole[1], Jacqueline McGrory[1], Titus Chelapurath[1], Froilan Galima[1], Valentina Zanovello[1], Carol Bartholomew[1], Sally Punzalan[1], Edwina Brown[1], Richard Corbett[1]

[1]*Imperial College Healthcare NHS Trust, United Kingdom*

Background and Aims: Early studies in peritonitis showed no difference in outcomes between anuric and non-anuric patients, despite pharmacokinetic studies showing the effect of residual renal function (RRF) on antibiotic clearance. Recent work identified a relationship between preserved RRF and treatment failure in gram-positive and culture-negative peritonitis. Our centre uses empiric vancomycin and gentamicin dosed by weight (both drugs) and by RRF (gentamicin). We sought to examine whether RRF is associated with treatment failure in our population.

Method: We retrospectively identified all episodes of PD peritonitis between January 2014 and July 2019 including demographic and clinical information. The RRF measured closest to the peritonitis episode was used. Treatment failure was defined as death, catheter removal or relapse.

Results: 189 peritonitis episodes occurred in 128 patients (43% female, mean age 61.3±17.9). 80 episodes were caused by gram-positive bacteria, 49 gram-negative, 51 culture-negative, 5 fungal and 4 polymicrobial. 21, 88 and 61 episodes occurred in patients with a creatinine clearance <0.5, 0.5-5, and >5ml/min respectively. Creatinine clearance data was unavailable in 21 patients.

Treatment failure occurred in 72 cases (38%) (19 relapses, 52 catheter removals, 7 deaths). Treatment failure for all bacterial peritonitis episodes was not affected by RRF as compared to anuric patients: 0.5-5 (OR 0.41, 95% CI 0.12-1.35, p 0.14) or >5 (OR 0.90, 95% CI 0.22-3.67, p 0.88). There was no difference in outcome in sub-group analysis by type of organism. Antibiotic concentrations did not differ between the RRF groups.

Conclusion: Although limited by small numbers we found no association between the degree of RRF and outcome. We hypothesise this is because we monitor antibiotic concentrations and therefore dose antibiotics appropriate to the level of RRF. In PD peritonitis regimes that adjust for RRF there is no impact of RRF on treatment outcomes.

P1209 ROLE OF NTPROBNP IN LONG-TERM PERITONEAL DIALYSIS PATIENTS

Luisa Pereira[1], Ana Rita Martins[2], Anabela Malho Guedes[1], Patricia Matias[2], Patricia Branco[2]

[1]Hospital de Faro, Centro Hospitalar Universitário do Algarve, Nephrology, Faro, Portugal and [2]Hospital de Santa Cruz, Centro Hospitalar Lisboa Ocidental, Nephrology, Lisboa, Portugal

Background and Aims: Plasma N-terminal fragment of pro brain natriuretic peptide (NTproBNP) concentration is elevated in cardiovascular diseases such as congestive heart failure, where increased levels of NTproBNP indicate cardiac dysfunction, hypervolemia, and higher risk of hospitalization and death. These associations have also been studied in patients with chronic kidney disease (CKD), where NTproBNP value remains controversial, especially in long-term peritoneal dialysis (PD) patients with respect to its pathophysiologic implications. This study aim was to determine whether NTproBNP was a predictor of hospital admissions and cardiovascular events among patients on automated (APD) and continuous (CAPD) ambulatory peritoneal dialysis.

Methods: This was a cross-sectional study which included stable patients from two Peritoneal Dialysis Units. Plasma NTproBNP concentration was measured in stable adult peritoneal dialysis patients attending for routine assessments on PD outpatient clinic.

In all patients, demographic variables, clinical and other laboratory parameters were recorded and analyzed. Descriptive statistics was performed. Groups were compared using independent t-test for comparison of continuous variables and Chi square test for categorical variables. In order to evaluate relationship between NTproBNP and the other variables multivariate logistic regression and Pearson bivariate analysis were used.

Results: The study enrolled 70 patients (male/female 44/26; mean age 55.3±14.6 years; APD/CAPD 25/45; PD duration 28±24.2months). One third (31.4%) of the patients was diabetic, 12.9% presented cardiac insufficiency and 20% had cardiovascular disease. Pearson bivariate correlation analysis revealed that patients with higher weekly kt/v (p=0.039), total fluid removal (diuresis and ultrafiltration) (p=0.027) and total weekly creatinine clearance (p=0.007) had lower NTproBNP values. These patients had also significant lower plasmatic creatinine and phosphorus levels. We found no significant association with residual kidney function, peritoneal transport (D/P creatinine), serum albumin levels and c-reactive protein.

We also found that patients with higher NTproBNP levels had significantly more cardiovascular events (p=0.010) and a trend for more common hospital admissions (p=0.066).

There were no significant differences regarding NTproBNP between the two modalities of peritoneal dialysis (APD and CAPD patients) or in patients who were PD first.

As expected, patients with cardiac dysfunction had significant higher NTproBNP values (p=0.004). Diabetic patients had higher NTproBNP levels, althought this difference was not significant.

Conclusion: Despite the inconsistency in the NTproBNP value among long-term PD patients, results from most studies concur that NTproBNP levels are closely associated with left ventricular dysfunction, morbidity and mortality in these patients. In our study, patients with higher NTproBNP levels had more cardiovascular events and a trend for more common hospital admissions. Regular monitoring of NTproBNP levels among PD patients may be useful for providing care for these patients. Plus, NTproBNP was associated with better PD efficacy, greater fluid removal and higher creatinine clearance, reinforcing clinical relevance of PD optimization. These results require confirmation in a prospective study.

P1210 EFFECT OF ICODEXTRIN OR GLUCOSE PERITONEAL DIALYSIS (PD) SOLUTIONS ON TRIGLYCERIDE AND OLEIC ACID LEVELS IN PD PATIENTS (EXIT TRIAL)

Sumi Lee[1], Yu In Jeong[1], DongHo Choi[1], Chungsik Lee[2], Young Ki Son[1], Seong Eun Kim[1], Won Suk An[1]

[1]Dong-A University Hospital, Department of Internal Medicine, Busan, Korea, Rep. of South and [2]Cheju Halla Hospital, Department of Internal Medicine, Korea, Rep. of South

Background and Aims: Dyslipidemia is a major cause of cardiovascular disease (CVD) and CVD incidence is definitely increased according to peritoneal dialysis (PD) vintage. The PD solutions contained glucose may affect on dyslipidemia including hypertriglyceridemia. The oleic acid (OA) content in the erythrocyte membrane was increased in patients with acute coronary syndrome and is significantly higher in PD patients than hemodialysis patients. We conducted this trial for comparing effect of icodextrin or glucose PD solutions on triglyceride and oleic acid levels in PD patients.

Method: This EXIT trial is an open label, randomized, cross-over multi-center trial. Twenty-two patients were enrolled and 15 patients finished this trial. Glucose group was initially exposed to glucose PD solutions for 6 months and then exposed to icodextrin PD solution for 3 months. Extraneal group was initially exposed to icodextrin PD solution for 3 months and then exposed to glucose PD solutions for 6 months.

Results: The enrolled patients were aged 63.6 $\pm$ 9.5 years old and mean PD duration was 10.8 $\pm$ 5.9 months. There were no significant differences of baseline clinical and laboratory data between glucose group and extraneal group. There was no significant decrease of triglyceride levels, erythrocyte membrane OA and monounsaturated fatty acid (MUFA) contents after 3 months exposure of icodextrin PD solution compared to baseline. However, there was a tendency of triglyceride levels decrease (p=0.093) after 3 months exposure with icodextrin PD solution and there was a tendency of triglyceride levels increase (p=0.078) after 3 months exposure with glucose PD solutions compared to baseline levels. Continuous 6 months exposure with glucose PD solution significantly increased triglyceride levels (p=0.041), LDL cholesterol levels, erythrocyte membrane OA (p=0.009) and MUFA compared to baseline levels.

Conclusion: Continuous exposure of glucose PD solutions may negatively affect on triglyceride and erythrocyte membrane OA contents. Combined use of icodextrin and glucose PD solutions may prevent lipid derangement (ClinicalTrial.gov number, NCT NCT02166359).

P1211 **IOT(INTERNET OF THINGS) FOLLOW-UP VS. CONVENTIONAL CARE IN PATIENTS WITH CONTINUOUS AMBULATORY PERITONEAL DIALYSIS: A RETROSPECTIVE, CASE-CONTROL STUDY**

Aihua Li[1], Mengjun Liang[1], Zongpei Jiang[1]

[1]*The Six Affiliated Hospital, Sun Yat-sen University, Department of Nephrology, Guangzhou, P.R. China*

Background and Aims: Peritoneal dialysis (PD) has been accepted as a home-based, more cost-effective renal replacement therapy worldwide. Increasing evidence indicates that patients on PD have clinical outcomes that are not optimistic than those on hemodialysis. The reasons for these observations are multifactorial and include lack of experience on self health-care, limited modality of follow-up, belated prescription adjustments, and shortage of management of the various complications. Internet of things (IoT), a novel technology that would improve access to and compliance in PD patients, has been designed and deployed to PD patients in our center for the nursing follow-up.

Method: A retrospective, case-control study enrolled 30 patients on continuous ambulatory peritoneal dialysis (CAPD) in The Six Affiliated Hospital of Sun Yat-sen University from 2018.09 to 2018.10. The patients were categorized into IoT group (15 patients) and conventional group in which patients was selected by propensity score matching for the gender, age, dialysis age and basic nephropathy. All the patients had been followed up for 3 months to assess their quality and compliance of PD. IoT follow-up was defined as the framework of home-based sphygmomanometer, electronic scale, weighing scale and portable application description (PAD) via bluetooth and the nurses in PD group could review the data timely over the internet and provide care management advice. Conventional care was defined as telephone or outpatient follow-up monthly.

Results: There were no differences among gender, age, dialysis age, and basic nephropathy distribution between the two groups. After 3-month follow-up, the weight compliance rate in IoT group seemed better than that in conventional group, with rate of 100% and 80%, p=0.068; the blood pressure compliance rate in IoT group seemed higher than that in conventional group, with rate of 60% and 46.7%, p=0.464. Nine patients (the rate of 60%) in IoT group, while only 2 patients (13.3%) in conventional group, had got alterations of hypotensive drugs, p=0.008. Eight patients (53.3%) in IoT group had acquired adjustments of PD doses, while no patient in conventional group had any changes, p=0.001.

Conclusion: Our preliminary results had indicated that IoT technology could provide innovations and timeliness for basic nursing care in PD follow-up. IoT devices would help to improve the availability and effectiveness of peritoneal dialysis.

P1212 PREDICTORS OF QUALITY OF LIFE IN PERITONEAL DIALYSIS: A SINGLE-CENTER EXPERIENCE

Carolina Figueiredo[1], Pedro Maia[1], Teresa Mendes[1], Helena Pinto[1], Alice Lança[1], Helena Sá[1,2], Rui Alves[1,2]

[1]Centro Hospitalar e Universitário de Coimbra, Nephrology, 561, Portugal and [2]Faculdade de Medicina da Universidade de Coimbra, Clínica Universitária de Nefrologia, Portugal

Background and Aims: Quality of life (QoL) is an important indicator of quality of healthcare. Measuring QoL and its correlates for peritoneal dialysis (PD) patients is very important for intervention and clinical decision-making. Being a technique performed by the patients themselves, their perspective of health related QoL is extremely important. The EuroQol questionnaire evaluates 5 QoL dimensions (mobility, self-care, usual activities, pain/ discomfort and anxiety/ depression) and includes a visual analogue scale (VAS) rated 0-100% that provides a quantitative measure of the patients' perception of their overall health.

Method: Data from 69 patients on peritoneal dialysis at our center were collected using EQ-5D-5L EuroQol questionnaire. Health state index (HSI) scores were calculated from individual health profiles using the Spanish value set (maximum score 1). Additional clinical and laboratory data was collected from the patient's medical files.

Results: Mean age of the population studied was 55,2 $\pm$ 14,0 years, and 66,7% (n=46) were male. Most patients were on PD $>$ 1 year (62,3%, n=43) and performing automated peritoneal dialysis (APD) (52,2%, n=36). Mean HSI was 0,88 $\pm$ 0,15 and mean VAS score was 75,1 $\pm$ 18,7.

Patients with weekly Kt/V $\geq$ 1,7 scored on average 0,09 points higher on the HSI (p=0,070) and 13,34 points higher in VAS (p=0,019), compared to patients with weekly Kt/V $<$ 1,7. Patients on PD $>$ 1 year scored on average 0,09 points lower on the HSI (p=0,017), mainly due to higher levels of anxiety/depression, and 11,9 points lower in VAS (p=0,005) than those $<$ 1 year.

Age did not significantly influence QoL, even when comparing patients $>$ 70 years with those $<$ 70 years old (HSI 73.0 $\pm$ 15.5 vs 75.4 $\pm$ 19.3, p=0.710 / VAS 0.82 $\pm$ 0.3 vs 0.89 $\pm$ 0.1, p=0.175). Likewise, when comparing continuous ambulatory peritoneal dialysis (CAPD) to APD, there was no significant difference in the scores of QoL. Gender, diabetes mellitus, arterial hypertension, cancer and infectious events related to PD in the last year did not influence QoL. Residual diuresis as an isolated factor did not significantly influence QoL scores. However, as it is a fundamental contributor to Kt/V, it may be indirectly associated with better QoL. A more detailed analysis was not possible as the number of patients with Kt/V $\geq$ 1.7 and no residual diuresis was, as expected, very low (n=4).

Conclusion: Perceived QoL in the elderly when compared to younger patients in PD was not inferior in our study, showing this option should be discussed individually with each patient.

Our results revealed time in PD negatively influences patients' perception of their own health, which may be due to patient's burden and exhaustion, and eventually lead to technique related complications.

Kt/V $\geq$ 1,7 was related to better QoL, either because higher dialysis adequacy leads to better QoL, or because patients who feel better have less tendency to neglect the technique.

Finally, we also found type of PD (CAPD vs APD) to have no significant influence on QoL, reinforcing the idea that it should be discussed and adapted to each individual patient.

P1213

ROLE OF PERITONEAL PHOSPHORUS TRANSPORT IN PERITONEAL DIALYISIS REGIMEN FOR THE MANAGEMENT OF HYPERPHOSPHATEMIA

Marc Xipell[1], Elena Guillen Olmos[1], Lida Rodas[1], Jose J Broseta[1], Angeles Mayordomo[1], Debora Bonache[1], Francisco Maduell[2], Manel Vera[1]

[1], Peritoneal Dialysis Department, Hospital Clínic, Barcelona. and [2], Hemodyalisis Department, Hospital Clínic, Barcelona.

Background and Aims: The ratio D/P-Creatinine (DP-Cr) obtained by the peritoneal equilibrium test (PET) is the most widely used parameter to characterize the type of peritoneal membrane transport, and it is used to determine the dialysis regimen for ultrafiltration (UF). It has been suggested that net UF influences the final clearance of solutes, so guiding ultrafiltration by D/P-Phosphorus (DP-P) instead of DP-Cr could have some added value in the management of hyperphosphatemia. The objective of this study is to define if there is a correlation between DP-P and DP-Cr, and if these are related to the clearance of phosphorus (P) and creatinine (Cr).

Method: retrospective analysis of PETs performed during 2016 and 2017 in our center. DP-Cr and DP-P were calculated, and in patients with 24h effluent sample the day of the PET, it was also analyzed weekly Kt/V-urea, and peritoneal Cr and P clearance (CrCl and PCl, respectively). Statistical analysis was done using t-Student test for independent data and Pearson correlation coefficient, with SPSS Statistical Package program v.23, establishing a significance level of $p<0.05$.

Results: 68 PETs were analyzed in 54 patients, mean age 60.4 years (SD 17), predominantly men (69% vs 31%). The mean plasma P, DP-Cr and DP-P were respectively 4.5 mg/dL (SD 1.2), 0.74 (SD 0.12) and 0.71 (SD 0.17). The correlation coefficient DP-P/DP-Cr showed a significant relationship ($r=0.84$, $p<0.001$), which was maintained when analyzing patients according to phosphorus levels: DP-P/DP-Cr with $P<5$ mg/dL ($r=0.81$); and $P\geq5$ mg/dL ($r=0.93$) ($p<0.001$).Patients in DP-P $\geq$50th percentile had P levels of 4.2 ($\pm$ 1.05), and those in$<$50th percentile had levels of 4.88 ($\pm$ 1.38) ($p<0.031$). Moreover, in patients with 24h effluent analyzed the day of the PET (n=35), the average PCl and CrCl was 4.1 and 2.85 ml/min, with statistical significant correlation ($r=0.92$, $p<0.001$).However, in these patients no relationship was found between DP-Cr and CrCl ($r=0.068$, $p=0.7$), nor between DP-P and PCl ($r=0.052$, $p=0.7$).

Conclusion: The DP-P/DP-Cr high correlation suggests that both parameters could be useful to classify the type of peritoneal transport. However, although patients with higher DP-P had better control of hyperphosphatemia, thus suggesting a direct positive relationship between DP-P and PCl, our data showed no correlation between them.

P1214 **RELATIONSHIP BETWEEN CHANGE IN DIALYSATE CONDUCTIVITY AND INTRAPERITONEAL VOLUME DURING PET**

Laura Rosales Merlo[1], Fansan Zhu[1], Peter Kotanko[1,3]

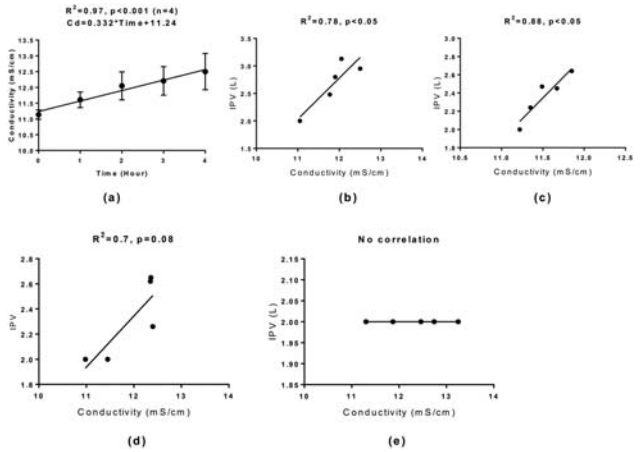
[1]Renal Research Institute, Research, New York, United States of America and [3]Icahn School of Medicine at Mount Sinai Hospital, Nephrology, New York, United States of America

Background and Aims: Bioimpedance spectroscopy (BIS) has been widely applied to measure fluid volume in dialysis patients. A fundamentally important, yet unanswered question is how changes in fluid conductivity affects the accuracy of BIS measurements. The aim of this study was to investigate whether the change in intraperitoneal volume (IPV) is – as hypothesized - linearly correlated with the change in dialysate conductivity during a peritoneal equilibrium test (PET).

Method: Four PD patients (age 58±13 years, three males, weight 87.8±28 kg) were studied during a standard PET. Segmental BIS was continuously measured with eight electrodes placed between rib and buttock on both sides of the body using a Hydra 4200 (Xitron Technologies Inc). IPV was calculated based on BIS recordings as recently published (Zhu, Kidney Blood Press Res 2019;44:1465–1475). Dialysate samples were collected hourly from baseline to the end of dwell. Dialysate conductivity was measured with a portable conductivity meter (CDH-280-KIT, Omega Engineering Inc, CT, USA).

Results: In all patients dialysate conductivity increased significantly ($p<0.0001$) from baseline (11.14±0.15 mS/cm) to the end of dwell (12.5±0.58 mS/cm) (Fig a). In 2 patients (Fig b and c) IPV and conductivity were linearly correlated; in one patient (Fig d) the relationship was nonlinear and absent in another one (Fig e).

Conclusion: Although the number of patients in this study was small, the results clearly indicated that dialysate conductivity increased linearly over time during PET. The correlation between dialysate conductivity and IPV is not linear and may be driven by other factors, such as dialysate electrolyte levels. In future studies measurements of dialysate electrolytes are necessary to better understand the drivers of the IPV / conductivity relationship.



Figures:

P1215 **INVERSE ASSOCIATION BETWEEN DIALYSATE OXALATE REMOVAL AND INTRAPERITONEAL INFLAMMATION IN PERITONEAL DIALYSIS PATIENTS**

Natalia Stepanova[1], Victoria Driianska[2], Lyudmyla Snisar[1], Larysa Lebid[1]

[1]State Institution «Institute of Nephrology of the National Academy of Medical Sciences», Nephrology and Dialysis, Kyiv, Ukraine and [2]State Institution «Institute of Nephrology of the National Academy of Medical Sciences», Immunology Laboratory, Kyiv, Ukraine

Background and Aims: Due to inadequate oxalate removal, hyperoxalemia is a well-established feature in end-stage renal disease (ESRD) patients. Considering the fact that oxalate is primarily removed by kidneys in healthy individuals, we hypothesized that oxalate elimination in peritoneal dialysis (PD) patients could be compensated by PD effluent (PDE). In addition, its dialysate concentration could be associated with intraperitoneal inflammation.

In the present study, we investigated oxalate excretion in PDE and its association with intraperitoneal inflammation in PD patients.

Method: We performed a cross-sectional single-center observational study involving 30 PD patients (17 women and 13 men). The average age was 48.3 ± 9.2 years. Among them, there were 11 (37%) diabetics and 19 (63%) non-diabetic patients. The mean time on PD was 32 [18.5-47] months.

Parameters of dialysis adequacy, cytokines concentration and oxalate removal levels with PDE were determined. The spectrophotometric method was performed for determining oxalate concentration in PDE using oxalate oxidase/peroxidase reagent (BioSystems, Spain). The ELISA method was used for the determination of interleukin-6 (IL-6) and monocyte chemoattractant protein-1 (MCP-1) measurements in dialysate.

For the statistical analysis, we used Kruskal-Wallis's t-test and Spearman's rank correlation test. The median (Me) and interquartile ranges [Q25 - Q75] were calculated according to abnormal distribution. All statistical analyses were performed using MedCalc.

Results: No differences in peritoneal oxalate, IL-6, and MCP-1 excretion between diabetics and non-diabetic patients were observed (Table 1).

However, the higher dialysate oxalate concentration was, the lower residual renal function was observed ($r = -0.69$; $p < 0.0001$). Surprisingly, increased dialysate oxalate level was associated with low IL-6 ($r = -0.54$; $p = 0.002$) (Fig. 1) and MCP-1 ($r = -0.7$; $p < 0.0001$) (Fig. 2) concentrations in PDE.

Conclusion: To the best of our knowledge, the association between PDE oxalate excretion and proinflammatory mediators' concentrations in PD patients has never been reported before. We suppose that peritoneal oxalate excretion might be involved in the intraperitoneal inflammation process. Further studies are needed to determine the possible pathogenetic role of dialysate oxalate removal in the conditions of intraperitoneal inflammation in PD patients.

Table 1. PDE levels of oxalate, IL-6, and MCP-1 in diabetic PD patients compared with non-diabetics.

	Diabetics (n = 11)	Non-diabetics (n = 19)	P
Oxalate (mg/d)	11.6 [10.4-13.7]	12.8 [10.1-13.4]	0.39
IL-6 (pg/ml)	51.1 [20.03-94.5]	29.4 [22.7-81.9]	0.29
MCP-1 (pg/ml)	501.5 [431-622]	605.7 [361-707]	0.88

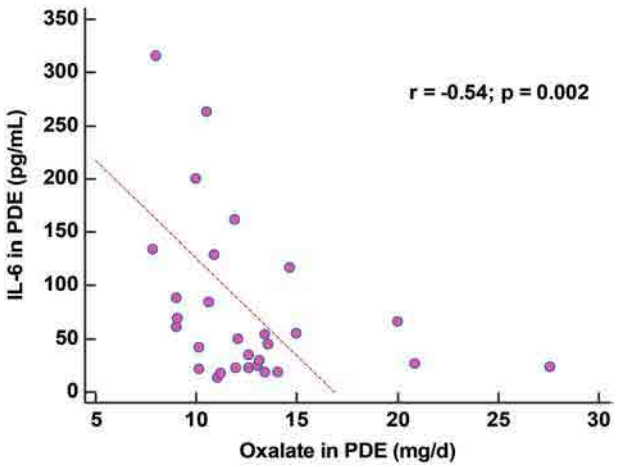


Figure 1. Association between dialysate oxalate and IL-6 concentrations in PD patients.

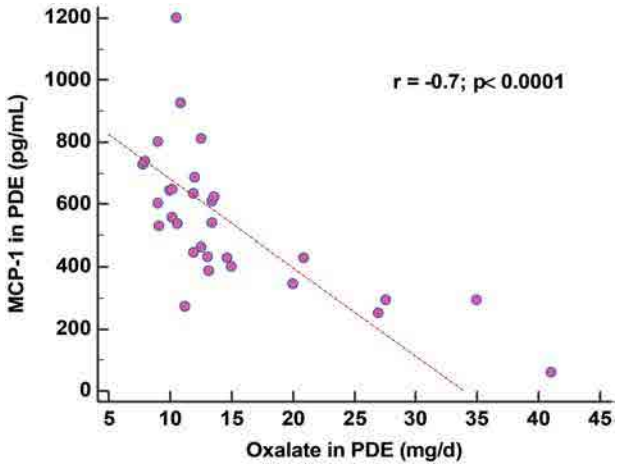


Figure 2. Association between dialysate oxalate and MCP-1concentrations in PD patients.

P1216 **EPIDEMIOLOGY OF HYPERTENSION IN PERITONEAL DIALYSIS USING CLINIC AND AMBULATORY BLOOD PRESSURE MONITORING.**

Vasilios Vaios[1], Panagiotis Georgianos[1], Georgia Vareta[1], Antonios Karpetas[1], Evangelia Ntounousi[2], Chrysostomos Dimitriadis[3], Aikaterini Papagianni[3], Pantelis Zebekakis[1], Vassilios Liakopoulos[1]

[1]AHEPA Hospital, Aristotle University of Thessaloniki, Peritoneal Dialysis Unit, 1st Department of Medicine, Thessaloniki, Greece, [2]University of Ioannina, Department of Nephrology, Ioannina, Greece and [3]Hippokration Hospital, Aristotle University of Thessaloniki, Department of Nephrology, Thessaloniki, Greece

Background and Aims: Earlier studies that were based on routine clinic blood pressure (BP) recordings suggested that the prevalence of hypertension is lower in patients on peritoneal dialysis (PD) than in those receiving maintenance hemodialysis. These studies, however, did not incorporate the "gold-standard" method of ambulatory BP monitoring (ABPM). The aim of the present study was to quantify the prevalence and control of hypertension in a cohort of 81 peritoneal dialysis (PD) patients using clinic and ambulatory BP recordings.

Method: Triplicate BP recordings were obtained after a 5-minute seated rest at clinic with the validated monitor HEM-705 CP (Omron, HealthCare). 24-hour ABPM was subsequently performed with the Mobil-O-Graph device (IEM, Germany). Hypertension was defined as (i) average clinic BP $\geq$140/90 mmHg or antihypertensive drug use and (ii) 24-hour BP $\geq$130/80 mmHg or current use of antihypertensive drugs.

Results: The prevalence of hypertension was 92.6% with clinic BP recordings and 93.8 with ABPM. In all, 75 participants (92.6%) were receiving therapy with an average of 2.4 antihypertensive medications. The rates of adequate control of hypertension were 49.3% with the use of clinic BP recordings and 39.5% with ABPM, respectively. In all, 6.2% of participants were classified as normotensives, 33.3% had concordant control of hypertension with both techniques, 40.7% had concordant lack of control confirmed by both techniques, 5% had "white coat" hypertension and 14.8% had masked uncontrolled hypertension.

Conclusion: This study suggests that the burden of hypertension among patients on PD is very high and that the wider use of ABPM is important to confirm the BP control status of these patients.

P1217 **VALUE OF MYCOBACTERIUM TUBERCULOSIS SPECIFY ELISOPT IN THE DIAGNOSIS OF PERITONEAL DIALYSIS-ASSOCIATED TUBERCULOUS PERITONITIS PATIENTS**

Qiuxia Fan[1], Xiaoyan Huang[1], Zibo Xiong[1], Jieyun Zhang[1], Yan He[1]

[1]*Peking University ShenZhen Hospital, Nephrology, Shenzhen, P.R. China*

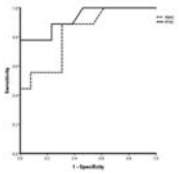
Background and Aims: Patients with ESRD undergoing chronic dialysis are 6 to 25 times more likely to develop tuberculosis (TB) than the general population. Tuberculous peritonitis is the most common form of tuberculosis infection in peritoneal dialysis patients. However, diagnosing active TB infection can be challenging, early and rapid diagnosis of tuberculous peritonitis has always been a challenge for nephrologists. *M.tuberculosis* antigen-specific IFN-γ production by peripheral blood mononuclear cells (PBMC) was determined by using an in-house ELISPOT assay by Institute of Hepatology of Shenzhen Third Hospital.In this study, we evaluated diagnostic performance of an *M.tuberculosis* antigen-specific gamma interferon enzyme-linked immunospot (ELISPOT) assay in continuous ambulatory peritoneal dialysis (CAPD) patients with tuberculous peritonitis.

Method: There were nine patients (1.29%) with tuberculous peritonitis among 700 CAPD patients. *M. tuberculosis* accounted for 2.84 % of all peritonitis.IFN-γ response in peripheral blood and peritoneal fluid were determined in 9 patients with tuberculous peritonitis(TBP),at the same time, 13 cases diagnosed with non-tuberculous peritonitis(NTBP) were enrolled.All patients were examined for tuberculosis-specific IFN-γ ELISPOT in peripheral blood and peritoneal dialysis fluid.

Results: 22 patients were recruited into this study, 9 were classified with confirmed tuberculosis peritonitis, 13 patients with bacterial or fungal peritonitis were enrolled as controls during the same period, in this patients, 3 were caused by Gram positive bacteria, 3 were caused by Gram negative bacteria, 3 were caused by fungus, 4 patients were negative athogenic bacteria culture .The AUC of ROC curve was 0.927 (95%CI:0.816–1.000,P=0.001) for ELISPOT on PFMC, which was higher than that of ELISPOT on PBMC (0.825,95%CI: 0.6490–1.000,P=0.011).When the cutoff value for the diagnosis of TBP was 40.5 SFCs/2 × 10^5 for ELISPOT on PBMC, with a sensitivity of 55.6%, a specificity of 92.3%,a diagnostic efficiency of 77.3%,The positive predictive value was83.3%, with negative predictive value of 75%,positive likelihood ratio of 7.2, and negative likelihood ratio of 0.48.The sensitivity, specificity,diagnostic efficiency,PPV, NPV, LR+, and LR- of the ELISPOT assay for the diagnosis of active TBP when performed on the PFMC were 77.8%, 84.6%, 81.8%, 77.8%, 84.6%, 5.05 and 0.26, respectively.Receiver operating characteristic(ROC) curves were used to estimate the diagnostic values of Elispot on PFMC and PBMC in 22 patients with confirmed TBP or NTBP.

Conclusion: IFN-γ release test can be used for early diagnosis of CAPD-related TBP; compared with peripheral blood, peritoneal dialysate may be a more effective and accurate way to diagnose CAPD complicated with tuberculous peritonitis.

Diagnostic accuracy estimates for Elispot assay on PFMC and PBMC



	AUC (95%CI)	sensitivity%	specificity%	diagnostic efficiency%	PPV%	NPV%	LR+	LR-
PFMC Elispot	0.927 (0.81-1.00)	77.8	84.6	81.8	77.8	84.6	5.05	0.26
PBMC Elispot	0.825 (0.64-1.00)	55.6	92.3	77.3	83.3	75	7.2	0.48

Figure:*FIG:M. tuberculosis* antigen-specifific IFN-γ response in PFMC ELISPOT assays is useful for diagnosis of TBP. The AUC of ROC curve was 0.927 (95%CI:0.816–1.000,P=0.001) for ELISPOT on PFMC, which was higher than that of ELISPOT on PBMC (0.825,95%CI: 0.6490–1.000,P=0.011).When the cutoff value for the diagnosis of TBP was 40.5 SFCs/2 × 10^5 for ELISPOT on PBMC, with a sensitivity of 55.6%, a specificity of 92.3%,a diagnostic efficiency of 77.3%,The positive predictive value was83.3%, with negative predictive value of 75%,positive likelihood ratio of 7.2, and negative likelihood ratio of 0.48.The sensitivity, specificity,diagnostic efficiency,PPV, NPV, LR+, and LR- of the ELISPOT assay for the diagnosis of active TBP when performed on the PFMC were 77.8%, 84.6%, 81.8%, 77.8%, 84.6%, 5.05 and 0.26, respectively. PBMC, peripheral blood mononuclear cells; PFMC, peritoneal fluid mononuclear cells;ROC: receiver operating characteristic;AUC:area under the receiver operating characteristic curve.

P1218 **OUTCOME OF RENAL REPLACEMENT THERAPY IN LEPTOSPIROSIS ASSOCIATED AKI - PERITONEAL DIALYSIS VS HEMODIALYSIS**

Sunu Alex[1]

[1]*Government medical college, Trivandrum, Nephrology, Trivandrum, India*

Background and Aims: Leptospirosis is a common zoonotic disease and acute kidney injury(AKI) is very commonly associated with it, often seen as a marker of disease severity. Renal replacement therapy(RRT) is often required in patients with clinical indications like uremia, oliguria, pulmonary edema and hyperkalemia. The two classical modalities employed for RRT are hemodialysis and peritoneal dialysis. We designed this study to evaluate the clinical outcome among patients with leptospirosis associated AKI requiring dialysis.

Method: : Basic clinical and demographic parameters of our patients were studied. The dialysis modality for each patient was decided based on their predominant clinical presentation. The duration of dialysis dependency and hospitalization along with final clinical outcome in terms of renal recovery or death were recorded. Appropriate statistical methods were used for analysis of results

Results: Thirty two patients underwent renal replacement therapy for leptospirosis associated AKI. Among them 22 received hemodialysis and 10 received peritoneal dialysis. Mortality in our group was 12.5%. Multiorgan involvement, need for mechanical ventilation and oliguric AKI were observed to be predictors of mortality along with hyperbilirubinemia, hypoalbuminemia, hyperkalemia and elevated creatinine phosphokinase levels. Peritoneal dialysis was observed to be associated with a shorter duration of dialysis dependency and hospitalization, however no significant impact on mortality was noticed.

Conclusion: Leptospirosis is a disease of great epidemiological significance in our part of the county. Prompt initiation of RRT in indicated patients leads to an acceptable clinical outcome with good renal recovery. Peritoneal dialysis is slowly losing popularity, which may be revived with proper training of medical personnel and good patient selection.

Table R1: Clinical profile of our patients

Clinical variable	Number	Percentage
Age		
Below 40 years	9	28.2
Above 40 years	23	71.9
Gender		
a .Males	28	87.5
b. Females	4	12.5
Duration of onset of symptoms		
Less than 4 days	11	34.4
4-6 days	18	56.2
More than 6 days	3	9.4

Table R2: Spectrum of clinical features in our patients

Clinical parameter	Number of patients	Percentage(%)
Fever	32	100
Myalgia	24	75
Conjunctival suffusion	22	68.75
Headache	20	62.5
Jaundice	20	62.5
Presence of favourable epidemiological setting	27	84.4
Hypervolemia	20	62.5
Hypovolemia	3	9.4
Euvolemia	9	28.1
Oliguria	15	46.9
Non oliguria	17	53.1
Hypotension	12	37.5
Presence of comorbidities	9	28.1
Hepatic dysfunction	28	87.5
Myocarditis	3	9.4
ARDS	2	6.3

Figure:

P1219 SLEEP AND PERITONEAL DIALYSIS

Maria Do Mar Menezes[1,1], Ana Carina Ferreira[1], Vasco Fernandes[1], Fernando Nolasco[1]

[1]*Hospital Curry Cabral, Nephrology Department, Lisboa, Portugal*

Background and Aims: Sleep is considered a basic human need according to Maslow. It helps in the individual's physical and psychological recovery. Nowadays, sleep disturbances are an increasingly frequent reality and they interfere negatively with quality of life. Poor sleep quality has a negative impact on the individual's health (attention, memory, Diabetes, Hypertension, immune system depression, mortality). Peritoneal dialysis (PD) may be an additional insult that is disturbing to its quality.

The aim of the study was to assess the quality and health of sleep in PD patients.

Method: We carried out a single-center study in 35 prevalent PD patients. We used the Pittsburgh Sleep Quality Scale (PSQI), which evaluates seven components (subjective quality, latency, duration, usual efficiency of sleep and sleep changes, medication use and daytime dysfunction) and which considers a good sleep quality when PSQI $\leq$5. We used a sleep health scale assessed by SATED PT (validated for the Portuguese population) and which considers 0 poor sleep health and 30 good sleep health.

Each patient answered both PSQI and SATED-PT questionnaires. Demographic and clinical variables were analyzed. Continuous variables are presented as means (standard deviation) or medians (interquartile range), depending on normality; categorical as frequencies. Univariate analysis was performed. STATA software was used and $p < 0.05$ was considered significant.

Results: Our cohort has 18 (51%) women, 34 (97%) Caucasians, mean age 49 $\pm$ 15 years, median dialysis time of 20.5 (8-33) months; 4 (11%) had a history of attempted construction of arteriovenous fistula and 7 underwent a short period of hemodialysis before starting PD (median 60 months). Charlson's median score was 4 (2-5). 21 patients (60%) were on automated PD, 14 on manual, 18 on Baxter system and 17 on Fresenius system.

Regarding sleep quality, the average obtained on the PSQI scale was 7 $\pm$ 3.4 and 60% had values$>$ 5. We found no correlations between these parameters and the demographic and clinical variables studied. We found that 36.4% of patients wake up earlier than expected, 43.8% get up to go to the bathroom, 30% have nightmares, 20% have pain while sleeping, 23.5% depend on sleeping medication, 34.3% have restless legs, all these parameters in a frequency greater than 3x week.

Regarding sleep health, the mean of the SATED scale was 22 $\pm$ 5.8 and only 2 patients (5.7%) had values $<$10. We found a negative correlation between the SATED value and time on dialysis ($p = 0.03$) and a positive correlation with BMI ($p = 0.04$). Only 1 patient with normal values lived alone ($p = 0.03$).

None of these scales (and respective sub-scales) correlated with the PD modality.

Conclusion: In conclusion, the majority of our patients have poor sleep quality but the small sample size limits further conclusions from this study.

P1220 **COMPARISON OF PERITONEAL DIALYSIS CATHETER INSERTION TECHNIQUES BY NEPHROLOGISTS: SURGICAL METHOD VS BLIND METHOD USING A TROCAR**

Seok Hui Kang[1], Jong Won Park[1], Kyu Hynag Cho[1], Jun Young Do[1]

[1]*Yeungnam University Medical Center, Internal Medicine, Daegu, Korea, Rep. of South*

Background and Aims: Successful PD requires timely peritoneal dialysis catheter (PDC) insertion and management of PDC related complications. Some societies have recently made an effort to increase PD and PDC insertion by nephrologists is an important issue. The aim of the present study was to evaluate comparative analysis of PDC insertion between blind and surgical methods by nephrologists.

Method: We reviewed medical records at a tertiary medical center in Korea and identified 249 adults who underwent first-time PDC insertion. All PDC insertions were performed using the blind or surgical methods. In our hospital during study period, two of three nephrologists performed the blind method routinely in all of eligible patients (blind group, n = 144). One of three nephrologists performed the surgical method in all of eligible patients (surgical group, n = 105). During follow-up, we collected data regarding peritoneal dialysis peritonitis (PDP), exit site and/or tunnel infection (ESI/TI). Catheter survivor was defined as maintaining of PD at July 2019 or PDC removal by PDC unrelated problems such as patient death due to PDC unrelated factors, kidney transplantation, patient demand, inadequate PD, improved renal function, poor oral intake due to abdominal distension, and colon cancer. Catheter non-survivor and/or PDC associated removal was defined as PDC removal by PDC related problems such as PDP, ESI/TI or PDC malfunction. Intervention-free non-survivor was defined as PDC revision, removal, or exchange by PDC related problems.

Results: Mean age at the PDC insertion in blind and surgical groups were 57.5 ± 13.7 and 56.3 ± 12.9 years, respectively ($P = 0.640$). There were no significant differences in age, sex, body mass index, underlying disease of ESRD, and Davies comorbidity index between the 2 groups. Mean follow-up durations were 37.0 ± 26.3 and 32.6 ± 23.4 months in the blind and surgical groups, respectively ($P = 0.172$). Total numbers of patients with one or more PDP events during follow-up period were 72 (50.0%) and 42 (40.0%) in blind and surgical groups ($P = 0.118$). Total numbers of PDP episodes were 157 and 100, respectively. Total numbers of patients with one or more ESI/TI events during follow-up period were 14 (9.7%) and 7 (6.7%) in blind and surgical groups ($P = 0.392$). Total numbers of ESI/TI episodes were 27 and 8, respectively. The 5-year PDC survival rates were 87.0% and 91.1% in the blind and surgical groups, respectively ($P = 0.995$, Figure 1). The 5-year intervention-free survival rates were 79.6% and 77.0% in the blind and surgical groups, respectively ($P = 0.723$). The leading cause of PDC removal was patient death. There was no significant difference in the distributions of cause of PDC removal in the 2 groups ($P = 0.335$). PDC associated removal rates in blind and surgical groups were 14 (18.4%) and 9 (16.4%), respectively ($P = 0.760$).

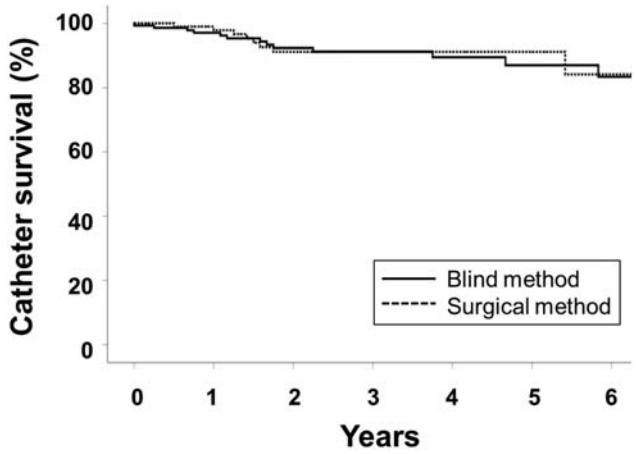


Figure 1. Catheter survival according to peritoneal catheter insertion methods.

Conclusion: Our study shows that catheter outcomes including infectious and mechanical complications and catheter survival are similar between blind and surgical insertion techniques by nephrologists.

P1221

THE VOXEL-BASED SPECIFIC REGIONAL ANALYSIS SYSTEM FOR ALZHEIMER'S DISEASE (VSRAD) BY MAGNETIC RESONANCE IMAGING SCAN IN PERITONEAL DIALYSIS (PD) PATIENTS, COMPARED WITH HEMODIALYSIS (HD) PATIENTS WITH ALZHEIMER'S DISEASE.

KAZUHITO TAKEDA[1]

[1]*Iizuka memorial Hospital, Nephrology, Iizuka City, Japan*

Background and Aims: Japan is currently moving towards an unprecedented aging society and chronic dialysis patients as well. As Aging population increases, in chronic dialysis patients as well, Mild cognitive impairment (MCI) and dementia cases are on the rise, and increasing burden on existing dialysis facilities. Our hospital has not only the outpatient department of Internal medicine, but also peritoneal and hemodialysis facilities, and Regional Dementia Center. We have accepted chronic dialysis patients, in our medical center and elderly ward, who are usually unable to maintain hospitalization or outpatient maintenance dialysis with cognitive impairment by collaborating with psychiatrists. Rehabilitation was instructed in all the patients by physiotherapists for the purpose of improving ADL. We investigated the current status of our PD patients, HD patients who experienced PD, and HD patients with Alzheimer's type dementia (AZ).

Method: A: Nine cases of hemodialysis (HD), who subsided peritoneal dialysis (PD), (including 2 DM cases:22%), Average age 75.4± 9.1 years old, 4 males, 5 females; average dialysis duration 322± 126 M:(HD-PD). B: Thirteen cases of PD, (including DM 3 cases: 23%), 6 males, 7 females; average age 71.6± 10.9 years old, average dialysis duration 286± 139 M:(PD). C: Fifteen cases of hemodialysis (HD) who was diagnosed as AZ (including 8 DM cases: 53%), Average age 76.6± 8.5 years old, 9 males, 6 females; average dialysis duration 53.9± 66.1 M:(HD-AD). We examined blood pressure (BP), and laboratory data. Analysis of the body fluid status; extracellular water/ total body water (ECW/TBW; IN BODY^{R}), Skeletal muscle index (SMI) was performed. Average Z-score points of MRI (assessment of hippocampus atrophy evaluation) and total brain atrophy was investigated by VSRAD.

Results: About 13 PD and 9 HD who experienced PD cases, there were 4 MCI cases, and no Alzheimer type dementia, or cerebrovascular dementia. About PD cases, average Hasegawa's formula expression average (HDS-R): 28.8±1.8, average BMI: 22.3± 2.9, average skeletal muscle mass index (SMI): 6.6± 1.0 kg/m^2, average Lipid ratio (%): 24.3± 7.8, average Z-score points of MRI : 1.02± 0.5 and total Brain atrophy was 4.3± 2.7 %. About HD-PD cases, one case had slight cerebrovascular dementia, and 2 cases are MCI; average Z-score was 1.2± 1.0 total Brain atrophy was 3.8± 1.4 %. Average SMI: 5.9± 1.3 kg/m^2, average BMI:20.7± 3.8, average Lipid ratio (%): 21.9± 8.1. Two cases died of malnutrition and sepsis. About 15 HD patients with Alzheimer type (AZ-type) dementia, average HDS-R: 10.4± 9.3, average BMI: 18.9± 2.2, average SMI: 4.7± 1.0 kg/m^2, average Lipid ratio (%): 23.5± 6.1, average Z-score points of MRI: 2.6± 0.9 and total Brain atrophy was 9.3± 5.7 %. One-year survival rate of HD patients with AZ was about 20% after transferring to our hospital. The data of SMI and LP% was relatively reserved in PD and HD-PD, but significantly low from that of HD-AZ, and therefore it might not be effective in rehabilitation because of muscle weakness in HD-AZ. There were almost no HD cases with overhydration (ECW/TBW). Almost all dialysis patients had simple some old cerebral infarctions by simple CT examination.

Conclusion: By CT and MRI image findings, almost PD cases had old low-density area in CT and no acute cerebral infarctions in MRI. The hippocampal atrophy and total brain atrophy of PD and HD-PD was extremely mild, but was very severe in HD-AZ. There were no cases with severe cognitive impairment between PD and HD-PD even if undergoing for over ten years.

P1222 CLINICAL OUTCOMES AND MORTALITY IN PERITONEAL DIALYSIS: WHAT ABOUT ELDERLY PATIENTS?

Amel Ayed[1], Meriem Ben salem[1], Faouzi Haouala[1], Mohamed Zied BEN BETTAIEB[1], Imen Chemli[1], Ahmed Letaief[1], Mouna Hammouda[1], Aloui Sabra[1], Habib Skhiri[1]

[1]*Fattouma Bourguiba University Hospital, nephrology, monastir, Tunisia*

Background and Aims: The burden of elderly patients initiating dialysis regimens is increasing around the world due to rising life expectancies. However, little is known regarding the results of elderly patients treated with peritoneal dialysis (PD). Thus, the aim of this study is to determine the clinical outcomes and to evaluate the survival rates as well as the predictors of mortality among this group.

Method: This is a retrospective descriptive study performed in the PD unit in Monastir - Tunisia from 1990 till december 2017. All patients aged $\geq$ 65 years were included. The epidemiological and clinico-biological data as well as the complications were collected. Overall and technique survival rates were analyzed.

Results: Of the total 304 patients who began PD during the study period, 55 met our inclusion criteria. The prevalence of elderly patients was 18.1%. The mean age was 73 $\pm$ 5 years (65-86) with a male predominance (65.5%). Our patients were diabetic, hypertensive and cardiac in 45%, 64% and 33% respectively. Histories of hemodialysis necessity prior to PD use were present in 43.6 % of the patients. PD exchanges were performed by a member of the family in for 87.3% of cases and they often choose the CAPD (80%). Peritonitis rate was 17.92 patient-months. During the follow-up period, transfers to hemodialysis (15 patients) and death (39 patients) were the most common causes of withdrawal from PD. Frequent peritonitis, ultrafiltration failure warranted transfers to hemodialysis in 27% and 40% respectively. Causes of death were mostly not related to PD (87.2%) and they included cardiovascular events (28.2%), sepsis (20.5%) as well as neoplasma (15.4%). The mean patient survival time was 16.4 years versus 23.3 years in the other group. The survival rates were 96%, 93.5%, 86.9% and 76.6% at 1, 3, 5 and 10 years after peritoneal dialysis initiation, respectively. Advanced age (p 0.04) and occurrence of peritonitis (p 0.02) were predictors of mortality. The mean technique survival duration was 48.6$\pm$2.7 months. The technique survival rates were 78%, 62.6%, 53.5% and 41% at 1, 2, 3 and 4 years, respectively. Peritonitis was the primordial predictor of technique survival.

Conclusion: Mortality among elderly patients seems to be higher in our study. Infectious complications and cardiovascular events were the main causes of death. Advanced age and occurence of peritonitis represented the main predictive factors of mortality.

P1223

PATIENT REMOTE MONITORING IN AUTOMATED PERITONEAL DIALYSIS: 2017-2019 CLINICAL EXPERIENCE IN A SINGLE CENTER

Gianpaolo Amici[1], Antonina Lo Cicero[2], Mery Zuccolo[2], Rosella Ferraro Mortellaro[2], Dino Romanini[2], Antonio Irlando[2], Loijze Celik[2], Alfonso Velardita[2]

[1]Nephrology and Dialysis Unit, San Daniele del Friuli and Tolmezzo Hospital, ASUFC, FVG, San Daniele del Friuli, Italy

Background and Aims: We conducted an observational study in a group of patients in automated peritoneal dialysis (APD) to evaluate the impact of the introduction and the long-term use of a telemedicine system for remote patient monitoring (RPM, Claria Sharesource Baxter).

Method: From April 1 2017 to December 31 2019 (33 months) we followed 42 APD patients with RPM, sex F 20 M 22, age 70±14 years, on PD treatment for median 10 (IQR 3-23) months, distance from the center 18±14 km in mountain and hill area. Have been studied 505 months of RPM overall, per patient median 9 (IQR 3-19) months, corresponding to 11685 APD sessions overall, per patient median 206 (IQR 52-457) sessions.

Results: Have been registered 1125 alarms (red flags) overall, per patient median 9 (IQR 1-45) alarms, rate 2.2 alarms patient-month (0.1 alarms per session). Analyzing the causes of the alarms: "dwell time lost" (>45 min) 1006 (89%), "drain anticipation" (>2 times) 22 (2%), "fill or dwell bypass" (>3 times) 15 (1%), "various causes" (>10 times) 86 (8%). "Various causes" alarm group sums mainly slow drain for set kinking and insufficient drain volume. We count 195 remote modifications of dialysis program overall, median per patient 3 (IQR 1-7), rate 0.02 patient month with a ratio 0.2 modifications per alarm. Looking to program modification, the alarm type specifically linked to modifications has been insufficient drain volume of the "various causes" group (36 events, 18% of all modifications). We found a positive correlation between the number of treatments and alarms ($r=0.534$, $p<0.001$). In the observation period the overall hospitalization days were 403, rate 0.8 days patient month, ratio 0.02 hospitalization days per APD RPM session and ratio 0.4 hospitalization days per alarm.

Conclusion: The study shows that APD with RPM improves patients' follow-up changing the organization of the center. In the long term the telemedicine system shows the advantages of a careful and daily monitoring. The rates of alarm, change of prescription and hospitalization resulted very low in our experience.

P1224 ROLE OF DIAGNOSTIC IMAGING DURING PERITONITIS IN PERITONEAL DIALYSIS PATIENTS

Khin Zar Li Lwin[1], Marjorie Foo[2], Htay Htay[2]

[1]MOH Holdings Pte Ltd, Internal Medicine, Singapore, Singapore and [2]Singapore General Hospital, Renal Medicine, Singapore, Singapore

Background and Aims: Peritonitis in peritoneal dialysis (PD) patients can be directly related to PD or secondary to intrabdominal infection (secondary peritonitis). The indication and role of imaging of abdomen during peritonitis in PD patients is unclear.

Method: This was a single center, retrospective study, including all the first episode of peritonitis in incident PD patients from the period of January 2013 to October 2017. Primary aim of the study was to identify the incidence of secondary peritonitis diagnosed by imaging of abdomen (defined as positive scan finding of intraabdominal lesions) in PD patients with peritonitis. Secondary outcomes were predictors for secondary peritonitis analyzed by multivariable logistic regression.

Results: There were total 527 incident PD patients during the study period. Of these, 153 patients (29%) developed at least one episode of peritonitis. The mean age of patients with peritonitis was 57.7 ± 3.4 years, 49 % were male, and 52% had diabetes mellitus. Out of 153, 78 patients (51%) underwent diagnostic imaging of abdomen to look for secondary peritonitis. Majority of them had contrast enhanced computed tomography (CT) scan (95%) and the remaining had non-contrast CT scan or ultrasound of abdomen. Of 78 patients who underwent scan, 12 patients (16%) were reported to have intra-abdominal lesions (secondary peritonitis) including colitis (n=2), pancreatitis (n=1), cholecystitis (n=4), appendicitis (n=1), intestinal obstruction (n=2), liver abscess (n=1), gastric cancer (n=1). According to the causative microorganisms, the positive scan finding of intra-abdominal lesions was more commonly observed in Gram-negative peritonitis (n=7, 58%), followed by fungal/mycobacterial peritonitis (n=2, 17%), Gram-positive peritonitis (n=2, 17%), polymicrobial peritonitis (n=1, 8%), but none (0%) in culture negative peritonitis. Among patients with Gram-negative peritonitis who underwent the imaging of abdomen, only 12% (7/58) were reported to have intra-abdominal lesions. In multivariable logistic regression, the presenting symptoms including fever (odds ratio (OR) 1.51, 95% confidence interval (CI) 0.40 – 5.68), abdominal pain (OR 1.08, 95% CI 0.24 -1.78), presence of cloudy of effluent (OR 0.66, 95% CI 0.19 -2.29), hypotension on presentation (OR 3.61, 95% CI 0.75 -17.46) or effluent white cell counts on presentation (OR 0.99, 95% CI 0.93 -1.05) were not significantly associated with secondary peritonitis.

Conclusion: A considerable number of patients underwent imaging of abdomen during peritonitis regardless of causative organisms, only a few of them had intra-abdominal lesions. Future prospective study is needed to guide the role of imaging in PD patients during peritonitis.

P1225

PREVALENCE AND PROGNOSTIC SIGNIFICANCE OF DIABETES IN PERITONEAL DIALYSIS: TECHNIQUE AND PATIENT SURVIVAL

Amel Ayed[1], Meriem Ben salem[1], Faouzi Haouala[1], Ayed Sinda[1], Imen Chemli[1], Ahmed Letaief[1], Ines Jafar[1], Mouna Hammouda[1], Aloui Sabra[1], Habib Skhiri[1]

[1]*Fattouma Bourguiba University Hospital, nephrology, monastir, Tunisia*

Background and Aims: Diabetes in recent years is climbing up as the number one cause of chronic kidney disease (CKD). Clinical statistics suggest that Diabetics on peritoneal dialysis (PD) tend to have a poorer prognosis than others.

Thus, the aim of this study is to determine the clinical outcomes and to evaluate the survival rates as well as the predictors of mortality among this group.

Method: It's a retrospective study carried out in the nephrology Department of Fattouma Bourguiba Hospital (Monastir, Tunisia) from 1990 to 2017 including 304 PD patients. We compared two groups: diabetic and non diabetic patients in term of survival and factors in correlation.

Results: A total of 110 diabetic versus 194 non diabetic patients were reported. The mean age of diabetic group was 55.14 ± 15 years with a sex ratio 2.33 (men/women). In addition to diabetes, comorbid diseases included hypertension (47.3%) and cardiopathy (32.7%). The mean Charlson score of diabetic group was 5.22±1.5 versus 2.72±1.23 in the other group. A total of 62.7% (n=69) of the patients performed PD with the help of another person mostly a member of the family. The PD modality often used was CAPD (71%). Only six patients made a compulsory choice to begin PD due to vascular access while sixty diabetics chose PD to maintain autonomy (54.5%). During the follow-up period, transfers to hemodialysis (40.9%) and death (53.6%) were the most common cause of withdrawal from PD. In total, 45 patients were transferred to hemodialysis because of infectious complications (31%), Ultrafiltration failure (31%), catheter dysfunction (27%), and psychological intolerance (11%). The death was unrelated to PD in 83% of cases mostly due to considerable burden of cardiovascular events (23 patients). The median survival of the diabetic patients was 15.8 years versus 20.8 years in non diabetic ones with significant difference between the 2 groups (p=0.0001). Diabetes was associated with worse prognosis (OR:147, p=0.0001). The median survival adjusted to the diabetes group was 180 months. Kaplan–Meier analysis showed that diabetes was associated with a significant increase in mortality (p=0.006). Global median survival of the technique was estimated to 68 months (95%, IC [47 ,90]), and it was correlated to the presence or the absence of diabetes. In fact, the technique survival among diabetic patients was estimated to 80% after 12 years and 25% after 20 years whereas, in the other group it approaches 90% and 35% respectively.

Conclusion: This study confirms the pejorative impact of diabetes in the technique and patient survival in DP. So, it stresses the importance of organizing appropriate care upstream to prevent the development of cardiovascular morbidities and infectious complications in DP.

P1226 MITOCHONIC ACID 5 (MA-5) AMELIORATES CG-INDUCED PERITONEAL FIBROSIS IN MICE

Hiro Inoue[1], Yoko Obata[1], Takehiro Suzuki[2], Miki Torigoe[1], Kenta Torigoe[1], Chitose Suzuki[2], Takaaki Abe[2], Takehiko Koji[3], Tomoya Nishino[1]

[1]Nagasaki University Graduate School of Biomedical Sciences, Department of Nephrology, Nagasaki, Japan, [2]Tohoku University Graduate School of Medicine, Division of Nephrology, Endocrinology and Vascular Medicine, Sendai, Japan and [3]Nagasaki University Graduate School of Biomedical Sciences, Department of Histology and Cell Biology, Nagasaki, Japan

Background and Aims: Peritoneal fibrosis is one of important complications induced by long-term peritoneal dialysis. Mitochondrial dysfunction causes an increase of oxidative stress and depletion of ATP. Thus, it may be associated with a variety of disease including fibrosis in several organs. Recently, mitochonic acid 5 (MA-5) was synthesized and its therapeutic potential for mitochondrial dysfunction in kidney disease models has been reported. In this study, we investigated the effect of MA-5 for peritoneal fibrosis model in mice.

Method: Peritoneal fibrosis was induced by intraperitoneal injection of chlorhexidine gluconate (CG) every other day for 3 weeks in C57/BL6 mice. MA-5 was administered at 2 mg/kg by gavage every day from the initiation of CG injection. Control mice received only a vehicle (distilled water). After 3 weeks of treatment, the animals were sacrificed and the peritoneal tissues were collected. The peritoneal sections were stained with Masson's trichrome for light microscopic examination and the fibrotic thickening of parietal peritoneum was measured on the randomly selected different regions on each section. The expressions of F4/80, which is a marker of macrophages, monocyte chemotactic protein 1 (MCP1), α-smooth muscle actin (α-SMA), and transforming growth factor-β (TGF-β) were evaluated by immunohistochemistry.

Results: The fibrotic thickening of parietal peritoneum was significantly attenuated in MA-5 treated mice compared with control mice (the thickness of submesothelial area: 100.24 +/- 13.67 vs 54.78 +/- 7.43 μm ($p<0.05$)). The numbers of TGF-β positive cells, α-SMA positive cells, MCP1 positive cells and infiltrating macrophages were significantly decreased in MA-5 treated mice than those in control mice.

Conclusion: These results suggest that MA-5 may have a therapeutic potential in the progression of peritoneal fibrosis as well as kidney disease models.

P1227

SURVIVAL OF PATIENTS TRANSFERRED FROM HEMODIALYSIS (HD) TO CHRONIC AMBULATORY PERITONEAL DIALYSIS (CAPD) DUE TO POOR ARTERIOVENOUS (AV) ACCESS

Ahad Qayyum[1]

[1]*Bahria International Hospital, Renal Unit, Lahore, Pakistan*

Background and Aims: This study was carried out to ascertain the 6 month survival of patients who were transferred from hemodialysis to peritoneal dialysis due to poor vascular access at tertiary care facility in Pakistan. PD remains an under-utilized and unpopular modality of renal replacement therapy. One of the major reasons for its unpopularity remains poor patient selection. Furthermore PD is used as a last resort when AV access for HD becomes impossible in Pakistan.

Method: This study was carried out over a 4 year period. All patients transferred from hemodialysis onto peritoneal dialysis were included in the study. A total of 23 patients of Pakistani decent were switched to peritoneal dialysis from hemodialysis because of poor AV access. All patients included in the study had undergone venograms and consultation with vascular surgeons to confirm that AV access henceforth was inadequate for hemodialysis to continue. After placement of the peritoneal dialysis catheter a 2 week rest period was given to each patient before CAPD was initiated. The 6 month survival of each patient from the point of being transferred to CAPD was noted.

Results: The mean age of patients included in the study was 58 years. 80% of the participants were known to have diabetes mellitus. 15 out of the 23 patients included in the study died within 6 months of starting peritoneal dialysis. 12 out of the 23 patients included had difficulties in achieving either required ultrafiltration or KT/V despite ensuring correct catheter placement and following standard CAPD good practices.

Conclusion: Patients being switched from hemodialysis to CAPD due to poor AV access carry a greater than 50% 6 month mortality rate. In a country where PD struggles to gain popularity, we need to be very selective in starting patients on this modality with a realization that PD cannot be kept as a last resort rather should be advocated as the first choice therapy. Only then can the true benefits of PD be exhibited.

P1228

IMPROVEMENT OF BODY WEIGHT MANAGEMENT, BETA2-MICROGLOBULIN LEVEL AND RESISTANCE TO ERYTHROPOIESIS-STIMULATING AGENTS BY HYBRID PERITONEAL DIALYSIS PLUS HEMODIALYSIS THERAPY

Kanako Fukasawa[1], Mizuya Fukasawa[2]

[1]University of Yamanashi Hospital, Department of Cinical Enginnering, Chuo, Japan and [2]University of Yamanashi Hospital, Department of Urology, Chuo, Japan

Background and Aims: Peritoneal dialysis (PD) has the advantages of not causing rapid changes in the body fluid levels or solute contents in the blood due to the continuous treatment on all days of the week, and of not needing the patients to visit the hospital 3 times a week or lie on a bed for 4 hours to receive treatment. PD alone can, however, not adequately remove all the uremic toxins and excess water, and the patients are likely to be resistant to erythropoiesis-stimulating agents (ESA). These drawbacks could be potentially improved if PD and hemodialysis (HD) were used together. The aims of the present study were to clarify the changes in the body weight, serum β2-microglobulin (β2MG) level, and resistance to ESA in PD patients switched from PD alone to PD-HD hybrid therapy (hybrid therapy).

Methods: The data of seven patients who were switched from PD alone to PD-HD hybrid therapy at our hospital were retrospectively analyzed to determine the changes in the body weight, serum β2MG level, dose of ESA (Darbepoetin Alfa) and the hemoglobin level before and at 3 months after the switch to hybrid therapy; in hybrid therapy, the patient received HD once a week and did not receive PD on that day. We also carried out a questionnaire survey to determine the changes in the feeling of well-being and quality of life of the patients after the switch to hybrid therapy.

Results and Discussion: The body weight decreased significantly from 67.4 ± 11.8 kg to 63.7 ± 8.7kg ($p = 0.0345$) after the switch from PD alone to PD-HD hybrid therapy, indicating that the control of the body fluids was much easier with hybrid therapy than with PD alone. The mean serum β2MG level in the patients decreased from 37.3 ± 11.6 μg/mL to 32.6 ± 5.9 μg/mL ($p = 0.1607$, not significant), ; in particular, in those patients in whom the serum β2MG levels were over 30 μg/mL, the level decreased significantly from 42.5 ± 8.7 μg / mL to 34.4 ± 6.1 μg / mL ($p = 0.0337$). The dose of ESA decreased significantly in all patients from 193 ± 74 μg/month to 69 ± 38 μg/month ($p = 0.006$), while the hemoglobin level remained unchanged (from 10.2 ± 1.7 g/dL to 11.2 ± 1.2 g/dL, $p = 0.1406$). In the questionnaire survey, almost all the patients expressed positive feelings about the switch of the treatment modality, such as "it became easier to go up the stairs," "improved working efficiency," and "comfortable feeling." Since the peritoneum was allowed to rest once in a week, on the day of the HD, it could also preserve peritoneal functions. Therefore, hybrid therapy was also considered to be effective from the viewpoint of performing PD over the long term.

Conclusion: We can expect easier management of the body fluid, efficient β2MG removal, and improvement of ESA resistance by switching the dialysis treatment modality from PD alone to HD-PD hybrid therapy.

P1229 PREVALENCE OF LIPID DISORDERS IN PERITONEAL DIALYSIS PATIENTS

Safa Fattoum[1], Barbouch Samia[1], Hajji Mariem[1], Tasnim Mesbahi[1], Braiek Nessrine[1], Imen Gorsane[1], Harzallah Amel[1], Ben Hmida Fathi[2], Ounissi Mondher[1], Ben Abdallah Taieb[1]

[1]Charles Niccolles Hospital, Internal Medecine, Tunis, Tunisia and [2]Charles Nicolles Hospital, Kidney pathology laboratory Irsp001, Tunis, Tunisia

Background and Aims: Lipid disorders are common in end stage renal disease patients. Renal replacement therapies and especially peritoneal dialysis (PD) results in further alteration rather than correction of lipidemia. The aim of this study is to precise the prevalence of the different lipid disorders of PD patients.

Method: It's a retrospective study conducted in our PD unit in December 2019. We collected all data concerning clinical characteristics of all patients currently in PD, as well as incidence of different lipid disorders.

Results: There were 90 patients with an average age of 45 years (extremes: 20.5 years and 80.6 years). The sex ratio is 1.25. Fourteen were diabetic (15.5%). All patients were on Automated PD (APD) except one on Continuous Ambulatory PD (CAPD). The average duration of PD was 40.5 months. The causal nephropathy was glomerular in 26,6 % (diabetic in 14 patients (15,5%)), hypertensive 13,3%,, interstitial in 16,66%., and undetermined in 27,7%. The average Charlson score was 3,2.

The average serum level of total cholesterol (TC) was 4,96 mmol/L, of triglycerides (TG) was 1,7mmol/L, of HDL-cholesterol(HDLc) was 0,93 mmol/L, and of LDL-cholesterol(LDLc) was 3,05 mmol/L.

Fifty one patients had dyslipidaemia: 13 had isolated hypercholesterolemia, 19 had isolated hypertriglyceridemia, and 19 had hypercholesterolemia and hypertriglyceridemia.

All dyslipidemic patients were on hypolipemic diet. Twelve (13,3%) were taking statin, no one was taking fibrate.

Conclusion: Chronic dialysis patients have several cardiovascular risk factors due to renal failure and comorbidities often associated. Dyslipidemia is a modifiable risk factor. It must be screened and treated to reduce morbidity and mortality.

P1230 **CHANGES IN CKD-MBD-REALTED MARKERS AND MIDDLE MOLECULAR WEIGHT SOLUTES (B2MG, A1MG)IN PATIENTS ON PD-HD COMBINATION THERAPY**

Tadashi TOMO[1], Takashi Sato[2], Jun Minaguchi[3]

[1]Oita University, Clinical engineering Research Center, Yufu, Japan, [2]Kaikoukai Central Clinic, Dialysis center, Nagoya, Japan and [3]Kawashima Hospital, Dialysis center, Tokushima, Japan

Background and Aims: According to a survey by the Japanese Society for Dialysis Therapy (as of December 31, 2017), among the 9,090 patients that underwent peritoneal dialysis (PD) in Japan, 1,765 patients were treated with PD in combination with once-weekly hemodialysis (HD) or hemodiafiltration (HDF) (PD-HD/HDF combination therapy); these patients accounted for 19.4% of the overall PD population. It has been confirmed that middle-molecular-weight solutes, such as β2MG, α1MG, that cannot be effectively removed by PD can be removed by HD/HDF in PD-HD/HDF combination therapy. In this study, we examined the changes in CKD-MBD-related markers (phosphorus, PTH, FGF-23 [molecular weight 32,000 Da], Fetuin-A [molecular weight 59,000 Da]) and middle-molecular-weight solutes (β2MG [molecular weight 11,800 Da] and α1MG [molecular weight 32,000 Da]) in nine patients on PD-HD combination therapy.

Method: We recruited nine patients (four men, five women) on PD-HD combination therapy with an underlying disease of chronic glomerulonephritis. The patients had a mean age of 66.2 years and a mean dialysis period of 49.1 months on PD alone and 32.1 months on PD combined with HD. The PD protocol included 2 L bag × 4/day (5 days, Monday–Friday; no therapy on Saturday and Sunday), and the HD protocol included 4 hours QB at 200 mL/min, QD at 500 mL/min, and Dialyzer Polysulfone (Asahi Medical Japan) every Saturday. Blood was collected before and after HD and before the next HD (1 week later) to measure CKD-MBD-related markers and middle-molecular-weight solutes. Kits to measure FGF-23 (Millipore, US) and Fetuin-A (Biovendor, Czech) were used.

Results: The levels of the different markers and solutes were as follows: phosphorus (mg/dL) (mean before HD: 5.31, mean after HD: 2.28 ($P < 0.01$), and mean before the next HD: 5.53); iPTH (pg/mL) (mean before HD: 131.9, mean after HD: 98.8, and mean before the next HD: 125.9); FGF-23 (pg/mL) (mean before HD: 785.3, mean after HD: 576.1 ($P < 0.01$), and mean before the next HD: 897); Fetuin-A (μg/mL) (mean before HD: 427.9, mean after HD: 423.1, and mean before the next HD: 428.75); β2MG (mg/L) (mean before HD: 36.31, mean after HD: 13.23 ($P < 0.01$), and mean before the next HD: 36.11); and α1MG (mg/L) (mean before HD: 141.9, mean after HD: 130.4, and mean before the next HD: 114.8).

Conclusion: β2MG and phosphorus levels were significantly decreased when PD was combined with HD, confirming that HD was able to eliminate them. Furthermore FGF-23 (molecular weight 32,000 Da) significantly decreased after HD but α1MG (molecular weight 30,000 Da) did not, suggesting that the decrease in FGF-23 was caused by the decrease in blood phosphorus concentration.

P1231 **ASSISTED PERITONEAL DIALYSIS IN ESRD PATIENTS**

Jelena Tosic Dragovic[1], Nada Dimkovic[1,2], Zdenka Majster[1], Tatjana Damjanovic[1], Ana Bulatovic[1], Radomir Naumovic[1,2]

[1]University Hospital Center Zvezdara, Nephrology, Belgrade, Serbia and [2]Faculty of medicine, Belgrade University, Belgrade, Serbia

Background and Aims: Peritoneal dialysis is an important form of treatment for patients with end stage chronic kidney failure requiring renal replacement therapy but its use may be limitted by growing number of elderly and disabled patients. Often, they choose an assisted peritoneal dialysis (assCAPD) as first option, that can be performed by relative or a nurs. The aim of this research was to analyse differences between two groups of patients (CAPD vs. assCAPD) in order to establish if two variants are comparable in regard of patients outcome.

Method: We analysed 61 patient divided into two groups (ass CAPD, N= 16 and CAPD, N= 45) who were dialysed in Zvezdara University hospital for more than 3 months and correlated number of peritonitis, exit site infections and overall mortality rates between two groups during the period of 60 months. Assistance was provided on the volontary basis by family member.

Results: Patients in assCAPD group were unsignificantly older (68±11vs. 60 ± 12 years) and had higher comorbidity score. The groups were homogeneous according the presence of diabetes mellitus, CRP and PTH levels. There were no significant difference between the two of groups in the number of peritonitis (p=0,77), exit site infections (p=0,37) and overall survival (p= 0,74, Figure 1.).

Conclusion: Family member provides very good assistance in peritoneal dialysis giving the results that are comparable to that of self-performing CAPD patients. This is therefore very successful treatmen option for a special population of ESRD patients who can not performe CAPD on their own.

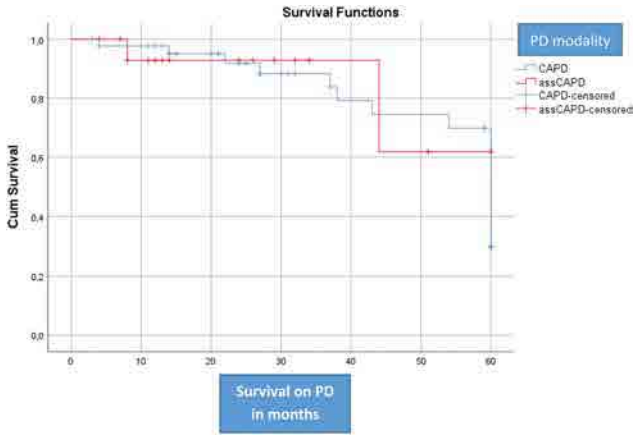


Figure:

P1232 COMPUTED TOMOGRAPHIC PERITONEOGRAPHY - GUARANTYING SAFER SURGICAL STRATEGIES

Pedro Alves[1], Ana Domingos[2], Henrique Patrício[1], João Ildefonso[3], Anabela Malho Guedes[2], Idalécio Bernardo[2], Pedro Leão Neves[2]

[1]Centro Hospitalar e Universitário do Algarve, Radiology, Faro, Portugal, [2]Centro Hospitalar e Universitário do Algarve, Nephrology, Faro, Portugal and [3]Centro Hospitalar e Universitário do Algarve, Surgery, Faro, Portugal

Background and Aims: Peritoneal Dialysis (PD) is currently the first option as renal replacement therapy to many patients, for several reasons, as personal flexibility, volemic management in cardiorenal patients, poor vascular access to dialysis, among others. Mechanical complications can be a drawback in these patients, which may occur during or after catheter placement. Abdominal wall hernias and dialysate leaks are relatively common and highly related to chronically increased intraperitoneal pressure. In this setting CT peritoneography is the technique of choice as it allows differentiation between a true hernia or a wall leakage.

Method: We describe a case of a 69-year-old man, with a personal history of polycystic kidney disease, colonic diverticulosis and hypertension, which opted for PD. The patient later developed a mechanical complication for which a proper diagnostic approach, namely through specific imaging, and surgical planning were essential.

Results: After 15 months without complications, it was detected a bulging in the periumbilical area, exacerbated by orthostatism. Changes in dialytic prescription included lower dialytic volumes during orthostatic period, with some improvements. The limitation of volumes and difficulty of drainage were limiting dialytic prescription and insufficient kt/V. An ultrasound (figure 1) and CT peritoneography (figure 2) were performed, revealing an hernial sac with peritoneal liquid leak, without any intestinal loop, approachable by minimally invasive surgery and local anesthesia.

Mini-laparotomy was performed, hernial sac was removed, without peritoneum aperture, with only a 4-day pause on PD technique.

Conclusion: CT peritoneography allowed the differentiation between this true hernia and a wall leakage, by providing accurate anatomical detail, allowing proper planning of surgical intervention. In this case, the patient had additional predisposing factors, namely polycystic kidney disease. Moreover, only a short pause on PD was necessary. Although some limitations exist, such as the use of iodinated contrast material and ionizating radiations, CT peritoneography is currently the gold standard for the evaluation of mechanical complications in PD; in addition to those mentioned, it is also useful for complications related to the catheter (kinking, entrapment, malposition), intrabdominal adhesions or loculated fluid collections.

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DIALYSIS. CARDIOVASCULAR COMPLICATIONS

P1236 EFFECTS OF SACUBITRIL-VALSARTAN IN HEART FAILURE WITH PRESERVED EJECTION FRACTION IN PATIENTS UNDERGOING PERITONEAL DIALYSIS

Sha Fu[1], Zhenjian Xu[1], Baojuan Lin[1], Junzhe Chen[1], Qiuyan Huang[1], Yanchun Xu[1], Anping Xu[1], Yangxin Chen[2], Ying Tang[1]

[1]Sun Yat-sen Memorial Hospital of Sun Yat-sen University, Nephrology, Guangzhou, P.R. China and [2]Sun Yat-sen Memorial Hospital of Sun Yat-sen University, Cardiovasology, Guangzhou, P.R. China

Background and Aims: Angiotensin receptor–neprilysin inhibitor (ARNI) sacubitril–valsartan is a landmark drug in heart failure with reduced ejection fraction (HFrEF), however, it remains unclear in patients with heart failure with preserved ejection fraction (HFpEF), especially the data of ARNI treatment on peritoneal dialysis (PD) patients with HFpEF are lacking. The present study was designed to determine the efficacy and safety of sacubitril–valsartan in patients with HFpEF undergoing peritoneal dialysis.

Method: We assigned end stage renal disease (ESRD)patients, receiving peritoneal dialysis for 3 months, with New York Heart Association (NYHA) class II to IV heart failure, left ventricular ejection fraction $\geq$ 50%, and elevated level of N-terminal pro–B-type natriuretic peptide (NT-proBNP) to receive sacubitril/valsartan treatment. Patients were regularly followed up after medication treatment. Wilcoxon matched-pair signed-rank (2 samples) tests were applied to investigate the alterations in Clinical and biochemical parameters as the efficacy before and after taking sacubitril–valsartan, and safety was also assessed.

Results: Twenty-one patients were recruited in this study. Compared with baseline levels, NT-proBNP levels (p=0.002) and heart rate (p=0.031) were markedly decreased after treatment with sacubitril/valsartan, signs and symptoms of heart failure (21/21 versus 15/21, p=0.021) and NYHA classification were notably improved after 3-12 months follow-up.

Conclusion: The present data suggested that sacubitril/valsartan treatment in the patients with HFpEF undergoing peritoneal dialysis was effective and safe, which is the first study about sacubitril/valsartan treatment for the PD patients with HFpEF, and it may bring the hope for these patients due to no other effective methods at present.

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P1237

TISSUE-NONSPECIFIC ALKALINE PHOSPHATASE, A CULPRIT DURING ARTERIAL MEDIA CALCIFICATION BUT INDISPENSABLE DURING PHYSIOLOGICAL BONE FORMATION/-MINERALIZATION IN RATS

Britt Opdebeeck[1], José Millan Luis[2], Anthony Pinkerton[2], Anja Verhulst[3], Patrick D'Haese[3], Ellen Neven[3]

[1]University of Antwerp, Laboratory of pathophysiology, Belgium, [2]Sanford Burnham Prebys Medical Discovery Institute and [3]University of Antwerp, Laboratory of pathophysiology

Background and Aims: Vascular media calcification is frequently seen in elderly and patients with chronic kidney disease (CKD), diabetes and osteoporosis. Pyrophosphate is a well-known calcification inhibitor that binds to nascent hydroxyapatite crystals and prevents further incorporation of inorganic phosphate into these crystals. However, the enzyme tissue-nonspecific alkaline phosphatase (TNAP), which is highly expressed in calcified arteries, degrades extracellular pyrophosphate into phosphate ions, by which pyrophosphate loses its ability to block vascular calcification. Here, we aimed to evaluate whether a TNAP inhibitor is able to prevent the development of arterial calcification in a rat model of warfarin-induced vascular calcification.

Method: To induce vascular calcification, rats received a diet containing 0.30% warfarin and 0.15% vitamin K1 throughout the entire study and were subjected to the following daily treatments: (i) vehicle (n=10) or (ii) 10 mg/kg/day TNAP-inhibitor (n=10) administered via an intraperitoneal catheter from start of the study until sacrifice at week 7. Calcium, phosphorus and parathyroid hormone (PTH) levels were determined in serum samples as these are important determinants of vascular calcification. As TNAP is also expressed in the liver, serum alanine aminotransferase (ALT) and aspartate (AST) levels were analyzed. At sacrifice, vascular calcification was evaluated by measurement of the total calcium content in the arteries and quantification of the area % calcification on Von Kossa stained sections of the aorta. The mRNA expression of osteo/chondrogenic marker genes (runx2, TNAP, SOX9, collagen 1 and collagen 2) was analyzed in the aorta by qPCR to verify whether vascular smooth muscle cells underwent reprogramming towards bone-like cells. Bone histomorphometry was performed on the left tibia to measure static and dynamic bone parameters as TNAP also regulates physiological bone mineralization.

Results: No differences in serum calcium, phosphorus and PTH levels was observed between both study groups. Warfarin exposure resulted in distinct calcification in the aorta and peripheral arteries. Daily dosing with the TNAP inhibitor (10 mg/kg/day) for 7 weeks significantly reduced vascular calcification as indicated by a significant decrease in calcium content in the aorta (vehicle 3.84 ± 0.64 mg calcium/g wet tissue vs TNAP inhibitor 0.70 ± 0.23 mg calcium/g wet tissue) and peripheral arteries and a distinct reduction in area % calcification on Von Kossa stained aortic sections as compared to vehicle condition. The inhibitory effects of SBI-425 on vascular calcification were without altering serum liver markers ALT and AST levels. Furthermore, TNAP-inhibitor SBI-425 did not modulate the mRNA expression of osteo/chondrogenic marker genes runx2, TNAP, SOX9, collagen 1 and 2. Dosing with SBI-425 resulted in decreased bone formation rate and mineral apposition rate, and increased osteoid maturation time and this without significant changes in osteoclast- and eroded perimeter.

Conclusion: Dosing with TNAP inhibitor SBI-425 significantly reduced the calcification in the aorta and peripheral arteries of a rat model of warfarin-induced vascular calcification and this without affecting liver function. However, suppression of TNAP activity should be limited in order to maintain adequate physiological bone mineralization.

P1238 **EVALUATION OF AN IN VITRO CO-CULTURE MODEL FOR TESTING EFFECTS OF CYTOPROTECTIVE ADDITIVES IN PERITONEAL DIALYSIS FLUIDS ON CARDIOVASCULAR OUTCOME**

Juan Manuel Sacnun[1,2], Rebecca Herzog[1,3], Maria Bartosova[4], Claus Schmitt[4], Klaus Kratochwill[1,3]

[1]Medical University of Vienna, Department of Pediatrics, Pediatric Nephrology and Gastroenterology, Vienna, Austria, [2]Zytoprotec, Vienna, Austria, [3]Medical University of Vienna, Christian Doppler Laboratory for Molecular Stress Research in Peritoneal Dialysis, Wien, Austria and [4]University of Heidelberg, Pediatric Nephrology, Heidelberg, Germany

Background and Aims: The composition of all currently available peritoneal dialysis (PD) fluids triggers morphological and functional changes in the peritoneal membrane. Periodic exposure leads to vasculopathy, hypervascularization, and diabetes-like damage of vessels, eventually leading to failure of the technique. Patients undergoing dialysis generally, have a high risk of cardiovascular events. It is currently unclear if there is a mechanistic link between peritoneal membrane failure and cardiovascular risk. In vitro and in vivo studies have shown that cytoprotective additives (e.g. dipeptide alanyl-glutamine (AlaGln) or kinase inhibitor lithium chloride (LiCl)) to PDF reduce peritoneal damage. Here, we developed an experimental model for investigating effects of these cytoprotective additives in PDF in the cardiovascular context.

Method: For modelling the peritoneal membrane in vitro, mesothelial and endothelial cells were co-cultured in transwell plates. Mesothelial cells were grown in the upper compartment and primary human umbilical vein endothelial cells (HUVEc) or primary microvascular cells were grown in the lower compartment. PDF with or without cytoprotective compounds, was added to the upper compartment to only expose mesothelial cells directly to different dilutions of the fluid. Effects on cell damage was assessed by quantification of lactate-dehydrogenase (LDH) release and live-dead staining of cells. Proteome profiles were analysed for both cell-types separately and in combination using two-dimensional difference gel electrophoresis (2D-DiGE) and liquid chromatography coupled to mass spectrometry (LC-MS). In vitro findings were related to PD-induced arteriolar changes based on abundance profiles of micro-dissected omental arterioles of children treated with conventional PD-fluids and age-matched controls with normal renal function.

Results: Marked cellular injury of HUVEc after PD-fluid exposure was associated with a molecular landscape of the enriched biological process clusters 'glucose catabolic process', 'cell redox homeostasis', 'RNA metabolic process', 'protein folding', 'regulation of cell death', and 'actin cytoskeleton reorganization' that characterize PD-fluid cytotoxicity and counteracting cellular repair process respectively. PDF-induced cell damage was reduced by AlaGln and LiCl both in mesothelial and endothelial cells. Proteome analysis revealed perturbation of major cellular processes including regulation of cell death and cytoskeleton reorganization. Selected markers of angiogenesis, oxidative stress, cell junctions and transdifferentiation were counter-regulated by the additives. Co-cultured cells yielded differently regulated pathways following PDF exposure compared to separate culture. Comparison to human arterioles confirmed overlapping protein regulation between endothelial cells in vitro and in vivo, proving harmful effects of PD-fluids on endothelial cells leading to drastic changes of the cellular process landscape.

Conclusion: In summary, this study shows harmful effects of PD-fluids also effecting endothelial cells and elucidates potential mechanisms by which cytoprotective additives may counteract the signalling axis between local peritoneal damage and systemic vasculopathy. An in vitro co-culture system may be an attractive approach to simulate the peritoneal membrane for testing direct and indirect effects of cytoprotective additives in PDF. When cultured and stressed in close proximity cells may respond differently. Characterisation of PD-induced perturbations will allow identifying molecular mechanisms linking the peritoneal and cardiovascular context, offering therapeutic targets to reduce current limitations of PD and ultimately decreasing cardiovascular risk of dialysis patients.

P1239 SHORT- AND LONG-TERM OUTCOME OF END-STAGE RENAL DISEASE PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

Hirota Kida[1], Shungo Hikoso[1], Akihiro Sunaga[1], Oeun Bolrathanak[1], Takayuki Kojima[1], Tomoharu Dohi[1], Tetsuhisa Kitamura[1], Katsuki Okada[1], Sinichiro Suna[1], Daisaku Nakatani[1], Hiroya Mizuno[1], Yasushi Sakata[1]

[1]*Osaka university, cardiology, suita, Japan*

Background and Aims: End-stage renal disease (ESRD) patients frequently have the coronary artery disease. However, the short- and long-term outcome of ESRD patients with acute myocardial infarction (AMI) is little known. The aim of this study was to clarify it.

Method: Using the database of the Osaka Acute Coronary Insufficiency Study (OACIS), 8702 consecutive AMI patients (male: 75.2%, mean age: 66.9±12.2yrs) from 2002 to 2013 were analyzed. We classified these patients into two groups, those with ESRD [ESRD group (n=271)] and without ESRD [No-ESRD group (n=8431)] and examined in-hospital or long-term all-cause mortality. ESRD was defined as eGFR<15ml/min/1.73m^2.

Results: ESRD group had higher frequency of diabetes (59.3% vs 37.8%, p<0.01), hypertension (90.1% vs 63.3%, p<0.01), Killip class≧2 (40.1% vs 21%, p<0.01), multi-vessel disease (69.3% vs 50.8%, p<0.01), and lower frequency of peak CK>3000 (21.7% vs 32.4%, p<0.01) than No-ESRD group. Mean follow-up period was 1041±721 days. In hospital mortality of ESRD group was 27% and No-ESRD group 7.2%. In patients who discharged alive (8027 patients), 1-year mortality of ESRD group was 12.2% and No-ESRD group 3.3%, 3-year mortality of ESRD group was 29.3% and No-ESRD group 8.7%. Kaplan-Meier analysis revealed that the all-cause mortality (log-rank p<0.01) was significantly higher in ESRD group than No-ESRD group. In ESRD patients who discharged alive (203patients), Cox univariate analysis after multiple imputation revealed that peak CK>3000 was significantly associated with an increased risk of mortality (Hazard ratio 2.67, 95% confidence interval 1.18to 6.07, p=0.031).

Conclusion: In patients with AMI, ESRD was significantly associated with worse short- and long-term outcome, suggesting that careful treatment might be required in ESRD patients with AMI, especially had peak CK>3000.

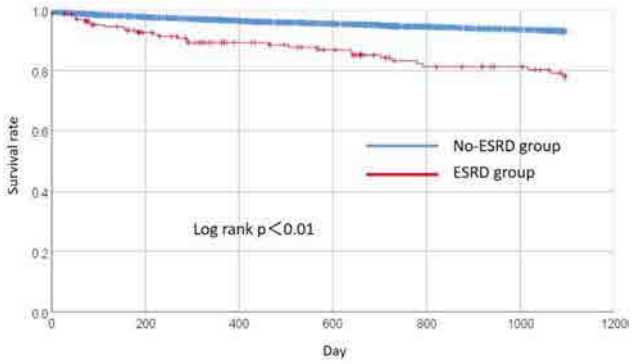


Figure:

P1240

EVALUATION OF COGNITIVE FUNCTION IN HEMODIALYSIS PATIENTS USING MAGNETIC RESONANCE SPECTROSCOPY: FIVE YEARS FOLLOW UP RESULTS

Shigeru Owada[1,2], Aki Hirayama[3], Teruhiko Maeba[2]

[1]Kita-Kashiwa Rehabilitation General Hospital, Kashiwa, Japan, [2]Asao Clinic, Kawasaki, Japan and [3]Tsukuba University of Technology, Center for Integrative Medicine, Tsukuba, Japan

Background and Aims: In Japan, the elderly population is increasing remarkably, and dialysis patients are aging as usual. According to statistics from the Japanese Society for Dialysis Therapy, at the end of 2017, the incidence of HD patients is estimated to be 3 per 1,000 population, and by the end of 2020, the average age will be over 70 years. Therefore, early diagnosis of cognitive impairment is an important issue. With the aging of dialysis patients, the number of cases showing cognitive dysfunction increase in addition to the decline of physical strength. The problem of the onset of dementia involves many difficulties in medical treatment and nursing.

Magnetic resonance spectroscopy (MRS) has been progressing from 1970s to evaluate neurological functions by measuring metabolites in the brain non-invasively. There are few reports using MRS for dialysis patients. In this study, we investigated the brain metabolites of hemodialysis (HD) patients with or without cognitive impairments using MRS and evaluated its usefulness for the diagnosis of cognitive disorder.

Method: A Toshiba MR device of 1.5 T was used. PRESS sequence was used to acquire water-suppressed 1H-MRS. Timing was TR/TE 2000/25 ms. Three kinds of brain metabolites, namely N-acethylaspartate (NAA), creatine (Cr) and mioinositol (MI) in the posterior cingulate gyrus were measured for 25 healthy adults (Cont group, 44±16 y.o.) and 84 HD patients (HD group, 74±11 y.o.), and ratios of NAA/Cr, MI/Cr and MI/NAA were calculated. The concentration of each metabolite was analyzed using LC model. HD patients were classified into three groups, namely normal cognitive function group (HD-N, n=25, 72±16 y.o.), mild cognitive impairment (HD-M, n=29, 74±9 y.o.) and dementia (HD-D, n=30, 79±8 y.) using MMSE test. Also, sequential changes of the brain metabolites were evaluated for 13 patients with worse cognitive function prospectively.

Results: HD patients showed a significant decrease of NAA and increases of MI and MI/NAA ratios compared to those of Cont group, suggesting that some metabolic abnormalities were inducted in HD. With a detailed classification of cognitive function in HD patients, NAA/Cr ratios were 1.69±0.17, 1.57±0.15, 1.71±0.20 and 1.54±0.22 in Cont, HD-N, HD-M and HD-D groups, respectively, and was significantly lower even in HD-N group than that of Cont group. MI/Cr ratios were 0.78±0.21, 0.90±0.21, 0.95±0.28 and 1.02±0.27 in Cont, HD-N, HD-M and HD-D groups, respectively, and those of HD-N/-M/-D were significantly higher than that of Cont group. Also, the value of HD-D was significantly higher than those in the other groups. MI/NAA ratios were 0.46±0.13, 0.56±0.17, 0.54±0.16 and 0.66±0.15, in Cont, HD-N, HD-M and HD-D groups, respectively. Again, those of HD-N/-M/-D were significantly higher than that of Cont group. HD-D group was highest among the HD patients.

In the prospective study, dementia progressed in 10 of 13 HD patients who were observed more than 5 years. The MI/NAA ratio increased in the patients with dementia progression (from 0.58±0.11 to 1.24±0.17) while that value of the patients without dementia progression showed no changes (from 0.51±0.14 to 0.55±0.18).

Conclusion: These result suggest that the measurement of metabolic fluctuation in the brain using MRS is useful for the diagnosis of cognitive function in HD patients. The MI/NAA value is a strong candidate for a predictive biomarker of dementia progression. In the future, research and development of measurements of various parts of the brain and their integration to show changes in the whole brain are desired.

P1241

CALCIFICATIONS IN DIFFERENT VASCULAR BEDS ACROSS THE SPECTRUM OF CHRONIC KIDNEY DISEASE INCLUDING CALCIFIC UREMIC ARTERIOLOPATHY: ARE SKIN PUNCH BIOPSIES USEFUL?

Anne Kristine Roendbjerg[1], Marianne Rix[2], Mette Gyldenløve[3], Dorrit Krustrup[4], Ilse Vejborg[2], Lars Lönn[2], Andreas Pasch[5], Lone Skov[3], Ditte Hansen[4]

[1]Roskilde Sygehus, Roskilde, Denmark, [2]Rigshospitalet, København, Denmark, [3]Gentofte Hospital, Hellerup, Denmark, [4]Herlev Hospital, Herlev, Denmark and [5]Calciscon Ag, Nidau, Switzerland

Background and Aims: Accelerated vascular calcification in different vascular beds is common in patients with chronic kidney disease (CKD). A severe form of vascular calcifications is calcific uremic arteriolopathy (CUA) presenting with painful ischemic skin lesions and high mortality. The prognostic value of skin biopsies in relation to CUA is unclear and the prevalence of skin vascular calcifications in different stages of CKD is sparsely described.

The aim of the study was to describe the occurence of small vesssel vascular calcifications in unaffected skin biopsies in relation to calcifications in other vascular beds across the spectrum of CKD including CUA.

Method: A cross-sectional cohort (total, n=39) comprising dialysis patients with current or previous CUA (CKD5D+CUA, n=9), dialysis patients without CUA (CKD5D-CUA, n=12), patients with CKD stage 3-4 (CKD3-4, n=12), and healthy kidney controls (control, n=6). The presence of vascular calcifications in the dermis and subcutis were assessed in 4 mm punch biopsies of unaffected skin from the lateral thigh. The presence of vascular calcification was evaluated by H&E, von Kossa and Alizarin staining. The presence of breast arterial calcifications (BAC) was evaluated by mammography, the abdominal aortic calcification score (AAC) by lateral lumbar X-ray and calcification propensity was measured by T_{50} reflecting the calcification propensity in blood.

Results: None of the included patients showed vascular calcifications in skin biopsies.

Declining kidney function was associated with presence of BAC, increased AAC and reduced T50 (Table).

No significant difference was found between CKD5D+CUA and CKD5D-CUA regarding BAC (p=1.000), AAC (p=0.815) or T50 (p=0.165). CKD5D+CUA compared to all other groups had no difference in BAC (p=0.109) and AAC (p=0.141) but reduced T50 (p=0.004). Dialysis patients (CKD5D±CUA) had significant more BAC (p=0.003), higher AAC (p<0.001) and lower T50 (p<0.001).

Conclusion: No vascular calcifications were found in punch biopsies from unaffected skin in patients with different stages of CKD including CUA. Despite imaging verified vessel calcification by BAC and AAC and increased calcification propensity by T_{50}. This suggest that conventional punch biopsies cannot be used to identify skin vascular calcification and thereby patients at risk for developing CUA.

	CKD5D+CUA	CKD5D-CUA	CKD3-4	Control	CKD5D±CUA
No.	9	12	12	6	21
Age (years)	71±8	68±7	70±8	69±4	70±7
Female No. (%)	3(33)	7(58)	3(25)	2(33)	10(48)
Skin vascular calcification No. (%)	0(0)	0(0)	0(0)	0(0)	0(0)
BAC present No. (%)	6(75)	8(67)	3(25)	0(0)*	14(70)***
AAC	21(16-24)	22(18-24)	15(5-18)	1(0-3)*	21(18-24)***
T50 (min.)	143±84**	200±89	290±97*	365±64*	177±90***

Presented as numbers (%), mean (SD) and median (IQR).
*p<0.05 compared to CKD5D+CUA.
**p<0.05 compared to others (CKD5D-CUA/CKD3-4/control).
***p<0.05 compared to non-dialysis (CKD3-4/control).

Figure:

P1242

THE RELATIONSHIP BETWEEN INTRADIALYTIC HYPOTENSION AND DIFFERENT BRAIN COMPONENTS VOLUME/ COGNITIVE FUNCTION IN MAINTENANCE HEMODIALYSIS PATIENTS

Ke Zheng[1], Yujun Qian[1], Tianye Lin[2], Fei Han[3], Feng Feng[2], Yicheng Zhu[3], Xuemei Li[1]

[1]Peking Union Medical College Hospital, Nephrology, Beijing, P.R. China, [2]Peking Union Medical College Hospital, Radiology, Beijing, P.R. China and [3]Peking Union Medical College Hospital, Neurology, Beijing, P.R. China

Background and Aims: Intradialytic hypotension (IDH) is common in maintenance haemodialysis patients, which is associated with disabling symptoms and interrupted treatment. Blood pressure fluctuations during haemodialysis may affect cerebral perfusion and subsequently brain atrophy and cognitive impairment. This study aimed to explore the correlation of IDH with brain atrophy and cognitive impairment.

Method: IDH was defined when the patients showed obvious hypotension symptoms during the dialysis procedure, such as dizziness, sweating or loss of consciousness, accompanied by blood pressure decrement, and needed to be treated by clinicians in the past one year. All patients received 3.0T MRI examination and cognitive function evaluation. We used the voxel-based morphometry (VBM) method to evaluate the changes of brain multi-component volume. All of the brain region (including gray and whiter matter, brain nuclei, ect.) volumes were measured by calculating the total number of voxels in each image data, with resampling voxel size of 1 mm. A wide range of cognitive tests was administered to evaluate cognitive function, including MMSE, MoCA, Philadelphia word learning test, Boston Naming Test, and trial making test. The cognitive function and brain multi-component volume of were compared between patients with and without IDH (IDH and no-IDH groups), and the correlation between brain volume and IDH was investigated by regression analysis.

Results: Totally 119 maintenance haemodialysis patients enrolled our study. 22 dialysis patients had the experience of IDH, and the prevalence is 18.5%. The patients with IDH had higher prevalence of diabetes and longer dialysis vintage (40.9% vs 16.5, p=0.011; 70.0 vs 41.0 months, p=0.054), they also had a lower post-dialysis SBP and DBP.

The MMSE scores and MoCA scores of patients with IDH and without IDH were similar (29.0 vs 29.0, p= 0.621; 23.5 vs 24.0, p= 0.273).

There was no difference in gray matter and white matter between IDH and no-IDH groups. But as for some important brain nuclei and parts associate with emotion and vision, like amygdala, cuneus and posterior cingulate, patient with IDH were smaller than patients without IDH (1.6±0.2 vs 1.7±0.2 mm3, p=0.009; 6.9±0.8 vs 7.4±1.0 mm3, p=0.031; 6.9±0.8 vs 7.4±0.9 mm3, p=0.024). The multiple-regression analysis showed that IDH was significantly associated with the volume atrophy of amygdala, cuneus and posterior cingulate (β=-0.12, p=0.009; β=-0.48, p=0.031; β=-0.48, p=0.026).

Conclusion: IDH was not rare in maintained dialysis patients. IDH may cause some specific brain components atrophy which may relative to emotion and visual changes in dialysis patients but was not associated with cognitive impairment and cognitive relative brain components.

P1243 ABSOLUTE BLOOD VOLUME VARIATIONS INFLUENCED BY DIALYSATE TEMPERATURE DURING HAEMODIALYSIS

Marta Álvarez Nadal[1], Irene Martin[1], Elizabeth Viera Ramírez[1], Milagros Fernandez Lucas[1]

[1]*Hospital Ramón y Cajal, Madrid, Spain*

Background and Aims: Intradialytic hypotension is a common complication in haemodialysis. Vascular refilling occurs to preserve haemodynamic stability. Recent studies report a feasible and noninvasive method to determine absolute blood volume, which would allow us to estimate vascular refilling during haemodialysis. During years, it has been proposed that lowering the dialysate temperature could improve intradialytic hypotension outcomes in patients undergoing chronic haemodialysis. The objective of this study is to analyze if lowering dialysate temperature modifies variations in absolute blood volume during haemodialysis.

Method: The study was performed in 51 patients under haemodialysis treatment. During two different sessions, relative blood volume was assessed using dialysate temperatures of 35.5°C (cool dialysate) and 36.5°C (neutral dialysate). Absolute blood volume and vascular refilling were calculated using *Kron et al* methodology (*Hemodial Int. 2016;20(3):484–91)*. Intradialytic hypotension was defined as a systolic blood pressure below 85 mmHg or a drop of pressure above 20 mmHg accompanied by symptoms. Statistical analysis was performed using paired t-Test or Wilcoxon rank sum.

Results: 31 episodes of intradialytic hypotension were observed, 14 under cool dialysate and 26 during neutral dialysate. We did not found statistically differences in absolute blood volume or in refilling volume between cool and warm dialysate temperature. In the group of patients with intradialytic hypotension (Table 1) we observed lower drop in absolute blood volume in the 35.5°C dialysate group (0.59 L) versus 36.5°C group (0.72 L). Although no statistically significant differences were found in vascular refilling volumes, when cool dialysate was used refilling tended to be higher.

Conclusion: It seems that in selected groups of patients the use of cool dialysate could improve absolute blood volume stability during HD treatments, although further studies are needed.

Table 1:

	Cool dialysate (35.5C)	Neutral dialysate (36.5C)	*p*-value
Initial ABV (L)	5.54	5.71	*NS*
Initial ABV - Final ABV (L)	0.59	0.72	0.014
Re˚lling volume (L)	2.32	2.29	*NS*
UF volume (ml)	2906.13	3013.16	*NS*
Vascular re˚lling fraction (%)	77.46	67.00	*NS*

P1244 MILD DIFFERENCES IN CARDIAC CALCIFICATION BETWEEN WILD TYPE AND SCLEROSTIN KNOCKOUT MICE WITH CKD

Annelies De Maré[1], Patrick D'Haese[2], Anja Verhulst[2]

[1]University of Antwerp, Wilrijk, Belgium and [2]University of Antwerp, Antwerpen, Belgium

Background and Aims: Ectopic soft tissue calcifications, especially cardiovascular calcifications, are frequently observed in patients with chronic kidney disease (CKD) and are associated with increased morbidity and mortality. Sclerostin, a well-known inhibitor of bone formation, shows significantly increased serum levels in CKD patients. Since the process of ectopic calcification shares many similarities with physiological bone formation, we investigated a possible role for sclerostin in ectopic calcification development.

Method: CKD was induced in wild type (WT) (n=21) and sclerostin knockout (Sost ko) mice (n = 21), both on a C57Bl6/J background, by the alternate administration of a 0.30% and 0.15% adenine supplemented diet, containing 1% phosphate. A normal renal function control group receiving standard mouse chow (WT C57Bl6/J n = 8) was also included in the study. Serum creatinine and phosphate levels were measured at the start and end of the study to assess CKD development. At sacrifice, the calcium content of the kidneys, heart and aorta was determined by flame atomic absorption spectrometry.

Results: The adenine-supplemented diet led to a clear induction of CKD in both the Sost ko and wild type mice, as reflected by increased serum creatinine (0.38 $\pm$ 0.09 mg/dL in control mice vs 0.65 $\pm$ 0.18 mg/dL in adenine-exposed mice, $p<0.0001$) and phosphate levels (9.12 $\pm$ 1.16 mg/dL in control mice vs 19.03 $\pm$ 3.11 mg/dL in adenine-exposed mice, $p<0.0001$). The Sost ko and WT mice receiving the adenine diet, developed the same degree of renal failure, since there were no differences in serum levels of creatinine ($p=0.0507$) and phosphate ($p=0.4890$). Significantly higher amounts of calcium were measured in the kidney (0.05 $\pm$ 0.01 mg/g wet tissue vs 3.70 $\pm$ 2.00 mg/g wet tissue, $p<0.0001$) and the heart (0.03 $\pm$ 0.01 mg/g wet tissue vs 0.07 $\pm$ 0.04 mg/g wet tissue, $p<0.0001$) of adenine-exposed mice, compared to mice receiving the control diet. Furthermore, Sost ko mice had a significantly higher calcium content in the heart compared to the WT mice with renal failure (0.05 $\pm$ 0.03 mg/g wet tissue in WT mice vs 0.08 $\pm$ 0.05 mg/g wet tissue in Sost ko mice, $p = 0.0029$). No differences were observed in aortic calcium content between control mice and mice with renal failure.

Conclusion: In this study we managed to develop a mouse model of CKD-induced soft tissue calcification in the heart and kidneys of the animals, however no calcifications developed in the aorta. The higher calcium content that was observed in the heart of Sost ko mice compared to WT mice, might be an indication of a protective function of sclerostin during ectopic cardiac calcification

P1245 **AORTIC ARCH CALCIFICATION AND PROGNOSIS IN HEMODIALYSIS PATIENTS**

Toyohiro Hashiba[1], Tomoko Honda[1], Satoru Kishi[1], Yuto Takenaka[1], Satoshi Furuse[1], Kyosuke Nishio[2], Kazunobu Masaki[2], Tatsuya Kano[3], Naobumi Mise[1]

[1]Mitsui Memorial Hospital, Internal Medicine, Chiyoda City, Japan, [2]Shinkoiwa Clinic, Internal Medicine, Katsushika City, Japan and [3]Shin-Koiwa Clinic Funabori, Internal Medicine, Edogawa City, Japan

Background and Aims: Aortic arch calcification (AAC) is associated with poor survival in dialysis patients, but long-term prognosis has not been examined well.

Method: In the present study, we investigated the prognostic impact of AAC among 321 chronic hemodialysis patients (211 males, 64±11 ages, dialysis history 10±8 years). ACC in chest X-ray was evaluated in 2012 and the patients were followed up for 7 years. The degree of AAC was classified into 4 categories as follows: Grade 0, no visible calcification; Grade 1, small spots of calcification or single thin calcification of the aortic knob; Grade 2, one or more areas of thick calcification; and Grade 3, circular calcification of the aortic knob.

Results: Calcification gravity was Grade 0 in 88 patients (27%), Grade 1 in 145 (45%), Grade 2 in 54 (17%) and Grade 3 in 34 (11%). All-cause mortality was significantly worse in patients with higher AAC grade (Grade 0: 19% (n=17), Grade 1: 35% (n=51), Grade 2: 46% (n=25), Grade 3: 71% (n=24); $p < 0.0001$). Univariate analysis showed AAC grade, age, cardiothoracic ratio, ischemic heart disease, cerebral vascular disease, albumin, hemoglobin, C-reactive protein and use of non-Ca phosphorus binders were significantly associated with all-cause mortality. In multivariate analysis, Grade 3 AAC, age and ischemic heart disease were independent risk factors for all-cause mortality.(Figure)

Conclusion: In our dialysis patients, higher gravity of AAC was independently associated with all-cause mortality. Gravity of AAC in chest X-ray is useful to predict prognosis of dialysis patients.

Risk Factors for all cause mortality	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
AAC Grade 1 vs. Grade 0	1.98	1.17–3.52	0.01*	1.28	0.75–2.31	0.38
Grade 2 vs. Grade 0	2.78	1.51–5.24	0.001*	1.74	0.94–3.30	0.08
Grade 3 vs. Grade 0	5.72	3.08–10.9	< 0.0001*	2.83	1.43–5.73	0.003*
Dialysis vintage (year)	1.00	0.99–1.00	0.15			
Age (year)	1.06	1.04–1.08	< 0.0001*	1.05	1.02–1.07	< 0.001*
Male	0.73	0.51–1.07	0.10			
Diabetes	1.28	0.88–1.83	0.19			
Hypertension	1.14	0.79–1.65	0.50			
Cardiothoracic ratio (%)	1.06	1.03–1.10	< 0.001*	1.02	0.98–1.06	0.28
Hyperlipidemia	0.91	0.61–1.33	0.62			
Ischemic Heart Disease	1.79	1.18–2.66	0.007*	1.66	1.07–2.51	0.02*
Cerebral Vascular Disease	1.81	1.23–2.64	0.002*	1.41	0.94–2.09	0.09
Albumin (g/dL)	0.18	0.10–0.34	< 0.01*	0.65	0.31–1.36	0.25
Hemoglobin (g/dL)	0.77	0.62–0.94	0.01*	0.88	0.70–1.11	0.29
C-reactive protein (mg/dL)	1.44	1.22–1.66	< 0.01*	1.14	0.93–1.39	0.20
Corrected Calcium (mg/dL)	0.99	0.70–1.41	0.97			
Use of $CaCO_3$	0.88	0.76–1.01	0.08			
Use of Non-Ca Phosphorus binders	0.63	0.44–0.91	0.01*	1.06	0.70–1.61	0.78
Use of Vit D	0.99	0.68–1.44	0.97			

Figure:

P1246 **CEREBRAL TISSUE REGIONAL OXYGEN SATURATION AND BLOOD PRESSURE IN HEMODIALYSIS PATIENTS**

Georgios Spanos[1], Styliani Paschou[1], Christos Dontsios[1], Stylianos Fragkidis[1], Christos Bantis[1], Livia Karmen Armentzoiou[1], Ellada Tsantekidou[1], Gerasimos Bamichas[1]

[1]General Hospital of Thessaloniki "G. Papanikolaou", Nephrology Department, Thessaloniki, Greece

Background and Aims: Patients undergoing hemodialysis (HD) often develop cerebral disease complications. Cerebral tissue regional oxygen saturation (rSO2) through near-infrared spectroscopy (NIRS) is a non-invasive method for cerebral tissue oxygenation monitoring. The aim of the study was to investigate the relationship between rSO2 and hemodialysis in stable HD patients. Additionally, we wanted to investigate how blood pressure during HD is associated with rSO2.

Method: This is a single centre cross-sectional study in clinically stable HD patients. Cerebral rSO2 was monitored at the forehead 10min before, during and 10min after HD, using an INVOS 5100C device (Medtronic, United Kingdom).

Results: Thirty-nine stable HD patients (23 men and 16 women; mean age, 62.4 ± 14.6 years were recruited. Dialysis vintage was 65.7 ± 72.1 months, 9 patients had diabetes mellitus, 12 had vascular disease while 14 were smokers. The baseline rSO2 levels (49.6±9.1 %) were significantly lower in HD patients compared with historic results on healthy subjects. We found no difference in rSO2 results in patients with diabetes mellitus, vascular disease or smoking. Although we found a decrease (figure) in rSO2 when patients start dialysis (10min before vs 10min after starting dialysis 49.6±9.1 vs 48.1±9.9 %, p=0.021) rSO2 value returned to baseline after dialysis (10min before vs 10min after dialysis 49.6±9.1 vs 49.9±5.9 %, p=ns. Systolic blood pressure scientifically dropped during the first hour of dialysis (146.7 ± 21.1 vs 137.3 ± 24.6, p=0.03) and systolic blood pressure drop correlated with rSO2. Three patients developed hypotensive episodes requiring iv fluids but these hypotensive episodes had no correlation with rSO2 variations.

Conclusion: Cerebral rSO2 decreases while patients are on dialysis but return to baseline after dialysis. Blood pressure variations correlate with rSO2 levels but rSO2 do not forecast hypotensive episodes on dialysis.

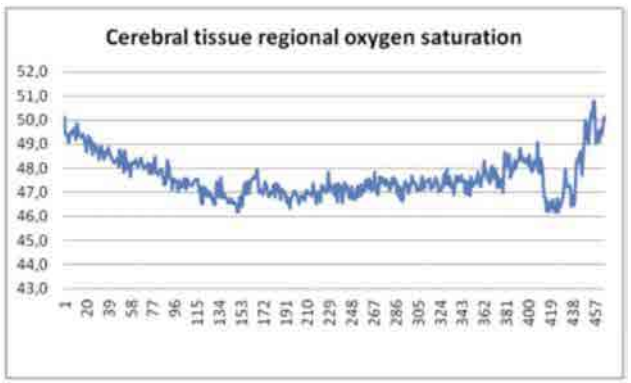


Figure:

P1247 **INTERDIALYTIC WEIGHT GAIN IN HEMODIALYSIS: EPIDEMIOLOGY AND OUTCOMES**

Issa Al Salmi[1,2], Yacoub Al Maimani[1], Fady Magdy[1], SUAD Hannawi[3]

[1]•••, *Muscat, Oman,* [2]*Oman Medical Specialty Board OMSB, Muscat, Oman and* [3]*Ministry of Health Head Office, Dubai, United Arab Emirates*

Background and Aims: Interdialytic weight gain (IDWG) has been linked to various complications in hemodialysis (HD) patients, especially cardiovascular (CV) complications. We aimed to evaluate the effect of IDWG in HD patients on the rate of hospital admissions over a 12-month period, and the impact of high IDWG on the frequency of IDH.

Method: The study included 120 patients; who had been receiving HD for at least 3 months. The presence of various comorbidities has been recorded including. Laboratory data included; serum creatinine, serum albumin, and hemoglobin level. The estimated IDWG was calculated based on the average between pre- and post- dialysis weights that were recorded on 3 consecutive dialysis sessions.

Results: Among those who had IDWG $\geq$ 4%, 81% of these patients had at least one hospital admission due to volume overload or the need for extra HD session(s). On the other hand, only 19% of those having IDWG $<$ 4% had been admitted or got extra HD sessions ($p<0.001$). Of those who were admitted (over 12 months) due to volume overload; 74.1 % had IDWG $\geq$ 4%, while 25.9% had IDWG $<$ 4% ($p< 0.001$). Regarding IDH, 87% of patients having IDWG $\geq$ 4% had at least one episode of IDH/week. On the other hand, only 22.5% of those with IDWG $<$ 4% had one episode of IDH/week ($p<0.001$). When analyzing those who had at least one IDH episode/week; 72.9% of them had IDWG $\geq$ 4%, while only 27.1% had IDWG $<$ 4% ($p<0.001$).

Conclusion: In HD patients, the frequency of hospital admission due to volume overload and the need for extra HD sessions is strongly related to the amount of IDWG ($>$ 4% in our patients), the same stands for the frequency of IDH. Thus, a control of IDWG in HD patient is of great importance, keeping in mind the importance the nutrition status of HD patients that may also impact IDWG.

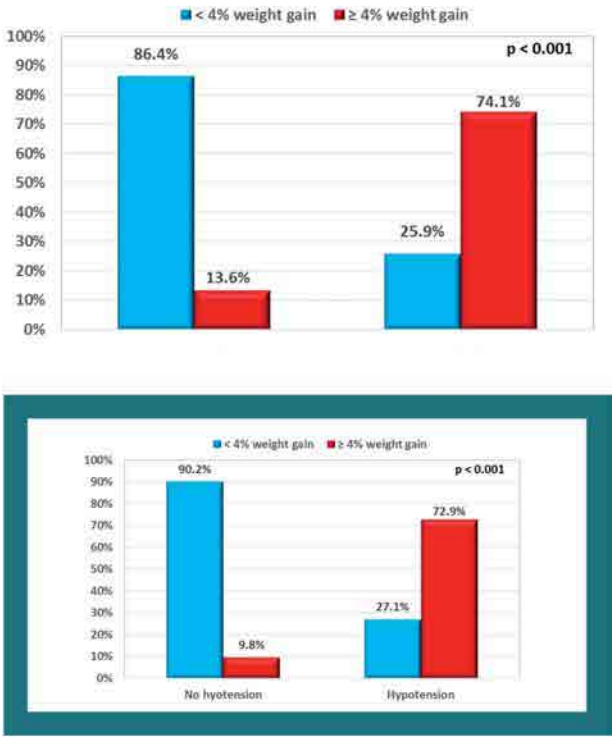


Figure 1.

P1248

DOES INCREMENTAL HAEMODIALYSIS PRESERVE NATIVE KIDNEY FUNCTION? A MULTI-CENTRE FEASIBILITY RANDOMISED CONTROL TRIAL

Enric Vilar[1,2], RAJA MOHAMMED KAJA KAMAL[1,2], Ewa Kislowska[1], Jocelyn Berdeprado[1], Bassam Alchi[3], James Burton[4,5], Andrew Davenport[6], Siva Sridharan[1,2], David Wellsted[2], Kenneth Farrington[1,2]

[1]Lister Hospital, United Kingdom, [2]University of Hertfordshire, United Kingdom, [3]Royal Berkshire Hospital, United Kingdom, [4]University of Leicester, United Kingdom, [5]Leicester Royal Infirmary, United Kingdom and [6]Royal Free Hospital, United Kingdom

Background and Aims: Incremental HD is a method of individualising haemodialysis (HD) dose according to level of residual renal function(RRF) such that as RRF reduces, HD dose is upwardly adjusted. Retrospective data suggest potential benefit of this approach in preserving RRF, a key predictor of survival for dialysis patients.

Method: A randomised, intention-to-treat, multi-centre trial was designed to determine the feasibility of a future definitive trial of incremental HD to establish if this approach preserves RRF. The trial was designed to estimate effect size of potential benefit in terms of RRF.

55 patients with RRF urea clearance$\geq$3ml/min/1.73m^2 BSA and within 3 months of starting HD were randomised across 4 UK dialysis centres to either conventional 3x weekly HD for 3.5-4 hours or incremental HD. The incremental HD protocol involved initiation of HD 2x weekly after randomization and upward adjustment of HD frequency and time as RRF was lost.

In the conventional HD arm, patients were dialysed to ensure Standard Kt/$V_{Dialysis}$>2.0. In the incremental HD arm, patients were dialysed to ensure Standard Kt/$V_{Dialysis}$+Standard Kt/$V_{Residual\ Renal\ Function}$>2.0 so both groups were dialysed to the same urea clearance target, except that urea clearance incorporated RRF in the incremental HD arm. Follow up was for 6 months (primary outcome data) but secondary outcome data will be for 12m. Patients were withdrawn for transplant, dialysis modality change or for patient choice.

The primary outcome was rate of change of RRF in the first 6 months after randomization (effect size of intervention). Recruitability, retainability, protocol adherence and rate of adverse events were also measured as a primary objective. As a secondary outcome, we determined proportion of patients with urea clearance$\geq$2 and $\geq$3ml/min / 1.73m^2 BSA at the 6 month time point. Impact of dialysis treatment was measured using questionnaire-based assessments at baseline and 6 months.

Results: 26 patients were randomised to standard HD and 29 to incremental HD. Baseline demographics including age, weight, haemoglobin, blood pressure, Charleson Comorbidity Index, were not significantly different between study arms. Baseline residual renal urea clearance was 5.1 $\pm$ SD 1.8 ml/min/1.73m^2 BSA in the standard HD arm and 5.72 $\pm$ SD 2.49 in the incremental HD arm. 6 months, residual renal urea clearance reduced to 2.68$\pm$SD 1.73 in the standard HD arm and 3.80$\pm$SD 1.85 in the incremental arm. In the first 6 months, 3 patients recovered to dialysis independence (standard arm=1, incremental arm=2). Slope of RRF was not significantly different between two arms (p=0.39). The proportion of patients with significant urea clearance>2ml/min/1.73m2 BSA at 6 months was significantly higher in the incremental HD arm (92%) compared to the standard HD arm (65%), p=0.032. Rate of major adverse cardiac events, fluid overload, hyperkalaemia, vascular access events, deaths and infections did not differ significantly between groups. There were 2 deaths in the standard HD arm (in 4025 patient days) versus 1 in the incremental HD arm in the first 6 months(4666 patient days).

There was no significant difference in Clinical Frailty Score, Montreal Cognitive Assessment score, depression score (PHQ-9), Quality of Life (EQ-5D-5L) and Illness Intrusiveness Rating Scale between groups at baseline and 6m time points.

Conclusion: Rate of loss of RRF (slope) was not significantly different between incremental HD and standard HD arms but incremental HD was associated with significantly higher probability of retaining urea clearance>2ml/min/1.73m2. There was no evidence of any clinical detrimental effect of incremental HD in terms of mortality, fluid overload or hyperkalaemic events. Incremental HD does not appear to be harmful and may confer a small benefit to preservation of residual renal function. A definitive study is required to define clinical benefits further.

P1249 SEVERE HEMODYNAMIC INSTABILITY DURING DIALYSIS - DRY, STUNNED OR ALLERGIC? STATE OF THE ART ECHOCARDIOGRAPHY COMBINED WITH SIMULTANEOUS LUNG ULTRASOUND

JOnas Öhman[1]

[1]*Turku University Hospital, Kidney Center, Turku, Finland*

Background and Aims: Intradialytic hypotension is a fairly common and serious adverse phenomenon. Associated comorbidities include e.g. heart failure, hypovolemia, allergic reactions with the dialysis apparatus and electrolyte disturbancies. Excessive ultrafiltration may explain later onset hypotension, but early-onset hemodynamic collapse remains poorly understood.

Preventive interventions may include incremental dialysis, increasing dry weight, increasing dialysis time and changing dialysis membranes/apparatus.

This study combines Echocardiography (Echo) and Lung Ultrasound (LUS) for hemodynamic phenotyping of patients with severe, early onset intra-dialytic hypotension. The aim is to figure out possible preventive strategies depending on underlying abnormalities.

Method: We enrolled dialysis patients with a symptomatic decrease in systolic arterial pressure < 90 mmHg requiring norepinephrine during the first 60 minutes of at least two consecutive dialysis sessions in our dialysis department. Echo + LUS was done simultaneously to everyone at baseline, i.e. BEFORE dialysis begun, and later at onset of a hypotension episode during dialysis. Patients with active bleeding or any other obvious temporary etiology for hypotension were excluded.

Echo concentrated especially on volemic state and filling pressures, while LUS evaluated the lungs and pleurae for signs of pulmonary congestion. Cardiac structure and function (e.g. valves, ejection fraction) was also evaluated.

Results: Between 1.10.2019 - 31.12.2019 10 patients were enrolled. All patients eventually required norepinephrine despite fluid challenge. No patients had signs or symptoms of an allergic reaction, such as urticaria or stridor/obstructive respiration, nor significant electrolyte disturbancies.

5/10 patients had severe systolic cardiac dysfunction at baseline (LVEF < 30 %) and these 5 patients also simultaneously showed signs of congestion and fluid overload on ultrasound.

On the contrary, the other 5/10 patients without severe cardiac failure all had low left-sided filling pressures and a collapsed inferior vena cava on Echo ALREADY at baseline, i.e. before initiation of dialysis. All of these hypovolemic patients had an excellent residual diuresis (> 1500ml/d).

All 10 patients in this study showed a significant drop in body volume measurement (BVM) -curves and left-sided filling pressures on Echo prior to onset of hypotension.

Of the 5 patients with severe cardiac dysfunction, 2/5 were transmitted into palliative care without dialysis, while 3/5 could be managed without future norepinephrine by longer, more frequent dialysis sessions using more convective and less diffusive dialysis.

Of the latter 5 "dry" patients without severe cardiac dysfunction, 3/5 had no more hypotensive episodes after increasing dry weight and using incremental dialysis programs, and the remaining 2 dry patients could be completely switched off dialysis due to vivid residual function.

3/5 of the "dry patients" had a baseline pulse pressure > 120 mmHg and 3 had coronary artery disease, both possibly predisposing to diastolic under-filling.

No patients in this study presented with significant myocardial stunning, defined as a > 10 % decrease in LVEF compared to baseline.

Conclusion: Severe, intra-dialytic hypotension requiring vasopressors may be prevented by individual tailoring of dialysis prescription. Ultrasound may help phenotyping patients requiring different dialysis strategies, including stopping dialysis entirely. Stunning and allergic reactions seemed rare.

At baseline, patients seemed to be mainly 1) either over-dialyzed (hypovolemic or hypo-osmotic) or 2) having significant cardiac disease, naturally requiring quite opposite preventive strategies. A decrease in left ventricular preload furthermore occurred in all patients at onset of hypotension, suggesting crossover of a patient-specific preload threshold.

P1250 **LOW SERUM URIC ACID LEVEL AND LEFT VENTRICULAR HYPERTROPHY : THE NEW PARADOXICAL ASSOCIATION IN HEMODIALYSIS PATIENTS**

GJULSEN SELIM[1], Angela Kabova[1], Blerim Bexheti[1], Zoran Janevski[1], Adrijana Spasovska Vasilova[1], Mimoza Milenkova[1], Aleksandra Canevska[1], Bojana Vrevezoska[1], Shkelqim Muharremi[1]

[1]University Clinic of Nephrology, Ss. Cyril and Methodius-University Skopje, Republic of North Macedonia, Skopje, Republic Of North Macedonia

Background and Aims: The association between serum uric acid (UA) and left ventricular hypertrophy (LVH) is controversial in chronic kidney disease, whereas in hemodialysis (HD) patients has not been studied until now. Thus, we evaluated the relationship of baseline and time-averaged UA with echocardiographic LVH over a 5-year period in HD patients.

Method: This longitudinal study was conducted on 225 prevalent HD patients over a 5-year period. Patients were stratified into 3 groups according to their baseline and time-averaged UA levels: lower group (UA<400μmmol/l), intermediate/reference group (UA between 400-450μmol/l) and higher group (UA>450μmol/l). Echocardiography was performed on a non-dialysis day and the presence of LVH was defined based on the left ventricular mass index (LVMI) >131 and >100 g/m^2, for men and women, respectively. The patients were followed during a 60 month period.

Results: During the 5-year follow-up, 81 patients died (36%), and the main causes of death were cardiovascular (CV) related (70%). Survival analysis show that patients with time-averaged UA<400 μmmol/l had a significantly higher all cause (log rank, p=0.003) and CV mortality (log rank, p=0.004) rate, compared to those with time-averaged UA between 400-450 μmmol/l and time-averaged UA>450μmol/l, but this difference was not statistically significant in terms of baseline UA level. A negative correlation was observed between LVH and time-averaged UA (r=-0.26, p=0.001), but not with LVH and baseline UA. Patients in lower time-averaged UA group had significantly higher LVMI compared to patients in intermediate and higher group (153.10± 59.89, 131.62±40.99, 131.19±44.49 g/m^2, p=0.029), but from the lowest to the highest baseline UA levels, LVH was not significantly different (146.99±59.20, 141.38±37.52, 126.85±42.48 g/m^2, p=0.07). Unadjusted odd ratio of LVH risk in the lower time-averaged UA compared to the reference time-averaged UA group was 3.11 (95% CI=1.38-7.05; p=0.006); and after adjustment for age, gender, diabetes and CV disease, ORs for LVH persisted significant only in the lower time-averaged UA group (OR = 2.82, 95% CI = 1.16–6.88, *P* = 0.002). On the contrary, baseline UA did not affect unadjusted and adjusted LVH.

Conclusion: In HD patients the prolonged exposure to hypouricemia is associated with LVH. This paradoxical association can only be explained by the hypothesis that uremic milieu in HD patients changes the influence of uric acid. However, these results should be the subject of further research.

P1251 **THROMBIN GENERATION ASSAY: A POTENTIAL TOOL TO STRATIFY THROMBOTIC RISK IN HEMODIALYSIS PATIENTS**

Ileana Kalikatzaros[1,2], Massimo Radin[1], Irene Cecchi[1], Savino Sciascia[1], Giacomo Forneris[1], Marco Pozzato[1], Renato Alberto Sinico[2], Dario Roccatello[1]

[1]Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, and SCDU Nephrology and Dialysis, S. Giovanni Bosco Hospital, Torino, Italy and [2]University of Milano-Bicocca, Milano, Italy

Background and Aims: Patients with Chronic Kidney Disease (CKD) in hemodialysis (HD) show both high thrombotic and hemorrhagic risks. However, routine laboratory techniques aimed to evaluate haemostasis, i.e. activated prothrombin time (PT) and activated partial thromboplastin time (aPTT), are not sensitive enough to detect mild hypocoagulable or hypercoagulable states in this population. Indeed, these methods evaluate the start-up phase of the coagulation, but omit the amplification stage in which an exponential increase of thrombin generation occurs.

Thrombin generation assay (TGA) is a second-level global coagulative test able to evaluate thrombin generation and decay. So far the TGA has never been used for assessing thrombotic risk in HD patients.

Method: This is a monocentric observational retrospective study conducted at San Giovanni Bosco Hospital and University of Turin, Italy.

After chart-reviewing of all patients with CKD in HD, we enrolled:

Group A) 100 Patients with CKD in HD, treated or not treated with warfarin

Group B) 60 Patients treated with Warfarin with normal kidney function

Group C) 60 Healthy Controls

Results: Compared to healthy donor patients on hemodialysis that were not treated with warfarin had significantly lower tLag (mean tLag 8.2±3.4 vs. 9.7±2.9, $p < 0.05$), lower tPeak (mean tPeak 14.3±6 vs. 16.2±4.7, $p < 0.05$), lower Peak (mean Peak 151.8±77.4 vs. 209.2±103.8, $p < 0.001$) and lower AUC (mean AUC 1624.5±564.4 vs. 2023±489.2, $p < 0.001$) (Figure 1).

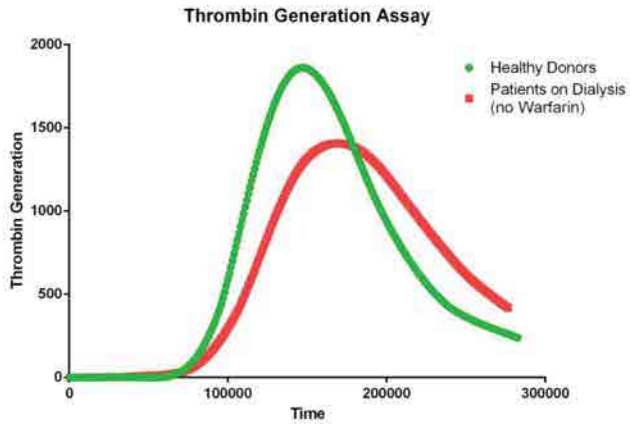


Figure 1: Compared to controls with normal renal function treated with warfarin, HD patients treated with warfarin had higher tLag (mean tLag 10.5±3.3 vs. 8.3±2.1, $p < 0.05$), higher tPeak (mean tPeak 16.5±4.9 vs. 13±2.9, $p < 0.05$).

Among HD patients who were not treated with warfarin, those with autoimmune conditions showed a pro-thrombotic TGA profile when compared to HD patients without autoimmune diseases, with significantly higher Peak (mean Peak 188.4±30 vs. 149.9±78.7, $p < 0.05$) and higher AUC (mean AUC 2066.9±138.2 vs. 1601.5±569, $p < 0.001$). Similarly, compared to patients without previous history of vascular events (59), patients with previous ischemic stroke or venous thrombosis (41), had significantly lower tLag (mean tLag 8±2.9 vs. 14.2±8.5, $p < 0.001$), lower tPeak (mean tPeak 14±5.6 vs. 21.7±12.3, $p < 0.05$), higher Peak (mean Peak 154.9±76.8 vs. 71.83±49.2, $p < 0.05$) and higher AUC (mean AUC 1653.7±548.7 vs. 863.4±501.4, $p < 0.05$).

Of note, a significant positive relationship was detected between the International Normalized Ratio (INR) and both tLag (Pearson 0.46, $p < 0.001$) and tPeak (Pearson 0.35, $p < 0.001$). INR was inversely correlated to Peak (Pearson -0.47, $p < 0.001$) and AUC (Pearson -0.61, $p < 0.001$) (Figure 2).

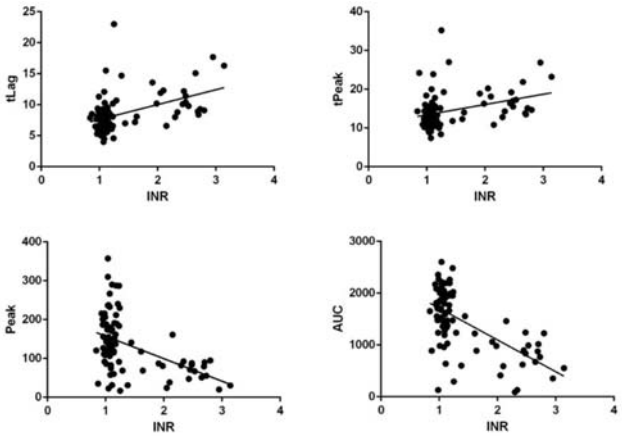


Figure 2: Conclusion: Identifying patients at high risk for cardiovascular diseases and thrombosis has an important impact on the management of patients with CKD in HD. In this study, we observed a prothrombotic TGA profile in patients with CKD in HD, especially those with autoimmune conditions or previous history of arterial events (especially ischemic stroke) or venous thrombosis. Prospective studies are needed to evaluate the possible clinical use of TGA as thrombotic risk stratification tool in HD patients.

P1252

ASSOCIATIONS OF SERUM SCLEROSTIN AND DKK-1 PROTEIN WITH FUTURE CARDIOVASCULAR EVENTS AND MORTALITY IN HEMODIALYSIS PATIENTS; A PROSPECTIVE COHORT STUDY.

EIRINI STAVRINOU[1], Panteleimon Sarafidis[1], Charalampos Loutradis[1], Evangelos Memmos[1], Danai Faitatzidou[1], Panagiotis Giamalis[1], Charalampos Koumaras[2], Asterios Karagiannis[2], Aikaterini Papagianni[1]

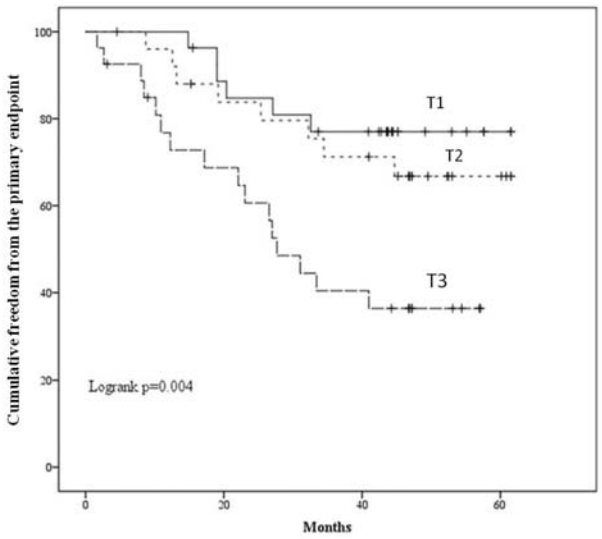
[1]Thessaloniki, Department of Nephrology, Hippokration Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece and [2]Thessaloniki, Second Propaedeutic Department of Internal Medicine, Hippokration Hospital, Aristotle University of Thessaoniki, Thessaloniki, Greece

Background and Aims: Sclerostin and Dickkopf-1 (Dkk-1) protein are inhibitors of the canonical Wnt/β-catenin bone pathway. Sclerostin but not Dkk-1 is associated with increased arterial stiffness. This study examined the prognostic significance of serum sclerostin and Dickkopf-related protein-1 (Dkk-1) levels for cardiovascular outcomes and mortality in hemodialysis patients.

Method: Serum sclerostin and Dkk-1 levels were measured with ELISA in 80 hemodialysis patients that were followed-up for a median of 45 months. Several factors that could interfere in the association of sclerostin and Dkk-1 with outcomes (including carotid-femoral pulse-wave-velocity (PWV), parathyroid hormone, calcium-phospate product and others) were assessed at baseline The primary end-point was a combination of all-cause death, non-fatal myocardial infarction, non-fatal stroke, coronary revascularization, hospitalization for decompensated heart failure and new-onset atrial fibrillation. Secondary end-points included cardiovascular and all-cause mortality.

Results: Cumulative freedom from the primary endpoint was significantly lower for higher tertiles of sclerostin (77.8%, 69.2%, and 40.7% for tertiles 1 to 3 respectively; log-rank-p=0.004). The corresponding risk for the primary outcome was gradually increasing for higher tertiles of sclerostin (Tertile 3: HR: 3.847, 95%CI: 1.502-9.851). No significant association was evident between sclerostin and all-cause mortality, whereas higher sclerostin levels presented a trend towards higher risk for cardiovascular mortality. Dkk-1 levels exhibited no association with the risk of the primary or the secondary endpoints. In stepwise Cox regression modeled analysis, sclerostin levels were associated with the primary outcome, independently of PTH, calcium-phosphate product, serum albumin, CRP and PWV levels (HR: 2.921, 95%CI: 1.401–6.090; p=0.004).

Conclusion: High serum sclerostin levels are associated with lower cumulative freedom and higher risk for a composite cardiovascular endpoint but not for all-cause mortality. Dkk-1 protein exhibited no association with the future risk of cardiovascular events.



	0	20	40	60
T1	27	23	19	2
T2	26	20	17	4
T3	27	17	10	0

Figure:

P1253 **ASSOCIATION OF PREDIALYSIS PULSE PRESSURE (PP) AND ITS INTRADIALYTIC VARIATIONS IN 5 YEAR MULTICENTER COHORT STUDY**

Valeriy Shilo[1,2], Ivan Drachev[3,4]

[1]MoscowState University for Medicine and Dentistry,, Nephrology for Postgraduates,, Moscow, Russia, [2]B. Braun Avitum Russlan Clinics, Moscow, Kurkino, MCVTP, Moscow, Russia, [3]Tver State Mecial University, Internal Disease, Tver, Russia and [4]B. Braun Avitum Rusland Clinics, MCVTP, Moscow, Russia

Background and Aims: Elevated PP, as a surrogate marker of elastic properties the arteries vessel wall, is important characteristics of the cardiovascular system and may be associated with poor survival both in the general eldery population with arterial hypertension and in patients on maintenance hemodialysis (HD). It has been shown, that increase predialysis PP in HD patients was associated with a higher risk of hospitalization or death, but the relationship between PP changes during HD was not well investigated in large prospective cohort studies. The aim of the study was to assess the effect of elevated predialisis PP and its intradialytic PP variations on survival in the Kaplan-Meir curves and in the Cox regression models.

Method: The retrospective cohort included patients who underwent maintenance HD in the large chain of B. Braun Avitum free standing HD units in Russia from 2011 to 2016 years (n = 3704). The mean age of the patients was 54,8±13,7 years, 45% were women and 55% men. All patients were on B. Braun Dialog+ Evolution dialysis machines with Adimea option for on-line KT/V measurement and synthetic alpha-polysulphone Xevonta series dialyzers (surface area 1,8, 2,0 and 2,3 sq. m.) The delivered dialysis dose, according to the Daugirdas 2nd generation formula was 1,6 ± 0.23 (spKt/V). Statistical analysis in a Kaplan-Meier curves and proportional Cox regression model were performed. The study used averaged BP data measured over the entire observation period and PP calculation. Patients were divided into subgroups according PP calculation <35, 35-55, 55-75 and more than 75 mm Hg. Variations in intradialytic PP (ΔPP) were divided into groups according to PP average change during HD procedure: -25 and lower decrease, -25 - -10, -10 - 0, 0 - 10, and 10 - 25 increase, mm Hg.

Results: From total cohort of 3704 patients, 207 (5,6%) has highly elevated PP (> 75 mmHg) and another 1549 (41,8%) has slightly elevated PP (55-75 mm hg). During the study, 393 deaths occurred. The Kaplan-Meyer survival curves clearly demonstrate that the worst survival rate occurs in the subgroup of patients with the markedly elevated predialysis PP (n=207, 35 deaths; HR = 1,7 CI = 1,3 – 2,6; p <0,001; Pic. 1). Then we analyze association of intradialytic PP changes and mortality in total cohort (n=3704) and the subgroups with elevated PP (n=1756). Both marked PP drop down and PP increase during HD worsen survival: the most poor demonstrate patients with highest decrease in PP (-25 mm Hg and more) and then with highest increase in PP (+10-25 mm hg) within HD procedure (Pic. 2).

In unadjusted Cox model predialytic PP and survival remain significant (p=0,01), but not PP changes (p=0,3). After multivariable adjustments in the Cox regression model with main demographic factors (age, treatment duration) and key laboratory indices (spKT/V, urea, creatinine, hemoglobin, albumin, Ca, PO4, PTH) there were no association between both predialysis PP and PP changes and mortality (p=0,9 and 0,1, respectively). Among the independent risk factors in our model, highest hazard ratio affecting survival has for ultrafiltration (UF) speed both for predialytic PP and PP variations (tabl. 1 and table 2).

Conclusion: In our study PP and its intradialytic variations show statistical significant association with mortality in single factor survival analysis and in unadjusted Cox regression model, but were not independent factor in adjusted multivariate HR model. UF speed has the highest impact on mortality in our model. We can hypothesize, that patients with elevated PP are vulnerable for high UF rate and prone for intradialytic hypotension and higher mortality on maintenance HD.

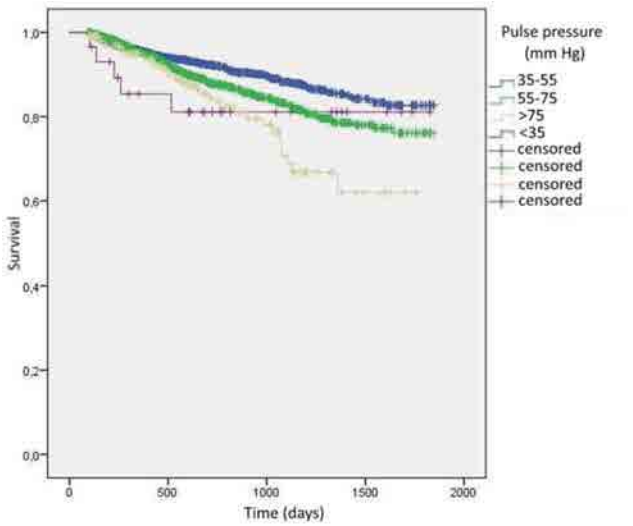


Figure:

Pic. 1. Association of predialytic PP level and survival (Kaplan-Meyer analysis). The subgroup with elevated PP (> 75 and 55-75 mm Hg) has the statistically significant poor survival.

Pic. 2. Association of intradialytic PP variations and survival (Kaplan-Meyer analysis) in subgroup with elevated PP (n=1756).

P1254 **CARDIAC TISSUE CHARACTERISATION AND AUTONOMIC FUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND ON HAEMODIALYSIS: A PILOT STUDY**

Mia Cokljat[1,2], Nicholas Bunce[3], Taigang He[3,4], Debasish Banerjee[1,5]

[1]St George's Hospital, Nephrology, United Kingdom, [2]St George's, University of London, Infection and Immunity Institute, United Kingdom, [3]St George's Hospital, Cardiology, United Kingdom, [4]St George's, University of London, Cardiovascular Imaging, United Kingdom and [5]St George's, University of London, United Kingdom

Background and Aims: Sudden cardiac death rates are higher in patients with CKD and on haemodialysis. Hypotheses include the presence of diffuse myocardial fibrosis secondary to fluid and toxin overload. Native T1, T2 and T2* mapping through cardiac magnetic resonance (CMR) is emerging as a novel technique to quantify myocardial fibrosis. This pilot study aimed to quantify cardiac morphological change using CMR native T1, T2 and T2* mapping and correlate with autonomic provocation testing, in CKD 3b-5 and haemodialysis patients.

Method: Patients with stable CKD 3b and higher, and patients on haemodialysis (CKD-haemodilaysis) underwent a non-contrast CMR, which included native T1, T2, T2* mapping. Autonomic provocation testing was performed using a dipolar ECG lead, followed by 14-days of recording. Results were compared between patient groups, and T1, T2, T2* maps compared to healthy controls using the student t test and Kruskal-Wallis tests.

Results: Nine CKD, eight haemodialysis and seven control patients were recruited (Table 1). Of the late-stage CKD patients, three were stage 3b, four were stage 4 and two were stage 5. There were no significant differences between the two patient groups in baseline characteristics (Table 1). There were no significant differences between CKD and CKD-haemodialysis patients in left ventricular end-diastolic volume index, left ventricular end-systolic volume index, right ventricular end-diastolic volume index, right ventricular end-systolic volume index, ejection fraction, and left ventricular mass index (71.1±15.2 vs. 80.51 ±21.9 ml/m^2, *p=0.316;* 24.4±7.09 vs. 34.4±19.4 ml/m^2, *p=0.171;* 67.11 ± 14.9 vs. 75.5±23.4 ml/m^2, *p=0.386;* 22.2±4.87 vs. 23.9±9.93 ml/m^2, *p=0.663*; 65.8±6.34 vs. 59.5±12.4 %, *p=0.200;* 48.4±8.60 vs. 50.5±11.0 g/m^2, *p=0.673*). T1 and T2 were significantly increased in CKD and CKD-haemodialysis patients compared to healthy controls (1259±57.7 vs. 1204±22.3 ms, *p=0.038* and 49.1±4.74 vs. 42.0±2.79 ms, *p=0.034*). There was no difference in T2* star (32.8±7.59 vs. 28.8±3.77, *p=0.291)*. There was no significant difference in native T1, T2 and T2* times between CKD and CKD-haemodialysis patients (1247±66.7 vs. 1273±45.7, *p=0.361;* 49.1±5.22 vs. 49.0±4.49, *p=0.960;* 34.1±7.57 vs. 31.3±7.81, *p=0.769)*. Mean percentage change of HR in CKD patients from lying to sitting to standing was 4.51%±6.66 and 11.5%±11.8 respectively. Mean percentage change of HR in CKD-haemodialysis from lying to sitting to standing was 2.15%±6.30 and 6.0%±4.45

	CKD *n = 9*	CKD-haemodialysis *n = 8*	Controls *n = 7*
Age	64 (±10.8)	71 (±11.6)	28.9 (±10.8)
Female *n (%)*	4 *(44.4)*	3 *(37.5)*	2 *(28.6)*
BMI *kg/m^2*	27.5 *(±5.0)*	27.2 *(±3.2)*	
Heart rate	68.3 *(±14.2)*	72 *(±9.72)*	
Systolic BP	146.6 *(±19.5)*	138.9 *(±28.7)*	
Diastolic BP	83.2 *(±8.41)*	73.6 *(±13.3)*	
CKD stage *n (%)*			
3b	3 *(33.3)*	0 *(0)*	
4	4 *(44.4)*	0 *(0)*	
5	2 *(22.2)*	8 *(100)*	
Creatinine μmol/L	295.1 *(±180.8)**	661.1 *(±195.7)**	
eGFR ml/min/1.73m^2	21.8 *(±9.67)**	6.75 *(±2.87)**	
Cardiovascular risks n *(%)*			
Diabetes	2 *(22.2)*	5 *(75)*	0 *(0)*
Hypertension	8 *(88.9)*	6 *(62.5)*	0 *(0)*
Smoking	2 *(22.2)*	4 *(50)*	0 *(0)*
Hypercholesteraemia	3 *(33.3)*	4 *(50)*	0 *(0)*
Personal history	0 *(0)*	2 *(25)*	0 *(0)*
Family history	0 *(0)*	1 *(12.5)*	0 *(0)*
Underlying renal disorder n *(%)*			
Diabetes	1 *(11.1)*	4 *(50)*	
Hypertension	2 *(22.2)*	1 *(12.5)*	
Polycystic kidney disease	2 *(22.2)*	0 *(0)*	
Membranous nephropathy	1 *(11.1)*	0 *(0)*	
Nephritis	0 *(0)*	2 *(25)*	
Ischaemic	0 *(0)*	1 *(12.5)*	
Nephrectomy	1 *(11.1)*	0 *(0)*	
Obstructive	1 *(11.1)*	0 *(0)*	
Tuberous sclerosis	1 *(11.1)*	0 *(0)*	
Haemoglobin g/L	116 *(15.4)*	115 *(21.6)*	
Adjusted calcium mmol/L	2.41 *(0.123)*	2.38 *(0.0523)*	
Phosphate mmol/L	1.21 *(0.187)*	1.35 *(0.454)*	
PTH pmol/L	10.8 *(3.99)*	37.4 *(51.7)*	

Figure: Table 1 showing demographic data * = significant difference between CKD and CKD-haemodialysis patients

respectively. There were no significant differences in postural HR variability between CKD and CKD-haemodialysis patients (*p=0.478* and *p=0.237)*.

Conclusion: In late stage CKD, cardiac volumes, mass, ejection fraction and native T1, T2 and T2* are comparable to those of patients on long-term haemodialysis. However native T1 and T2 times are significantly elevated in later stage CKD and haemodialysis, compared to healthy controls. Heart rate changes over postural provocation are comparable between CKD and CKD-haemodialysis patients, although autonomic response is reduced compared to previously published data in healthy controls. Processes that drive myocardial fibrosis may start earlier in CKD pathogenesis.

P1255 **DIASTOLIC BLOOD PRESSURE IS ASSOCIATED WITH BRAIN ATROPHY IN HEMODIALYSIS PATIENTS: A SINGLE CENTER CASE CONTROL STUDY**

Keren Cohen-Hagai[1], Feda Fanadka[2], Tania Grumberg[3], Guy Topaz[4], Naomi Nacasch[1], Meidad Greenberg[5], Tali Zitman-Gal[1], Sydney Benchetrit[1]

[1]MEIR MEDICAL CENTER, NEPHROLOGY, KFAR SABA, Israel, [2]MEIR MEDICAL CENTER, RADIOLOGY, KFAR SABA, Israel, [3]MEIR MEDICAL CENTER, ANESTHESIA, KFAR SABA, Israel, [4]MEIR MEDICAL CENTER, MEDICINE C, KFAR SABA, Israel and [5]MEIR MEDICAL CENTER, PEDIATRIC NEPHROLOGY, KFAR SABA, Israel

Background and Aims: Brain atrophy (BA) is a common finding in neuroimaging of hemodialysis (HD) patients, representing a parenchymal cerebral damage. Likely contributing factors to BA are age, chronic hypertension, diabetes mellitus and other cardiovascular risk factors of atherosclerosis that are also common among HD patients. BA may also occur due to focal ischemia and hypoperfusion during HD. However, data on optimal blood pressure (BP) in these patients are limited. The goal of this study was to determine whether the prevalence and severity of BA would be higher among HD patients with lower BP.

Method: A blinded neuroradiologist graded BA of all HD patients who underwent brain non-contrast computerized tomography (CT) from 2015 to 2017 in our institution. Age-and sex-matched patients with normal kidney function who underwent brain CT during the same period and technique served as the control group

Results: A total of 280 patients were included in this retrospective study, with average BP of 140/70 mmHg among HD patients and 142/75 mmHg in the control group. BA was more common in dialysis patients and its severity increased with age and traditional cardiovascular risk factors. We observed a significant negative correlation between diastolic BP (DBP) at dialysis initiation and BA. Average DBP decreased with increasing severity of BA. These findings were observed in both HD and non-CKD patients.

Conclusion: Brain atrophy was associated with lower DBP, which may induce cerebral hypoperfusion and ischemia. This finding should discourage over-treatment of hypertension in hemodialysis patients.

P1256

THE ASSOCIATION PROTEIN-ENERGY WASTING AND INFLAMMATION STATUS WITH MORTALITY AFTER LOWER EXTREMITIES REVASCULARIZATION IN PATIENTS ON HAEMODIALYSIS

Hiroshi Takahashi[1], Yoshitaka Kumada[2], Hideki Ishii[3], Norio Umemoto[4], Ryuta Ito[4], Yukio Yuzawa[1], Naotake Tsuboi[5]

[1]Fujita Health University, Nephrology, [2]Matsunami General Hospital, Cardiovascular Surgery, [3]Nagoya Graduate School of medicine, Cardiology, [4]Nagoya Kyoritsu Hospital, Cardiology and [5]Fujita Health University, Nephrology, Japan

Background and Aims: Although lower extremity revascularization has been commonly performed in chronic haemodialysis (HD) patients with peripheral artery disease (PAD), poorer prognosis still remains major problems in such population. Recently, protein-energy wasting (PEW) or malnutrition have been considered to be strongly associated with chronic inflammation and advanced atherosclerosis in HD patients. We investigated the association of geriatric nutritional risk index (GNRI) as a surrogate marker of the PEW, C-reactive protein (CRP) and these joint role with prediction of amputation and/or mortality after lower extremity revascularization in chronic HD patients.

Method: We enrolled a total of 862 HD patients (age 67±10 years, diabetes 62.9%, critical limb ischemia 53.5%) who successfully underwent lower extremity revascularization (552 with endovascular therapy and 310 with bypass surgery). Patients were divided into tertiles according to GNRI levels; tertile 1 (T1): <80.0, T2: 80.0-96.6and T3: >96.6, and CRP levels; T1: <2.0mg/l, T2: 2.0-12.6mg/l and T3: >12.6mg/l, respectively. They were followed up for up to 8 years.

Results: During follow-up period (median: 43 months), 63 (7.3%) patients needed major amputation and 202 (23.4%) patients died. Kaplan-Meier analysis shows that amputation-free survival rates for 8 years were 47.5%, 51.6% and 66.5% in T1, T2 and T3 of GNRI, and were 65.8%, 58.7% and 33.2% in T1, T2 and T3 of CRP, respectively ($p<0.0001$ in both). After adjustment for age, previous coronary artery disease and critical limb ischemia as covariates with $p<0.05$ by univariate analysis, declined GNRI [hazard ratio (HR) 2.18, 95% confidence interval (CI) 1.57-3.07, $p<0.0001$ for T1 vs. T3] and elevated CRP (HR 1.78, 95%CI 1.24-2.59, $p=0.0016$ for T3 vs. T1) were identified as independent predictors of amputation and/or mortality. In the combined setting of both variables, the risk of amputation and/or mortality was 3.77-fold higher (95%CI 1.97-7.69, $p<0.0001$) in theT1 of GNRI with T3 of CRP than in the T3 of GNRI with T1 of CRP. Similar results were obtained for amputation and mortality, respectively (Figure).

Conclusion: Among HD patients undergoing lower extremity revascularization, those with pre-procedural declined GNRI and elevated CRP frequently experienced amputation and/or mortality, furthermore, combination of both variables could stratify the risk of amputation and/or mortality.

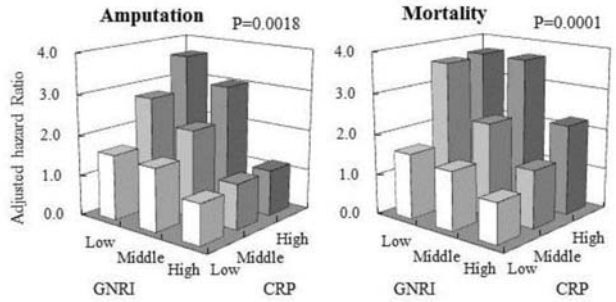


Figure:

P1257 **SERTRALINE ADMINISTRATION TO PREVENT INTRADIALYTIC HYPOTENSION: A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED, CROSSOVER STUDY (SLATAN STUDY)**

Prit Kusirisin[1]

[1]*Chiang Mai University, Internal medicine, Chiang Mai, Thailand*

Background and Aims: Intradialytic hypotension (IDH) is the most common intradialytic complication ranging from 15-50% in chronic hemodialysis patients and increases morbidity and mortality in this population. According to pathophysiology, various strategies have been applied to treat this condition. Autonomic dysfunction is the one of the factors leading to IDH and is commonly found in elderly and diabetes patients. The use of sertraline to improve autonomic function was done in some small studies but the benefits was inconclusive, especially in diabetic patients. This study aimed to clarify an efficacy of sertraline regarding IDH in hemodialysis patients.

Method: We conducted a single-center, randomized, double-blinded, placebo-controlled, crossover study on chronic hemodialysis patient who had IDH in at least 25% of their dialysis sessions. Each patient received either sertraline or placebo for 4 weeks and were crossed to the other group after washout period for 4 weeks. Sertraline was started at the dose of 50 mg/day during the first week and was increased to 100 mg/day from week 2 to week 4. Matching placebo was adjusted using the same protocol as sertraline. The primary outcome was an incidence of IDH. Secondary outcomes included an incidence of IDH in subgroup of the patients with and without diabetes, the changes of blood pressure during hemodialysis session, and incidence of adverse events. Intention-to-treat analysis was applied to all data analyses.

Results: A total of 37 patients were enrolled into the study (48.6% males, mean age of 64.0±15.5 years, mean dialysis vintage of 2.4±2.4 years). All patients in sertraline group completed the study; however, 4 patients in placebo group dropped out due to adverse effects. Baseline characteristics did not differ between both groups. By analysis of crossover design, an incidence of IDH in sertraline group was significantly lower than placebo group (2.5±2.3 episodes versus 4.2±2.7 episodes during study period of 4 weeks, p for treatment effect <0.001, p for period effect = 0.802, and p for sequence effect = 0.811). In subgroup of diabetes patients, an incidence of IDH in sertraline group was 2.5±2.2 episodes versus 4.4±2.8 episodes in placebo group (p for treatment effect = 0.001, p for period effect = 0.491, and p for sequence effect = 0.382). However, there was no difference in incidence of IDH between the two groups in non-diabetes patients. There was no significant difference of adverse events between the two groups.

Conclusion: Among patients undergoing chronic hemodialysis with intradialytic hypotension, administration of sertraline significantly decreases intradialytic hypotension episodes. In addition, diabetes patients may confer more benefit from the treatment compared with non-diabetes status.

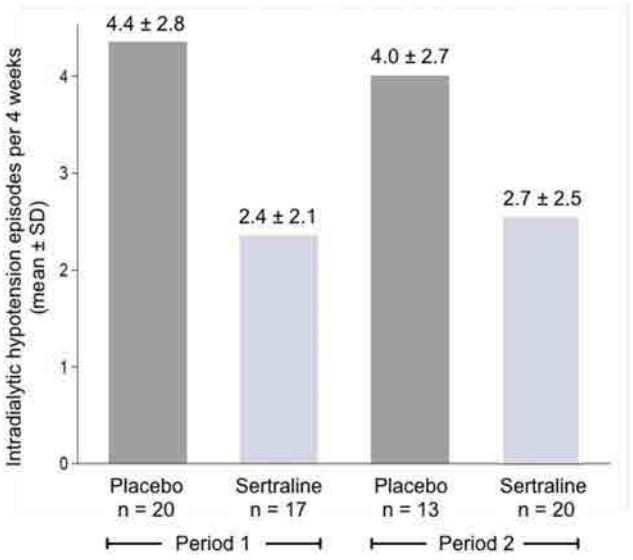


Figure: I ncidence of intradialytic hypotension in each treatment period

P1258

CLINICAL COMPARATIVE STUDY OF AORTIC ARCH CALCIFICATION IN PATIENTS WITH MAINTENANCE PERITONEAL DIALYSIS AND HEMODIALYSIS

Junhui Li[1], Niansong Wang[2]

[1]Shanghai Jiaotong University Affiliated Sixth Peoples Hospital, Nephrology, Shanghai, P.R. China and [2]Shanghai Jiaotong University Affiliated Sixth Peoples Hospital, Nephrology, shanghai, P.R. China

Background and Aims: Vascular calcification is known to be an important risk factor in patients with dialysis, However, the comparative study on vascular calcification between peritoneal dialysis (PD) and hemodialysis (HD) is less. The aim of this study was to analyze the presence, risk factors of aortic arch calcification (AAC), and compare the prognosis in maintenance PD and HD patients.

Method: Using retrospective analysis method, 177 patients with PD and 147 patients with HD were included in the study. The extent of AAC was evaluated by chest X-ray examination. The demographic characteristics and clinical data were collected and compared between PD group and HD group. Binary logistic regression analysis was performed to evaluate risk factors associated with the aortic arch calcification.

Results: The incidence of AAC in HD group (59.86%) was significantly higher than that in PD group (37.29%). Multivariate analysis showed that age, residual renal function (RRF) and serum phosphate were the independent risk factors for calcification of PD patients and the odds ratio (OR) values were 1.133, 1.039, 0.762 and 18.186, respectively. Similarly, age, RRF, calcium-phosphorus product and LDL were the risk factors of HD patients and their respective OR values were 1.125, 0.509, 2.755 and 3.221. Compared with patients without AAC, the presence of moderate-severe AAC was associated with greater risk of mortality, and the OR values were 17.833 and 20.056 in PD group and HD group, respectively.

Conclusion: Our findings suggest that the AAC was more common in HD patients. Older age and lower RRF are common independent risk factors for AAC in PD and HD patients. Moderate to severe AAC a ppears to be associated with increased risk of mortality.

P1259

RELATIONSHIP BETWEEN NT-PROBNP AND ELECTROCARDIOGRAPHIC FINDINGS IN PREVALENT HEMODIALYSIS PATIENTS

Shouichi Fujimoto[1], Yuji Sato[2], Masao Kikuchi[3], Hiroko Inagaki[4], Toshihide Hayashi[5], Nobuhiko Joki[5]

[1]Faculty of Medicine, Miyazaki, University of Miyazaki, Department of Hemovascular Medicine and Artificial Organs, Miyazaki, Japan, [2]University of Miyazaki Hospital, Dialysis Division, Miyazaki, Japan, [3]University of Miyazaki Hospital, Department of Nephrology, Miyazaki, Japan, [4]Faculty of Medicine, University of Miyazaki, Miyazaki, Collaboration Labo. M&N, Miyazaki, Japan and [5]Toho University Ohashi Medical Center, Division of Nephrology, Tokyo, Japan

Background and Aims: There are several reports showing on the relationship between electrocardiographic (ECG) findings and prognosis in dialysis patients. We recently reported that among various ECG findings, T-wave of lead aVR (aVRT) amplitude revealed the strongest and significant association with cardiovascular disease (CVD) events and all-cause mortality in prevalent dialysis patients (Ther Apher Dial, 2017). We also reported that BNP level was significantly associated with CVD-related mortality and all-cause mortality in our cohort study (Ren Fail, 2018; Sci Rep, 2019). On the other hand, BNP levels have been reported to be higher among elderly and women and lower in people with higher body mass index. However, there is no report showing the correlation between NT-proBNP and ECG findings.

Method: From our Miyazaki Dialysis Cohort, we extracted patients who had both ECG findings and NT-proBNP data and did not have atrial fibrillation. We examined the relationship between log NT-proBNP level and various ECG findings using Spearman analysis as a cross-sectional study.

Results: We analyzed 519 hemodialysis patients (44.1% women, mean age was 66.1 years old, median dialysis vintage was 105 months) without atrial fibrillation. Diabetes mellitus was the underlying disease in 25.0% and a history of CVD was found in 25.2% of all patients. Median and IQR (25-75 percentile) of NT proBNP was 4150 (1980-8960). Log NT-proBNP level was significantly correlated with aVRT magnitude (mV), electrical left ventricular high voltage (mV), QTc time (ms), and T-wave amplitude of I lead (mV) ($r=0.289$, $p<0.01$; $r=0.248$, $p<0.01$; $r=0.271$, $p<0.01$; $r=-0.282$, $p<0.01$, respectively). However, log NT-proBNP did not show significant correlation with heart rate, PR interval and QRS duration. These significant correlations between these ECG findings and log NT-proBNP were higher in men compared with women.

Conclusion: Although some ECG findings and BNP level are factors associated with CVD events and death, there was also a significant correlation between these two factors. There has been no report showing the relationships between these two factors, and it may be useful in considering BNP levels in dialysis patients.

P1260

INTRA CRANIAL AND HEART VALVES CALCIFICATIONS IN HEMODIALYSIS PATIENTS - INTERRELATIONSHIP AND CLINICAL IMPACTS

KEREN COHEN HAGAI[1], Feda Fanadka[2], Tania Grumberg[3], Guy Topaz[4], Naomi Nacasch[1], Meidad Greenberg[1], Tali Zitman-Gal[1], Sydney Benchetrit[1]

[1]Meir medical center, Nephrology, Israel, [2]Meir medical center, Radiology, Israel, [3]Meir medical center, Anesthesiology, Israel and [4]Meir medical center, Internal medicine C, Israel

Background and Aims: Arterial calcification is an integral component of active atherosclerosis and is an independent risk factor for cardiovascular disease. Intra-cranial calcification (ICC) in hemodialysis (HD) patients has a prevalence of about 90%, and its severity is correlated with age, hemodialysis vintage and mineral bone disease.

Heart valves calcifications are also considered as a local manifestation of atherosclerosis and have been associated with poor cardiovascular outcomes.

This study assessed the correlation between valvular and ICCs in hemodialysis patients and its clinical impact on mortality.

Method: A blinded neuroradiologist graded ICC of all HD patients who underwent non-contrast brain computerized tomography (CT) from 2015 to 2017 in our institution. Valvular calcifications were recorded according to echocardiography study. Only hemodialysis patients with available echocardiography and brain CT were included.

Results: This retrospective study included 119 hemodialysis patients (mean age 70.6±12.6 years, 57.1% male). Of the total cohort, 19 (16%) had no cardiac or brain calcifications and 65 (54.6%) had both valvular and intracranial calcifications. Considering the patients with no calcification as the reference group yielded adjusted odds ratios for all-cause mortality of 3.68 (95%CI 1.55-8.75) among patients with any brain calcifications, p=0.002. ICC was the most important predictor of mortality in the study cohort.

Conclusion: We found an independent association between ICC and the risk of death among hemodialysis patients. Assessing ICC in non-contrast CT may contribute to the risk stratification of HD patients. These calcifications are no less important than valvular calcifications are. Additional studies are needed to confirm these findings.

P1261 **DIAGNOSTIC VALUE OF TEMPORARY OCCLUSION OF ARTERIO-VENOUS HIGH FLOW FISTULA DURING RIGHT HEART CATHETERISATION IN PATIENTS WITH PULMONARY HYPERTENSION**

Eugene Zeltyn-Abramov[1], RUSTAM ISKHAKOV[2], NATALYA BELAVINA[3], NATALIYA KLOCHKOVA[4], NADIA FROLOVA[3]

[1]City Hospital 52, Nephrology, Moscow, Russia, [2]Moscow City Hospital 52, Intensive care unit, Moscow, Russia and [4]City Hospital 52, Intensive care unit, Moscow, Russia

Background and Aims: Pulmonary hypertension (PH) is prevalent in patients with functioning high-flow arterio-venous fistula (HFAVF) and associated with congestive heart failure (CHF). The real incidence and possible causes of this phenomenon is a matter of debate. Hemodynamic effects of HFAVF is considering as one of the reasons for PH formation. The subject of study was the impact of HFAVF on selected parameters of central hemodynamics. In particular, the diagnostic relevance of test of temporary HFAVF occlusion (TTO) was evaluated during right heart catheterization (RHC).

Method: A total of 13 patients were enrolled: 8 - after kidney transplantation (KT) with preserved allograft function and 5 - on maintenance hemodialysis (HD). All of them demonstrated clinical presentation of CHF III-IV class (NYHA). Severe PH and diastolic disfunction (DD) were observed at a baseline: echocardiographic systolic pulmonary arterial pressure sPAP (mmHg): M=59 (SD 13), ratio of mitral early diastolic inflow velocity (E) (pulsed wave Doppler) to average of septal and lateral mitral annular early-diastolic peak velocity (e′) (tissue Doppler imaging) E/e′ M=18 (SD 5). The ones who have comorbid conditions that cause PH were excluded. All patients bore an upper arm HFAVF, flow of the AVF (Qa) measured by Doppler ultrasonography was markedly high (Qa): M = 3,8 l/min (SD 1,2), the cardio-pulmonary recirculation (Qa/CO): M = 51% (SD 13). All patients underwent RHC and TTO AVF. Echocardiography (Echo) was performed initially and on the follow up (8 weeks after AVF closure/flow reduction). Statistical analysis was performed using the STATISTICA 13 software (Wilcoxon, T-test).

Results: The results of RHC and Echo data are presented in tables 1, 2.

As can be seen from the table data, all cases demonstrated instrumental features of high output CHF (HO CHF) in accordance with patient's clinical status. TTO of HFAVF resulted in statistically significant decrease in CO and CI values, but no changes in PAP parameters were observed. Taking into account clinical and instrumental features of advanced CHF, HF AVF was closed in 8 patients after KT and in 2 patients on HD. 3 patients on HD underwent AVF flow reduction up to Qa not exceeding 1,1 l/min. Follow-up demonstrated complete resolution of CHF and dramatic improvement of DD, reduction in CO, CI, sPAP, volume parameters.

CO, cardiac output; CI, cardiac index; sPAP, systolic pulmonary arterial pressure; meanPAP, mean pulmonary arterial pressure; RAP, mean right atrial pressure; PCWP, pulmonary capillary wedge pressure; LV EDVi, left ventricular end-diastolic volume index; LAVi, left atrial volume index; RAVi, right atrial volume index;

Conclusion: PH is a component of AVF-induced HO CHF and could be classified as postcapillary one. TTO confirms significant HFAVF contribution to specific changes of parameters of central hemodynamics due to HO CHF. TTO does not impact on PAP values and therefore is not valid to clarify PH genesis per se.

Table 1. Results of RHC and TTO

Parameters	Before TTO AVF Me (25% 75%)	TTO AVF Me (25% 75%)	P value
CO l/min	7,2 (6,6 8,9)	6 (5,5 6,5)	0,0014
CI l/min/m^2	3,9 (3,7 5,0)	3,2 (2,7 3,5)	0,0015
sPAP mmHg	51 (48 68)	52 (45 70)	p>0,05
meanPAP mmHg	34 (30 35)	33 (29 34)	p>0,05
RAP mmHg	9 (8 13)	9 (6 13)	p>0,05
PCWP mmHg	21 (17 25)	22 (16 27)	p>0,05

Table 2. Results of Echo monitoring

Parameters	Before AVF closure/flow reduct. M (SD)	After AVF closure/ flow reduct. M (SD)	P value
CO l/min	7,1 (2,2)	5,2 (1,3)	0,0003
CI l/min/m^2	3,8 (1,0)	2,8 (0,7)	0,0001
sPAP mmHg	59 (13)	29 (4)	0,00006
LV EDVi ml/m^2	96 (10)	74 (10)	0,0001
LAVi ml/m^2	63 (13)	37 (6)	0,00003
RAVi ml/m^2	50 (15)	24 (9)	0,0003

P1262 VASCULAR CALCIFICATION OF ABDOMINAL AORTA AND COMMON ILIAC ARTERY AFTER KIDNEY TRANSPLANTATION

Kentaro Nakai[1], Shutaro Yamamoto[1], Haruka Tomooka[1], Megumi Inoue[1], Chiaki Kohara[1], Tomoya Shukuri[1], Keita Takae[1], Takehiro Nishiki[2], Kentaro Motoyama[2], Koji Mitsuiki[1]

[1]Japanese Red Cross Fukuoka Hospital, Division of Nephrology and Dialysis Center, Fukuoka, Japan and [2]Japanese Red Cross Fukuoka Hospital, Department of Surgery, Fukuoka, Japan

Background and Aims: Vascular calcification is a risk factor for cardiovascular disease and mortality in dialysis and transplant patients. Previous studies have shown that coronary artery calcification correlates with cardiovascular mortality. However, it is not known whether vascular calcification of the abdominal aorta and common iliac artery (CIA) may impact clinical outcomes after kidney transplantation. The aim of this study was to identify the risk factors of vascular calcification after kidney transplantation.

Method: In this retrospective study, we assessed 100 patients who underwent kidney transplantation between 2008 and 2017. Of these, 62 patients received a computed tomography (CT) scan of the abdomen twice with an interval of at least 6 months. We examined the characteristics of vascular calcification of the abdominal aorta and iliac artery and divided the patients into three groups based on dialysis modality before transplantation: hemodialysis (HD group), peritoneal dialysis (PD group) and preemptive kidney transplantation (PEKT group). Then, we identified the risk factors for the progression of calcification. Abdominal aortic calcification was assessed based on the aortic calcification index (ACI), and calcification of CIA was assessed based on the maximal thickness of calcification.

Results: At baseline, abdominal aortic calcification was present in 66% of patients, and the median ACI was 10 [0-30]. Calcification of the CIA was present in 62% of patients, and maximal thickness of the CIA was 2.4 mm [0-4.6]. The mean duration of follow-up was 68 $\pm$ 29 months, and the mean interval of CT was 40 $\pm$ 29 months. After kidney transplantation, the progression rate of ACI and maximal thickness of CIA were 1.6 $\pm$ 2.5 per year and 0.17 $\pm$ 0.41 mm per year, respectively. The maximal thickness of CIA calcification was significantly higher, and ACI tended to be higher in the HD group than in the PEKT group. Age, male gender, diabetes mellitus and dialysis vintage were the independent variables related to both ACI and maximal thickness of CIA calcification. The progression rates of ACI and maximal thickness of CIA were comparable among the three groups in terms of dialysis modality. Age and rejection within the first 6 months were independent risk factors for ACI progression, and diabetes mellitus was an independent risk factor for progression of maximal thickness of CIA. No significant association was found between the progression of vascular calcification and dialysis-related parameters, including dialysis modality and vintage.

Conclusion: This study suggests that dialysis vintage was the independent variable related to calcification of the abdominal aorta and common iliac artery, whereas dialysis modality was not a significant predictor of vascular calcification and its progression in these blood vessels.

P1263 ASSOCIATION OF LEFT VENTRICULAR HYPERTROPHY AND ADIPOCYTOKINES IN PATIENTS ON DIALYSIS

Cristina Catarino[1], Maria do Sameiro Faria[1,2], José Pedro Lopes Nunes[3], Susana Rocha[4], Maria João Valente[1], Susana Coimbra[1,5], Petronila Rocha-Pereira[1,6], Elsa Bronze-da-Rocha[1], Nuno Bettencourt[2], Ana Beco[2], Sofia Homem Melo Marques[2], José Gerardo Oliveira[3,7], José Madureira[8], Vasco M.P. Miranda[9], Luís Belo[1], Alice Santos-Silva[1]

[1]UCIBIO, REQUIMTE, Laboratory of Biochemistry, Department of Biological Sciences, Porto, Portugal, [2]Hemodialysis Clinic of Felgueiras, Felgueiras, Portugal, [3]Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal, [4]LAQV, REQUIMTE, Laboratory of Applied Chemistry, Department of Chemical Sciences, Porto, Portugal, [5]CESPU, Institute of Research and Advanced Training in Health Sciences and Technologies (IINFACTS), Gandra PRD, Portugal, [6]Health Science Research Centre, University of Beira Interior, Covilhã, Portugal, [7]Hemodialysis Clinic of Porto, Porto, Portugal, [8]NefroServe, Hemodialysis Clinic of Barcelos, Barcelos, Portugal and [9]Hemodialysis Clinic of Gondomar, Gondomar, Portugal

Background and Aims: Cardiovascular (CV) disease events are the major cause of death in end-stage renal disease (ESRD) patients on dialysis. Left ventricular hypertrophy, myocardial stress and disturbances in nutritional status are common findings in ESRD patients on dialysis. The adipokines, adiponectin and leptin, are known as important mediators of cardiometabolic risk in obesity, although their role in ESRD patients is poorly clarified.

N-terminal pro B-type natriuretic peptide (NT-proBNP) is synthesized within cardiac myocytes, in response to cardiac wall stress.

Our aim was to study the association of left ventricular hypertrophy with adipokines (adiponectin and leptin), myocardial stress (ProBNP) and nutritional status (BMI and albumin) in ESRD patients on dialysis.

Method: This study included 196 ESRD patients on dialysis (hemodiafiltration and high-flux hemodialysis). LVH was defined by a value of LVMI $>$ 115 g/m2 in men and 95 g/m2 in women. Patients were divided into two groups - LVH (n=131) and non-LVH (n=65).

Left ventricular mass (LVM) was evaluated through echocardiographic studies, corrected for body surface area and the values are presented as LVM index (LVMI).

LVMI, clinical and analytical variables (age, body mass index, dialysis vintage, dialysis adequacy, albumin, adiponectin, leptin, NT-proBNP and hemoglobin concentration) were evaluated.

Results: The prevalence of LVH was 66.8%; LVH patients presented significantly higher levels for NT-proBNP, and significantly lower levels for hemoglobin, when compared with non-LVH patients; a trend towards (P=0.052) lower leptin values were observed. No differences were observed between groups, for age, BMI, dialysis vintage, URR, Kt/V, eKt/V, ultrafiltration volume, albumin and adiponectin.

In LVH patients, we found that LVMI presented significant positive correlations with NT-proBNP and with adiponectin; and, significant negative correlations with markers of dialysis adequacy (URR and eKt/V) and leptin.

Conclusion: Our data suggest that a higher LVMI in ESRD patients is associated with higher myocardial stress, with lower leptin and higher adiponectin levels, showing no association of these adipokines with increased cardiovascular risk and with worsening of left ventricular hypertrophy. Further studies are needed to understand the roles of these adipokines, considering the controversial association with left ventricular hypertrophy, a cardiovascular risk condition.

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P1264 **LOW PHOSPHATE AND LOW CALCIUM LEVELS PREDICT A HIGHER RISK FOR CARDIOVASCULAR EVENTS OF MAINTENANCE HEMODIALYSIS PATIENTS.**

Kuragano Takahiro[1], Takeshi Nakanishi[1]

[1]*Hyogo College of Medicine, Division of Kidney and dialysis, Nishinomiya, Japan*

Background and Aims: It has been reported that higher serum levels of phosphate (P) and calcium (Ca) are associated with a higher risk of cardiovascular disease (CVD) and premature death of maintenance hemodialysis (MHD) patients. Thus, several clinical guidelines recommend that serum P and Ca levels in MHD patients be maintained within the optimal range. However, in the current situation in which the guidelines have penetrated widely, there are few reports that have investigated the association between chronic kidney disease (CKD)-mineral and bone disorder (MBD)-related factors and adverse events in MHD patients.

Method: The study design was a 3-year multicenter, observational study. A total of 989 MHD patients were enrolled in this study. The blood levels of Hb, ferritin, iron, total iron-binding capacity, β2-microglobulin, creatinine, total protein, albumin, total cholesterol, Ca and P were measured every 3 months. The blood levels of high-sensitivity C-reactive protein (hCRP) and intact parathyroid hormone (int-PTH) were also measured every six months. The correlation between CKD-MBD factors and adverse events was evaluated by the time-dependent Cox hazard model.

Results: In 82% of patients, 83% of patients, and 78% of patients, serum P levels, serum Ca levels, and int-PTH levels, respectively, were maintained in the target ranges ($3.5 \leq P \leq 6.0$ mg/dL, $8.4 \leq Ca \leq 10.0$ mg/dL, $60 \leq$ int-PTH ≤ 240 pg/mL) that were recommended by the 2012 guidelines of the Japanese Society for Dialysis Therapy. After correcting for age, sex, past history of CVD, Hb, albumin, and hCRP, compared with the patients with target levels of P, patients with low P levels (<3.5 mg/dL) had a significantly higher risk for CVD (P=0.042, HR: 2.27), hospitalization (P=0.034, HR: 2.44), and all-cause mortality (P=0.03, HR: 2.29). On the other hand, there was no association between higher serum P levels and adverse events. Compared with the patients who maintained target int-PTH levels, patients with lower (<60) (P=0.025, HR: 1.46) and higher (>240 pg/mL) (P=0.04, HR: 1.44) int-PTH levels had a significantly higher risk for hospitalization. There was no significant correlation between serum Ca and adverse events. Furthermore, compared with the patients who maintained the target levels of both Ca and P, the patients with target Ca and low P levels (P=0.042, HR: 2.75) had a significantly higher risk for CVD. Compared with the patients who maintained the target levels of both Ca and P, the patients with low Ca and low P levels (P<0.001, HR: 4.4) and target Ca and low P levels (P=0.22, HR: 2.0) had a significantly higher risk for hospitalization.

Conclusion: After correcting for several clinical factors, we found that patients who maintained low serum P levels had a significantly higher risk for CVD and all-cause mortality than patients who maintained higher Ca and P levels. Undoubtedly, extremely high serum P, Ca, and int-PTH levels should be treated according to the guidelines. However, in the current situation in which the guidelines have penetrated widely, CKD-MBD management, in which the clinical conditions of low P, Ca, and int-PTH are considered, is needed.

P1265

INTRA-DIALYTIC RELEASE OF EXTRACELLULAR VESICLES (EVS) IS INDEPENDENT OF THE MODE OF DIALYSIS A COMPARISON BETWEEN STANDARD HEMODIALYSIS (SHD), COOL HD (CHD), LOW-VOLUME HEMODIAFILTRATION (LVHDF) AND HIGH-VOLUME HDF (HVHDF): THE HOLLANT STUDY

Paul A Rootjes[1], Camiel De Roij van Zuijdewijn[1], Menso J. Nubé[1], Gertrude Wijngaarden[1], Rienk Nieuwland[2], Najat Hajji[2], Chi Hau[2], Muriel Grooteman[1]

[1]*Amsterdam UMC, locatie VUmc, Nephrology, Amsterdam, Netherlands and*
[2]*Amsterdam UMC, locatie AMC, Lab. Exp. Clinical Chemistry, Amsterdam, Netherlands*

Background and Aims: Treatment with high-volume HDF is associated with a better survival than standard HD. The underlying mechanism is unknown, but may depend on a lower level of intra-dialytic tissue damage. We compared tissue injury, as measured by the release of EVs during four dialysis treatment modalities.

Method: Chronic hemodialysis (CHD) patients were included in an open, cross-over, randomized fashion (n=14). EV release was measured by a calibrated flow cytometer (Apogee A-60) after antibody labeling. EVs are defined as cell-derived particles with a diameter <1.000nm and a refraction index (RI) <1.42. Two HD modalities were studied: *sHD, t dialysate 36,5° C (sHD) and cHD, t dialysate 35,5° C* and two HDF modalities *(t dialysate 36,5° C): lvHDF with a convection volume (CV) <15 L/session and hvHDF with a CV >23 L/session.*To establish the cellular origin of EVs, EVs were labelled with (anti-) CD45 (leukocytes), CD62e (activated endothelial cells), CD62p (activated platelets), CD144 (vascular endothelial cadherin), CD61 (platelets), CD235a (erythrocytes) and connexin-43 (myocardial and endothelial cells), and with the general EV marker lactadherin. Differences between the 4 dialysis modalities were investigated by comparing pre- and post-dialysis and the delta (post- minus pre-dialysis) EV concentrations by Friedman's test.

Results: As shown in the figures below, CD61, lactadherin and CD144 increased during the 4 modalities (1=sHD,2=cHD,3=lvHDF,4=hvHDF). The overall increase (sum of all modalities) in connexin-43. In Table 1, the concentrations of EVs before- and after dialysis are shown with a p-value for the difference (post- minus pre-dialysis). No significant differences were found in pre- and post-dialysis and delta EV concentrations between the 4 dialysis modalities (data not shown).

Conclusion: From this analysis the following conclusions can be drawn: 1) except for CD62e, which declined, all measured EVs increased significantly during dialysis (Table 1). 2) Although not all EVs increased similarly during the 4 modalities (Fig 1), in terms of tissue damage no modality appears more advantageous than the other.

Table 1: intradialytic EV changes: means of 4 modalities, delta's and p-values post vs pre-dialysis

EV concentration (10^7/mL)	Pre-dialysis	Post-dialysis	delta	p-value (post- vs pre)
CD45	0.277	0.337	0.060	<0.0005
CD61	0.397	0.932	0.535	<0.0005
CD62p	0.031	0.074	0.043	<0.0005
CD235a	0.839	1.570	0.731	<0.0005
CD62e	0.991	0.048	-0.943	0.03
CD144	0.021	0.163	0.142	0.03
Connexin-43+	0.098	0.282	0.184	0.002
Lactadherin	2.826	5.176	2.35	<0.0005

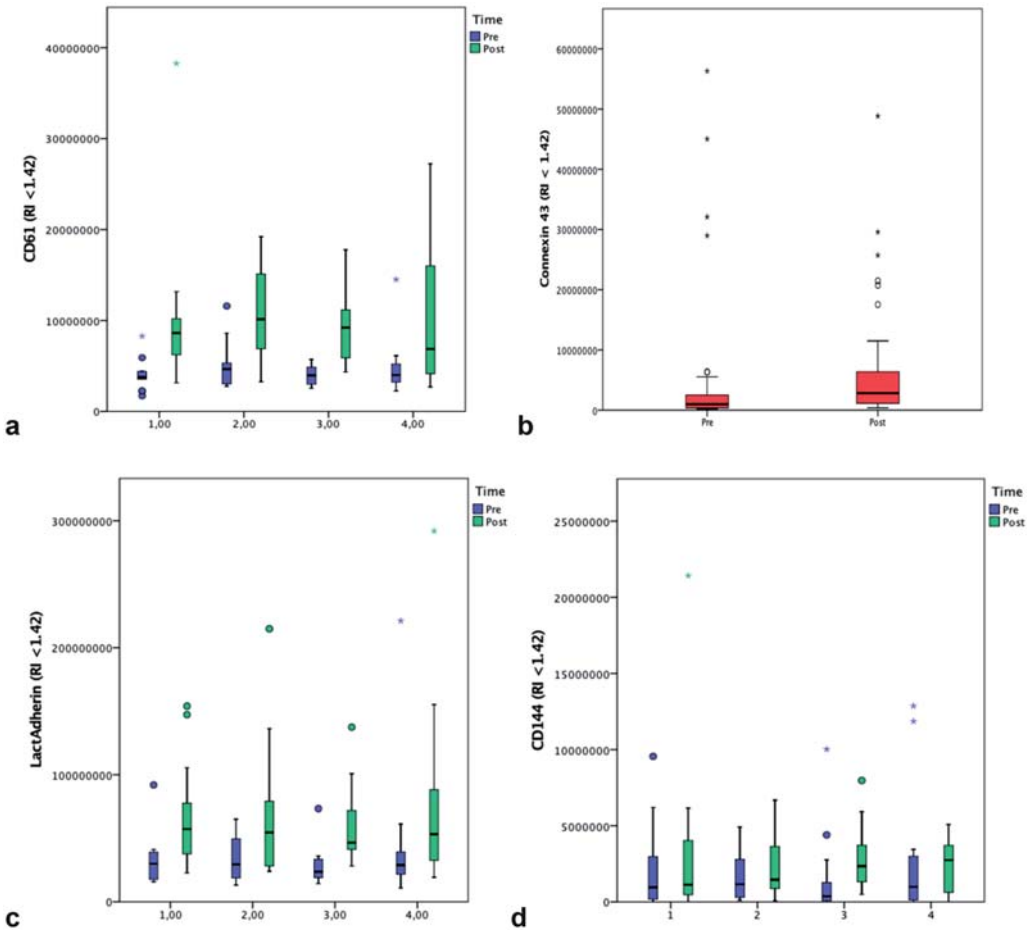


Figure 1: Absolute EV concentrations (mL-1) before and after dialysis: a:CD61, b:connexin-43, c:lactadherin, d:CD144. RI<1.42 (refraction index). Modality of dialysis (1= sHD, 2= cHD, 3= lvHDF, 4= hvHDF).

P1266 SERUM MALONDIALDEHYDE-MODIFIED LOW-DENSITY LIPOPROTEIN LEVEL IS A RISK FOR AORTIC STIFFNESS IN MAINTENANCE HEMODIALYSIS PATIENTS

Jia-Sian Hou[1], Chia-Wen Lu[1], Bang-Gee Hsu[1,2]

[1]Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Division of Nephrology, Hualien, Taiwan, R.O.C. and [2]Tzu Chi University, School of Medicine, Hualien, Taiwan, R.O.C.

Background and Aims: Circulating oxidized malondialdehyde LDL (MDA-LDL) induced macrophage apoptosis, the release of higher levels of matrix metalloproteinases and TNF-α, therefore, act as a marker of oxidative stress and are associated with atherosclerotic cardiovascular diseases. We evaluated the association between serum MDA-LDL levels and aortic stiffness in patients with hemodialysis (HD).

Method: A total of 155 patients with HD were enrolled in this study. Carotid-femoral pulse wave velocity (cfPWV) value was measured by a validated tonometry system (SphygmoCor). Patients with cfPWV >10 m/s were used to define the aortic stiffness group, while values ≤ 10 m/s were regarded as the control group, according to the ESH-ESC 2013. Serum MDA-LDL levels were measured using a commercial enzyme-linked immunosorbent assay.

Results: 68 patients (43.9%) had aortic stiffness and higher percentages of diabetes ($p < 0.001$), hypertension ($p = 0.017$), and had older age ($p = 0.038$), higher systolic blood pressure ($P = 0.021$), serum MDA-LDL level ($p < 0.001$) compared to subjects with control group. After adjusting for factors significantly associated with aortic stiffness by multivariable logistic regression analysis revealed that serum MDA-LDL levels (odds ratio (OR): 1.014, 95% confidence interval (CI): 1.007–1.021, $p < 0.001$), diabetes (OR: 2.893, 95% CI: 1.300–6.437, $p = 0.009$), and hypertension (OR: 2.408, 95% CI: 1.066–5.436, $p = 0.034$) were the independent predictors of aortic stiffness in HD patients. Multivariable forward stepwise linear regression analysis also showed that serum logarithmically transformed MDA-LDL level (log-MDA-LDL, $\beta = 0.404$, adjusted R^2 change = 0.265, $p < 0.001$), diabetes ($\beta = 0.233$, adjusted R^2 change = 0.055, $p = 0.001$), and hypertension ($\beta = 0.132$, adjusted R^2 change = 0.014, $p = 0.048$) were the independent predictors of cfPWV values in HD patients. The area under the receiver-operating characteristic (ROC) curve predicting aortic stiffness by serum MDA-LDL level in HD patients was 0.721 (95% CI: 0.643-0.790, $p < 0.001$).

Conclusion: In this study, high serum MDA-LDL level was positively associated with cfPWV values and thus was related to aortic stiffness in HD patients.

P1267 **EFFECT OF SODIUM AND ULTRAFILTRATION MODELING VERSUS LOW TEMPERATURE DIALYSATE IN PREVENTION OF INTRADIALYSIS HYPOTENSION: A SINGLE CENTRE STUDY FROM INDIA**

Vaibhav Tiwari[1], Anurag Gupta[1], Yogeshman Anand[1], Vinant Bhargava[1], Manish Malik[1], Ashwani Gupta[1], A K Bhalla[1], Devinder Singh Rana[1]

[1]*Sir Ganga Ram Hospital, New Delhi, India*

Background and Aims: Symptomatic intradialytic hypotension is the most frequent complication in patients receiving hemodialysis. It complicates 5 to 30 percent of all dialysis treatments. In our study, we aimed to compare the effect of sodium and ultrafiltration modeling versus low-temperature dialysate on the occurrence of intradialytic hypotensive episodes.

Method: Single center, prospective, randomized trial. Patients with chronic kidney disease (CKD) stage V on maintenance hemodialysis (HD) for at least twice weekly for a minimum of 3 months were observed for the occurrence of $\geq$1 intradialytic hypotensive episode per month. After full filling the inclusion and exclusion criteria, patients were randomized 1:1 ratio into two groups based on computer-generated randomization numbers allotted to them by the dialysis coordinator.

Group 1: Underwent dialysis with sodium and Ultrafiltration modeling (Linearly decreasing dialysate sodium from 141 mmol/L to 128 mmol/L and linearly decreasing ultrafiltration rate).

Group 2: Underwent dialysis with low-temperature dialysate (36 degrees Celsius).

Primary outcome was number of hypotensive episodes per month. Secondary outcomes were interdialytic weight gain and ultrafiltration volume per session.

Results: A total of 320 patients were observed for 3 months in our centre. Intradialytic hypotension was found in 18.75 % of patients. Diabetic nephropathy (61.66%) was the leading cause of end-stage renal disease in these patients. There was no significant difference between the two groups in mean arterial blood pressure, hemoglobin, cardiac status, and serum albumin before dialysis. Both groups had a similar incidence of intradialytic hypotensive episodes ($P > 0.05$). Interdialytic weight gain and ultrafiltration volume removed per session were also similar in both groups.

Conclusion: Sodium and ultrafiltration modeling and low-temperature dialysate were both equally effective in the prevention of intradialytic hypotensive episodes.

P1268

MIXING ARTIFICIAL INTELLIGENCE AND CLINICAL OUTREACH TO REDUCE RISK OF FLUID OVERLOAD HOSPITALIZATION IN PATIENTS WITH END-STAGE RENAL DISEASE

Joanna Willetts[1], Andrew Long[1], Amanda Rivenbark[2], Jeffrey Hymes[3], Len A Usvyat[1], Sheetal Chaudhuri[1], Franklin Maddux[4]

[1]Fresenius Medical Care, Global Medical Office, Waltham, United States of America, [2]Fresenius Medical Care North America, Fresenius Kidney Care, Waltham, United States of America, [3]Fresenius Medical Care North America, NA Medical Office, Waltham, United States of America and [4]Fresenius Medical Care AG & Co. KGaA, Global Medical Office, Bad Homburg, Germany

Background and Aims: Fluid overload is associated with increased morbidity and mortality in hemodialysis (HD) patients. In-patient treatment of fluid overload was previously estimated to occur at a rate of 13.7 episodes/100 patient-years and estimated to cost $266 million over a 2.5-year period (Arneson 2010). We developed a model to predict which patients treated at a large dialysis provider are at imminent risk of hospitalization due to fluid overload and may benefit from additional interventions.

Method: We built a machine learning (ML) model using clinical and HD treatment data to identify which patients have the highest risk of hospital admission for fluid overload within 7 days of the current outpatient dialysis treatment. Next, we partnered with a team of remote nurses who perform chart reviews, needs identification, and communication outreach when warranted with the goal to reduce hospital admissions. Patients were identified from the ML model and displayed in a worklist on a computer dashboard, ranked by their risk score on that day. The computer dashboard also contained relevant clinical information to enhance the patient review process.

Results: Model results from prospective data (> 9M predictions in a two-month period) show the model has an area under the receiver operating curve (AUROC) of 0.79, sensitivity of 65%, and specificity of 78% (Figure 1). Weekly chart reviews increased 18% from 26 weeks before the pilot compared to 14 weeks after the pilot began; total communication outreach increased 31% across the same time frame. Further, the nurses using the dashboard anecdotally reported that the dashboard reduced the amount of time required to decide to perform a chart review or perform communication outreach.

Conclusion: Our predictive model successfully identifies patients at high risk for fluid overload hospital admissions. Understanding the nurse workflow, how they manage this patient population, and which components can be made more efficient enabled them to increase the number of chart reviews and communication outreach.

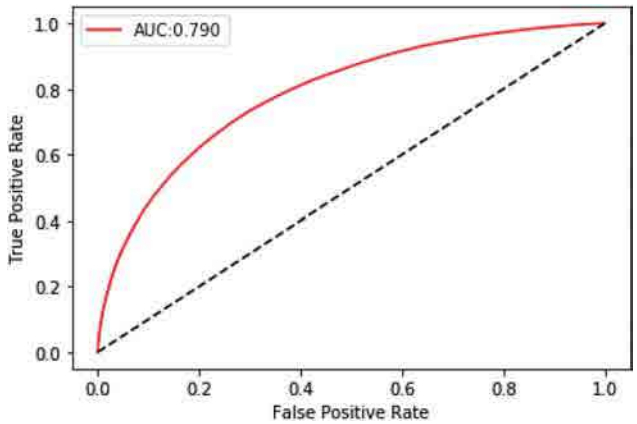


Figure:

P1269

EXERCISE TRAINING FOR IMPROVING SLEEP QUALITY IN PATIENTS WITH END-STAGE KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Jueyao Liang[1,2], Xindong Qin[1], Guobin Su[1], La Zhang[1], Huanyu Liu[2], Yifan Wu[1], Xusheng Liu[1]

[1]Nephrology Department, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, P.R. China and [2]The Second Clinical Medical School, Guangzhou University of Chinese Medicine, Guangzhou, P.R. China

Background and Aims: Sleep disorders are commonly experienced by patients with end-stage kidney disease (ESKD) which influence the quality of life severely and may cause high risk of cardiovascular events. People with ESKD may constrain the use of neuroleptic medications which can lead to dependence if used in the longer-term. As non-pharmacological intervention, exercise training was suggested as based therapy to improve the quality of life. We conducted a systematic review to assess the efficacy of exercise training for improving sleep quality in dialysis patients with ESKD.

Method: Randomised controlled trials (RCTs) that evaluated the effects of regular exercise training on sleep quality in patients with ESKD were included. Searching was conducted in CENTRAL, EMBASE, PUBMED, CINAHL, WEB OF SCIENCE, and 3 Chinese databases (CBM, CNKI, WANFANG), date from inception to May 2019. Risk of bias was assessed. The quality and strength of evidence were evaluated by GRADE framework. Study selection, data extraction and methodological quality assessment were performed independently by two researchers. Results were reported as mean differences (MD) for continuous outcomes, with 95% confidence intervals (CI). This systematic review was registered in the PROSPERO (CRD42019141630).

Results: Twelve RCTs were included, which involving 753 participants. Methodological quality of studies and strength of evidence were assessed from low to moderate. Eleven trials included patients who receiving regular hemodialysis (HD) and one trial included patients that receiving either regular HD or continuous ambulatory peritoneal dialysis (CAPD). The major type of exercise was aerobic training during hemodialysis session (7 RCTs), followed by intradialytic resistance exercise, intradialytic mixed training, and interdialytic aerobic exercise. Most studies set exercise 3 times per week with moderate intensity, lasting 20∼60 minutes per session, and treatment duration for 2∼6 months. The Pittsburgh Sleep Quality Index (PSQI) questionnaire, Kidney Disease Quality of Life (KDQoL-SF) questionnaire, University of Massachusetts Weekly Sleep Questionnaire (UMass WSQ), visual analogue scale (VAS), and sleep fragmentation index (SFI) based on patient-reported outcomes were measured for testing sleep quality. By measuring with PSQI questionnaire (scale 0-21, lower is better), the sleep quality was improved with regular exercise comparing with usual care (5 RCTs, 296 participants, MD -4.92, 95%CI -6.54 to -3.30, I^2=88%, moderate certainty evidence). The result was similar with KDQoL-SF questionnaire (4 items assessing sleep quality, higher is better) (3 RCTs, 328 participants, MD 8.75, 95%CI 2.06 to 15.43, I^2=54%, low certainty evidence). However, there was no significant different in sleep diary by measuring with UMass WSQ (2 RCTs, 46 participants, MD -0.48, 95%CI -4.05 to 3.09, I^2=59%, low certainty evidence). There was only one study measured with VAS and SFI, so we didn't analyze it into meta-analysis.

Conclusion: Regular exercise appeared to be beneficial to improve sleep quality in patients with dialysis, especially intradialytic aerobic training. Given the growing challenge of pharmacological dependence, there is necessary to design high quality RCTs for non-pharmacological interventions such as exercise training.

P1270

INCREASED SCLEROSTIN, BUT NOT DKK-1 PROTEIN, IS ASSOCIATED WITH ELEVATED PULSE WAVE VELOCITY IN HEMODIALYSIS SUBJECTS

EIRINI STAVRINOU[1], Panteleimon Sarafidis[1], Charalampos Koumaras[2], Charalampos Loutradis[1], Panagiotis Giamalis[2], Konstantinos Tziomalos[3], Asterios Karagiannis[2], Aikaterini Papagianni[1]

[1]Thessaloniki, Department of Nephrology, Hippokration Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece, [2]Thessaloniki, Second Propaedeutic Department of Internal Medicine, Hippokration Hospital, Aristotle University of Thessaoniki, Thessaloniki, Greece and [3]Thessaloniki, First propaedeutic Department of Internal Medicine, AHEPA Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece

Background and Aims: Sclerostin and Dickkopf-1 (Dkk-1) protein are inhibitors of the canonical Wnt/β-catenin bone pathway. Pilot data suggest that sclerostin may be involved in vascular changes in CKD, but data on Dkk-1 effects are scarce. This is the first study investigating simultaneously the associations of sclerostin and Dkk-1 with arterial stiffness in hemodialysis patients.

Method: 80 patients on chronic hemodialysis had carotid-femoral pulse wave velocity (PWV), central BP and wave reflections evaluated with applanation tonometry (Sphygmocor) in a mid-week non-dialysis day. Serum levels of sclerostin and Dkk-1 were measured with ELISA. A large set of demographic, co-morbid, laboratory and drug parameters were used in the analyses.

Results: Subjects with PWV>9.5 m/sec (high arterial stiffness group, n=40) were older, had higher BMI, higher prevalence of hypertension, diabetes and coronary-heart-disease and higher peripheral SBP, central SBP, C- reactive protein and serum sclerostin (p=0.02), but similar Dkk-1 compared to subjects with low PWV. When dichotomizing the population by sclerostin levels, those with high sclerostin had higher PWV than patients with low sclerostin levels (10.63±2.71 vs 9.77±3.13, p=0.048). Increased sclerostin (>200 pg/ml) was significantly associated with increased PWV (>9.5 m/s) (HR:2.778, 95%CI:1.123-6.868, per pg/ml increase); this association remained significant after stepwise adjustment for Dkk-1, iPTH and calcium x phosphate product. In contrast, no association was noted between Dkk-1 and PWV (HR: 1.000, 95%CI: 0.416-2.403).

Conclusion: Serum sclerostin is associated with PWV independently of routine markers of CKD-MBD in hemodialysis patients. In contrast Dkk-1 has no association with arterial stiffness and is rather not pathophysiologically involved in relevant vascular changes.

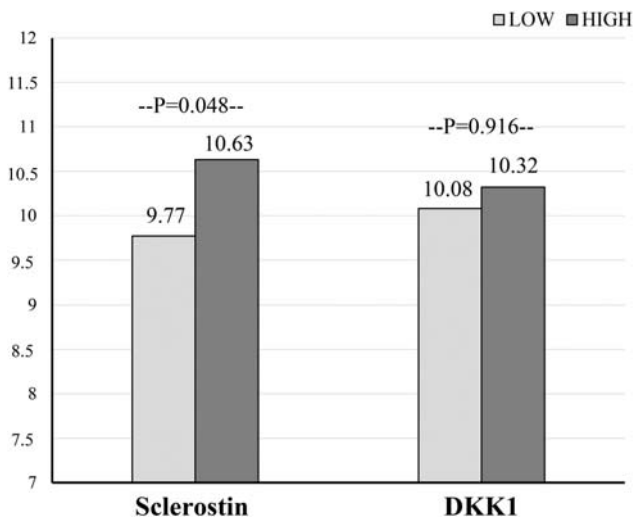


Figure:

P1271

PARADOXICAL EFFECT OF ALDOSTERONE ON CARDIOVASCULAR OUTCOME IN MAINTENANCE HEMODIALYSIS PATIENTS

Young-Ki Lee[1], Sun Ryoung Choi[1], Hayne Cho Park[1], Do Hyoung Kim[1], Ajin Cho[1], Juhee Kim[1], Jong-Woo Yoon[1], Jung-Woo Noh[1], Min-Kyung Kang[1]

[1]*Hallym University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of South*

Background and Aims: Patients with end-stage renal disease have an increased risk of cardiovascular (CV) mortality and left ventricular diastolic dysfunction (LVDD) is known to contribute to its high occurrence. Although high serum aldosterone level is involved in the development of CV complications in general population, this association is unclear in patients undergoing hemodialysis (HD). We aimed to determine the impact of serum aldosterone on LVDD and CV mortality among HD patients.

Method: We performed a prospective cohort study of maintenance HD patients without CV disease. Patients were divided into two groups according to the median level of serum aldosterone (44 ng/dL). All patients underwent echocardiography to evaluate diastolic dysfunction. Proportions of LVDD and CV mortality were compared between high and low aldosterone groups.

Results: We enrolled a total of 60 adult patients (mean age 57.9±12.1 years, male 30.0%). Low aldosterone group had an increased left ventricular diastolic dimension compared with high aldosterone group (52.2±8.4 vs. 50.3±5.2 mm, p=0.033). The E/è ratio (19.5±7.5 vs. 14.6±5.2, p=0.024) was significantly higher among patients in low aldosterone group compared to high aldosterone group. There were no significant differences either in ejection fraction, LVMI, or the proportion of LVH between two groups. Low log-aldosterone (odds ratio 0.403; 95% confidence interval 0.188-0.862) and large left atrial dimension (1.308; 1.114-1.536) were independent risk factors for LVDD. In addition, cox regression analysis demonstrated that low log-aldosterone was an independent predictor of CV mortality in HD patients (hazard ratio 0.505; 95% confidence interval 0.294-0.869, p=0.014).

Conclusion: Low serum aldosterone was not only associated with LVDD but also an independent predictor of CV mortality among HD patients.

P1272 **ECFECT OF MELATONIN ON DYSLIPIDEMIA IN HEMODIALYSIS PATIENTS**

Nargesossadat Zahed[1,2], Marjan Pouyamehr[3], Adineh Taherkhani[4]

[1]Shahid beheshti university of medical science, Nephrology, Tehran, Iran, [2], [3]Shahid beheshti university of medical science, Internal medicines, Tehran, Iran and [4]Shahid beheshti university of medical science, Internal medicine, Tehran, Iran

Background and Aims: Cardiovascular disease is one of the major causes of death in hemodialysis patients.

Lipid metabolism abnormalities and increased inflammatory factors are related factors.

In recent studies melatonin inhibits dyslipidemia and reduces inflammatory factors by inhibiting LDL-c oxidation.

The purpose of this study was to evaluate the effect of melatonin supplement on hyperlipidemia and c reactive protein (CRP) level in hemodialysis patients.

Method: In this clinical trial ,the inclusion criteria were as follows:age older than 18 years, undergoing dialysis for at least 3 months,triglyceride >150mg/dL,HDL-c<40 mg/dL in males, HDL-c<50 mg/dL in females and serum CRP>5 mg/l

Exclusion criteria were:

Patients with a history of stroke, myocardial infarction, peripheral vascular disease, malignancy, heart failure, liver cirrhosis, active liver disease, history of infection, hospitalization one month ago, hepatitis B and C.HIV, and taking corticosteroid, statin, Non-steroidal anti-inflammatory drugs.

Among 200 hemodialysis patients,only 28 patients fulfilled the inclusion criteria..

Patients were treated with Melatonin supplements 3 mg per day at bedtime during 12 weeks. Serum lipid profile and CRP level were measured after 12 weeks.

Five patients were excluded, 2 patients underwent kidney transplantation, and three patients did not cooperate.

Data were analyzed by SPSS 20 software. Normal distributed quantitative data were expressed as the mean ± SD and qualitative data was expressed as frequency and percentage.

Wilcoxon matched pairs test was used to compare the two groups according to the type of study that had no normal distribution and the number of participants (less than 30) and study type (pre-test and post-test). P <0.05 was considered as the level of significance.

Results: A total of 23 patients completed the treatment protocol.Baseline demographic characteristics of patient are shown in Table 1.Parcipitant was composed of 13 male and 10female .The participants' mean age was 30.6± 11.6.Etiology of ESRD was diabetes in 13(56/5%)and hypertension in5(21.7%)patients and other causes was 5(21/7%).

After treatment mean total cholesterol levels decreased from 139.95 ± 35.49 mg/dL to 131.13 ± 34.96 mg/dL (p value =0.194) which was not statistically significant. But the decrease in serum triglyceride level was statistically significant ,from 242.08 ± 101.05 mg/dL decreased to 178.00 ± 48.02 mg/dL (pvalue = 0.004).HDL-c increased significantly after treatment from 36.20 ±7.08 mg/dL to 40.16 ±4.35mg/dL (pvalue =0.032).

Serum CRP levels did not decreased.The limitations of our study were the small sample size and short duration of the investigation.

Conclusion: Melatonin supplement improves triglyceride and HDL-c in hemodialysis patients but has no effect on total cholesterol-c and CRP in hemodialysis patients.

Table1 Patient characteristics

Properties	*Values*
Age(year)	
Mean ± Standard deviation	60.30 ± 16.11
Middle	61.00
Domain (min-max)	59 (32-91)
Sex	
Female	10 (43.5%)
Male	13 (56.5%)
Age of starting dialysis (year)	
Mean ± Standard deviation	57.29 ± 17.19
Middle	55.00
Domain (min-max)	60 (29-89)
Etiology of ESRD	
DM	13 (56.5%)
HTN	5 (21.7%)
Others	5 (21.7%)

Table 2 Mean,standard deviation and P-value of triglyceride, total cholesterol, HDL and CRP before and after

	Before treatment with melatonin *Mean (±SD)*	**After treatment with** melatonin *Mean (±SD)*	0P-**value**
Triglyceride	242.08 (±101.05)	178.00 (±48.02)	0.004
Total cholesterol	139.95 (±35.49)	131.13 (±34.96)	0.194
HDL	36.20 (±7.08)	40.16 (±9.35)	0.032
CRP	16.23 (±12.98)	25.43 (±20.92)	0.346

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EFFECTS OF ABDOMINAL AORTIC CALCIFICATION PROGRESSION ON OUTCOMES IN MAINTENANCE HEMODIALYSIS PATIENTS

Zhe Wang[1]

[1]*The Second Hospital of Tianjin Medical University, Kidney disease and blood purification department, Tianjin, P.R. China*

Background and Aims: Vascular calcification is the risk factor for cardiovascular event, cardiovascular mortality and all-cause mortality in maintenance hemodialysis (MHD) patients. We investigated the effects of abdominal aortic calcification (AAC) progression on outcomes in MHD patients.

Method: 111 patients who were on MHD between Jun. 2014 and Oct. 2014 in the dialysis center and finished the AAC examination at baseline and two years later were included prospectively. We evaluated the progression of AAC by AAC score (AACs) at baseline and two years later. According to the change of AACs, the patients were divided into rapid AAC progression group (change of AACs>median) and non-rapid AAC progression group (change of AACs≤median). We investigated the effects of AAC progression on outcomes in MHD patients in the follow-up period. Kaplan-Meier analysis was used to compare their survival rate. Uni- and multivariable Cox proportional hazard regression models were used to determine the risk factors of all-cause mortality, cardiovascular mortality and cardiovascular events.

Results: The presence of AAC was 78.4% (87/111), rapid AAC progression was seen in 54 patients, and non-rapid AAC progression was seen in 57 patients. The mean follow-up duration was 27.9(27.1, 28.0) months. Kaplan-Meier analysis showed that patients in rapid AAC progression group had a higher risk of mortality as compared to patients in non-rapid AAC progression group (P=0.017). Multivariate Cox regression analysis demonstrated that high baseline AACs (HR=1.135, 95%CI~1.001~1.286, P=0.048), hypoproteinemia (HR=0.789, 95%CI 0.640~0.972, P=0.026) were independent risk factors for all-cause mortality. High baseline AACs (HR=1.187, 95%CI 1.038~1.356, P=0.012), low spKt/V (HR=0.103, 95%CI 0.013~0.801, P=0.030) were independent risk factors for cardiovascular mortality. Low spKt/V (HR=0.018, 95%CI 0.003~0.115, P=0.000), hypoproteinemia (HR=0.736, 95%CI 0.608~0.890, P=0.002) were independent risk factors for cardiovascular events.

Conclusion: Abdominal aortic calcification progression may increase the risk of cardiovascular events and death in MHD patients. Severity of abdominal aortic calcification, adequacy of dialysis, and nutritional status are predictors of outcomes in MHD patients.

Table 1. The multivariate Cox regression analysis for all-cause mortality

Variables	β	HR (95%CI)	P
Baseline AACs	0.125	1.135 (1.001, 1.286)	0.048
Albumin	-0.238	0.789 (0.640, 0.972)	0.026

Table 2. The multivariate Cox regression analysis for cardiovascular mortality

Variables	β	HR (95%CI)	P
Baseline AACs	0.171	1.187 (1.038, 1.356)	0.012
spKt/V	-2.272	0.103 (0.013, 0.801)	0.030

Table 3. The multivariate Cox regression analysis for cardiovascular events

Variables	β	HR (95%CI)	P
spKt/V	-4.041	0.018 (0.003-0.115)	0.000
Albumin	-0.307	0.736 (0.608-0.890)	0.002

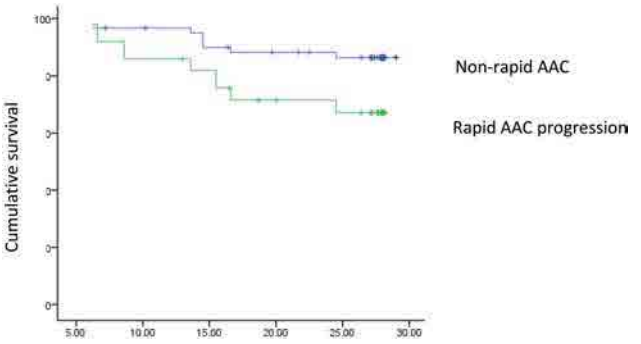


Figure 1. Kaplan-Meier survival curve for all-cause mortality (P=0.017 by log-rank test).

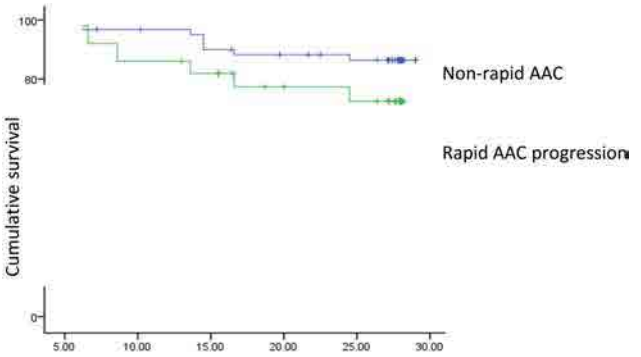


Figure 2. Kaplan-Meier survival curve for cardiovascular mortality (P=0.074 by log-rank test).

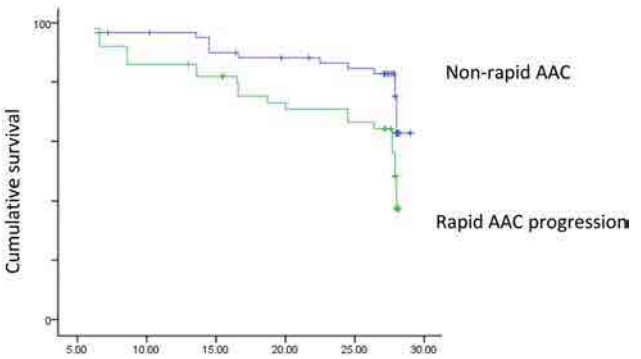


Figure 3. Kaplan-Meier survival curve for cardiovascular events (P=0.006 by log-rank test).

P1274 THE CHARACTER OF CARDIAC REMODELING AND VALVE CALCIFICATION IN TYPE 2 DIABETIC PATIENTS WITH END-STAGE RENAL DISEASE

Oleksandr Susla[1], Mykola Shved[1], Zoriana Litovkina[1], Svitlana Danyliv[1], Anatoliy Gozhenko[2]

[1]I. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine and [2]Ukrainian Scientific Research Institute of Transport Medicine, Odesa, Ukraine

Background and Aims: Systematic analysis of cardiac remodeling features in type 2 diabetic patients with end-stage renal disease (ESRD) is important both in stratification of cardiovascular risk and in choice of adequate treatment strategies. The lack of number and fragmentation of studies, the ambiguity of their data regarding the problem of myocardial reconstruction and cardiac valve calcification (CVC) under these conditions have substantiated the need for this study, its relevance and purpose.

Method: 136 ESRD patients on chronic hemodialysis (HD) were included in this observational cross-sectional study (men, 78; age, 53.9±1.0 years; HD duration, 47.6±4.2 months). The study was performed in accordance with the provisions of the Declaration of Helsinki last revision. Depending on the presence/absence of diabetic nephropathy (DN) all patients were divided into two groups: the 1st one – without DN (n=88); the 2nd one – with DN (n=48). A complete ultrasound examination of the cardiac structure and function including CVC analysis was performed. Data are presented as means±SEM. Mann-Whitney U-test was used for comparison of the quantitative variables, χ^2-test – qualitative ones.

Results: Left ventricular (LV) hypertrophy (93.8 vs. 78.4%, p=0.020) and eccentric hypertrophy (47.9 vs. 28.4%, p=0.023) were diagnosed more often in patients with DN than those without diabetes. Prevalence of pseudonormal and restrictive types of LV diastolic dysfunction (62.5 vs. 28.4%, p<0.001), systolic dysfunction (27.1 vs. 9.1%, p=0.006) and pulmonary hypertension (PH) (64.6 vs. 35.2%, p=0.001) were significant in the 2nd group. CVC (66.6 vs. 38.6%, p=0.002), combined calcification of mitral (MV) and aortal (AV) valves (35.4 vs. 13.6%, p=0.003), stenoses of MV (16.7 vs. 3.4%, p=0.007) and AV (39.6 vs. 15.9%, p=0.004), and insufficiency of MV (66.7 vs. 44.3%, p=0.013) and AV (35.4 vs. 14.8%, p=0.006) were recorded more often in HD patients with DN. LV myocardial mass index (181.0±7.2 vs. 155.0±5.3 g/m^2, p=0.001) as well as right ventricle (RV) diameter (2.80±0.09 vs. 2.47±0.04 cm, p=0.003) were also greater in the 2nd group.

Conclusion: In type 2 diabetic patients with ESRD occurs maladaptive cardiac remodeling with predominance of unfavourable (especially eccentric) types of LV hypertrophy, RV dilatation, PH, severe LV diastolic and systolic dysfunction, and widespread combined calcification of MV and AV with the valve defects. The identification of risk factors for the progression of the pathological reconstruction of myocardium and CVC in HD patients with DN will be the subject of our further research.

P1275

PARAOXONASE 1 (PON1) GENE POLYMORPHISMS, PON1 EXPRESSION IN PBMCS, AND SERUM PON1 ACTIVITY CONCERNING DYSLIPIDEMIA AND RELATED COMORBIDITIES IN HEMODIALYSIS (HD) PATIENTS

Alicja Ewa Grzegorzewska[1], Ewa Iwańczyk-Skalska[2], Paulina Adamska[1], Leszek Niepolski[4], Adrianna Mostowska[2], Wojciech Warchoł[5], Paweł Jagodziński[2]

[1]Poznan University of Medical Sciences, Department of Nephrology, Poznań, Poland, [2]Poznan University of Medical Sciences, Department of Biochemistry and Molecular Biology, Poznań, Poland, [4]B.Braun Avitum Poland, Dialysis Center, Nowy Tomyśl, Poland and [5]Poznan University of Medical Sciences, Department of Ophthalmology, Poznań, Poland

Background and Aims: PON1 may prevent atherosclerosis influencing lipid metabolism and exerting antioxidant and anti-inflammatory activities. We focused on serum PON1 activity in HD patients concerning dyslipidemia, coronary heart disease (CHD), myocardial infarction (MI), and cerebral stroke (CS). PON1 activity was related to *PON1* polymorphisms, *PON1* expression in PBMCs, and demographic, clinical, and laboratory data.

Method: In 93 HD patients (men 55, age 66.7, 18.3 – 86.2 years, renal replacement therapy duration 3.9, 0.2 – 22.3 years, CHD 25, MI 15, CS 9), dyslipidemia was diagnosed by K/DOQI guidelines. The TG/HDL-cholesterol ratio of $\geq$3.8 indicated atherogenic dyslipidemia. Standard diagnostic rules were applied for CHD, MI, and CS recognition. PON1 activity was measured in serum using an automated PON1 assay kit. *PON1* polymorphisms were genotyped by high-resolution melting curve analysis (rs662) or using predesigned TaqMan SNV Genotyping Assay (rs854560 and rs705379). In 46 subjects, the relative *PON1* transcript level was determined in PBMCs using reverse transcription-quantitative polymerase chain reaction analysis.

Results: In univariate analyses, the lower serum PON1 activity the higher frequency of mixed dyslipidemia (LDL $\geq$ 100 mg/dL, TG $\geq$ 200 mg/dL, non-HDL $\geq$ 130 mg/dl; $\beta \pm$ SE: -21.4 $\pm$ 10.0, P = 0.035) and the higher serum TG levels ($\beta \pm$ SE: -1.06 $\pm$ 0.49, P = 0.034). Normalized serum PON1 activity (the PON1/HDL ratio) correlated positively with male sex ($\beta \pm$ SE: 0.56 $\pm$ 0.25, P = 0.029), atherogenic dyslipidemia ($\beta \pm$ SE: 0.67 $\pm$ 0.25, P = 0.008), and cigarette smoking ($\beta \pm$ SE: 0.86 $\pm$ 0.42, P = 0.043). After adjustment for gender, cigarette smoking, urine output, living in rural area, and serum phosphorus, significance was maintained between normalized serum PON1 activity and atherogenic dyslipidemia ($\beta \pm$ SE: 0.54 $\pm$ 0.24, P = 0.028), male sex ($\beta \pm$ SE: 0.51 $\pm$ 0.24, P = 0.037) and cigarette smoking ($\beta \pm$ SE: 0.93$\pm$0.41, P = 0.024) as well as revealed for living in rural area ($\beta \pm$ SE: 0.55 $\pm$ 0.26, P = 0.039), urine output ($\beta \pm$ SE: -0.14 $\pm$ 0.07, P = 0.046), and zinc supplementation ($\beta \pm$ SE: 1.5 $\pm$ 0.67, P = 0.029). PON1 activity (101, 27.7 – 213 U/L) and normalized PON1 activity (2.27, 0.57 – 7.10) were not influenced by *PON1* polymorphisms and did not yield differences in patients stratified by CHD, MI, CS, and dyslipidemic patterns except atherogenic dyslipidemia. The latter relationship was caused by a correlation between serum PON1 activity and TG (r = -0.220, P = 0.034). *PON1* transcript was detected in PBMCs of 9 subjects. They showed a higher prevalence of the AG + GG genotypes of *PON1* rs662 (77.8% vs. 34.3%, P = 0.027), a higher serum CRP level (7.8, 2.8 – 46.8 mg/L vs. 3.9, 0.4 – 23.0 mg/L, P = 0.042), and a lower albumin (3.9, 2.6 – 4.5 g/dL vs. 4.2, 3.2 – 4.6 g/dL, P = 0.025) compared with the results of 37 subjects without the *PON1* expression. The relative *PON1* transcript level did not correlate with serum PON1 activity (r = 0.042, P = 0.915).

Conclusion: In HD patients, serum *PON1* activity is associated with atherogenic dyslipidemia but not with already developed CHD and history of MI or CS, even after adjustment for several confounding variables. Illegitimate *PON1* transcription occurs in uremic PBMCs at very low level and is influenced by *PON1* rs662 polymorphism and upregulated by inflammation. PON1 could be considered as a therapeutic target in prevention of atherosclerosis and its complications in uremic patients.

P1276 EXPLORING POSSIBLE PREDICTORS OF STRUCTURAL DETERIORATION AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION IN HEMODIALYSIS PATIENTS

Satoshi Masuyama[1], Masayuki Mizui[1], Koichi Maeda[2], Toru Kuratani[2], Yusuke Sakaguchi[1], Yasushi Sakata[3], Yoshiki Sawa[2], Yoshitaka Isaka[1]

[1]Osaka University Graduate School of Medicine, Nephrology, Suita, Osaka, Japan, [2]Osaka University Graduate School of Medicine, Cardiovascular Surgery, Suita, Osaka, Japan and [3]Osaka University Graduate School of Medicine, Cardiology, Suita, Osaka, Japan

Background and Aims: Transcatheter aortic valve implantation (TAVI) is an effective treatment for aortic stenosis (AS) in high-risk patients, such as those who are suffering ESRD on hemodialysis. We previously showed that long-term survival of hemodialysis patients underwent TAVI was lower than that of non-hemodialysis patients but was comparable with that of hemodialysis patients treated with surgical aortic valve replacement. It is known that hemodialysis is a high risk of the bioprosthetic structural valve deterioration (SVD) after valve replacement surgery. Consistently, higher incidence of re-TAVI operation due to restenosis was observed in hemodialysis patients than in non-hemodialysis patients (Odds ratio [OR]:29.4, $p<0.001$).

In this study, we aimed to identify predictors of SVD in post-TAVI hemodialysis patients.

Method: From April 2012 to December 2015, 24 patients on hemodialysis were selected to receive TAVI for the treatment of AS in Osaka University Hospital. Demographic and laboratory data at pre- and post-operation were compared between patients who underwent re-TAVI (valve-in-valve) (SVD group) and those who did not (no-SVD group).

Results: During the follow-up period (maximal 7 years), 4 out of 24 patients required re-TAVI (valve-in-valve) operation because of SVD. Although serum calcium, phosphate, and PTH levels before operation were comparable between SVD group and no-SVD group, serum magnesium levels were significantly lower in SVD group. Lower serum magnesium quartiles were associated with a higher risk of SVD (OR 5.83, $p=0.036$). While effective orifice area index (EOAi) of aortic valve at 1 week after TAVI was similar between the 2 groups, EOAi improvement at 1 month was significantly poorer in SVD group than in no-SVD group (1.70 ± 0.15 vs 2.50 ± 0.56, $p = 0.049$).

Conclusion: The higher incidence of re-TAVI due to SVD in hemodialysis patients could be related with pre-operative low magnesium levels and with one-month post-operative low EOAi improvement.

This was a single center observational study, and the number of patients was very small so that our data would not be necessarily applicable for every patient. Further investigation is necessary for identifying a prognostic predictor of SVD, which will lead to the prevention of unfavorable re-operation in hemodialysis patients.

P1277

EFFECT OF HEMODIALYSIS ON PERIPAPILLARY CHOROIDAL THICKNESS AND OPTIC NERVE HEAD PARAMETERS MEASURED BY SWEPT-SOURCE OPTICAL COHERENCE TOMOGRAPHY

Won June Lee[1], Yong Un Shin[1], Mincheol Seong[1]

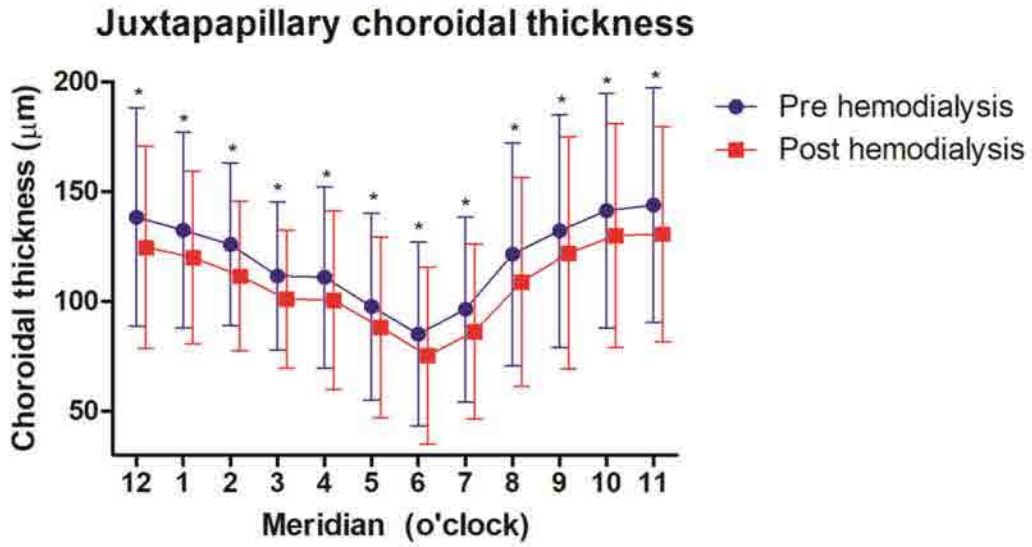
[1]*Hanyang University College of Medicine, Ophthalmology, Seoul, Korea, Rep. of South*

Background and Aims: To investigate the effect of hemodialysis (HD) on peripapillary choroidal thickness (PCT) and optic nerve head (ONH) parameters by swept-source optical coherence (SS-OCT) and other ophthalmologic parameters in patients with end-stage kidney disease (ESKD).

Method: A prospective observational study was performed on 29 patients who underwent HD for ESKD. Detailed ophthalmologic examinations and SS-OCT were performed immediately before and after HD. The PCT were measured using the modification tool in the built-in OCT image viewer program. The ONH parameters including rim area (RA) and vertical cup-to-disc ratio (VCDR) were obtained using built-in software. Changes in PCT, and ONH parameters before and after HD were statistically analyzed.

Results: Average PCT significantly decreased from 127.3 ± 49.2 before HD to 117.1 ± 50.9 after HD (P<0.001). The RA increased and VCDR decreased significantly after HD (P=0.001 and P=0.027, respectively). Disc area did not show significant change after HD (P=0.648). Significant correlation was found between changes in PCT and changes in macular choroidal thickness (rho=0.547, P=0.002).

Conclusion: We observed significant decrease in PCT and significant changes in ONH parameters after HD. Our study suggest that HD can give influence on the ONH and its surrounding structure.



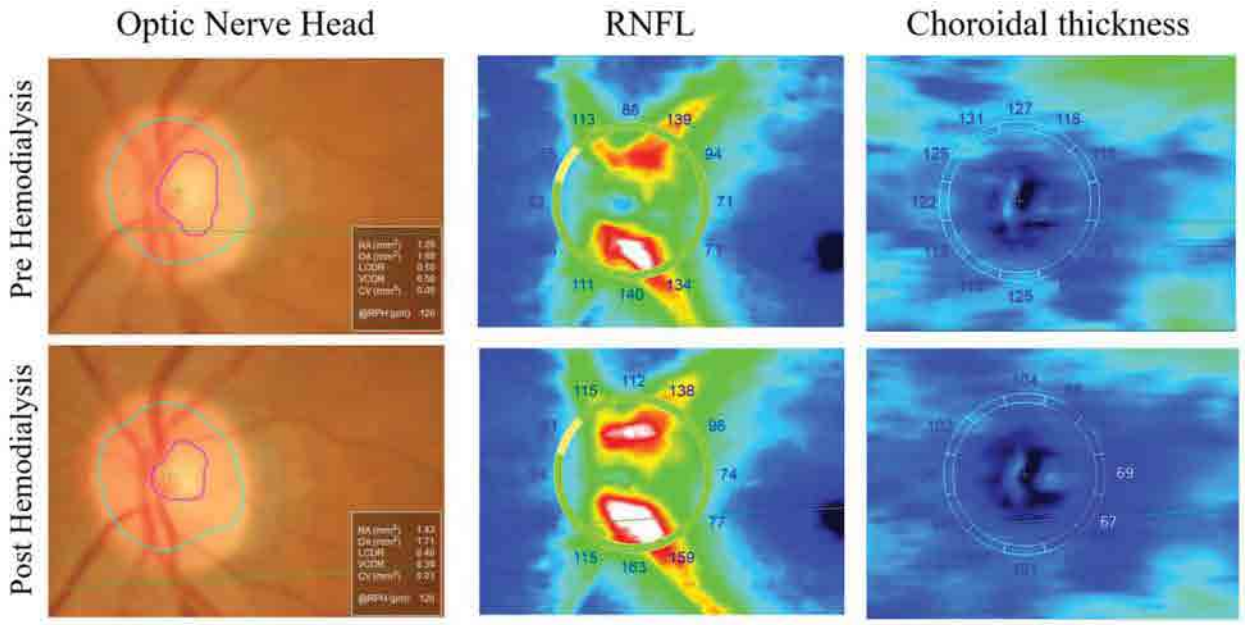


Figure:

P1278 DIALYSIS IN TREATMENT OF CONGESTIVE HEART FAILURE

Vesna Ristovska[1]

[1]*Medical Faculty, University Sts Cyril and Methodius, Department of Nephrology, Skopje, Republic Of North Macedonia*

Background and Aims: The advanced congestive heart failure (CHF), may provoke functional kidney disturbances with insufficient and resistant to conservative therapy water excretion. The treatment of the chronic renal failure (CRF) with active dialysis related to ultrafiltration (UF), may overcome the renal diuretics resistance with diuresis restoration and oedema elimination. The aim of the study was to define the indications for active, discontinued UF in setting of the CHF refractory to drugs, especially in the treatment of oedema.

Method: We investigated 12 patients, mean age 62,4+/-5,3 years, with incipient renal failure, but advanced congestive heart failure. Seven of them were males and 5 females. The indication for discontinued UF, was the severe expressed heart failure, reduced diuresis and initial renal insufficiency. In all investigated patients, before and after each UF procedure, the serum sodium and potassium, blood urea nitrogen (BUN), creatinin and osmolality were detected. The body weight, abdominal and crural parameters were noted before and after dialysis.

Results: The recovery was achieved in 10 patients with CHF, but 2 patients out of 12 have not demonstrated satisfactory response to UF. The biochemical features encountered to CHF patients suggest chronic hyponatriemia, hypokalemia and hypovolemia. Proteinuria range 1,2 to 3,6 g/l, was present in 6 patients. The clinical data were performed with oedema formation, reduced diuresis and dispnea. Mean UF rate achieved after several dialysis was 12,4+/- 7,6, lit.

Conclusion: Chronic heart failure in chronic renal patients, with severe oedemas is an indication for UF therapy, even if the values of BUN and creatinin are not increased. Reduction of the body weight and the extracellular volume, contribute for improved survival in these patients. However the risk of complications is high and not always with successful treatment.

P1279 **INSULIN RESISTANCE IN HEMODIALYSIS PATIENS**

Pavel Filinyuk[1], Aleksander Rumyantsev[2]

[1]St Petersburg University, Department of Faculty Therapy, 199034, Russia and [2]Saint Petersburg University, Department of Faculty Therapy, 199034, Russia

Background and Aims: insulin resistance (IR) is a decrease in the biological response of sensitive tissues to insulin. IR is known as an adverse risk factor in cardiovascular disease, which largely determines the prognosis of patients receiving hemodialysis (HD). But this issue is not well understood. For the screening of IR, special indices have been developed that characterize the sensitivity of tissues to insulin. The aim of the study was to compare the methods of screening for IR in patients receiving HD in relation to the markers of systemic inflammation and atherogenic dyslipidemia (AtD).

Method: 124 patients receiving HD for 75.4 ± 44.5 months were examined including 66 men and 58 women aged 57.6 ± 13.6 years. For IR screening, the Homeostatic Model Assessment-1 and 2 indices (HOMA-1 and HOMA-2), the Quantitative Insulin Sensitivity Check Index (QUICKI) and triglycerides / glucose (Tri/G) were used. Patients were examined in accordance with the recommendations of KDIGO. Data analysis was carried out using "STATISTICA 10.0".

Results: fasting insulin levels were elevated in 19% of patients. But, the calculated indices were consistent with the idea that IR is much more common. So, the IR index in the HOMA -1 model was increased in 47%, in the HOMA -2 model - in 33%, in the QUICKI model - in 36%, the TriH indicator - in 91%. The sensitivity of peripheral tissues in the HOMA-1 and HOMA-2 models was equally reduced by 35-40%.

The results of the correlation analysis between indicators of IR and plasma concentration of C-reactive protein and lipid profile are presented in table 1.

Informativeness of IR indicators depending on the presence of obesity is presented in table 2

We were also interested in whether insulin resistance affects the development of clinical manifestations of atherosclerosis, cardiac arrhythmias, and heart failure. An analysis of this relationship did not reveal. Only the IR index in the HOMA-1 model with a value of more than 2.7 units was associated with a 4.5-fold increase in the risk of developing clinical manifestations of atherosclerotic lesions ($\chi 2 = 4.582$ $p = 0.032$). Statistically significant it was only in men. Given our data, perhaps IR is one of the reasons for the higher morbidity and mortality of men at HD.

Conclusion: a comparison of IR models allows us to distinguish HOMA-2 as the most accurate index. The highest correlation with systemic inflammation and AtD was in the HOMA-1 and HOMA-2 indices.

Table 1

Indicator	CRP	LDL	HDL	TG
HOMA-1IR	0,225	0,406	-0,356	0,325
p	0,007	0,0001	0,0001	0,0001
HOMA-1The sensitivity of peripheral tissues to insulin, S%	-0,215	-0,400	0,240	-0,280
p	0,010	0,0001	0,004	0,0008
HOMA-2IR	0,316	0,417	-0,387	0,315
p	0,0001	0,0001	0,0001	0,0001
HOMA-2The sensitivity of peripheral tissues to insulin, S%	-0,299	-0,402	0,328	-0,290
p	0,0003	0,0001	0,0002	0,0005
QUICKI	-0,215	-0,084	0,345	-0,372
p	0,010	0,323	0,0001	0,0001
Tri/G	0,037	-0,081	-0,399	–
p	0,664	0,341	0,0001	–

Note: CRP - C-reactive protein, LDL - low density lipoproteins, HDL - high density lipoproteins, TG – triglycerides.

Table 2

Indicator	HOMA-1	HOMA-2	QUICKI	Tri/G
Sensitivity	0,731	0,542	0,792	0,955
Speci˚city	0,529	0,727	0,475	0,119
Likelihood ratio of a positive result	1,552	1,985	1,509	1,084
Likelihood ratio of a positive result	0,509	0,630	0,438	0,378
Accuracy	0,630	0,724	0,616	0,329

P1280

IMPACT OF HAEMODIALYSIS IN PATIENTS UNDERGOING BYPASS SURGERY FOR PERIPHERAL ARTERY DISEASE WITH CRITICAL LIMB ISCHEMIA - 10-YEAR FOLLOW-UP STUDY -

Yoshitaka Kumada[1], Hideki Ishii[2], Norio Umemoto[3], Ryuta Ito[3], Hiroshi Takahashi[4]

[1]Matsunami General Hospital, Cardiovascular Surgery, [2]Nagoya University Graduate School of Medicine, Cardiology, [3]Nagoya Kyoritsu Hospital, Cardiology and [4]Fujita Health University, Nephrology

Background and Aims: Although lower extremities bypass surgery has been commonly performed as the standard option to treat peripheral artery disease with critical limb ischemia (CLI) even in patients on haemodialysis (HD) as well as general population, higher amputation and/or mortality rates still remains major clinical problems after bypass surgery in this population. In this 10-year follow-up study, we investigated the impact of HD on outcomes after surgical revascularization in patients with CLI.

Method: A total of 464 patients undergoing successfully elective bypass surgery were enrolled. We compared 304 HD patients with 335 limbs and 160 non-HD (NHD) patients with 183 limbs during 10 years follow-up period. Primary outcome was amputation-free survival (AFS) rate defined as freedom rate from composited endpoint with major amputation (limb amputation above ankle level) or all-cause mortality. To minimize the differences of clinical characteristics between the two groups, propensity score-matching with all baseline variables was performed.

Results: Prevalence of diabetes (55.6% vs. 33.8%), ulcer/gangrene (99.1% vs. 63.5%) and infra-popliteal artery disease (58.9% vs. 32.5%) were significantly higher in HD group compared to NHD group ($p<0.0001$ in all). Pre-procedural C-reactive protein (CRP) levels was also higher in HD group [14.0 (4.0-51.5) mg/l vs. 7.0 (2.0-34.0) mg/l, $p=0.0015$]. Inversely, age was younger in HD group than in NHD group (67 ± 9 years vs. 72 ± 8 years, $p<0.0001$). The 30-day mortality rate was comparable (3.3% in HD group vs. 1.3% in NHD group, $p=0.16$). During follow-up period (median of 48 months), 53 amputation (17.4%) and 102 death (33.6%) in HD group, and 17 amputation (10.6%) and 23 death (14.4%) in NHD group occurred, respectively. The 10-year AFS rate was significantly lower in HD group compared to NHD group [41.3% vs. 71.3%, hazard ratio (HR) 2.33, 95% confidence interval (CI) 1.64-3.41, $p<0.0001$). Similarly, limb salvage rate and survival rate was also lower in HD group than in NHD group (72.1% vs. 87.5%, HR 1.90, 95%CI 1.12-3.39, $p=0.016$, and 51.8% vs. 80.4%, HR 2.78, 95%CI 1.80-4.48, $p<0.0001$, respectively). In the propensity score-matched cohort, having no significant differences of all baseline characteristics between HD and NHD group (n=125 in each), the 10-year AFS rate and survival rate was still lower in HD group compared to NHD group (53.1% vs. 72.8%, HR 2.11, 95% CI 1.34-3.39, $p=0.0012$ and 58.6% vs. 84.9%, HR 3.72, 95% CI 2.09-7.06, $p<0.0001$, respectively). However, the limb salvage rate was statistically comparable between the two group (81.9% vs. 84.2%, HR 1.13, 95%CI 0.55-2.38, $p=0.74$). In addition, pre-procedural CRP levels could predict major amputation in HD patients (HR 1.06, 95%CI 1.01-1.10, $p=0.024$) but not NHD patients (HR 1.09, 95%CI 0.93-1.25, $p=0.27$).

Conclusion: The long-term AFS rate and survival rate were markedly lower in HD patients compared to NHD patients. However, the limb salvage rate was even between HD and NHD after adjustment for clinical characteristics. These results suggest that detection at the early stage of PAD may potentially improve the poor outcome. Pre-procedural inflammation status may also specifically affects the poor outcome in HD group.

P1281 **CLINICAL CHARACTERISTICS OF OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME IN MAINTENANCE HEMODIALYSIS PATIENTS**

Yan Qin[1], Dan Yuan[1], Rong Huang[1], Xuemei Li[1]

[1]*Peking Union Medical College Hospital, Renal Division, Beijing, P.R. China*

Background and Aims: To explore the clinical characteristics of obstructive sleep apnea hypopnea syndrome (OSAHS) in maintenance hemodialysis patients.

Method: 42 patients with maintenance hemodialysis in our hemodialysis center from April 2019 to December 2019 were enrolled for night-time sleep breathing monitoring. The patients were divided into the OSAHS group(n=25) and the non-OSAHS group(n=17) defined by AHI. The OSAHS group was further divided into a mild group (n=14) and a moderate-severe group (n=11). The clinical datas, sleep breathing monitoring datas, and echocardiographic parameters of the OSAHS group and the non-OSAHS group, the mild OSAHS group, and the moderate-severe OSAHS group were compared.

Results: 1. There were no differences in gender, age, dialysis age, spKt / V, BMI, TBW, ECW, ICW, E / I ratio, Ca, P, HB, and diastolic blood pressure between the the OSAHS group and the non-OSAHS group. 2. Incidence of left ventricular concentric hypertrophy (84.0% VS 47.1%, P = 0.011), left ventricular wall thickness (12.0 VS 10.2, P = 0.029) and systolic blood pressure (147.0 ± 9.6 VS 139.4 ± 13.8, P = 0.041)) in OSAHS group was significantly higher than the non-OSAHS group; 3: There was no statistical difference in serum carbon dioxide binding capacity (CO2CP) between the two groups (23.1 ± 2.7 VS 23.8 ± 2.6, P = 0.392), but the daily intake of sodium bicarbonate in the OSAHS group was higher than that of the non-OSAHS group (2.5 ± 1.0 VS 1.5 ± 0.5, P = 0.004); the CO2CP of the moderate-severe OSAHS group was lower than that of the mild group (21.7 ± 2.2 VS 24.2 ± 2.7, P = 0.019), the left ventricular wall thickness was significantly higher than the mild group (11.4 ± 1.4 VS 12.6 ± 1.1, P = 0.025).

Conclusion: Clinicians should pay attention to the early diagnosis and prevention of OSAHS in maintenance hemodialysis patients. Because the dialysis population is different from the general population of OSAHS patients, the serum CO2CP of this population is negatively correlated with the degree of OSAHS, and clinicians need to pay particular attention to the amount of sodium bicarbonate to correct acidosis.

P1282 **BODY COMPOSITION AND VENTRICULAR FUNCTION IN HEMODIALYSIS, CLOSED COMPARTMENTS?**

Javier Carbayo[1], Soraya Abad Esttebanez[2], Eduardo Verde[2], Alejandra Muñoz de Morales[2], Ángela González-Rojas[2], Adriana Acosta[2], Andrés Delgado[2], Luis Alberto Sã¡nchez Cã¡mara[2], Almudena Vega[2], Marian Goicoechea[2]

[1]Hospital General Universitario Gregorio Marañón, Nephrology, Madrid, Spain and [2]

Background and Aims: Right ventricular dysfunction is common among hemodialysis (HD) patients and it has been recently described as a marker of cardiovascular morbidity and mortality. Nevertheless, mechanisms responsible for have not been clearly elucidated. Volume overload, retrograde left ventricular dysfunction, pulmonary hypertension, left-right shunt and mineral bone disease have been related. Similarly, body composition and chronic fluid overload are closely linked to survival in dialysis patients. However, there are no data about correlation between body composition and echocardiographic parameters in previous studies

The aim of this study was to assess the relationship between body composition and changes in right and left ventricular function in patients on maintenance hemodyalisis.

Method: We conducted a retrospective and longitudinal observational cohort study over a population of 78 patients on maintenance hemodyalisis at a single hospital. They were on chronic hemodyalisis program of three weekly sessions of 240 minutes duration.

A transthoracic echocardiogram (TTE) and a bioimpedance (BI) were performed in the same month, in the first inter-dialysis day of the week, being the patients asymptomatic and clinically stable, at the beginning and at the end of the study. The follow-up time since the completion of first and second ETT and BI was 19.5 months, with an average total follow-up of 29.7 months. Cardiovascular and general mortality events were recorded during that period.

Echocardiography data about cardiac cavities measurement, ventricular and valvular function was collected. Left ventricular ejection fraction was evaluated by Simpson's method (LVEF, %) and right ventricular function by tricuspid annular plane systolic excursion (TAPSE, mm).We gathered information about fluid status and corporal composition. Statistical analysis was performed using SPSS Statistics, version 21 (SPSS, Inc., Chicago, IL, USA).

Results: Patients with RV dysfunction (35.7%), determined as TAPSE < 20, experienced a higher mortality rate (20%) compared to those who maintained TAPSE ≥ 20 (63.2%), who had a mortality rate of 2.3%. These results were statistically significant in the Kaplan-Meier survival analysis (Log Rank 6.65; $p = 0.010$). There were not statistically significant differences regarding age, diabetes, years on dialysis and status of volume overload between patients with and without right ventricular dysfunction. No significant differences were found between any other of the echocardiography parameters and overall mortality.

Equally, neither bioimpedance measure at the beginning of the study was associated with mortality. Patients who had an FTI above the average (9.20 kg / m2) suffered a greater fall in TAPSE (-1 $\pm$ 4.3 mm) ($p = 0.032$) and LVEF (-4.2 $\pm$ 6.8) ($p = 0.045$), regarding those with lower FTI: TAPSE +2.3 $\pm$ 4.3 and LVEF +3.7 $\pm$ 10.4. These results seems to be related to a disproportionate LTI/LTI index rather than a greater total mass of fat due to patients with FTI $>$ 9.2 kg/m2 had a mean LTI/FTI index of 1.1, meanwhile those with FTI $<$ 9.2 kg/m2 a mean LTI/FTI of 5.9. No statistically significant relationship was found with absolute or relative volume overload, nor with changes in them over time.

Conclusion: The results presented suggest that high fat tissue index, and an underlying lower LTI/FTI index, could be associated with a higher risk of right and left ventricular dysfunction, which has been associated with higher mortality in hemodialysis patients.

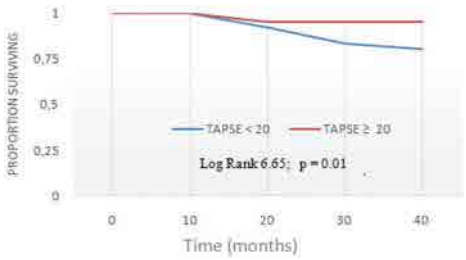


Figure 1. Kaplan-Meier curves for survival regarding right ventricular function at the beginning of the study.

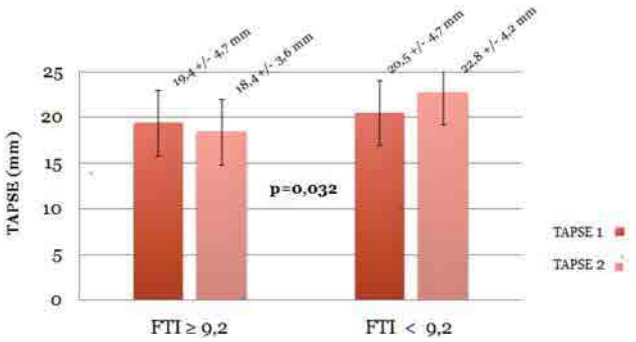


Figure 2. Differences in right ventricular function (determined as TAPSE, mm) over time according to initial value of fat tissue index (FTI).

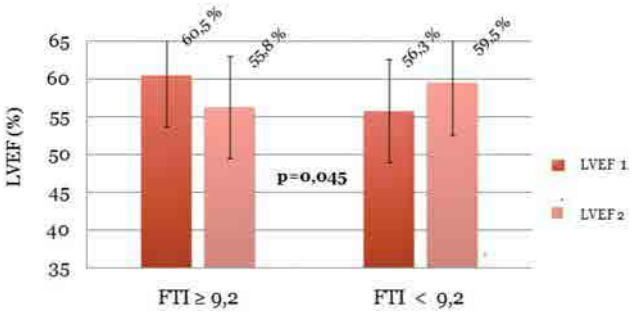


Figure 3. Differences in left ventricular function (determined as LEVF, %) over time according to initial value of fat tissue index (FTI).

P1283

BASELINE CHARACTERISTICS IN THE "IPACK-HD" STUDY (INHIBIT PROGRESSION OF CORONARY ARTERY CALCIFICATION WITH VITAMIN K IN HEMODIALYSIS PATIENTS): A PHASE 2, MULTI-CENTRE, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PILOT TRIAL

Corinne Babiolakis[1], Deborah Zimmerman[2], Louise Moist[3], Andrew Day[4], Patrick Norman[5], Mandy Turner[6], Jocelyn Garland[7], Michael Adams[6], Sarah Booth[8], Daren Heyland[4], Rachel Holden[1]

[1]Queen's University, Medicine, Kingston, Canada, [2]University of Ottawa, Canada, [3]University of Western Ontario, Medicine, Canada, [4]Queen's University, Critical Care Medicine, Canada, [5]Kingston Health Sciences Centre, Canada, [6]Queen's University, Biomedical and Molecular Sciences, Canada, [7]Queen's University, Medicine, Canada and [8]Tufts University, Canada

Background and Aims: The leading cause of mortality for patients with end-stage kidney disease (ESKD) is cardiovascular disease (CVD). This is due, in part, to vascular calcification (VC) where calcium becomes deposited within arterial walls causing narrowing of the arteries and altering their flexibility. Matrix Gla protein (MGP), a vitamin k-dependent protein, is a key local inhibitor of VC and becomes up-regulated adjacent to sites of calcification. There is a very high prevalence of vitamin K deficiency in patients across the chronic kidney disease (CKD) spectrum and vitamin K has been shown to prevent VC in experimental models. To date, no trial has examined whether vitamin K supplementation prevents the progression of coronary artery calcification in patients with ESKD, a group in which high risk has been established. The aim of the iPACK-HD pilot study is to determine whether a trial to determine whether vitamin K has a favourable effect on coronary artery calcium (CAC) scores in patients with ESKD is feasible.

Method: The iPACK-HD pilot trial is a phase 2 multi-centre, double-blind, randomized, placebo-controlled clinical trial conducted in three sites (Kingston, Ottawa and London) in Ontario, Canada. Adult patients with ESKD on chronic dialysis with a baseline CAC score of $\geq$30 Agatston units (AUs) are randomized to receive 10 mg of vitamin K1 or matching placebo administered post-hemodialysis 3x/week for a total of 12 months. Exclusions include medical conditions that require anticoagulation and a history of either coronary artery bypass, grafting or stenting. Randomization is stratified based on diabetes and study centre. Baseline CAC scores are determined by computed tomography (CT) and demographic and laboratory data at study entry are obtained by participant interview and medical chart review.

Results: A total of 85 participants are randomized into this trial. Baseline characteristics of trial participants are reported as mean $\pm$ SD, median [IQR], or %. The mean age is 63 $\pm$ 13 years. There are a higher proportion of males (57%) than females and whites (85%) compared to all other ethnicities. Forty-four percent of participants have diabetes and 77% have hypertension. Dialysis vintage is 0.9 [0.4,2.7] years. Most participants take calcium-based phosphate binders (89%) and over half of participants take an HMG-CoA reductase inhibitor (53%) or vitamin D (61%). Clinical laboratory values are presented in Table 1. Total median CAC and volume calcium scores are 587 [252,1416] AUs and 482 [206,1170] mm^3, respectively. Sixty-five (76%) participants had a study exit CT scan performed upon completion of the study. Of 156 doses, a median of 150 [123,155] were received and 2 [1,6] were missed.

Conclusion: Participants in the iPACK-HD study have a high burden of calcification but are similar in baseline characteristics to the Canadian hemodialysis population. Loss to trial completion is 24%, but the most frequent reason is kidney transplantation. Adherence to study drug is very high with few reported side effects.

Table:

Clinical Laboratory Test	**Value**(mean $\pm$ SD or median [IQR])
HgB (g/L)	108.2 $\pm$ 12.9
Albumin (g/L)	34.3 $\pm$ 4.6
Alkaline Phosphatase (IU/L)	90.0 [68.0,111.0]
Creatinine (μmol/L)	678.4 $\pm$ 206.5
Kt/V	1.7 $\pm$ 0.3
Total cholesterol (mmol/L)	4.2 $\pm$ 1.3
HDL (mmol/L)	1.1 $\pm$ 0.3
LDL (mmol/L)	1.9 $\pm$ 1.1
Triglycerides (mmol/L)	2.2 [1.2,4.0]
Serum Phosphate (mmol/L)	1.7 $\pm$ 0.4
Serum Total Calcium (mmol/L)	2.2 $\pm$ 0.2
Serum Parathyroid Hormone (pmol/L)	31.3 [15.2,49.4]

P1284 DIASTOLIC DYSFUNCTION IS A STRONG PREDICTOR OF MORTALITY IN DIALYSIS PATIENTS

Elvana Rista[1], Vilma Cadri[2], Ilir Akshija[2], Nestor Thereska[2], Ariana Strakosha[2], Myftar Barbullushi[2], Endri Harja[3]

[1]hygeia Hospital Tirana, Dialysis-Transplantation, Tirana, Albania, [2]Mother Teresa, Tiranë, Albania and [3]Hygeia Hospital, Tiranë, Albania

Background and Aims: The prevalence of cardiovascular disease in dialysis patients is quite high. This is the leading mortality cause and the main reason for hospital admissions in this population. Diastolic dysfunction is an important predictor of cardiovascular events.

The aim of this study is to calculate the prevalence of diastolic dysfunction (DD) and to identify any significant association of mortality and the grade of DD in chronic dialysis patients with preserved systolic function

Method: This is a prospective study of 310 consecutive patients who were enrolled from 2012-2019. All patients are dialysis dependent for chronic kidney disease (CKD) getting treatment at Nephrology-Dialysis &Transplantation Unit at Hygeia Hospital Tirana. LVH, diastolic dysfunction and cardiac valve pathology contributing to this were diagnosed by transthoracic echocardiography (TTE) criteria. DD was graded as: grade I (mild), grade II (moderate) and grade III (severe). The survival rate was analysed by Kaplan-Meier curves and Cox regression analysis.

Results: Mean age was 51.9±15.6 years; 62.6 % of pts were male, with a mean dialysis vintage of 49 months. 85 % of pts had preserved ejection fraction 50 % or more. LVH was observed in 79.1% of pts. LVED diameter (mm) 52±7 LVESd (mm) 33.7±6.8. Cardiac valve changes were diagnosed as follows: Aortic valve- 35% of patients resulted normal on ultrasound examination, 47% and 17% of pts had leaflet sclerosis and calcifications respectively with normal valve function. 25 % and 7% had some degree of aortic valve regurgitation and stenosis. Mitral valve examination resulted in 9% normal and in 84% of pts with some degree of regurgitation. Arterial hypertension was found in 95.1% of the patients. Diastolic dysfunction was detected in 55% of pts. Of them, 64.5% were deemed to have grade I diastolic dysfunction, 26.7% grade II, 8.7% grade III. During follow up, 25.5% of the patients with DD, died. The analysis of survival curve showed that grade III, 5.2 CI [3.86; 6.64], was associated with higher mortality compared with grade I 11.06 CI [10.01; 12.04] and grade II 11.65 CI [8.5; 14.8], $p<0.001$.

Conclusion: Diastolic dysfunction is ubiquitous echocardiography finding in patients treated with hemodialysis. Grade of diastolic disfunction tend to predict mortality of dialysis patients. 7-year survival analysis shows grade III to be associated with high mortality rates. A multidisciplinary approach is needed in order to predict, prevent and treat these conditions to improve outcomes.

P1285 **ACTIVE FLUID MANAGEMENT IMPROVES LEFT VENTRICULAR FUNCTION AND MECHANICS IN HEMODIALYSIS PATIENTS: A RANDOMIZED TRIAL**

Zoran Paunic[1], Milica Dekleva-Manojlovic[2], Natasa Markovic-Nikolic[2], Nada Dimkovic[3]

[1]Special Hospital for Hemodialysis "Fresenius Medical Care" Belgrade, Belgrade, Serbia, [2]Zvezdara University Medical Center, Clinical Department for Cardiovascular Diseases, Belgrade, Serbia and [3]Zvezdara University Medical Center, Clinical Department for Nephrology, Belgrade, Serbia

Background and Aims: Relative hypervolemia or overhydration (ROH) above 15% of the normally hydrated body extracellular volume (ECV), assessed by bioimpedance spectroscopy (BIS), puts chronic hemodialysis (HD) patients at an increased risk of cardiovascular (CV) incidents and death, as numerous studies have shown. It has also been reported that the reduction of ROH to the value below 15% of ECV can positively affect hypertension and some aspects of the left ventricle (LV) function and morphology. The concept of Active Fluid Management (AFM) has been developed and it hypothesized that maintaining average (weekly) predialysis overhydration (AWOH) below 15% of ECV will preserve heart function and structure and thus lead to fewer CV complications. The purpose of this study was to investigate the effects of AFM concept guided by BIS on cardiac morphology, mechanics and function in chronic HD patients.

Methods: Randomized prospective single-center study lasted 9 months and included BIS naive HD patients from the Dialysis unit of Zvezdara University Medical Center in Belgrade with HD vintage greater of 3 months. BIS was performed by Body Composition Monitor (BCM). In accordance with the AFM concept, BIS was applied to patients in the Active group every time their average weekly ROH (AWOH) exceeded 15% of their normal ECV and their dry weight (DW) was time-adjusted according to the findings along with clinical assessment. In the Control group, patients were treated in accordance with the standard clinical practice. Cardiac structural and functional characteristics were obtained at the beginning and the end of the study by using 2-dimensional Doppler echocardiography and spackle tracking modality. Cardiac markers (high-sensitivity C-reactive protein, Troponin T and N-terminal pro-brain natriuretic peptide) were measured at the same time.

Results: The study included 42 patients (25 M) in the Active group and 41 patients (23 M) in the Control group. Patients from both groups were of similar age (56.1 $\pm$ 11.5 vs. 57.5 $\pm$ 13.2 years, $p = 0.6$) and HD vintage (79.9 $\pm$ 59.2 months vs. 95.3 $\pm$ 80.0 months, $p = 0.6$). 73 patients completed the 9 months study, 38 in the Active group and 35 in Control group. Within the Active group, recommended AWOH lower than 15% ECV has 55% at start and 76% of patients at the end of study ($p< 0.01$). In parallel, there were improvements in their LV ejection fraction (LVEF), from 41.3 $\pm$ 9.3% to 44.0 $\pm$ 8.8% ($p < 0.01$), LV end systolic volume index, from 40.2 $\pm$ 12.5 to 35.8 $\pm$ 13.5 ml/m^2 ($p < 0.05$), LV mass indexed at height at 2.7 (LVMI$^{2.7}$) from 62.8 $\pm$ 19.7 g / m$^{2.7}$ to 57.7 $\pm$ 16.9 g/m$^{2.7}$ ($p <0.01$) and Global radial strain (GRS) - from 18.6 $\pm$ 10.2% to 21.8 $\pm$ 12.2% ($p <0.05$). In the Control group, there were signs of LV diastolic function worsening at the end of the study: E/A ratio increased from 1.0 $\pm$ 0.3 to 1.2 $\pm$ 0.6 ($p < 0.01$), as well as E/e' lateral ratio from 10.6 $\pm$ 5.0 to 11.1 $\pm$4.1 ($p <0.01$) and right ventricle systolic pressure (RVSP) from 34.8 $\pm$ 10.2 mmHg to 38.8 $\pm$ 8.3 mmHg ($p <0.05$). This worsening of LV diastolic function in the Control group correlated with the increased level of one of the cardiac markers, N-terminal pro-brain natriuretic peptide (NT-proBNP) - from 5810.0 (3339.0-15627.0) pg/ml to 8024.0 (4433.0-17467.0) pg/ml ($p <0.04$).

Conclusion: Active Fluid Management leads to the improvement of left ventricle systolic function and prevents worsening of diastolic function in the observed hemodialysis patients. This concept implemented could favourably affect the clinical course of hemodialysis patients in daily clinical practice.

P1286 **THE RELATIONSHIP BETWEEN PROTEIN-BOUND UREMIC TOXINS AND TARGET CARDIOVASCULAR PROTEINS IN HEMODIALYSIS PATIENTS**

Mei-Chuan Kuo[1,2,3], Ping-Hsun Wu[1,4,5,6], Yi-Ting Lin[1,4,5,6], Yi wen Chiu[1,2,3], Shang-Jyh Hwang[1,2,3], Jiun-Chi Huang[1,7], Szu-Chia Chen[7,8], Su-Chu Lee[2], Shih-Shin Liang[8]

[1]Kaohsiung Medical University, Faculty of Medicine, College of Medicine, Kaohsiung, Taiwan, R.O.C., [2]Kaohsiung Medical University Chung-Ho Memorial Hospital, Division of Nephrology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C., [3]Kaohsiung Medical University, Faculty of Renal Care, College of Medicine, Kaohsiung, Taiwan, R.O.C., [4]Kaohsiung Medical University Chung-Ho Memorial Hospital, Department of Family Medicine, Kaohsiung, Taiwan, R.O.C., [5]Kaohsiung Medical University, Graduate Institute of Clinical Medicine, College of Medicines, Kaohsiung, Taiwan, R.O.C., [6]Uppsala University, Department of Medical Sciences, Uppsala, Sweden, [7]Kaohsiung Municipal Siaogang Hospital, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C. and [8]Kaohsiung Medical University, Department of Biotechnology, College of Life Science, Kaohsiung, Taiwan, R.O.C.

Background and Aims: Uremic toxins are crucial non-traditional risk factors for cardiovascular disease in patients with chronic kidney disease (CKD). Indoxyl sulfate (IS) and p-cresyl sulfate (PCS) were associated with all-cause and cardiovascular mortality in CKD patients, but possible mechanisms have not been fully elucidated. Herein, we explored the association between protein-bound uremic toxins and 181 cardiovascular-specific proteins in patients receiving hemodialysis (HD).

Method : In the discovery phase, we investigated associations between circulating free form IS and PCS and cardiovascular-specific protein levels quantified by a proximity extension assay of 333 stable HD patients with correction for multiple testing. In the second phase, the independent association was assessed using multivariable-adjusted models. The associations of IS or PCS with *cardiovascular-specific proteins* levels on a continuous scale were also evaluated.

Results : Free form IS was negatively associated with six proteins (C-C motif chemokine 15, complement component C1q receptor, perlecan, bleomycin hydrolase, cluster of differentiation 166 antigen, and signaling lymphocytic activation molecule family member 5) and positively associated with one protein (fibroblast growth factor 23). Free form PCS was negatively associated with three proteins (C-C motif chemokine 15, complement component C1q receptor, and interleukin-1 receptor-like 2). Adjusting the multivariable models for classical cardiovascular risk factors at baseline yielded similar results.

Conclusion : Protein-bound uremic toxins (IS and PCS) were associated with several *cardiovascular-specific* proteins involved in cell adhesion, endothelial barrier function, inflammation, complement system, and phosphate homeostasis. Multiplex proteomics appears to be a promising way to explore novel aspects of uremic toxin pathophysiology.

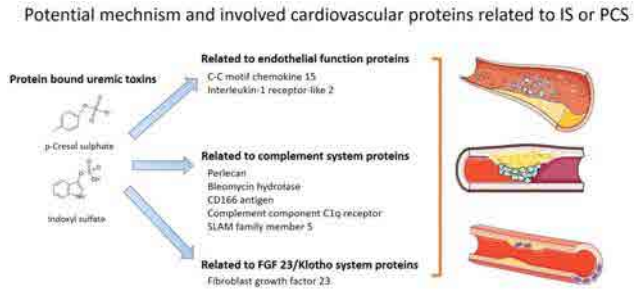


Figure:

P1287

A COMPARATIVE STUDY OF BLOOD PRESSURE VARIABILITY INDICES BETWEEN PATIENTS UNDERGOING PERITONEAL DIALYSIS AND THOSE UNDER HEMODIALYSIS OR WITH CHRONIC KIDNEY DISEASE.

Maria Eleni Alexandrou[1,2], Charalampos Loutradis[1], Dimitrios Sarris[1], Nikolaos Kouris[1], Maria Schoina[1], Georgios Tzanis[1], Chrysostomos Dimitriadis[1], Vasileios Sachpekidis[3], Dorothea Papadopoulou[2], Eugenia Gkaliagkousi[4], Aikaterini Papagianni[1], Gianfranco Parati[5], Panteleimon Sarafidis[1]

[1]Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece, [2]Department of Nephrology, Papageorgiou General Hospital of Thessaloniki, Thessaloniki, Greece, [3], Department of Cardiology, Papageorgiou General Hospital of Thessaloniki, Thessaloniki, Greece, [4]Aristotle University of Thessaloniki, 3rd Department of Internal Medicine, Papageorgiou General Hospital of Thessaloniki, Thessaloniki, Greece and [5]University of Milano-Bicocca, Department of Cardiovascular, Neural, and Metabolic Sciences, San Luca Hospital, Istituto Auxologico Italiano and Department of Medicine and Surgery, Milan, Italy

Background and Aims: Blood pressure variability (BPV) indices have been independently associated with cardiovascular events and mortality in hemodialysis (HD) patients. Data on short-term BPV in patients on peritoneal dialysis (PD) are totally absent. This study examined short-term BPV parameters of patients undergoing PD in comparison to HD and pre-dialysis chronic kidney disease (CKD) patients.

Method: 38 PD patients were matched for age, gender and dialysis vintage with 76 HD in 1:2 ratio patients and for age and gender with 38 patients with CKD stage 2-4 in 1:1 ration. BPV parameters [standard deviation (SD), weighted SD (wSD), coefficient-of-variation (CV) and average-real-variability (ARV)] were calculated from data from 48hour (PD, HD) and 24hour (CKD) ambulatory BP monitoring according to validated formulas.

Results: There were no significant differences in BPV indexes studied between PD and HD patients but all BPV indexes in these patients were numerically higher than those in CKD patients. Systolic ARV was significantly higher in PD or HD compared with pre-dialysis CKD during the first and the second interdialytic 24hour periods, both daytime period and nighttime 2 (1st 24hour period: PD:11.86±3.19; HD:11.23±3.45; CKD:9.81±2.49, p=0.016, 2nd 24hour period: PD: 12.18±4.11; HD: 12.96±4.57; CKD: 9.81±2.49, $p<0.001$). Analysis of diastolic ARV and systolic and diastolic wSD showed similar results. There were no differences with regards to dipping pattern and systolic and diastolic CV during all periods studied.

Conclusion: BPV indices are similar between PD and HD patients and higher compared to CKD counterparts. Despite what was theoretically expected, PD patients demonstrate high fluctuations in BP in the absence of abrupt shifts in volume.

P1288

FACTORS ASSOCIATED WITH THE ANKLE BRACHIAL INDEX TRAJECTORY OVER TIME AMONG PATIENTS RECEIVING HAEMODIALYSIS

Manae Harada[1], Yuta Suzuki[1,2], Takaaki Watanabe[2], Shohei Yamamoto[2], Yusuke Isobe[2], Keigo Imamura[2], Haruka Ito[2], Sachi Yamabe[2], Shun Yoshikoshi[2], Yasuo Takeuchi[3], Yoriko Horiguchi[4], Naoyoshi Aoyama[5], Atsuhiko Matsunaga[2], Atsushi Yoshida[4]

[1]Sagami Circulatory Organ Clinic, Rehabilitation, Sagamihara, Japan, [2]Kitasato University Graduate School of Medical Sciences, Sagamihara, Japan, [3]Kitasato University School of Medicine, Nephrology in Internal Medicine, Sagamihara, Japan, [4]Sagami Circulatory Organ Clinic, Hemodialysis Center, Sagamihara, Japan and [5]Kitasato University School of Medicine, General Medicine, Sagamihara, Japan

Background and Aims: Measurement of the ankle brachial index (ABI) is a simple, noninvasive means of diagnosing peripheral arterial disease. Additionally, a lower ABI has also been shown to be associated with a higher mortality rate. A high prevalence of a low ABI has been reported in patients with chronic renal failure, especially among patients receiving haemodialysis. Therefore, identifying factors that predict a decline in the ABI is important for developing treatment strategies. However, little is known about the factors associated with a decline in the ABI over time in patients receiving haemodialysis. Furthermore, most patients receiving haemodialysis have low levels of daily physical activity and are thus prone to arteriosclerosis. Here, we examined the factors including the level of physical activity associated with the ABI trajectory over time among patients receiving haemodialysis.

Method: The subjects were 236 outpatients (mean age of 64.2±12.0 years, 148 men, mean body mass index of 22.0±4.1 kg/m^2) receiving maintenance haemodialysis thrice a week at a haemodialysis centre. The exclusion criteria for the study were as follows: major amputation of a lower extremity at baseline and lower-extremity peripheral revascularization and amputation of a lower extremity during follow-up. The ABI was determined using a blood pressure pulse-wave inspection apparatus (Form3; Omron Colin, Tokyo, Japan). The lowest values of ankle pressure were used for the calculations. As background factors for the patients, we investigated age, sex, body mass index, haemodialysis vintage, comorbidities (diabetes, cerebrovascular disease, and cardiovascular disease), serum chemistry (haemoglobin and albumin), and level of physical activity. The patients were classified with a low level of physical activity if they used a wheelchair at home or in the hospital or required walking assistance. The ABI and background factors were investigated at baseline and 1, 2, and 3 years. To determine factors associated with the ABI trajectory over time, we conducted multivariate generalised estimating equations analysis.

Results: The mean ABI at baseline was 1.12 (median = 1.16; 25th–75th percentile = 1.07–1.21). Age (-0.02 per year; 95% confidence interval, -0.003 to -0.001), cardiovascular disease (-0.06 per year; 95% confidence interval, -0.115 to -0.023), and level of physical activity (-0.09 per year; 95% confidence interval, -0.135 to -0.041) were associated with the ABI trajectory over time.

Conclusion: Increased ageing, the incidence of cardiovascular disease, and a decreased level of physical activity are independently associated with a decline in the ABI over time. Clinical attention should be paid to low physical activity levels among patients receiving haemodialysis. Studies should examine whether interventions for low physical activity levels can improve the trajectory of the ABI in patients receiving haemodialysis.

P1289

CIRCULATING HIGH SENSITIVITY CARDIAC TROPONIN-T WAS AN IMPORTANT PREDICTIVE MARKER FOR CARDIOVASCULAR EVENTS IN HEMODIALYSIS PATIENTS

Su-Chu Lee[1], Ping-Hsun Wu[1,2,3,4], Yi-Ting Lin[2,3,4,5], Pei-Yu Wu[6], Szu-Chia Chen[3,6], Mei-Chuan Kuo[1,3,7], Yi wen Chiu[1,3,7]

[1]Kaohsiung Medical University Chung-Ho Memorial Hospital, Division of Nephrology, Department of Internal Medicine, Kaohsiung, Taiwan, R.O.C., [2]Kaohsiung Medical University, Graduate Institute of Clinical Medicine, College of Medicines, Kaohsiung, Taiwan, R.O.C., [3]Kaohsiung Medical University, Faculty of Medicine, College of Medicine, Taiwan, R.O.C., [4]Uppsala University, Department of Medical Sciences, Uppsala, Sweden, [5]Kaohsiung Medical University Chung-Ho Memorial Hospital, Department of Family Medicine, Kaohsiung, Taiwan, R.O.C., [6]Kaohsiung Municipal Siaogang Hospital, Department of Internal Medicine, kaohsiung, Taiwan, R.O.C. and [7]Kaohsiung Medical University, Faculty of Renal Care, College of Medicine, Kaohsiung, Taiwan, R.O.C.

Background and Aims: High sensitivity cardiac troponin-T (hs-cTnT) are prognostic markers in patients with stable cardiovascular (CV) disease but limited study investigated the CV outcome association in asymptomatic patients receiving hemodialysis (HD). We evaluated the prognostic value of hs-cTnT in predicting CV events in stable HD patients.

Method: A total of 341 stable HD patients was included in this prospective cohort study. Baseline hs-cTnT was measured by Roche hs-cTnT assays. Patients were followed up for 3 years or until first CV event, which was defined a composite endpoint of acute coronary syndrome, ischemic stroke, or hospitalization for heart failure. Cox proportional hazards model was used to determine independent predictors of CV events. The importance of hs-cTnT compared to other clinical parameters was evaluated by random forests algorithm in Gini index.

Results: The HD patients enrolled in this study was 59.2 ± 11.5 87 years old, 53.4% male, 42.5% had diabetes, 76.8% had hypertension, 17.6% had coronary artery disease, and 9.1% had cerebrovascular disease. In multivariate Cox regression analysis, the circulating hs-cTnT levels were independent associated with CV events (HR 2.31; 95% CI 1.21-4.40; *p*-value=0.011) after adjusting for confounders. Multivariable model showed prognostic significance, with the c-statistics of 0.75. The addition of baseline hs-cTnT to established risk factors improved risk prediction of CV events (c-statistics of 0.76; integrated discrimination improvement = 0.02, $P = 0.049$). Gini index demonstrated hs-cTnT was more important than other clinical parameters for CV events prediction.

Conclusion: Circulating hs-cTnT levels independently predicted CV events in chronic HD patients. CV risk in HD patients could be stratified according to hs-cTnT levels. The results suggest the useful property of hs-cTnT as an end-organ damage marker reflecting subclinical cardiac injury.

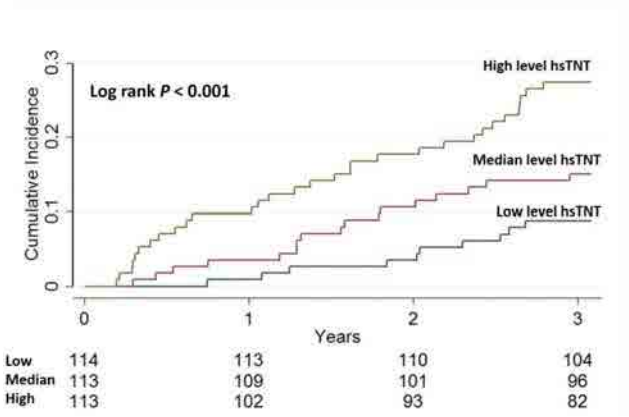


Figure: Cumulative incidence of cardiovascular events across tertiles (Q1–Q3) of baseline high sensitivity cardiac troponin T level

P1290 RISK FACTORS FOR PROGRESSION OF CORONARY ARTERY CALCIFICATION OVER 5 YEARS IN HEMODIALYSIS PATIENTS

Ahmed Alayoud[1], Azizi Mounia[2], Jabrane Marouan[1], Mohammed Arrayhani[1]

[1]IBN ZOHR University, Faculty of Medicine and Pharmacy, agadir, Morocco and
[2]Military Hospital Agadir, Division of Nephrology, agadir, Morocco

Background. Although progression of coronary artery calcification (CAC) has been established as an important marker for cardiovascular morbidity, very few studies have studied it in end-stage renal disease patients. Thus we examined and evaluate risk factors of calcification changes in dialysis patients.

Method: Among 28 hemodialysis (HD) patients, CAC was measured in Agatston units at baseline and after five years using the 64 multi-slice ultra-fast CT. The HD patients were classified as progressors or no progressors according to the change in the CAC score across these 2 measurements.

Results: Over an average 63 months follow-up, participants without CAC at baseline had no incident CAC .The progression of CAC was slow and was found only in 6 patients (21.4%) . It was significantly associated with several cardiovascular risk factors, namely, older age (p=0.03), diabetes (p=0.05), male sex (p=0.02), hypercholesterolemia (p = 0.05), anemia (p=0.017), inflammation (p=0.05), and hyperphosphataemia (p=0.012) . However, calcemia, parathormone levels, dialysis duration, tobacco, high blood pressure and dialysis dose did not seem to influence the progression of CAC in our series. A strong association was found between basal calcification scores and Delta increment at 5 years.

Conclusions: Our study suggests that CAC progression in dialysis is a complex phenomenon, associated with several risk factors with special regard to elevated basal scores. This progression can be avoided or slowed with appropriate management which must begin in the early stages of chronic kidney disease

P1291 **PULMONARY HYPERTENSION VERSUS PULMONARY CONGESTION IN HAEMODIALYSIS PATIENTS IN RELATION TO INCREASED INTER DIALYTIC WEIGHT GAIN**

Magdy ElSharkawy[1,2], Lina Khedr[1,2], Ali Abdel Rahman[3], Ahmed El Shimy[4], Ahmed Shebl[1]

[1]Nasser Institute Hospital, Nephrology department, Cairo, Egypt, [2]Ain-Shams univeristy faculty of medicine, nephrology, Cairo, Egypt, [3]NHTMRI, Department of Radiology, Cairo, Egypt and [4]Faculty of Medicine - Ain Shams University, Department of Radiology, Cairo, Egypt

Background and Aims: Volume overload is considered as an important clinical problem in HD patients. It is associated with morbid situations such as pulmonary hypertension and lung congestion. to assess the effect of increased (IDWG) on pulmonary hypertension, and lung congestion.

Method: This observational cross sectional study was conducted at on 60 HD patients, that were divided into Group I: 30 patients with an IDWG $< 3.5\%$ and, Group II: 30 patients with an IDWG $> 3.5\%$ of their dry weight. Pulmonary artery pressure was measured by echo and patients classified according to PAP into mild, moderate and severe pulmonary hypertension. Lung congestion in all patients was measured by lung ultrasound and patients classified into minimal, mild, moderate and severe lung congestion.

Results: Our study showed that pulmonary hypertension prevalence was 30% while lung congestion was 100%. Patients with increased IDWG $> 3.5\%$ (group 2) had pre HD higher PAP than those with IDWG $< 3.5\%$ (group 1) and patients with IDWG $> 3.5\%$ had more change in their PAP post HD session than those with IDWG $< 3.5\%$ but no significant difference between the change after the HD session in both groups. HD duration is an important factor in PH development over years. There is a significant relation anemia and hypercalcemia with PH. Patients with more increased IDWG $> 3.5\%$ (group 2) had higher pulmonary congestion than those with IDWG $< 3.5\%$ (group 1) and patients with IDWG $< 3.5\%$ had more change in their lung congestion level after the HD session than those with IDWG $> 3.5\%$ but no statistical significance between the change in both groups. There was a significant relation between HD therapy duration with pulmonary congestion measured prior to the session.

Conclusion: on the short term increased IDWG affect lung congestion more than pulmonary hypertension.

P1292 DECREASES IN ANGIOGENIC T CELLS ARE PREDICTIVE BIOMARKERS OF VASCULAR DYSFUNCTION AND ATHEROSCLEROSIS IN CHRONIC KIDNEY DISEASE

Natalia Carrillo-Lopez[1,2], Javier Rodriguez-Carrio[1,3], Catalina Ulloa[4], Beatriz Martín-Carro[1,2], Carmen Rodriguez-Suarez[4], Maria Vittoria Arcidiacono[1], Belinda Fernandez-Mariño[5], Jorge B. Cannata-Andia[1,2,6], Ana Suarez[3], Adriana S Dusso[1,2]

[1]Hospital Universitario Central de Asturias, Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Bone and Mineral Research Unit, Oviedo, Spain, [2]REDinREN-ISCIII, [3]University of Oviedo, Area of Immunology, Department of Functional Biology, Oviedo, Spain, [4]Hospital Universitario Central de Asturias, Division of Nephrology, Oviedo, Spain, [5]Hospital Universitario Central de Asturias, Department of Radiology, Oviedo, Spain and [6]University of Oviedo, Department of Medicine, Oviedo, Spain

Background and Aims: The stratification of early cardiovascular (CV) risk is a major unmet need in chronic kidney disease (CKD). Since angiogenic T-cells are emerging mediators of vascular homeostasis and have been linked to CV disease (CVD), this study evaluated the frequency of circulating angiogenic T-cells in CKD patients undergoing peritoneal dialysis (CKD-5D) and their potential as predictive biomarkers of CVD.

Method: In 30 peritoneal dialysis patients and 16 matched healthy controls (HC), we quantified: Vascular calcification (by Kauppila Index); left carotid intima media thickness (lc-IMT by ultrasound), carotid adventitial vasa vasorum density (an early marker of atherosclerosis stage, by Superb Microvascular Ultrasound Image), pulse wave velocity (a marker of vascular stiffness and dysfunction, using the Complior Analyzer), angiogenic T cell frequency in blood (by Flow cytometry) and the traditional 10-year CVD risk (using the SCORE chart).

Results: As expected, CKD-5D patients exhibited higher Kauppila index ($p<0.001$), lcIMT ($p=0.010$) and adventitial vasa vasorum density ($p=0.008$) than HC. Angiogenic-T cell frequency was decreased in CKD compared to HC (1.68(1.05) vs. 3.33(1.44)%, $p<0.001$). In CKD-5D patients, angiogenic-T cell frequency was not associated with blood pressure, cholesterol levels or time on dialysis (all $p>0.05$) and did not correlate with Kauppila ($r=-0.350$, $p=0.080$) or lcIMT ($r=-0.154$, $p=0.600$), but strongly associated negatively with both pulse wave velocity ($r=-0.734$, $p<0.001$) and with adventitial vasa vasorum (newly formed vasa vasorum) number: $r=-0.640$, $p=0.006$; or density: $r=-0.813$, $p<0.001$). Angiogenic-T cell levels paralleled pulse wave velocity (B[95% CI]: -0.083[-0.155, -0.010], $p=0.028$; $R2=0.531$) and adventitial vasa vasorum -15.049[-26.705, -3.392], $p=0.015$; $R2=0.598$) and improved the prediction model over that of the SCORE chart ($R2=0.360$ and $R2=0.336$, respectively).

Conclusion: Angiogenic-T cell frequency was decreased in CKD-5D patients and could be considered as biomarkers of vascular dysfunction and early atherosclerosis stage.

P1293 **WARFARIN INCREASES THE RISK OF VASCULAR CALCIFICATION IN HAEMODIALYSIS PATIENTS: A MULTICENTER CASE-CONTROL STUDY**

Rezzan Eren Sadioğlu[1], Evren Üstüner[2], İhsan Ergün[3], Tevfik Ecder[4], Gökhan Nergizoglu[1], Kenan Keven[1]

[1]Ankara University School of Medicine, Ibni Sina Hospital, Department of Nephrology, Ankara, Turkey, [2]Ankara University School of Medicine, Ibni Sina Hospital, Department of Radiology, Ankara, Turkey, [3]Ufuk University School of Medicine, Department of Nephrology, Ankara, Turkey and [4]Demiroglu Bilim University School of Medicine, Department of Nephrology, İstanbul, Turkey

Background and Aims: Vascular calcifications (VC) are highly prevalent in maintenance haemodialysis patients and it is a recognized risk factor for increased mortality. Previous experimental studies showed the relation between warfarin which has been prescribed frequently in dialysis patients and VC. The aim of this study is to investigate the association between VC and warfarin use in haemodialysis patients.

Method: This was a cross-sectional, observational, multicenter study. VC were assessed using Adragao (AS; pelvis and hands) and Kauppila (KS; lateral lumbar spine) scores in 76 haemodialysis patients from six centers. There were 32 patients (4.5%) being treated with warfarin for at least 1 year out of a total 711 haemodialysis patients and we included 44 control patients with matching parameters of age, sex and dialysis vintage to the study. Clinical characteristics, concomitant treatments, laboratory results were recorded and possible risk factors related to VC were analyzed.

Results: Of the patients, 47% were females, mean age was 65.8 ± 9 years, 23% were diabetics, their mean dialysis vintage was 68.39 ± 38.5 months and mean Kt/V 1.66 ± 0.27. No significant differences in clinical characteristics and basic laboratory results were found between control and warfarin group. In warfarin group, median Kauppila score was higher than control [11 vs 6.5, (25%-75% percentile, 5 vs 15), P=0.032] and percentages of Kauppila score >6 patients were higher, as well (76,6% vs 50%; P=0.029). Median Adragao score was not significantly different between two groups [7 vs 6, (%25,%75 percentile 6 vs 8), P=0.177]. Logistic regression analysis revealed that warfarin treatment was independently associated with Kauppilla scores of >6 (OR 3.28, 95% CI 1.17-9.22, P=0.024).

Conclusion: The results of this study showed that warfarin is a strong risk factor for vascular calcifications, especially in aorta of haemodialysis patients.

Table 1. Basic characteristics of the patients and summary of the results

Parameter	Warfarin (+) n=32	Warfarin (-) n=44	P value
Age (mean±SD)	67.6±9	64.54±8.3	0.143
Female/Male	14; 43%/18; 56%	22; 50%/ 22; 50%	0.646
Dialysis vintage (months, mean±SD)	74.9±44.2	63.6±33.4	0.209
Kt/V	1.62±0.2	1.7±0.2	0.205
Diabetes mellitus +/- (n,%)	6, 18%	12, %27	0,427
Warfarin usage time (months, mean±SD)	65.9±9.7	NA	NA
Kauppilla score (median,-min-max)	11 (1-24)	6,5 (1,20)	**0,032**
Kauppilla score >6 (n, %)	23, 76.6%	22, 50%	**0,029**
Adragao score (median, min-max)	7 (2-8)	6 (0-8)	0,177
Adragao score ≥ 3 (n, %)	30, 93.7%	41, 93.1%	0,638
Serum calcium (mean±SD)	8.82±0.5	8.78±0.5	0.778
Serum phosphorus (mean±SD)	4.62±0.87	4.84±0.89	0.279
Serum parathyroid hormone (mean±SD)	376.23±192.8	457.36±251.2	0.116
Serum albumin (mean±SD)	3.81±0.38	3.91±0.52	0.361
Serum hemoglobin (mean±SD)	11.43±1.1	11.6±1.57	0.595
Serum C-reactive protein (mean±SD)	14.3±12.2	13.8±15.4	0.881

Figure:

P1294 **AMBULATORY BLOOD PRESSURE PROFILE IN PERITONEAL DIALYSIS COMPARED TO HEMODIALYSIS AND CHRONIC KIDNEY DISEASE PATIENTS.**

Maria Eleni Alexandrou[1,2], Charalampos Loutradis[2], Nikolaos Kouris[2], Dimitrios Sarris[2], Maria Schoina[2], Georgios Tzanis[2], Chrysostomos Dimitriadis[2], Vasileios Sachpekidis[3], Dorothea Papadopoulou[1], Eugenia Gkaliagkousi[4], Aikaterini Papagianni[2], Gianfranco Parati[5], Panteleimon Sarafidis[2]

[1], Department of Nephrology, Papageorgiou General Hospital of Thessaloniki, Thessaloniki, Greece, [2]Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece, [3], Department of Cardiology, Papageorgiou General Hospital of Thessaloniki, Thessaloniki, Greece, [4]Aristotle University of Thessaloniki, 3rd Department of Internal Medicine, Papageorgiou General Hospital of Thessaloniki, Thessaloniki, Greece and [5]University of Milano-Bicocca, Department of Cardiovascular, Neural, and Metabolic Sciences, San Luca Hospital, Istituto Auxologico Italiano and Department of Medicine and Surgery, Milan, Greece

Background and Aims: Hypertension is highly prevalent in dialysis patients and is often poorly controlled. Data on the ambulatory blood pressure (BP) profile of patients undergoing peritoneal dialysis (PD) are scarce. The aim of this study is to compare the ambulatory BP profile of PD patients with that of hemodialysis (HD) and to pre-dialysis CKD patients.

Method: 38 patients undergoing PD were matched in a 1:2 ratio for age, gender and dialysis vintage with 76 HD patients and in a 1:1 ratio for age and gender with 38 CKD stages 2-4 patients. Patients under PD and HD underwent 48-hour and CKD patients 24-hour ambulatory BP monitoring. BP levels were compared for the 48hour, 1st and 2nd 24hour, daytime and nighttime periods. Two-way mixed ANOVA analysis for repeated measurements was used to evaluate the effect of dialysis modality and time on ambulatory BP in PD and HD.

Results: During all periods studied, SBP and DBP were numerically higher but not statistically different in PD than in HD patients. SBP was significantly higher in PD or HD compared with predialysis CKD (PD:138.38±20.97; HD:133.75±15.5; CKD:125.52±13.4 mmHg, p=0.003; PD vs CKD: p=0.003; HD vs CKD: p=0.041 accordingly); significant differences were also evident during the daytime and nighttime periods. DBP displayed a similar trend in the total period studied (PD:82.34±15.22; HD:80.47±11.13; CKD:76.81±7.82 mmHg, p=0.108), but the difference significant only during the second nighttime period. Repeated-measurements analysis showed no effect of dialysis modality and no interaction between modality and time on ambulatory BP during all periods studied.

Conclusion: Average BP levels are similar between PD and HD patients, but higher for both groups compared to CKD counterparts. The dialysis modality had no significant effect on ambulatory BP profile.

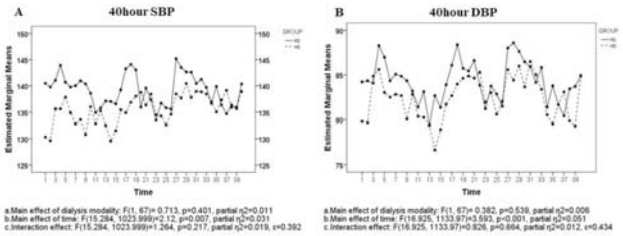


Figure:

P1295

OBSERVATION ON THE EFFECT OF DIGOXIN COMBINED WITH BENAZEPRIL HYDROCHLORIDE ON THE MAINTENANCE OF CHRONIC HEART FAILURE IN HEMODIALYSIS PATIENTS

Shidong Feng[1], Rui Jing[2]

[1]Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China, Department of Nephrology, Xi'an, P.R. China and [2]Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China., Department of Nephrology, Xi'an, P.R. China

Background and Aims: To observe the effect of digoxin combined with benazepril hydrochloride on the heart structure and function of chronic heart failure in patients with maintenance hemodialysis.

Method: Choose 36 patients with maintenance hemodialysis, chronic heart failure (NYHA II - III) from 2016 to 2017 in our department. The patients were randomly divided into three groups: control group 1: digoxin (0.125mg/ day), control group 2: benapril hydrochloride (20mg/ day), and observation group: digoxin (0.125mg/ day) + benapril hydrochloride (20mg/ day), with 12 people in each group. There was no statistical difference in the clinical baseline data of the three groups of patients. The experiment mainly observed left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDV), serum troponin T, I (TnT, TnI), and serum n-terminal brain natriuretic peptide precursor (NT-proBNP), human component bioelectrical impedance analysis (BCM), the blood pressure. No other RAAS inhibitors were allowed for all patients. The observation period was 1 year.

Results: 1. According to the findings of cardiac ultrasound, LVEF value increased significantly and LVEDV decreased significantly in the observation group. There was a statistical difference between the observation group and the control group ($P<0.05$), while there was no statistical difference between the two control groups. 2. Serum examination showed that TnT, TnI, nt-probnp were significantly decreased in the observation group, there was a statistical difference between the observation group and the two control groups ($P<0.05$), there was no statistical difference between the two control groups. 3. During the observation period, there was no significant difference in the incidence of hyperkalemia among the three groups ($P>0.05$).

Conclusion: A large dose of benazepril hydrochloride combined with a small dose of digoxin, had significant effect on the cardiac structure and function of chronic heart failure in patients with maintenance hemodialysis.

P1296 CARDIAC COMPLICATIONS OF ARTERIOVENOUS FISTULAS IN PATIENTS WITH END-STAGE RENAL DISEASE

Nessrine Breik[1], Hela Jbeli[1], Safa Fattoum[1], Imen Ouertani[1], Badreddine Ben kaab[1], Ikram Mami[1], Lilia Ben Fatma[1], Soumaya Beji[1], Wided Smaoui[1], Fethi Benhmida[2], Lamia Rais[1], Mohammed Karim Zouaghi[1]

[1]La Rabta Hospital, Department of Nephrology, Dialysis and Transplantation, Tunis, Tunisia and [2]Charles Nicolle Hospital, Research Laboratory of Kidney Diseases (LR00SP01), Tunis, Tunisia

Background and Aims: Current literature suggests the arteriovenous fistula (AVF) to be the preferred type of vascular access for hemodialysis. However, AVFs have significant and potentially deleterious effects on cardiac functions particularly in the setting of preexisting heart disease. The aim of this study is to compare the clinical and echocardiographic evolution after creation of a proximal AVF and a radial AVF.

Method: We conducted a retrospective descriptive study including all chronic hemodialysis patients through AVF. Group 1 (G1) included patients with proximal AVF and group 2 (G2) patients with radial AVF.

Results: Twenty-four patients were collected in G1 and the average age was 55 years. G2 included 13 patients with a mean age of 44 years. Systolic blood pressure decreased after AVF creation in both groups (G1: 62.5%, G2: 45%, NS). A dyspnea was noted in 70% of cases of G1 and 38.4% of cases of G2 (NS). The interventricular septum was thickened in 20.8% of cases of G1 and 38.4% of G2 (NS). Left ventricular (LV) dilatation was observed in both groups with LV diastolic telegram diameter increase of 58% in G1 versus 10% in G2 ($p = 0.04$). A decrease in LV ejection fraction was found in 62.5% in G1 and 46.1% in G2 ($p = 0.066$). The major cardiac complications in G1 were acute coronary syndrome in 5 patients and atrial fibrillation in 4 cases after an average of 60 months and 35 months, respectively. No cardiac complications were noted in G2.

Conclusion: AVFs remain the preferred type of vascular access for chronic hemodialysis therapy because they are associated with better long-term patency and fewer complications compared with synthetic grafts. Its seat will depend on the vascular state and the cardiac status of the dialysis patient.

P1297 **PULMONARY HYPERTENSION VERSUS PULMONARY CONGESTION IN HAEMODIALYSIS PATIENTS IN RELATION TO INCREASED INTERDIALYTIC WEIGHT GAIN**

Magdy ElSharkawy[1,2], Lina Khedr[1,2], Ahmed El Shimy[3], Ali Abdel Rahman[2,4], Ahmed Shebl[2]

[1]Ain-Shams univeristy faculty of medicine, nephrology department, Cairo, Egypt, [2]Nasser Institute Hospital, Nephrology department, Cairo, Egypt, [3]Ain-Shams univeristy faculty of medicine, Department of Radiology, Cairo, Egypt and [4]NHTMRI, Department of Radiology, Cairo, Egypt

Background and Aims: Volume overload is considered as an important clinical problem in HD patients. It is associated with morbid situations such as pulmonary hypertension and lung congestion. to assess the effect of increased (IDWG) on pulmonary hypertension, and lung congestion.

Method: This observational cross sectional study was conducted at on 60 HD patients, that were divided into Group I: 30 patients with an IDWG $< 3.5\%$ and, Group II: 30 patients with an IDWG $> 3.5\%$ of their dry weight. Pulmonary artery pressure was measured by echo and patients classified according to PAP into mild, moderate and severe pulmonary hypertension. Lung congestion in all patients was measured by lung ultrasound and patients classified into minimal, mild, moderate and severe lung congestion.

Results: Our study showed that pulmonary hypertension prevalence was 30% while lung congestion was 100%. Patients with increased IDWG $> 3.5\%$ (group 2) had pre HD higher PAP than those with IDWG $< 3.5\%$ (group 1) and patients with IDWG $> 3.5\%$ had more change in their PAP post HD session than those with IDWG $< 3.5\%$ but no significant difference between the change after the HD session in both groups. HD duration is an important factor in PH development over years. There is a significant relation anemia and hypercalcemia with PH. Patients with more increased IDWG $> 3.5\%$ (group 2) had higher pulmonary congestion than those with IDWG $< 3.5\%$ (group 1) and patients with IDWG $< 3.5\%$ had more change in their lung congestion level after the HD session than those with IDWG $> 3.5\%$ but no statistical significance between the change in both groups. There was a significant relation between HD therapy duration with pulmonary congestion measured prior to the session.

Conclusion: on the short term increased IDWG affect lung congestion more than pulmonary hypertension.

P1298

SEASONAL VRIABILITIES OF HOME AND CLINIC BLOOD PRESSURE IN HEMODIALYSIS PATIENTS ARE DPEND ON VOLUME STATUS AND TEMPERATURE CHANGE IN MULTICENTER OF VARIOUS DISTRICTS IN JAPAN

Munekazu Ryuzaki[1], Motoaki Komatsu[1], Hidehisa Soejima[2], Kazuaki Soejima[2], Itaru Ebihara[2], Tsuyoshi Imai[2], Chikao Yasunaga[2], Yasushi Suzuki[2], Makoto Hiramatsu[2]

[1]Saiseikai Central Hospital, Nephrology, Tokyo, Japan and [2]Saiseikai Dialysis Collaborate Research Association, Kumamoto, Japan

Background and Aims: In general population, there are weekly and seasonal variabilities of blood pressure (BP) which are supposed to be the risk of cardiovascular disease. Home BP is well correlated to the cardiovascular risk compared to clinic BP. We already reported home and clinic BP of hemodialysis (HD) patients fluctuate seasonally partly due to temperature. The aim of this study is to determine in large number of HD patients whether the seasonal BP variability correlates to the volume status and temperature.

Method: One hundred sixty nine dialysis patients (93 male, 76 female) in ten Saiseikai hospitals in various districts in Japan were recruited. All patients were asked to measure BP at least four times a day in a sitting position, twice consecutively in the morning after urination before breakfast and medication and twice consecutively in the evening just before going to bed. The mean of twice measurements was defined as the data of measurement time. Data from Oct. 2015 to Oct. 2017 were analyzed. If the dialysis were performed 3 times a week (Mon, Wed, Fri), Monday was defined as 1st day. If the dialysis were performed on Tue. Thurs. and Sat., Tuesday was defined as 1st day. Seasonal variabilities in morning home BP and night home BP were evaluated. Seasonal changes in clinic BP just before and after HD were also evaluated in 61 patients.

Results: Weekly home BP variability in the morning, 1st day 153±16 / 78±13 mmHg, 2nd day 144±28 / 76±12, 3rd day 150±14 / 77±13, 4th day 142±26 / 75±13, 5th day 149±14 / 77±12, 6th day 144±24 / 76±13, 7th day 149±16 / 78±13. Systolic home BPs in 1st, 3rd and 5th days were significantly elevated compared with 2nd, 4th and 6th days. Morning home BP significantly elevated gradually from 6th, 7th and to 1st day. Lowest SBP in the morning was 4th day but not 6th day which was the same as the previous result (CJASN 3: 416-422, 2008). Seasonal variability of morning home BP in 1st day was evident with the rise in autumn and winter (spring 153±19 / 78±12, summer 146±17 / 77±12, autumn 158±16* / 80±12, winter 156±19* / 80±13, * $p<0.05$ vs summer) (figure). There was almost same seasonal morning home BP variability in 4th day which had the lowest value of morning home BP in a week. Seasonal changes of night home BP in 5th day were not significant through four seasons, which night was supposed to be the driest volume status in a week. Seasonal changes in clinic BP just before and after HD, in 1st day before HD: spring 147±19 / 74±13 mmHg, summer 144±20 / 71±11, autumn 150±19 / 74±13, winter 147±21 / 74±12. Systolic BP in autumn was significantly elevated compared to summer. In the other clinic BPs before and after HD in 3rd and 5th days, there were no significant seasonal changes observed. Seasonal changes of highest temperature were significant (spring 19.9±3.1*°C, summer 30.9±2.6, autumn 23.3±2.7*, winter 8.5±2.8*, *$p<0.05$ vs summer). Morning BP of 1st day in a randomly selected patient was correlated with highest temperature ($r=-0.397$ $p<0.0001$).

Discussion: There is seasonal home BP variability probably due to temperature change because BP was correlated well with temperature. Seasonal morning BP variability was evident in the 1st day of the HD week, but this seasonal home BP variability was disappeared measuring BP in the night without volume overload. We assumed that vasoconstriction due to change in temperature was enhanced by volume overload and sympathetic activation in the morning.

Conclusion: In the large number of HD patients in multicenter of various districts in Japan, seasonal BP variabilities were affected by the volume status and temperature.

P1299 **SODIUM ZIRCONIUM CYCLOSILICATE FOR THE TREATMENT OF PERSISTENT HYPERKALAEMIA IN PREVALENT HAEMODIALYSIS PATIENTS: EXPERIENCE FROM CLINICAL PRACTICE.**

Owain Brooks[1], Ashraf Mikhail[1], Chris Brown[1], Mark Gumbleton[2], Justine Jenkins[2], Kaitlin Boyle[2]

[1]Swansea Bay University Health Board, Department of Nephrology, Swansea, United Kingdom and [2]Cardiff, School of Pharmacy and Pharmaceutical Sciences, Cardiff, United Kingdom

Background and Aims: Sodium zirconium cyclosilicate (SZC) (Lokelma®) is a new oral potassium binder. In September 2019 the UK National Institute for Health and Care Excellence (NICE) did not recommend SZC for dialysis patients due to a lack of evidence. The recent DIALIZE phase 3b randomised controlled trial concluded that SZC is an effective and well-tolerated treatment for hyperkalemia in haemodialysis (HD) patients. We offer an insight into SZC treatment in HD patients with persistent hyperkalaemia in clinical practice.

Method: Adult prevalent HD patients prescribed SZC for persistent hyperkalaemia were included for analysis. The highest pre-dialysis serum potassium (sK^+) values were recorded each month before (M-6 to M-1) and after (M1 to M5) SZC initiation. The primary efficacy measure was a reduction in sK^+ with SZC treatment.

Results: Sixteen patients (mean age 53.5 years, 56.3% male) were included for analysis. 43.8% (n=7) were diabetic. At the time of SZC initiation 43.8% (n=7) received HD via arteriovenous fistula, 12.4% (n=2) via arteriovenous graft and 43.8% (n=7) via tunnelled central venous catheter. The mean Urea Reduction Ratio [SD] was 68.5% [10.8] and the mean [SD] pre-HD bicarbonate was 22.8mmol/L [2.7]. The dialysate potassium prescription was 2mmol/L for 93.8% of patients (n=15) and 1mmol/L for 6.2% of patients (n=1). The mean [SD] achievement of prescribed dialysis hours over the previous 4 weeks was 93.5% [12.2]. 68.8% (n=11) had previous treatment with calcium polystyrene sulfonate and 12.5% (n=2) with patiromer. 18.8% (n=3) were currently prescribed a renin-angiotensin-aldosterone system inhibitor. 93.8% (n=15) had received dietetic advice. SZC starting doses ranged from 5g four times a week on non-dialysis days to 10g three times a day.

Mean [SD] sK^+ at month-1 (M-1) (immediate pre-treatment period) was 7.38mmol/L [0.31]. Mean [SD] sK^+ at month 1 (M1) was 6.37mmol/L [1.21]. The statistical difference between these groups was p=0.0023 (paired two-tailed T-test). Figure 1 includes mean maximum monthly pre-dialysis sK^+ from M-6 to M5.

SZC was stopped in two patients (after M1 with sK^+ 5.0mmol/L and after M4 with sK^+ 4.3mmol/L) as it was no longer clinically indicated. Two patients became non-compliant (clinician-suspected or confirmed by patient) with SZC after M2 (sK^+ 6.7mmol/L and sK^+ 6.4mmol/L). Subsequent sK^+ values would not reflect treatment with SZC in these patients. Figure 2 includes mean maximum monthly sK^+ for the 12 patients on SZC from M-3 to M5.

ANOVA and post-hoc Dunnett's tests were undertaken to compare SZC treatment months (M1, 2, 3, 4 and 5) to the immediate pre-treatment period (M-1). ANOVA was close to significance (p=0.058), with post-hoc corrected for multiple comparisons finding the data to be significant for M1 vs. M-1 (p=0.045) and M5 vs. M-1 (p=0.018). The same tests across M1 through M5 revealed no significant difference (p=0.968 ANOVA and p=0.555 Dunnett's), demonstrating that continued treatment with SZC to M5 did not result in a further decline in sK^+.

Conclusion: Sodium zirconium cyclosilicate is effective in reducing pre-dialysis sK^+ in patients with moderate and severe hyperkalaemia undergoing haemodialysis in clinical practice.

P1300 **CARDIOVASCULAR COMPLICATIONS IN HEMODIALYSIS PATIENTS**

Helaoui Fadwa[1]

[1]*Hospital Charles Nicolle, nephrology, Tunis, Tunisia*

Background and Aims: Cardiovascular complications are the leading cause of morbidity and mortality among dialysis patients. We aim to determine the cardiac damage showed by trans-thoracic ultrasound and to identify the various factors associated with it.

Method: Fourty chronic hemodialysis patients have benefited of transthoracic ultrasound during this year (2019). Clinical findings were collected from patients' medical files. Data collected included demographics, Clinical Status and echocardiographic parameters. All the patients included in this study gave their consent. Data were collected and analysed using SPSS software. Chi-squared test with a level of significance of 0.05 was used for the qualitative variables.

Results: The mean age of our population is 53.1 (range: 26-78) with a sex ratio equal to 0.9. 72.5% of patients are hypertensive; 27.5% of patients are diabetic. Only 2 patients to be coronary. In this study, 11 patients remained asymptomatic while 29 patients (75.5%) presented with cardiac symptomatology: 39.7% complained of chest pain, 27.5% presented with acute dyspnea and 24,1% a pericardial rub. Rhythm disorders were objectified in electrocardiography in 3 patients (1 ventricular extrasystole and 2 cardiac arrhythmia by atrial fibrillation). Twenty percent of the cardiac ultrasounds performed are without abnormalities. Cardiac ultrasound revealed the presence of valvulopathies in 40% with 20% valve calcifications. Left ventricular hypertrophy is evident in 55% of patients, 45% of whom are hypertensive. Segmental hypokinesia was observed in 27.5% and pulmonary hypertension was observed in 37.5%. Cardiac ultrasound also showed dilated right cavities in 22.5% of cases and dilated left cavities in 32.5%. Dilatation of the inferior vena cava is observed only in 3 patients. Pericarditis is highlighted in 37.5% of which 36.3% are of medium abundance and 18.1% are of great abundance without signs of compression. Clinical data were correlated with echocardiographic findings. A correlation was found between left venticular hypertrophy and hypervolemia (p=0.001) and between perdialytic hemodynamic instability and ischemic cardiopathy (p=0.04) as well as pulmonary hypertension and vascular access dysfunction (p=0.02).

Conclusion: Cardiovascular complications are very common in chronic hemodialysis population. The left ventricular hypertrophy is the main cause of heart disease with predominance of high blood pressure as an associated comorbidity.

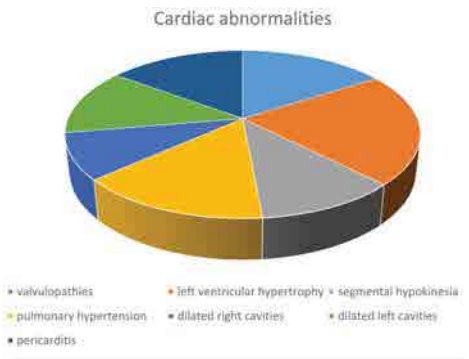


Figure:

P1301

CLINICAL OUTCOMES OF ORAL ANTICOAGULATION AND NO ANTICOAGULATION AMONG END-STAGE RENAL DISEASE PATIENTS ON MAINTENANCE HEMODIALYSIS WITH ATRIAL FIBRILLATION: A SINGLE-CENTER PROSPECTIVE COHORT STUDY

Eratosthenes Polito[1], Grecia Darunday[1]

[1]*Perpetual Succour Hospital, Section of Adult Nephrology, Department of Internal Medicine, Cebu City, Philippines, The*

Background and Aims: Progress has been made over the past six decades in the world of hemodialysis, however it still remained as an ongoing challenge for clinicians since it is coupled with an increasing incidence of dysrhythmia that brings a high cardiac mortality in the first year. Many of these patients will have a risk profile lending to oral anticoagulation with warfarin as the traditionally mainstay of therapy for this indication or a non-vitamin K oral anticoagulants (NOACs) in some because of ease of administration and comparable efficacy. There may be convincing as well as contrasting arguments regarding its use, but without well-conducted clinical trials, it is definitely impossible to consider the indication of oral anticoagulation therapy in this special group of population.

This study aims to determine the difference in clinical outcomes between oral anticoagulation and no anticoagulation therapy among End-Stage Renal Disease patients on maintenance hemodialysis with atrial fibrillation in Perpetual Succour Hospital, and to provide local data on the prevalence and frequency of oral anticoagulation and no anticoagulation therapy in this group of patients.

Method: This is a single-center, prospective, observational cohort study conducted in a tertiary hospital in Cebu City, Cebu. All diagnosed End-Stage Renal Disease patients with chronic atrial fibrillation on maintenance hemodialysis for at least 3 months.

Results: A total of 188 ESRD patients on maintenance hemodialysis at The Kidney Service-Perpetual Succour Hospital were identified from May 1, 2017 through October 31, 2018, of which 74 (39.4%) subjects had a documented coexisting chronic atrial fibrillation at the time of recruitment but only 69 individuals were included in the analysis. At enrollment, 59 (85.5%) patients were identified to have no oral anticoagulation therapy and 10 (14.5%) were already receiving oral anticoagulation. Ischemic strokes was more prevalent (80%, $p=<0.0001$) among patients who were on oral anticoagulant. Likewise, patient differ significantly in terms of intracranial hemorrhage (30%, $p=0.0004$) and gastrointestinal bleeding (50%, $p=<0.00001$) were noted among patients receiving oral anticoagulation therapy. In relation to over-all mortality, acute myocardial infarction, peripheral arterial occlusive disease and caciphylaxis, there was no sufficient evidence to show significant difference between two groups.

Conclusion: This study suggests that the use of oral anticoagulation did not prevent ischemic strokes in ESRD patients on maintenance hemodialysis with chronic atrial fibrillation. Further, it was associated with increased risk for intracranial hemorrhage and gastrointestinal bleeding. Lastly, there was no significant difference in relation to all-cause mortality, acute myocardial infarction, peripheral arterial occlusive disease and calciphylaxis between the two study groups.

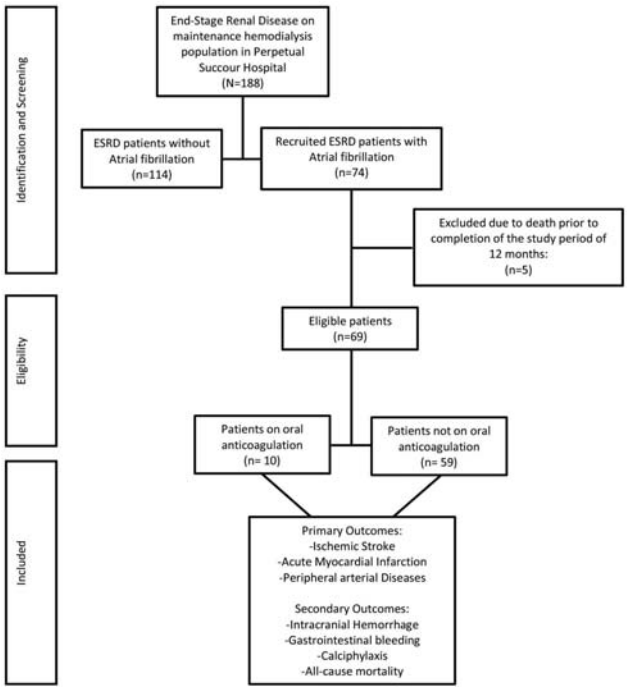


Figure 1. Flow diagram illustrating the details on how the study population were obtained.

P1302

NONINVASIVE ASSESSMENT OF PULMONARY HYPERTENSION USING QUANTITATIVE IMAGING IN HEMODIALYSIS PATIENTS

Fabio Salerno[1,2,3], Tamas Lindenmaier[2], Alexander Matheson[1,2], Rachel L. Eddy[1,2], Marrissa McIntosh[1,2], Justin Dorie[3], Grace Parraga[1,2], Christopher McIntyre[1,3]

[1]Western University, Medical Biophysics, London, Canada, [2]Robarts Research Institute, London, Canada and [3]The Lilibeth Caberto Kidney Clinical Research Unit, Medicine - Nephrology, London, Canada

Background and Aims: Pulmonary hypertension (PH) is highly prevalent in the hemodialysis (HD) patient population. Right heart catheterism remains the gold standard for PH diagnosis and etiological stratification – this makes a comprehensive investigation of PH challenging in these patients. The PEPPER study suggested that postcapillary PH is the most common form of PH in HD patients, as the result of volume overload and left ventricular dysfunction. We hypothesized that novel quantitative imaging-derived biomarkers, such as pulmonary vessel volume and pulmonary artery volume, would improve our insight on the relationship between PH, volume status and left ventricular dysfunction in HD patients. In this study, we explored the combined role of noncontrast chest CT and echocardiography to investigate PH in a sample of HD patients.

Method: Study participants underwent noncontrast chest CT and doppler echocardiography on a non-HD day. To avoid potential confounders, chronic hemodialysis patients with previously diagnosed chronic lung disease, cancer and infections were excluded, and smoking history was limited to 20 packs/year. Pulmonary vessel volume was automatically segmented and measured using commercial software (VIDA Diagnostics Inc., Coralville, USA). Total pulmonary artery (PA) volume was segmented manually from CT, including 25 mm of the main, left and right pulmonary arteries starting from the bifurcation; volumes were calculated using a combination of in-house software (3D Quantify, Robarts Research Institute, London, Ontario, Canada; MATLAB MathWorks, Inc., Natick, Massachusetts, USA). PA volume and pulmonary vessel volume were indexed by body surface area (BSA), to correct for body size. Left atrial volume and PA systolic pressure were measured from doppler echocardiography according to current clinical guidelines. Associations between quantitative imaging biomarkers and demographics were assessed with Pearson and Spearman correlation, as appropriate. Linear fitting was performed with linear regression.

Results: Five HD patients were studied. Two patients had PA systolic pressure ≥ 35 mmHg. Preliminary analysis showed a nonlinear trend correlation between PA systolic pressure and pulmonary vessel volume/BSA (Panel A), PA systolic pressure and pulmonary artery volume/BSA (Panel B). Additionally, pulmonary vessel volume showed a significant, positive linear correlation with total pulmonary artery volume (Panel C) and left atrial volume (Panel D).

Conclusion: Preliminary correlations between pulmonary vessel volume, pulmonary artery volume, left atrial volume and PA systolic pressure suggest that intravascular volume and left ventricular dysfunction may play a significant role in determining PH in HD patients. Quantitative imaging allows screening for PH and provides additional, noninvasive, and relevant clinical information on the pathophysiology of PH in HD patients.

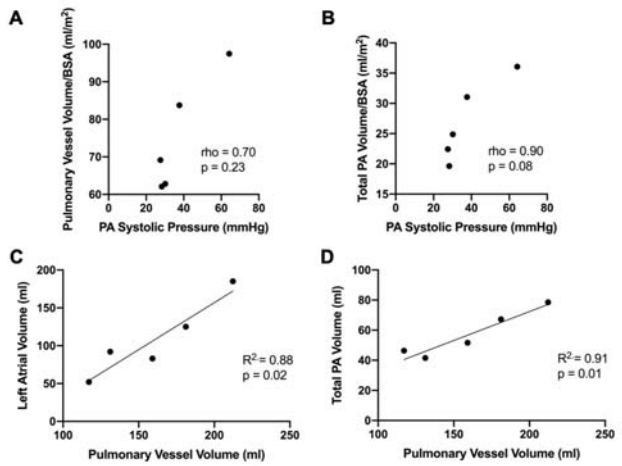


Figure 1.

Correlation for PA Systolic Pressure (mmHg) with pulmonary vessel volume/BSA and total PA volume/BSA (Panels A and B, respectively). Correlation for pulmonary vessel volume with left atrial volume and total PA volume (Panels C and D, respectively).

P1303

ASSOCIATION BETWEEN PULSE PRESSURE AND EXTRACELLULAR TO INTRACELLULAR WATER RATIO IN HEMODIALYSIS PATIENTS

Robert Ekart[1,2], Gasper Keber[2], Benjamin Dvorsak[3], Masa Knehtl[3], Radovan Hojs[2,3]

[1]UNIVERSITY MEDICAL CENTRE MARIBOR, CLINIC FOR INTERNAL MEDICINE, DEPT. OF DIALYSIS, Maribor, Slovenia, [2]UNIVERSITY OF MARIBOR, FACULTY OF MEDICINE, MARIBOR, Slovenia and [3]UNIVERSITY MEDICAL CENTRE MARIBOR, CLINIC FOR INTERNAL MEDICINE, DEPT. OF NEPHROLOGY, MARIBOR, Slovenia

Background and Aims: Optimal fluid management is a challenge in patients with end-stage kidney disease (ESRD) on maintenance hemodialysis (HD). Multifrequency bio-impedance spectroscopy (MBIS) is a non-invasive method to estimate body composition, including estimates of extracellular water (ECW) and intracellular water (ICW) and the ratio between both spaces (ECW/ICW). Pulse pressure is a significant risk factor of cardiovascular disease and death in general and dialysis population. Our study aimed to analyse the correlation between systolic, diastolic and pulse pressure with body composition status in ESRD patients before HD.

Method: We performed a retrospective single-centre cohort study in 93 HD patients. The body composition was measured using the portable whole-body MBIS device, Body Composition Monitor-BCM(®) (Fresenius Medical Care, Bad Homburg, Germany). Blood pressure was measured with OMRON monitors.

Results: The mean age of patients was 64 ± 13 years, mean dialysis vintage 63 (1-352) months, 61% were men, all patients had arteriovenous fistula as vascular access. Sixty-nine (74.2%) patients were fluid overload (FO) with > 1.1 L overhydration. Other data are presented in table 1. We found a statistically significant correlation between the pulse pressure and ECW/ICW ratio (r=0.258; P=0.033) in FO patients. In contrast, there was no significant correlation between systolic, diastolic blood pressure and ECW/ICW ratio in FO patients.

Conclusion: Only pulse pressure and not systolic or diastolic blood pressure values measured before HD are associated with ECW/ICW ratio in FO patients.

Variable	*All patients (N=93) Mean ± SD*	*Fluid overload patients (N=69) Mean ± SD*	*NOT fluid overload patients (N=24) Mean ± SD*	*P value*
Age (years)	64.3 ± 13	64.3 ± 13	64.1 ± 12	0.943
Dialysis vintage (months)	63.2 ± 64	65.8 ± 68	55.8 ± 49	0.509
Systolic blood pressure (mmHg)	151 ± 21	151 ± 22	149 ± 19	0.708
Diastolic blood pressure (mmHg)	78 ± 13	79 ± 13	75 ± 12	0.168
Pulse pressure (mmHg)	73 ± 21	72 ± 22	75 ± 21	0.654
MBIS: Extracellular water (ECW) (L)	18.1 ± 4.2	19.03 ± 4.2	15.4 ± 3.1	**<0.0001**
MBIS: Intracellular water (ICW) (L)	18.8 ± 4.4	19 ± 4.5	18.3 ± 4.4	0.527
MBIS: ECW/ICW	0.97 ± 0.14	1.01 ± 0.13	0.84 ± 0.1	**<0.0001**
MBIS: Overhydration (L)	2.14 ± 1.9	2.83 ± 1.6	0.16 ± 1	**<0.0001**

P1304 **FIBROBLAST GROWTH FACTOR (FGF23) AND CARDIOVASCULAR MORTALITY IN DIALYSIS PATIENTS: A 10 YEAR PROSPECTIVE SINGLE CENTER STUDY**

Gülay Demirtaş[1], Sadan Turgut[2], Sabahat Ozdem[2], Gultekin Suleymanlar[2], Üstün Yılmaz[1], Fevzi F. Ersoy[2]

[1]Antalya Education and Research Hospital, Antalya, Turkey and [2]Antalya Akdeniz University Faculty of Medicine, Antalya, Turkey

Background and Aims: The aim of the study is to evaluate whether circulating fibroblast growth factor 23 (FGF23) predicts cardiovascular mortality in dialysis patients, independent of markers of calcium-phosphate metabolism and cardiovascular risk factors.

Method: A prospective observational study at Akdeniz University Medical Center including 51 peritoneal dialysis patients and 27 hemodialysis patients was undertaken from 01/2009 to 12/2019. Plasma C-terminal FGF23 concentrations in addition to other measures of mineral metabolism were performed at baseline. Patients were followed for all-cause mortality, cardiovascular mortality, non-fatal MI, non-fatal stroke, coronary revascularization, heart failure hospitalization and atrial fibrillation.

Results: The mean age of patients 48± 15 years. During a ten year follow up period, there were 47 deaths. The median plasma FGF23 level was 321 pg/ml (interquartile range 51-1784 pg/ml). Patients were stratified by their baseline FGF23 levels according to the tertiles. Cumulative survival analysis by tertiles of FGF23 were made with the Kaplan-Meier survival curve. Kaplan Meier analysis with log-rank did reveal a significant difference between the groups (p=0,048).

Conclusion: Higher FGF23 levels are associated with an increased incidence of cardiovascular mortality in dialysis patients, independent of other markers of calcium-phosphate metabolism and cardiovascular risk factors.

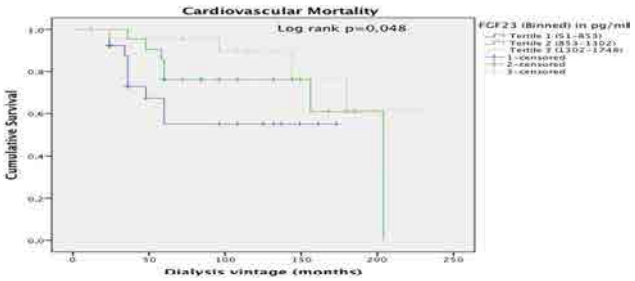


Figure:

P1305 **CARDIAC OUTPUT AND ESTIMATED UPPER BODY BLOOD FLOW**

Jochen Raimann[1], Gwendolyn Derk[2], Maria Fox[2], Elizabeth Poozhikunnel[2], Stephan Thijssen[1], Kenneth Wilund[2], Peter Kotanko[1,3]

[1]Renal Research Institute, Research Division, New York, United States of America, [2]University of Illinois at Urbana Champaign, United States of America and [3]Icahn School of Medicine at Mount Sinai Health System, United States of America

Background and Aims: Cardiopulmonary monitoring during hemodialysis has the potential to improve dialysis adequacy, prevent adverse events, improve quality of dialysis patients' lives and reduce mortality risks. Under stable conditions the knowledge of upper body oxygen consumption, the difference between arterial and venous oxygen saturation (ScvO2) and hemoglobin concentrations allow the calculation of estimated UBBF (eUBBF; Rosales 2019). We studied the association between eUBBF and cardiac output during hemodialysis.

Method: In patients with a central venous catheter as the vascular access, we simultaneously measured intradialytic central-venous oxygen saturation and hemoglobin levels once per minute using the Crit-Line Monitor (Fresenius Medical Care North America, Waltham, USA). Concomitantly we measured cardiac output (CO) using the Task Force Monitor (CNSystems, Graz, Austria). We depicted CO and eUBBF as box-whiskers in 5 minute periods from 20 to 180 minutes, tested the minute-level time series for stationarity using the Dickey-Fuller test, employed differencing to make the time series stationary, and tested for linear associations using cross-correlations and determined if the CO time series was useful to predict the eUBBF time series using the Granger Causality test.

Results: We studied 13 patients (59±14 years, 5 (38%) male, 93±22 kg pre-dialysis weight 170±7 cm tall) during 34 hemodialyses. CO and UBBF was 4.7±1.0 and 1.3±0.4 L/min, and showed a small trend downward for CO during hemodialysis. Cross-correlations showed no remarkable correlations for all treatments, Granger causality index was less than 20% in 8 treatments however without clearly discernible patterns.

Conclusion: Despite variability in the CO the eUBBF remains stable, a dynamic which pathophysiologically appears plausible. While testing for linear associations yielded no significant relationships, based on the Granger causality test there nevertheless appears to be some form of a relationship which requires some further investigation which will need to also include aspects such as fluid overload, body temperature and total peripheral resistance. Based on this data, cardiopulmonary monitoring appears possible and yields a reliable continuous overview of the hemodynamic status of a patient.

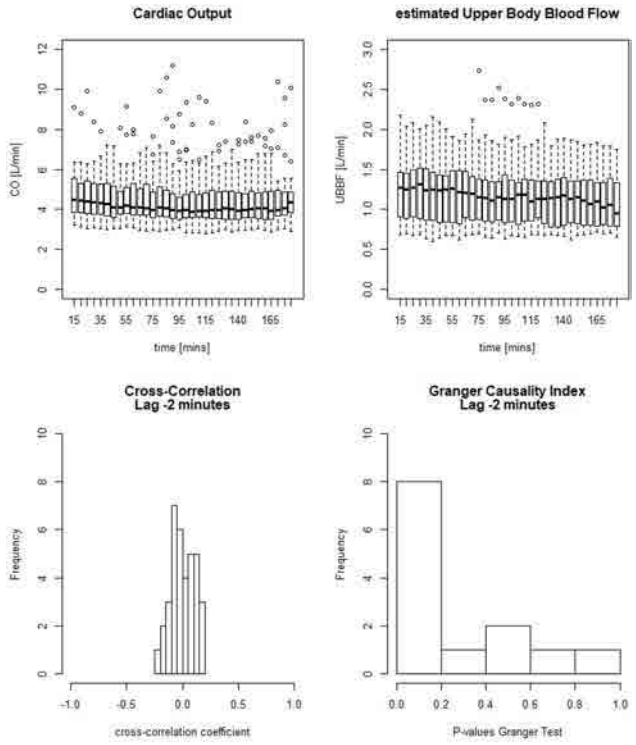


Figure: Dynamic of cardiac output and estimated upper body blood flows during 34 hemodialyses; correlation coefficient from cross-correlations and Granger Causality index at a lag of -2 minutes.

P1306 **EFFECT OF A SUPERVISED PERI- DIALYTIC EXERCISE PROGRAM ON SERUM ASYMMETRIC DIMETHYLARGININE IN MAINTENANCE HEMODIALYSIS PATIENTS**

Yaser Ammar[1], Ahmad Awad[2]

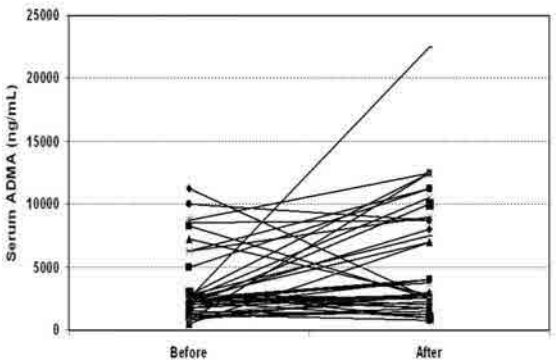
[1]Alexandria University, Medical Research Institute, Internal Medicine, Alexandria, Egypt and [2]Alexandria University, Medical Research Institute, Chemical Pathology, Alexandria, Egypt

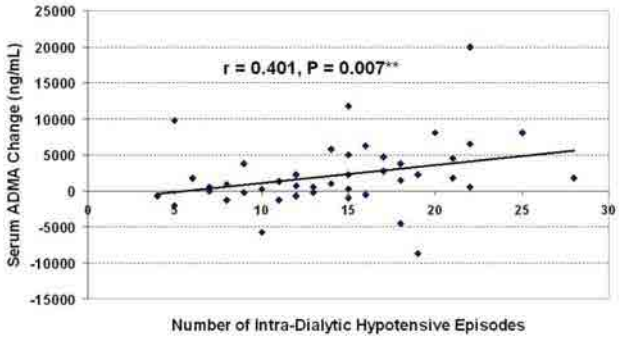
Background and Aims: End-stage renal disease (ESRD) patients treated with maintenance hemodialysis (MHD) have high cardiovascular disease morbidity and mortality. Accumulation of asymmetric dimethylarginine (ADMA), an endogenous nitric oxide synthase inhibitor, has been strongly implicated in endothelial dysfunction, premature atherosclerosis, vascular events and mortality. Regular physical exercise effectively decreased serum ADMA in several studies. This potential should be explored among MHD patients.

Method: Forty four middle-aged ESRD patients treated with thrice-weekly MHD for >6 months completed a 6 months regimen of peri-dialytic lower limb exercise comprising pre-dialytic 10-12 stretching cycles and 20-30 minutes of intra-dialytic pedalling cycles. Plasma ADMA, CRP, other laboratory parameters and overall physical activity level were assessed initially and at the end of the study.

Results: S.ADMA increased from a median of 2375 to 3000 ng/mL (P=0.016). 31 patients sustained an increase in S.ADMA (ADMA_Inc), whereas 13 patients had a declining or stable S.ADMA (ADMA_Dec). Compared with ADMA_Inc, ADMA_Dec patients had significantly higher Kt/V (P=0.02), significantly higher grade of basal general physical activity level (P=0.017) and significantly less intra-dialytic hypotension episodes (IDHs) (P=0.019). The increase in S.ADMA and the post- study S.ADMA level had statistically significant positive correlations with number of IDHs (r=0.401,P=0.007 and r=0.305,P=0.044, respectively).

Conclusion: A 6 months program of combined aerobic and resistance peri-dialytic exercise failed to reduce S.ADMA in most MHD patients studied. A modest S.ADMA decline, however, occurred in patients with higher basal exercise level, higher Kt/V, and less IDHs. A potential benefit of peri-dialytic exercise in decreasing S.ADMA may be promoted by a multidisciplinary approach targeting increased physical activity, improved dialysis efficiency and prevention of IDHs.





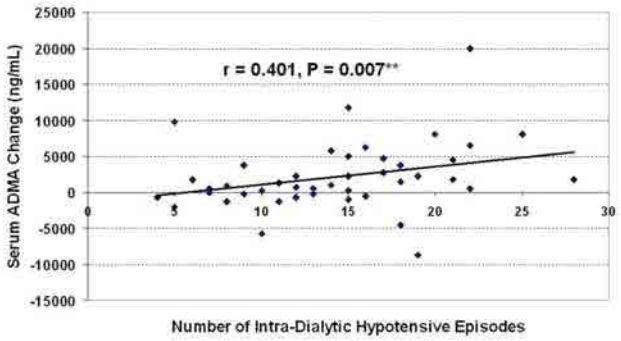


Figure:

P1307 HEMORRHAGIC VERSUS ISCHEMIC RISK IN PATIENTS WITH ATRIAL FIBRILLATION ON HEMODIALYSIS

Mariana Sousa[1], Pedro Bravo[1], Cristina Santos[1], Aura Ramos[1]
[1]*Hospital Garcia de Orta, Almada, Portugal*

Background and Aims: Patients with renal replacement therapy and atrial fibrillation (AF) have a particularly high risk of both stroke and bleeding, but no high-quality evidence-based recommendations exist to properly manage these patients. Therefore, we aim to evaluate the ischaemic versus the haemorrhagic risk in a hemodialysis (HD) population.

Method: We selected patients that started hemodialysis in our hospital between 2011 and 2015. Only incident patients that were on regular hemodialysis treatment for more than 3 months were considered. Both patients that already had AF before HD, or developed AF during the follow-up, were included. At the time of AF diagnosis or beginning of HD, the risk factors were analyzed based on CHA_2 DS_2 -VASC and HAS-BLED scores. The outcomes were hemorrhagic events (only the events that needed hospitalization were taken into account), ischaemic events (i.e. that result from embolic arterial ischaemia) and death related to any of these events.

Results: From 302 incident patients on hemodialysis, 46 (15.23 %) were included. Mainly man (65%), with a mean age of 75 ± 10 years old. Most of the patients (63%) already had AF when they started hemodialysis. There was no significant difference between the incidence of ischaemic and haemorrhagic events (p=0.219). Three patients died of an ischemic event and two of haemorrhagic shock.Twenty one patients (45.6%) started oral anticoagulation. No difference was found between the proportion of haemorrhagic events between patients with oral anticoagulation and patients with no anticoagulation (p=0.157). Similarly, oral anticoagulation was not associated with any effect on the incidence of ischaemic events (p=0.366). The results after adjustment for the risk factors included in the HAS-BLED and CHA_2 DS_2-VASC scores were the same.

Previous stroke, transient ischaemic attack or thromboembolic event significantly increased the risk of an ischaemic event, when adjusted to oral anticoagulation, age, diabetes, vascular disease and hypertension (OR 6.78, C.I 95% 1.236-37.278, p=0.028). This risk factor was not associated with an increase of haemorrhagic events. No other risk factor included in the scores was associated with any significant effect in the outcomes.

Conclusion: As we know, AF increases the risk of ischaemic events in general population. However, in hemodialysis patients, we didn't observe any difference between the incidence of ischaemic and haemorrhagic events. Therefore, the benefit of oral anticoagulation in such patients remains questionable. It is worth noting that patients with previous stroke, transient ischemic attack or thromboembolic event seem to have higher risk of new ischaemic events. In these patients, there may be some advantage in oral anticoagulation. Since this is a single center, retrospective, observational study, these results should be interpreted with caution.

Ischaemic events	*p value*	*Odds ratio*	95% C.I.	
			Inferior	Superior
Hypertension	,494	,396	,028	5,636
Diabetes Mellitus	,921	,923	,189	4,499
Previous stroke, transient ischaemic attack or thromboembolic event	,028**	6,789	1,236	37,278
Vascular disease	,349	2,257	,411	12,398
Anticoagulation	,448	,510	,090	2,901
Age>65 years old	,354	3,434	,253	46,584
Constant	,371	,169		

Figure: Impact of risk factors on ischaemic events. Abbreviations C.I: Confidence interval **p value <0.05

P1308

PHOSPHATE-LOWERING USING SUCROFERRIC OXYHYDROXIDE: CALCIFICATION PROPENSITY (T50) IN HEMODIALYSIS PATIENTS. POST-HOC ANALYSES OF A RANDOMIZED, CONTROLLED CLINICAL TRIAL.

Ursula Thiem[1], Rodrig Marculescu[2], Andreas Pasch[3], Maria Haller[1], Daniel Cejka[1]

[1]Ordensklinikum Linz, Medicine III - Nephrology, Transplantation, Rheumatology, Linz, Austria, [2]Medical University of Vienna, Laboratory Medicine, Wien, Austria and [3]Calciscon AG, Nidau, Switzerland

Background and Aims: Lowering serum phosphate with sucroferric oxyhydroxide (SO) therapy reduces calcification propensity (measured with the T_{50} test) in hemodialysis patients (Cejka et al. Abstract FR-PO149, ASN Kidney Week 2019). Intriguingly, we observed considerable inter-patient variability for changes in T_{50} in response to SO treatment, despite similar reductions in serum phosphate.

Method: Post-hoc analysis of a randomized, controlled cross-over study investigating the effects of serum phosphate lowering using oral phosphate binder therapy with SO on calcification propensity (T_{50}). Patients with changes of serum phosphate of approximately -0.5 mmol/l between phosphate binder wash-out and high dose (2000 mg/d) SO and were selected and classified as "responders" (showing profound changes in T_{50}) and "non-responders" (showing very little change in T_{50}). Data are shown as means ± SD.

Results: "Responders" (N=4) and "non-responders" (N=4) showed similar degrees of lowering of serum phosphate with high-dose SO treatment (-0.47 ± 0.06 vs. -0.49 ± 0.01 mmol/l). "Responders" showed marked increases in T_{50} (+108 ± 26 min), but "non-responders" did not (+6 ± 24 min). When comparing other laboratory parameters during the wash-out phase between "responders" and "non-responders", no obvious difference in single parameters or pattern of laboratory parameters was apparent for ionized calcium (1.11 ± 0.1 vs. 1.01 ± 0.1 mmol/l), phosphate (1.76 ± 0.31 vs. 2.06 ± 0.47 mmol/l), T_{50} (285 ± 82 vs 271 ± 38 min), albumin (3.9 ± 0.2 vs. 4.1 ± 0.4 g/dl), magnesium (1.07 ± 0.17 vs. 0.98 ± 0.14 mmol/l), bicarbonate (22.0 ± 3.6 vs. 24.1 ± 3.0 mmol/l), iPTH (301 ± 156 vs. 463 ± 303 pg/dl) or iFGF23 (6903 ± 9480 vs. 1097 ± 927 pg/ml).

Conclusion: Similar degrees of phosphate lowering do not lead to a similar improvements in T50. T_{50} "responders" versus "non-responders" cannot be identified using current standard laboratory parameters.

P1309

RIGHT VENTRICULAR-PULMONARY ARTERIAL UNCOUPLING IN PATIENTS ON CHRONIC HEMODIALYSIS WITH SEVERE RIGHT VENTRICULAR REMODELING

Gregorio Romero-González[1,2], Agnes Diaz-Dorronsoro[2,3], Ana De la Fuente[3], Susanna Ravassa[2], Nuria Garcia-Fernandez[1], Paloma Leticia Martin-Moreno[1], Javier Lavilla[1], Omar González[1], Miguel A. Rojas[1], Ignacio Lorenzo[1], Isabel García-Trigo[1], Noelia Ania[1], Elena Osácar[1], Ana Sabalza[1], Pilar Amézqueta[1], Begoña López[2], Arantxa González[2], Javier Diez[1,2,3]

[1]University of Navarra Clinic, Nephrology Department, Pamplona, Spain, [2]CIMA (Center for Applied Medical Research) University of Navarre, Cardiovascular Disease, Pamplona, Spain and [3]University of Navarra Clinic, Cardiology Department, Pamplona, Spain

Background and Aims: Patients on chronic hemodialysis (HD) may present right ventricular (RV) dysfunction and increased pulmonary artery pressure (PA). The aim of the current study is to describe the RV-PA coupling in chronic patients on HD.

Method: This study explored the adequacy of RV-PA coupling in 41 patients on HD. They underwent a comprehensive transthoracic Doppler echocardiography, and were stratified in accordance with the severity of RV remodeling defined by the presence of RV dilation (tricuspid annulus $\geq$40 mm) and RV systolic dysfunction (tricuspid annulus systolic excursion plane [TAPSE] $<$17 mm). RV-PA coupling was estimated by the TAPSE to PA systolic pressure (TAPSE:PASP) ratio.

Results: Three groups of patients were identified: No RV remodeling (Group 1, n=26), mild-to-moderate RV remodeling (Group 2, n=11) and severe RV remodeling (Group 3, n=4). Compared to patients from Groups 1 and 2, patients from Group 3 exhibited significant lower TAPSE values ($p<0.001$), a tendency to higher PASP values (p=0.054) and significant lower TAPSE:PASP ratio values (p=0.012). C-reactive protein levels and were directly correlated with PASP (r=0.405, p=0.017) and inversely with TAPSE (r=-0.311, p=0.041) and the TAPSE:PASP ratio (r= -0.392, p=0.015) in all patients. These echocardiographic parameters were not correlated with other biochemical, hemodynamic or anthropometric parameters.

Conclusion: These findings suggest that RV-PA coupling is markedly decreased in HD patients with severe RV remodeling. The role of systemic inflammation in RV remodeling and RV-PA uncoupling in HD patients warrants further studies.

P1310 **STUDY OF RISK FACTORS AND PREVALENCE OF PULMONARY HYPERTENSION IN CKD 5D PATIENTS ON HEMODIALYSIS**

Shankar Prasad Nagaraju[1], Ganesh Paramasivam[2], Ravindra Attur Prabhu[1], Dharshan Rangaswamy[1], Indu Ramachandra Rao[1], Srinivas Vinayak Shenoy[1], Mohan V Bhojaraja[1], Vasudeva Guddattu[3]

[1]Kasturba Medical College, Manipal,Manipal Academy of Higher Education, Manipal,India, Nephrology, Manipal, India, [2]Kasturba Medical College, Manipal,Manipal Academy of Higher Education, Manipal,India, Cardiology, Manipal, India and [3]Prasanna School of Public Health, Manipal Academy of Higher Education,Manipal, Department of Statistics, MANIPAL, India

Background and Aims: Pulmonary hypertension (PH) in chronic kidney disease stage 5D (CKD5D) patients on haemodialysis (HD) is associated with increased morbidity and mortality. We studied the risk factors and prevalence of PH in patients on HD at our centre. We also studied its association with oxidative stress and markers of inflammation.

Method: After ethics committee clearance, we conducted a cross-sectional study on CKD5D patients at our centre from June 2016 to May 2017. Patients on maintenance HD for at least 3 months were included. Demographic, clinical, biochemical and transthoracic echocardiography details were collected. PH was defined as estimated mean pulmonary artery pressure (mPAP) greater than 25 mm Hg at rest. PH was further categorized into mild (mPAP b/w 25-40mmHg), moderate (mPAP b/w 40-60mmHg) and severe PH (mPAP > 60mmHg). Serum thiol and C Reactive protein (CRP) were studied as markers of oxidative stress and inflammation respectively. Data was analysed using SPSS version 16.

Results: Out of 52 patients, 28 (54%) had PH. Twenty four out of these patients had mild PH (Figure 1). None had severe PH. The baseline characteristics of patients with and without PH are shown in Figure 2. No clinical or biochemical factors ($p>0.05$) were found as significant risk factors in our study. CRP (p-0.76) (inflammatory marker) and Thiol levels (p-0.36) (oxidative stress marker) did not had any relationship with occurrence of PH. (Table 1).

Conclusion: CKD 5D patients on HD have high prevalence of PH. There were no identifiable risk factors. The prevalence of PH was not influenced by dialysis vintage,

Table 1 : Demographic, clinical, biochemical, echocardiographic findings of study population (CKD 5D on haemodialysis) with and without pulmonary hypertension

Characteristics	Total (52)	PH(Yes)(28)	PH(No)(24)	P value
Clinical				
Age(years) ##	**57(47,68)**	**57(46,66)**	**57(52,68)**	**0.31**
Sex(Male)	**40**	**19**	**21**	**0.09**
DM*	**17**	**10**	**7**	**0.61**
DM Duration	**4.4(3,9)**	**4.4(3,9)**	**4.4(3,9)**	**0.65**
HTN#	**51**	**28**	**23**	**0.12**
HTN duration	**10(5,10)**	**10(4,11)**	**11(5,12)**	**0.54**
Residual urine (UOP<100 ml)	**34**	**20**	**14**	**0.32**
Access (AV Fistula)	**48**	**26**	**22**	**0.13**
CVA $	**2**	**1**	**1**	**0.91**
IHD +	**7**	**3**	**4**	**0.53**
SMOKING	**2**	**1**	**1**	**0.27**
Dialysis Vintage(Months)	**36(22,91)**	**30(22,84)**	**47(24,97)**	**0.42**
WEEKLY Ultra˚ltration (ml/hour/kg)	**15(11,18)**	**15(11,18)**	**15(11,18)**	**0.83**
Biochemical Characteristics				
HgB (g/L)##	**9.7(8.8,10.5)**	**9.1(8.6,10.5)**	**10.2(9.2,10.8)**	**0.14**
Calcium(mg/dl)##	**8.5(8.1,8.9)**	**8.7(8.2,9.0)**	**8.2(7.9,8.9)**	**0.16**
Phosphorous(mg/dl)##	**4.4(3.2,5.6)**	**4.5(3.2,5.1)**	**4.7(3.5,6.5)**	**0.08**
Albumin(g/L)##	**4.05(3.8,4.2)**	**4.1(3.9,4.2)**	**4(3.7,4.1)**	**0.12**
PTH(ug/ ##	**333(175,561)**	**366(182,544)**	**219.4(156,520)**	**0.66**
Ferritin (mg)##	**1214(990,1781)**	**1224(1037,1987)**	**1204(376,1681)**	**0.64**
CRP (mg/dl)	**2.1(1.3,5.3)**	**2(1.3,5.8)**	**2.2(1.5.4)**	**0.76**
THIOL(umol/L)	**266(182,605)**	**304(146,776)**	**223.9(187,417)**	**0.36**
Echocardiographic ˚ndings				
Ejection Fraction (%)##	**63.5(57.7,66)**	**62(53,65)**	**65(62,67)**	**0.31**
LVH Left Ventricular Hypertrophy(LVH)	**37**	**18**	**19**	**0.49**
Regional wall motion abnormality(RWMA)	**7**	**4**	**3**	**0.63**
Tricuspid regurgitation(TR)	**43**	**28**	**15**	**0.001**
Mitral Regurgitation(MR)	**32**	**23**	**9**	**0.002**
Left Ventricular systolic dysfunction(LVSD)	**9**	**8**	**1**	**0.09**
Left ventricular diastolic dysfunction(LVDD)	**13**	**8**	**5**	**0.58**
Right ventricular Systolic dysfunction(RVSD)	**4**	**4**	**0**	**0.07**

*DM- Diabetes Mellitus,

#HTN-Hypertension, $CVA-Cerebro vascular Accident, + IHD –Ischemic heart disease,

**CRP – C reactive Protein, THIOL MDA,

###Mean,

##Median

ultrafiltration, paratharmone levels, presence of co-morbidities, oxidative stress or inflammation.

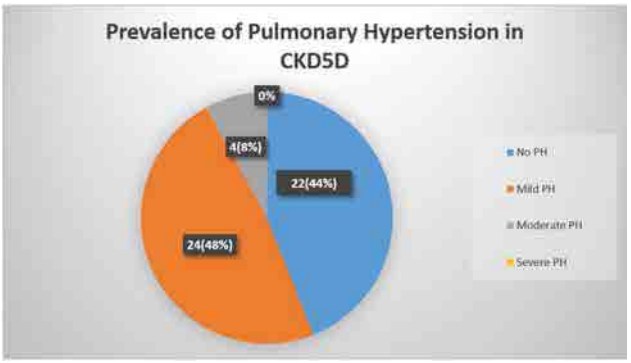


Figure 1:

DIALYSIS. VASCULAR ACCESS

P1318 EPIDEMIOLOGY OF BLOODSTREAM INFECTIONS IN A SCOTTISH HAEMODIALYSIS POPULATION WITH FOCUS ON VASCULAR ACCESS METHOD

Kirsty Crowe[1], Beth White[1], Nitish Khanna[1], Peter Thomson[1]
[1]*Queen Elizabeth University Hospital, United Kingdom*

Background and Aims: Haemodialysis (HD) vascular access infections account for approximately 28% of infection-associated hospitalisations in patients with end-stage renal disease[1]. Traditionally there has been focus on *Staphylococcus aureus (S. aureus*) infections, however there is increasing recognition of the burden of Gram-negative bloodstream infection (BSI) in the HD population[2,3].

Epidemiological analysis has enabled surveillance of the impact of antimicrobial protocols on BSI rate and outcome[2]. Scottish Registry data reflects that access methods are changing alongside the HD population phenotype, with increasing use of arterio-venous graft (AVG) and central venous catheters for incident and prevalent HD access[3].

In this study, the rate of BSI in a contemporary Scottish HD cohort is reported by microbial species and vascular access type: arterio-venous fistula (AVF), AVG, tunnelled central venous catheter (TCVC) or non-tunnelled central venous catheter (NTCVC).

Method: The Strathclyde Electronic Renal Patient Record (SERPR) database for the West of Scotland was utilised to obtain retrospective observational data all adult patients attending inpatient and outpatient renal services across seven dialysis units between 1st January 2017 and 31st December 2017.

All BSIs were analysed as separate episodes if more than 14 days apart, regardless of the suspected source of infection, and expressed as events per 1000 HD days. The number of days each patient was exposed to each vascular access subtype was calculated utilising the prospectively recorded HD access observations. Prevalent HD vascular access type was noted for each BSI.

Results: There were 786 patients who underwent HD with 217 503 total HD days over the study period. A total of 147 separate BSIs occurred, involving 115 patients. A total of 168 organisms were encountered in these BSIs. There were 49 BSIs during 126, 674 HD days using AVF access, 14 BSIs during 25, 511 AVG HD days, 81 BSIs during 64, 353 TCVC HD days and 3 BSIs during 965 NTCVC HD days. Table 1 outlines the BSI rates by vascular access and organisms identified

Staphylococci-related BSI comprised the majority of events (51.7%), with *S. aureus* implicated in 47% of these BSIs. Coagulase-negative staphylococci were the most commonly identified organisms in the AVF, TCVC and NTCVC groups, with *S. aureus* the leading organism in the AVG group. Gram-negative organisms accounted for the next largest proportion of BSIs (27%) and were more prevalent in the TCVC and NTCVC groups.

Conclusion: AVF access subtype was associated with the lowest BSI rate, and NTCVC the highest which is in keeping with previous studies and one of the drivers for AVF as the preferred HD access type internationally. Staphylococci continue to represent a large proportion of BSIs in this cohort, however other organisms are prevalent. BSIs caused by Gram-negative organisms and *Candida* species were represented more heavily in the TCVC and NTCVC population, perhaps representing co-morbidity of these groups.

Table 1. Bloodstream infection rates by organism and vascular access subtype

No of BSIs per 1000 HD days	Bloodstream Infection Causative Organism(s)							
	All	*Staphylococcus aureus*	Coagulase negative staphylococcus	*Streptococcus* spp.	*Enterococcus* spp.	Other Gram positives	Gram-negatives	*Candida* species
All	0.68	0.17	0.23	0.04	0.02	0.10	0.20	0.02
AVF	0.39	0.03	0.16	0.05	0.02	0.06	0.13	0.01
AVG	0.55	0.31	0.00	0.00	0.00	0.20	0.08	0.00
TCVC	1.26	0.39	0.42	0.03	0.02	0.16	0.36	0.05
NTCVC	3.11	0.00	2.07	0.00	1.04	0.00	1.04	1.04

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P1319 **AMBIGUOUS RESULTS OF CENTRAL VEIN STENOSIS ENDOVASCULAR TREATMENT IN HEMODIALYSIS PATIENTS**

Aleksei Zulkarnaev[1], Zurab Kardanakhishvili[2], Boris Baykov[3]

[1]Moscow Regional Research and Clinical Institute, Surgical department of transplantation and dialysis, Moscow, Russia, [2]M. E. Zhadkevich Moscow City clinical hospital, Department of vascular surgery, Moscow, Russia and [3]Moscow Hospital for war veterans No. 2, Department of vascular sur, Moscow, Russia

Background and Aims: Balloon angioplasty (BA) without the use of stents has unsatisfactory results, which may cast doubt on its expediency. At the same time, BA is a very expensive treatment method. We conducted a comprehensive comparative analysis of the native arteriovenous fistula (AVF) patency rates in hemodialysis patients with central venous stenosis (CVS) after endovascular BA and «open» palliative surgery.

Method: A retrospective study included 80 patients with confirmed central vein stenosis: subclavian, brachiocephalic veins, vena cava inferior, or multiple lesions. The main group included 39 patients who underwent percutaneous balloon angioplasty. The control group included 41 patients who did not have balloon angioplasty for various reasons. In this patients we performed only «open» palliative interventions: thrombectomy, proximalization of arteriovenous anastomosis, AVF blood flow reduction.

Results: Functional primary patency (the time interval between the start of AVF using and the first intervention) did not differ: groups were comparable in time of stenosis manifestation (fig. 1A). Primary patency (the time interval between the first and second interventions) after BA was statistically significantly better than in the main group (fig. 1B), but difference was minimal: median survival in the study group of 8 months [95% CI 6; 10] vs. - 6 months [95% CI 4.9; 7.1].

There was the strong negative correlation between the primary patency and functional primary patency in the main group ($r = –0.627$ [95%CI –0.787; –0.388], $p < 0.0001$) but not in the control group ($r = 0.049$ [95%CI –0.262; –0.351], $p = 0.7599$). Thus, the later manifestation of CVS related with lower effectiveness of BA.

The functional secondary patency (total duration of AVF use) in the main group was significantly better: median survival was 47 months [95% CI 40.9; 53.1] vs. 34 months [95% CI 29.8; 38.2] as well as secondary patency (the time interval between the first intervention and the complete cessation of AVF use): median survival was 16 months [95% CI 12.5; 19.5] vs. 7 months [95% CI 4.9; 9.1] (fig. 1 C and D).

The occlusion-free period from the moment of starting the AVF use (functional primary assisted patency – fig. 1E) was higher in the main group, but difference was minimal: median survival was 39 months [95% CI 36.5; 41.5] vs. 32 months [95% CI 27.5; 36.5], as well as occlusion-free period from the moment of the first surgical

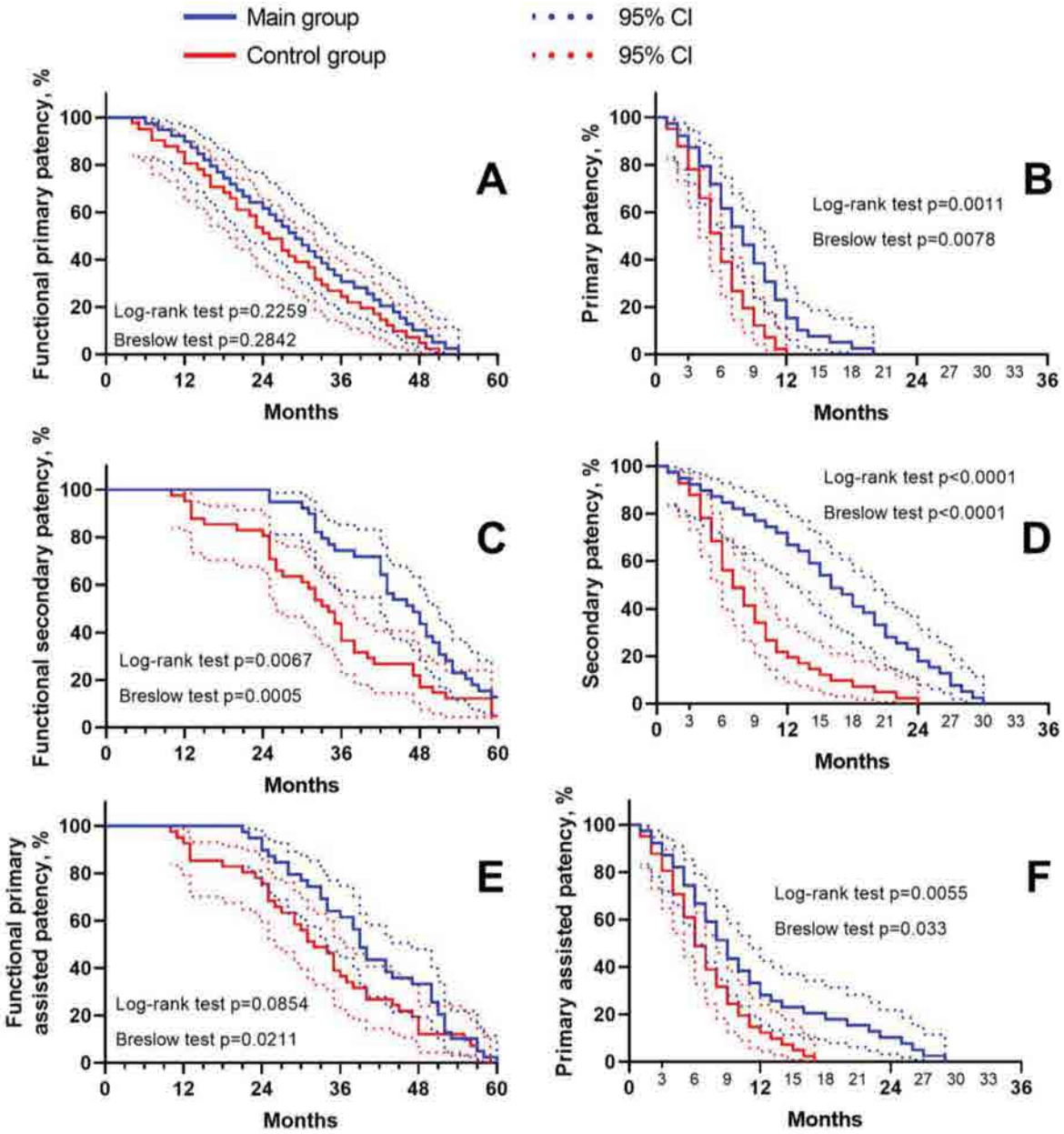


Figure:

intervention (primary assisted patency – fig. 1F) median survival was 9 months [95% CI 7; 11], in the control group - 7 months [95% CI 5.6; 8.4].

The need for open interventions was lower in the main group: 0.374 [95% CI 0.24; 0.556] and 2.451 [95% CI 1.1963; 3.023] per 10 patient-months, incidence rate ratio (IRR)= 0.153 [95% CI 0.095; 0.237], $p<0.0001$; as well as overall need for interventions:

1.511 [95% CI 1.225; 1.843] and 2.451 [95% CI 1.963; 3.023] per 10 patient-months, IRR 0.617 [95% CI 0.461; 0.825] p=0.0011.

The value of AVF volume blood flow had a strong negative correlation with the primary patency in both groups ($r = –0.529$, $p = 0.0027$; $r = –0.419$, $p = 0.0101$).

Conclusion: 1. Central vein stenosis is inevitably leads to loss of vascular access on the ipsilateral side. 2. Balloon angioplasty allows to extend the period of AVF use but it is not a radical treatment method of CVS. 3. The results of balloon angioplasty are significantly affected by the length of the period from the start of AVF use to the CVS manifestation. 4. Multiple repeated BA are apparently justified in patients for whom the possibility of creating a new vascular access is doubtful. 4. The AVF volume blood flow is an important factor determining the severity of CVS clinical manifestations and the need for repeated surgical interventions.

P1320 **ASSESSMENT OF ARTERIOVENOUS FISTULA DYSFUNCTION WITH ACCESS STENOSIS IN HEMODIALYSIS PATIENTS USING SMART-PHONE VIDEOS**

Lin-Chun Wang[1], Fansan Zhu[1], Ohnmar Thwin[1], Lela Tisdale[1], Xia Tao[1], Vaibhav Maheshwari[1], Alhaji Cherif[1], Norbert Shtaynberg[2], Kamran Karimi[2], Dean Preddie[2], Stephan Thijssen[1], Peter Kotanko[1,3]

[1]Renal Research Institute, New York, United States of America, [2]Azura Vascular Care, New York, United States of America and [3]Icahn School of Medicine at Mount Sinai, New York, United States of America

Background and Aims: Vascular access dysfunction is one of the leading causes of morbidity and a major contributor to healthcare costs in hemodialysis (HD) patients. Inexpensive, non-invasive tools for routine assessment of vascular access function are needed. Hemodynamically relevant stenoses in arteriovenous fistulas (AVF) lead to a reduction in access flow rate (Q_a) and changes in blood flow patterns in the AVF that may be picked up by palpation and auscultation. We hypothesized that these changes in blood flow patterns can not only be felt and heard but also seen, i.e., that they may be detectable in video recordings done with commercially available smartphones after digital motion augmentation.

Methods: We studied HD patients with AVF dysfunction requiring balloon angioplasty and/or stenting. One-minute video recordings of the skin above the AVF and Q_a measurements were conducted before and after the endovascular intervention. Videos were recorded with an iPhone 6S (Apple Inc., Cupertino, CA, USA). Q_a was measured by HVT100 endovascular flowmeter (Transonic Systems Inc., Ithaca, NY, USA). Significant access stenosis was defined as a >50% reduction of luminal diameter. Degree of stenosis was assessed by angiography. Frame-to-frame pixel changes in video images were amplified using "Eulerian Video Magnification" (Massachusetts Institute of Technology, MA, USA; http://people.csail.mit.edu/mrub/evm/#code). The time-domain data were then transformed into the frequency-domain signals. Fifty random 10-second segments were sampled per one-minute video, and the frequency with the lowest magnitude (F_{min}) was determined in each sample (example shown in Fig. 1). The average F_{min} was then assessed for its association with the degree of AVF stenosis.

Results:

Ninety subjects were studied (Table 1). AVF interventions were successful in all patients. Post-intervention Q_a (1638 ± 714 ml/min) was on average 1.23-fold higher than pre-intervention Q_a (1373 ± 684 ml/min; P<0.01, paired t-test). Subjects were grouped by degree of stenosis, and the number of subjects in each category is shown in Fig. 1B. Higher degrees of stenosis were associated with greater increases in Q_a from before to after the intervention (P<0.01, one-way ANOVA; Fig. 1C). Interestingly, the degree of AVF stenosis was also positively related with the change in F_{min} from before to after the intervention (P=0.08, one-way ANOVA; Fig. 1D).

Conclusion:

Simple smartphone video recordings of AVF appear to contain frequency-domain information that correlates with hemodynamic changes caused by AVF stenoses. While the F_{min} metric employed in our analysis is not ideal, these results should encourage the quest for other parameters that exhibit higher correlations with vascular access dysfunction. If successful, this would allow commercially-available smartphones to be used as ubiquitous tools for quick, non-invasive, ambulatory surveillance of AVF function, thereby allowing timely referrals and avoidance of emergency interventions.

Table 1. Patient Characteristics

	All (n=90)	Diabetes (n=58)	No diabetes (n=32)
Age [years]	63.27 ± 14.3	65.5 ± 13.3	59.3 ± 14.3
Sex [F/M]	41 / 49	25 / 33	16 / 16
Race			
White	12 (13.3%)	6 (10.4%)	6 (18.8%)
Black	50 (55.6%)	35 (60.3%)	15 (46.9%)
Other	28 (31.1%)	17 (29.3%)	11 (34.3%)
Ethnicity			
Hispanic	22 (24.4%)	15 (25.9%)	7 (21.9%)
Not Hispanic	68 (75.6%)	43 (74.1%)	25 (78.1%)
Diabetes	58 (64.4%)	58 (100%)	0 (0 %)
Hypertension	79 (87.8%)	55 (94.8%)	24 (75%)
CAD	18 (20%)	15 (25.9%)	3 (9.4%)
HD Vintage [years]	4.1 ± 3.5	4.5 ± 4.0	3.5 ± 3.5
Weight [kg]	78.6 ± 21.5	80.0 ± 21.2	76.2 ± 21.5
BMI [kg/m^2]	27.6 ± 6.9	28.0 ± 6.9	26.8 ± 6.9

Values are means ± SD or count (%) as appropriate. BMI: body mass index, CAD: coronary artery disease.

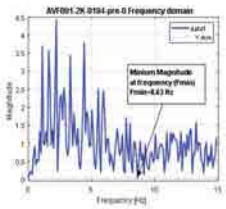


Fig 1A. Sample frequency domain analysis

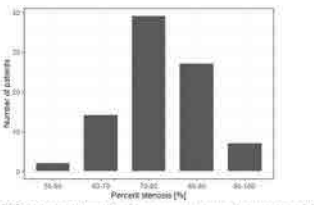


Fig 1B. Number of patients in each representative group of percent stenosis

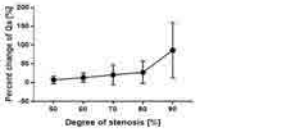


Fig 1C. Percent change of Qa versus degree of stenosis. Percent changes are expressed relative to pre-intervention values.

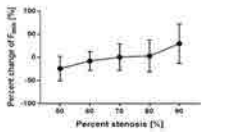


Fig 1D. Percent change of F_{min} versus percent stenosis

Figure:

P1321 PLASMATIC OSTEOPONTIN: A PREDICTOR OF VASCULAR ACCESS DYSFUNCTION IN HEMODIALYSIS PATIENTS

Nirvana Sadaghianloo[1,2], CONTENTI Julie[2,3], Vido Sandor[4], Carboni Joseph[1], Bonnet Sophie[5], Serge Declemy[1], Nathalie M. Mazure[2]

[1]Centre Hospitalier Universitaire de Nice - Hôpital Pasteur, Vascular Surgery, Nice, France, [2]Centre Méditérranéen de Médecine Moléculaire - INSERM U1065, Nice, France, [3]Centre Hospitalier Universitaire de Nice - Hôpital Pasteur, Emergency medicine, Nice, France, [4]Centre Hospitalier Universitaire de Nice - Hôpital Pasteur, Nephrology and Hemodialysis, Nice, France and [5]Centre Hospitalier Universitaire de Nice - Hôpital Pasteur, Clinical Research and Innovation, Nice, France

Background and Aims:

Despite recommendations for a close follow-up of arteriovenous fistulas (AVF), thrombosis rate reaches 10% each year. Conventional follow-up modalities remain a burden for hemodialysis patients. We tested the hypothesis that osteopontin (OPN), a pro-inflammatory molecule related to intimal hyperplasia, could be a biological marker of stenosis, and could thereby allow a screening of patients at risk for AVF dysfunction.

Method:

Our prospective study (NCT03270358) compared the rate of plasmatic OPN between patients with a good-functioning AVF (control group, N= 39) and patients who required surgical or endovascular revision of their AVF because of a stenosis (stenosis group, N= 37). Blood samples were taken in the AVF, at the time of AVF cannulation in control patients, and at the time of AVF revision in stenosis patients. For each patient, blood from the contralateral arm was also analyzed as a between-subject control (paired *t* test). Cardiovascular risk factors, ongoing medications, and OPN rates (ELISA technique) were compared among the groups (uni- and multivariate analysis). The ROC curve determined sensitivity and specificity of the marker for the detection of stenosis.

Results:

Patients' characteristics were similar between the 2 groups (mean age, 70 years; men, 63%; AVF duration; 39 months), apart from diabetes (control group, 33%; stenosis group, 57%; p=0.04). The rate of OPN was similar between the AVF arm and the contralateral arm (p=0.11), but significantly increased in the stenosis group compared to the control group (655 vs. 452 ng/mL, respectively, p=0.02). There was no statistically significant difference in OPN rate for diabetics and non diabetics (two-way ANOVA, p= 0.50). Sensitivity was 89% for a threshold >293ng/mL and specificity was 80% for a threshold >567ng/mL (AUC: 0.70; 95%CI: 0.57-0.81; p=0.004). Patients with an OPN rate ≥293ng/mL and those with an OPN rate ≥567ng/mL had respectively 8.87 and 15.62 higher odds to have a stenosis than patients with an OPN rate <293ng/mL (binomial regression, p<0.01).

Conclusion:

Plasmatic OPN rate in hemodialysis patients can be measured simply, in a blood sample taken at the time of AVF cannulation, and is strongly correlated to the presence of a symptomatic AVF stenosis. This biomarker could help the physician choose which patient need a comprehensive examination of his/her AVF with duplex ultrasound or fistulogram.

P1322 EFFECTS OF HAEMODIALYSIS ARTERIOVENOUS FISTULA CREATION ON CARDIAC STRUCTURE AND FUNCTION

Sokratis Stoumpos[1,2], Alastair Rankin[1], Pauline Hall Barrientos[3], Peter Thomson[2], Ram Kasthuri[3], David Kingsmore[2], Giles Roditi[3], Patrick Mark[1,2]

[1]University of Glasgow, Cardiovascular Research Centre, Glasgow, United Kingdom, [2]Queen Elizabeth University Hospital, Renal and Transplant Unit, Glasgow, United Kingdom and [3]Queen Elizabeth University Hospital, Radiology, Glasgow, United Kingdom

Background and Aims:

Arteriovenous fistula (AVF) is considered the preferred type of access for maintenance haemodialysis. The creation of an AVF may contribute to maladaptive cardiovascular remodelling. We conducted a study to evaluate the effect of AVF creation on cardiac structure and function in patients with end-stage renal disease (ESRD).

Method:

In this prospective cohort study, patients with ESRD listed for AVF creation underwent cardiac magnetic resonance imaging at baseline and at 6 weeks. All participants had ultrasound measurements of AVF blood flow at 6 weeks. The primary outcome was the change in left ventricular (LV) mass. Secondary outcomes included changes in LV volumes, left atrial volume, LV ejection fraction, LV global longitudinal strain, cardiac output/index, and septal thickness.

Results:

A total of 65 patients were enrolled, of whom 40 had an AVF creation and completed both scans. Patients were divided into 2 groups based on AVF blood flows: 22 in the high flow group ($\geq$ 600mL/min) and 18 in the low flow group ($<$ 600mL/min). On the second cardiac magnetic resonance scan, a mean increase of 7.4 g (95% CI, 1.1–13.7, P=0.02) was observed in LV mass; in the high flow group the mean increase was 15.5 g (95% CI, 7.3–23.8) compared with a small decrease of 2.5 g (95% CI, −10.6 to 5.6) in the low flow group (P=0.003). Significant increases in LV end-diastolic volumes, cardiac output, and cardiac index were also seen after AVF creation ($P<0.04$). No significant changes were observed in LV ejection fraction (P=0.52), LV end-systolic volumes (P=0.12), and LV global longitudinal strain (P=0.21).

Conclusion:

Creation of AVF in adults with ESRD resulted in significant increase of LV myocardial mass early after surgery.

P1323 HEMODIALYSIS TUNNELED CATHETER-RELATED BACTEREMIA: THIRTEEN-YEAR OBSERVATIONAL STUDY.

Marina Almenara Tejederas[1], Wenceslao Aguilera Morales[1], María Ángeles Rodríguez-Perez[1], Salia Virxinia Pol Heres[1], Mercedes Salgueira Lazo[1]

[1]*Hospital Universitario Virgen Macarena, Servicio de Nefrología, Sevilla, Spain*

Background and Aims: Tunneled catheter-related bacteremia (TCRB) is a common and severe cause of bacteremia among hemodialysis (HD)-dependent patients. TCRB have reported incidence of 0.5 to 5.5 events per 1000 catheter days and are associated with increased morbidity and death. The main objetive of our study is determinate the incidence of TCRB in our hospital and, secondarily, to analyze our microbiology, recurrence and reinfection rates.

Method: The study is an observational retrospective evaluation of medical records of patients in whom a TC for HD was implanted in the period from January 1, 2005, to December 31, 2018. The TC were implanted by nephrologists, following a preimplantation and management protocol agreed with the Infectious Diseases Unit.

Patients were followed up from TC insertion until the study end date or first of recovery kidney function, kidney transplantation, transition to peritoneal dialysis or death. CRB definition was according Spanish Clinical Guidelines on Vascular Access for Haemodialysis: positive blood culture accompanied by fever or clinical signs of sepsis, without another posible site of infection. We recorded demographic, clinical and TC-related variables (conditions of catheter insertion, site of catheter insertion and duration of use, etc.). Exclusion criteria for our study were the lack of clinical follow-up due to belonging to a different hospital area.

Results: A total of 393 TC were implantated over a period of 13 years. After applying exclusion criteria, we investigated 341 TC implanted in 279 patients: 265 into the intern jugular vein, 71 into the subclavian and 5 in femoral vein. The mean age of the included patients was 63 (range 19-93 years). Fifty-one percent of catheter was implanted in male patients. Forty-six percent of the patients suffered from diabetes mellitus. In 55% of the cases, the cause of CT implantation was the difficulty of creating an internal vascular access.

In total there were 91 CRB in 58 patients, with a rate of 0.48 infections per 1000 catheter days (figure 1), occurring at median 461 days (range 143-443 days) after catheter insertion. Within that group, 82.4% occurred after 6 months from the implementation of the CPT. Only 6 (6.59%) took place in the 30 days after implantation. Gram-positive organisms accounted of 85%, with a predominance of Staphylococcus epidermidis (47%) followed by Staphylococcus aureus (25%). A broad spectrum of Gram-negative bacteria accounts for 14% of patients. Nineteen TC were removed by CRB, with a rate of 5.5% of total functioning TC. CRB was the cause of death in 7 of the 279 patients (2.5%). During the study, 12 (13% of CRB) recurrences and 30 (32% of CRB) reinfections events have been identified.

Conclusion: The incidence of CRB in our population was found to be lower that previous studies. It usually appears in the long term, with Gram-positive germs as the most frequently involved. The temporality and low recurrence rate suggest that our protocol has been effective.

The high rate of reinfection orients a certain individual predisposition to suffer from CRB. Identification of potential predicting risk factors could reduce the morbimortality of these patients.

Figure 1. Incidence of CRB during the follow-up period.

	Implanted TC	Functioning TC	Functioning TC days	N° CRB	CRB rates/ year	Accumulated CRB rate	Removed TC
2005	8	8	848	0	0	0	0
2006	20	28	5624	4	0,71	0,61	0
2007	21	46	11077	7	0,63	0,62	0
2008	27	58	11556	10	0,86	0,72	5
2009	16	47	11222	4	0,35	0,61	1
2010	8	40	11625	9	0,77	0,65	0
2011	12	41	8237	13	1,57	0,78	3
2012	13	35	9453	8	0,84	0,78	0
2013	25	56	12864	6	0,46	0,73	2
2014	28	67	15081	7	0,46	0,69	0
2015	31	75	17333	3	0,17	0,61	0
2016	39	97	23130	7	0,30	0,56	3
2017	44	112	24599	10	0,40	0,54	4
2018	49	115	24846	3	0,12	0,48	1
TOTAL	342	115	187495	91	0,54	0,48	19

P1324 **TARGETING ZERO INFECTIONS IN HEMODIALYSIS PATIENTS. AN EXPERIENCE OF ONLY TWO CATHETER-RELATED BLOODSTREAM INFECTION (CR-BSI) OVER A PERIOD OF 1430 DAYS**

Claudio Luders[1], Carlucci Gualberto Ventura[1], Fabio DiNizo[1], Felicio Lopes Roque[1]

[1]*Hospital Sírio-Libanês, Hemodialysis, São Paulo, Brazil*

Background and Aims: Patients undergoing hemodialysis (HD) through a tunneled central venous catheter are exposed to several risks. Catheter-related bloodstream infection (CR-BSI) is the second major cause of death in this population. To reduce the incidence of CR-BSI we conducted a non-randomized pre-post intervention study aimed to eliminate all preventable CR-BSI.

Method: A quasi-experimental study was conducted in an intra-hospital hemodialysis unit with 15 HD machines and attending 70 patients until March 2019, and 24 machines and 90 patients from that date until today. The CDC, CR-BSI criteria for dialysis event surveillance protocol, defined as the presence of a positive blood culture with the suspect source report as the vascular access or uncertain was used to define CR-BSI. A sequential implementation of evidence-based interventions, associated in literature with the reduction of CR-BSI rate, were developed between January 2011 and January 2020. The intervention package included: 1. Alcohol based gel delivery system fixed in every HD machine to enhance hand hygiene adherence 2. A new strict aseptic protocol for connecting/disconnecting HD lines that included: 2.1 Wrapping catheter rubs for 1-2 minutes with alcoholic chlorhexidine-saturated gauze before removal catheters caps 2.2 Nurses and patients wear masks during catheter manipulation 2.3 Apply a sterile fenestrate drape with sterile gloves before removing the caps 2.4 The scrub-the-hub aseptic technic after removing the caps with alcoholic chlorhexidine-saturated gauze 2.5 Precocious use of Tissue Plasminogen Activator (rTPA) to correct inadequate blood flow, avoiding excess of catheter manipulation 3. Use of chlorhexidine-impregnated dressing changed once a week 4. Training all nurse staff admitted, catheter care skill evaluation semiannually, re-training when necessary and monthly infection rate feedback 5. Use of citrate 30% as lock solution.

Results: During the follow-up period (January 2011 to January 2020) a mean of 45 patients (range 30-55) used tunneled catheter as vascular access each year. The mean age was 69±15 years (range 11-96 years), with 60% of patients been diabetic. After implementation the of the new strategies we observed a continuous reduction in the CR-BSI rate: 2010 the year before strategies implementation CR-BSI rate was 1.1/1000 catheter-days; 2011 CR-BSI rate 0.6/1000 catheter-days; 2012 CR-BSI rate 0.6/1000 catheter-days; 2013 CR-BSI rate 0.1/1000 catheter-days; 2014 CR-BSI rate 0.1/1000 catheter-days; 2015 CR-BSI rate 0.2/1000 catheter-days; 2016 CR-BSI rate 0.2/1000 catheter-days; 2017 CR-BSI rate 0.0/1000 catheter-days, 2018 CR-BSI rate 0.08/1000 catheter-days, and 2019 CR-BSI rate 0.06/1000 catheter-days. Between April 10th of 2016 and January 10th of 2020, a 1430 days period, we observed only 2 CR-BSI. Between April 10th of 2016 and January 3rd of 2018 there was a period of 633 days with no CR-BSI.

Conclusion: Implementation of several evidence-based practices and continuous education can reduce CR-BSI in HD patients to a very low level. Targeting zero infection proposing to eliminate all preventable infection should be the routine practice of all dialysis units.

P1325 VASCULAR ACCESS OUTCOMES IN A FRAIL HAEMODIALYSIS POPULATION

Alice Radley[1], Wan Wong[2], Tara Collidge[1], Peter Thomson[1]

[1]Queen Elizabeth University Hospital, Renal and Transplant Unit, Glasgow, United Kingdom and [2]Queen Elizabeth University Hospital , Renal and Transplant Unit, Glasgow, United Kingdom

Background and Aims: Current guidelines recommend the pursuit of arteriovenous (AV) access over central venous catheter (CVC) access in haemodialysis (HD) populations. The limitations of this approach are increasingly recognised, and are particularly relevant when considering frail patients with relatively high levels of comorbidity and limited life expectancy. In such patients AV access may incur more invasive procedures, whereas CVC access may incur heightened risks of infection.

This study aimed to evaluate the association between HD access modality and access complications, hospitalisation and mortality in a cohort of HD patients with frailty.

Method: We performed a retrospective analysis of prospectively recorded data from the Strathclyde Electronic Renal Patient Record concerning HD patients from 01/10/2017 to 21/09/2019. HD patients with a Rockwood clinical frailty scale (CFS) $\geq$6 were identified with baseline demographic data being recorded from date of first CFS $\geq$6 to census date 21/09/19 or death. We recorded the first vascular access modality at study inception and the modality at the time of census or death.

Episodes of TCVC associated sepsis were determined using both clinical diagnosis in patient case records and positive blood cultures. Episodes were regarded as separate where positive blood cultures occurred $\geq$14 days apart. An inpatient admission was regarded as a discharge date $\geq$24 hours following admission. These were then further categorised as unscheduled or elective.

Results: 139 patients were identified with CFS $\geq$6. Median age was 72 years and 51% were female. Median follow-up was 1.1 years with total 50861 observed HD days. 52.3% patients were deceased at census.

Table 1 illustrates vascular access modality at initial CFS. CVC accounted for the greatest proportion of dialysis access days (50.3%) compared to AVF (40.7%) and AVG (8.9 %).

Table 1: Vascular access modality at first clinical frailty score

	No. of patients	TCVC (%)	non-TCVC (%)	AVF (%)	AVG (%)
Total	139	53.6	4.3	32.9	8.6
CFS 6	87	52.9	6.9	29.9	10.3
CFS 7	49	55.1	0	36.7	4.1
CFS 8&9	5	40.0	0	40.0	20.0

There was no significant difference in mortality between vascular access modalities over the follow-up period (50.7% CVC; 55% AVF; 54.5% AVG, p=0.18).

In total, 5244 HD exposed days (10.3%) were spent as an inpatient during follow-up, of which 5120 (98%) were unscheduled and 119 (2%) were elective.

The AVG group had the highest rate of inpatient bed days (138/1000 HD days) when compared to CVC (107/1000 HD days) and AVF (94/1000 HD days). Both AVG and CVC were associated with more inpatient bed days than AVF ($p<0.0001$ for each).

Patients who started with CVC and transitioned to AV access had a rate of 86/1000 HD days. This was significantly lower than those who remained CVC throughout (p=0.0001).

There were 24 recorded events of CVC associated sepsis during follow-up, occurring at a rate of 0.8 per 1000 HD days. Rates of CVC associated sepsis were similar between CFS 6 (0.6 per 1000 HD days) and CFS 7 (1.1 per 1000 HD days), p=0.21. The CVC associated staphylococcus aureus bacteraemia (SAB) rate for the overall population was 0.2 per 1000 HD days.

AVG sepsis occurred at a rate of 0.2 per 1000 HD days and there were no incidences of AVF sepsis in those who continued with AVF throughout the follow-up period.

Conclusion: CVC was the most prevalent access modality in this frail HD population. Rates of CVC associated sepsis and SAB were similar to published bloodstream infection rates and existing local data (Murray et al QJM 2014). Although absolute events were low, increasing frailty from CFS 6 "moderately frail" to CFS 7 "severely frail" did not appear to influence rate of CVC associated sepsis. Patients with CVC and AVG had greater inpatient bed days than those with AVF. Transitioning from CVC to AV access reduced inpatient bed days. However, the choice of vascular access modality did not influence mortality overall.

P1326 **NATIVE AVF ANEURYSMS RECONSTRUCTION: THE MULTI-CENTER EXPERIENCE**

Aleksei Zulkarnaev[1], Boris Baykov[2], Ewgenii Strugaylo[3], Zurab Kardanakhishvili[4], Natalia Fominykh[1], Vadim Stepanov[1]

[1]Moscow Regional Research and Clinical Institute, Surgical department of transplantation and dialysis, Moscow, Russia, [2]Moscow Hospital for war veterans No. 2, Department of vascular surgery, Moscow, Russia, [3]Dolgoprudny Central city hospital, Department of surgery, Dolgoprudny, Russia and [4]M. E. Zhadkevich Moscow City clinical hospital, Department of vascular surgery, Moscow, Russia

Background and Aims: to analyze the results of surgical correction of native arteriovenous fistula (AVF) aneurysms in hemodialysis patients.

Method: A retrospective observational study included 158 patients who underwent various surgical interventions. 87 patients (55.1%) underwent pre-emptive surgeries. 71 patients (44.9%) underwent surgeries after AVF thrombosis («on demand» surgery).

In the presence of high-flow AVF or in a case of high risk of fistula vein rupture, aneurysmorrhaphy was performed, which was supplemented by transposition of the reconstructed vein – fig. 1. In a case of paraanastomotic stenosis of the vein, aneurysmorrhaphy was enhanced by arteriovenous anastomosis proximalization. In a case of local proximal or distal stenosis of the functional segment of the vein, aneurysmorrhaphy was supplemented with stenosis plastic using the wall of the resected aneurysm. In a case of prolonged proximal stenosis or totally thrombosed proximal aneurysm, the fistula blood flow was switched to *v. basilica* with its transposition. In the case of a totally thrombosed distal aneurysm, it was excised and proximal AVF was created.

Results: In the case of pre-emptive surgeries, secondary patency was 69% [95% CI 44.9; 84.2] after 4.8 years (maximum follow-up). In the case of on-demand surgeries the secondary patency was 45.6% [95% CI 23.6; 65.2] after 4.3 years (maximum follow-up) – fig. 2. HR (log rank test) pre-emptive vs. on demand surgeries 0.296 [95% CI 0.147; 0.592], inverse HR = 3.381 [95% CI 1.674; 6.827], p = 0.0002.

The risk AVF function loss was lower in patients who received pre-emptive surgeries compared with patients who received on-demand surgery: 2.642 [95% CI 1.406; 4.519] versus 6.268 [95% CI 3.927; 9.49] per 100 patient-years, incidence rate ratio (IRR) = 0.422 [95% CI 0.207; 0.834] (inverse estimate IRR=2.372 [95% CI 1.2; 4.842]), p = 0.0127.

The need for CVC was also lower in patients who received pre-emptive surgeries: 1.728 [95% CI 1.38; 2.136] versus 2.821 [95% CI 2.292; 3.434] per 10 patient-years, IRR=0.6125 [95% CI 0.4576; 0.8185] (inverse estimate IRR= 1.633 [95% CI 1.222; 2.185]), p = 0.0009.

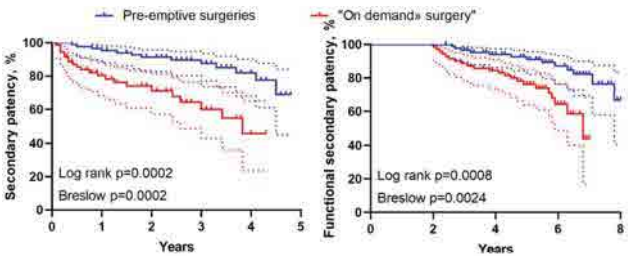
Moreover, the number of operations was significantly higher in patients who underwent pre-emptive surgeries: 4.207 [95% CI 3.654; 4.821] versus 2.963 [95% CI 2.421; 3.59] per 10 patient-years, IRR=1.42 [95% CI 1.124; 1.802] (inverse estimate IRR= 0.704 [95% CI 0.555; 0.89]), p=0.0031.

In almost all cases, fistula vein aneurism has been associated with various hemodynamic disorders. The median volume blood flow Qa was 2.9 [interquartile range - IQR 1.9; 3.8] l/min., (minimum. 1 l/min., max. 4.5 l/min.). Reconstruction in most cases led to significant change in Qa ($p<0.0001$). After reconstruction, the Qa median was 1.8 [IQR 1.6; 2.1] l/min. (minimum 1.4 l/min., max. 2.1 l/min). It is noteworthy that in patients with low Qa values, Qa increased slightly, and at high values, it decreased significantly. However, additional methods of blood flow reducing were not used. The median of the Qa difference was -1.2 [IQR -1.9; -0.2] l/min. (minimum -2.7 l/min, max. 1 l/min.).

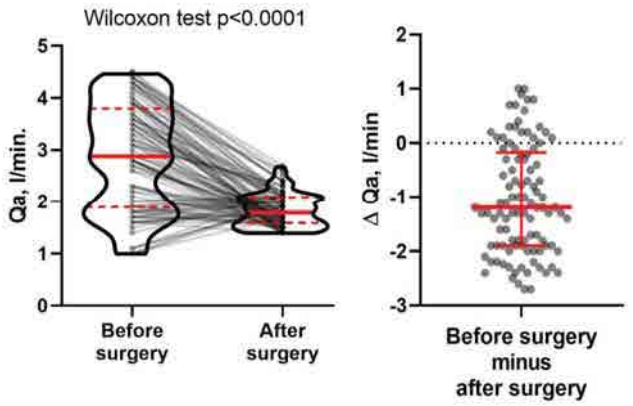
Conclusion: The indication for surgical treatment is not just aneurism, but its complications, the high risk of complications development or a combined pathology. Preventive surgical interventions can significantly extend the AVF patency and reduce the need for central venous catheters, however, this is achieved by significantly increasing the number of surgeries. The concept of routine monitoring of a normally functioning AVF by a surgeon should replace the concept of on-demand surgery in case of AVF thrombosis or development of other serious complications.



Figure:



1.



2.

P1327 STATUS OF AV FISTULA AFTER SUCCESSFUL RENAL TRANSPLANT ; A SINGLE CENTRE STUDY

Pratim Sengupta[1], Tarpan Sasmal[1], Sumanta Biswas[1]

[1]*ILS Hospital, Nephrology, Kolkata, India*

Background and Aims: Functioning AV-Fistula is considered the Achilles hill of ESRD patients. After successful renal transplantation considering the risk of graft failure or recurrence of disease all attempts are made to preserve the functional AV fistula except few clinical situations like high output cardiac failure, steal phenomenon or large aneurysm with risk of rupture where voluntary closure of AVF is preferred. Even with care and attention a significant number of AV-Fistula closes spontaneously. In this retrospective study we analyzed the fate of AVF after successful renal transplantation.

Method: The medical records 800 renal transplant recipients in last 15 years were analyzed with the objective to find out the outcome of AVF after transplant. Data were systematically charted and analyzed by SPSS V.23.01

Results: Out of 800 renal transplantation in last 15 years, excluding patients on CAPD or temporary catheter or AVgraft; 680 patients data were finally analyzed. Out of this 680 functioning AVF, 86 patients lost follow up and hence status of AVF could not be retrieved. Among rest 594 recipients, AV fistula was closed spontaneously in 184 cases (31.1%), and only 5 patients required planned AVF closure due to large aneurysm (2 cases), trauma and impending rupture (2 cases), cosmetic reason (1 cases). Incidence of spontaneous fistula closure was significantly higher among females than male recipients ($p=0.001$). Majority (62%) of the spontaneous closure occurred immediate post transplant period (within 7 days after transplant) and rest 26.4% within 1month and 9.2% in between 1 and 4 month. Only 2.4% fistula closed after 4 month of transplant. In the Tacrolimus era there is no significant difference in the rate of spontaneous closure with the patients who received cyclosporine ($p=0.78$). However among patient who received injectable cyclosporine the spontaneous closure was significantly higher ($p=0.001$). Factors which could be attributable to the rate of closure are, need of peripheral cannulation in perioperative period in the fistula arm ($r^2=0.89$), operative time more than 2and half hr ($r^2=0.78$), more than 2 unit of blood transfusion ($r^2=0.85$) during operation and dialysis vintage through AVF less than 6 month ($r^2=0.77$). There was no observed difference in rate of spontaneous closure among patients who received induction and who don't ($p=0.08$). In subgroup analysis among induction with basiliximab or thymoglobulin there was no significant difference in spontaneous fistula closure (p=0.07).

Conclusion: Spontaneous closure of AV fistula observed in 31.1% patients with successful renal transplantation. It is more common in female recipients and 97.6% of spontaneous closure takes place within 4month of transplant. The factors which are attributable for spontaneous closure are cannulation in the fistula arm, injectable cyclosporine use, operative time more than 2and half hr, blood transfusion more than 2 units, during operation.

P1328

EFFECTIVENESS OF MUSIC FOR ALLEVIATING PAIN DURING HAEMODIALYSIS ACCESS CANNULATION: A MULTI-FACILITY, SINGLE-BLIND, RANDOMISED CONTROLLED TRIAL

Tatsuyoshi Ikenoue[1], Masatsugu Kishida[2], Yosuke Yamada[3], Mineaki Kitamura[4], Emi Inayama[5], Kanae Takahashi[6], Ayumi Shintani[6]

[1]Kyoto University Graduate School of Medicine, Human Health Science, Kyoto, Japan, [2]National Cerebral and Cardiovascular Center, Department of Nephrology, Suita, Japan, [3]Shinshu University School of Medicine, Department of Nephrology, Matsumoto, Japan, [4]Nagasaki University Hospital, Department of Nephrology, Nagasaki, Japan, [5]Mihama Narita Clinic, Department of Nephrology, Narita, Japan and [6]Osaka City University Graduate School of Medicine, Department of Medical Statistics, Osaka, Japan

Background and Aims: Repeated needle pain during haemodialysis (HD) access cannulations is a serious problem for HD patients. Although the efficacy of music for alleviating pain and anxiety is well established, there is insufficient scientific evidence related to its effectiveness in alleviating pain during access cannulations during HD. This study aimed to investigate the effects of music on reducing pain during access cannulating in HD patients.

Method: A prospective, multi-facility, single-blind, crossover, randomised controlled trial was conducted. The intervention included listening to Mozart and a white-noise control condition. Patients were randomly allocated to either an 'Early-group' or a 'Later-group'. All patients who underwent cannulation wore headphones without sound in the first and third weeks (No-sound period). The Early-group received cannulation while listening to Mozart's Sonata for Two Pianos in D major (K.448) during the second week (Music period), and white noise during the fourth week (White noise period). The Later-group received cannulation while listening to white noise first, followed by Mozart in the fourth week. During each period, the music or no-music protocol started 8 minutes prior to the cannulation, and participants finished listening after HD began. The Visual Analogue Scale (VAS) was used to measure pain and anxiety during cannulation and the VAS scores for pain and anxiety were compared for the music and no-music settings. We evaluated the ratio of outcome measures between the music and white noise periods with the repeated measure mixed effect regression. We analysed the effects according to the intention-to-treat principle. Two-sided-significance-level was set at 0.05.

Results: In total, one hundred and twenty-one patients were enrolled in this study, across four facilities. The median age was 64 years, and there were 84 males (69.4%). Sixty-five patients (53.7%) used analgesics for alleviating pain. The median VAS pain score was 28 and VAS anxiety score was 19 in No-sound period. The Mozart music setting had a 12.2% (95% confidence interval (CI): 2.3 to 21.1, p=0.017) lower VAS score than the white noise setting. On the other hand, there was no significant difference in the VAS anxiety score between the two groups, that is the Mozart music setting had a 7.96% (95% CI: -4.70 to 18.4, p=0.172) reduction compared to the white noise setting.

Conclusion: We examined the effects of Mozart's music on alleviating pain using scientific methods. The music appears to reduce pain of access cannulation in HD patients. Although the trial assessed the effects of music using a single musical composition, the study did not clarify the effects of music on the physical, emotional, and cognitive status of patients. Further studies in this direction are required.

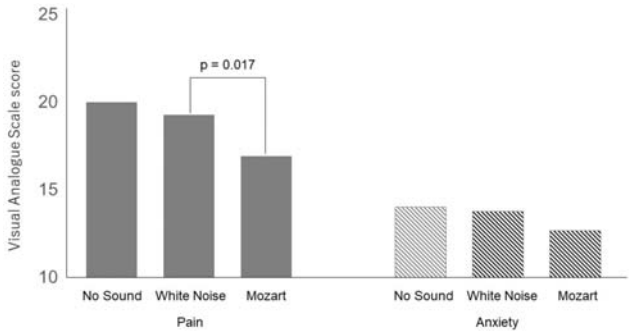


Figure. The effect of the Mozart's music compared to the white-noise.

Figure:

P1329 **STENTING VERSUS ISOLATED BALLOON ANGIOPLASTY FOR CENTRAL VEIN STENOSIS IN HEMODIALYSIS PATIENTS**

Aleksei Zulkarnaev[1], Zurab Kardanakhishvili[2], Boris Baykov[3]

[1]Moscow Regional Research and Clinical Institute, Surgical department of transplantation and dialysis, Moscow, Russia, [2]M. E. Zhadkevich Moscow City clinical hospital, Department of vascular surgery, Moscow, Russia and [3]Moscow Hospital for war veterans No. 2, Department of vascular, Moscow, Russia

Background and Aims: comparative analysis of the results of isolated balloon angioplasty (BA) and BA with stenting of central veins stenosis in patients on hemodialysis.

Method: A retrospective study included 62 patients with confirmed stenosis of the central veins: subclavian, brachiocephalic veins, vena cava inferior, or multiple lesions. In 39 patients, stents are not used; isolated balloon angioplasty (BA) was performed. In 23 patients we used bare metal stents.

Results: Functional primary patency (the time interval between the start of AVF using and the first endovascular intervention) did not differ in the groups – fig. 1A; HR 1.142 [95% CI 0.6875; 1.897], p = 0.5994.

The use of stents leads to increase primary patency (the time interval between the first and second endovascular interventions) – fig. 1B; HR 2.064 [95% CI 1.252; 3.404], p = 0.0017.

The use of stents allows to increase the functional secondary patency (total duration of use of the AVF) – fig 1C; HR 2.099 [95% CI 1.272; 3.463], p = 0.0016.

Secondary patency (the time interval between the first endovascular intervention and the complete cessation of the use of AVF) was higher after BA with stenting: HR 2.03 [95% CI 1.232; 3.347], p = 0.0021; fig 1D.

The use of stents allows to increase functional primary assisted patency (non-occlusive period from the start of AVF use) – fig. 1E and primary assisted patency (non-occlusive period from the first surgical intervention) – fig 1F: HR 1.936 [95% CI 1.175; 3.188], p= 0.0053 and HR 2.0 [95% CI 1.213; 3.295], p = 0.0042.

The need for open reconstructive interventions after the first BA or BA with stenting was the same 0.374 [95% CI 0.24; 0.556] and 0.45 [95% CI 0.291; 0.664] per 10 patient-months, incidence rate ratio (IRR)= 0.831 [95% CI 0.471; 1.464] p=0.521.

The need for endovascular interventions did not differ between isolated BA and BA with stenting 1.137 [95% CI 0.8913; 1.43] and 0.827 [95% CI 0.606; 1.104] per 10 patient-months, IRR=1.374 [95% CI 0.952; 1.999] p=0.09.

Total need for surgical interventions (open + endovascular) also did not differ: 1.511 [95% CI 1.225; 1.843] and 1.277 [95% CI 0.997; 1.611] per 10 patient-months, IRR 1.183 [95% CI 0.872; 1.612] p=0.2822.

We found a strong negative correlation between functional primary patency and primary patency (r = -0.627; p <0.0001) – fig. 2, as well as a between functional primary patency and secondary patency in patients after isolated BA (= -0.53; p = 0.0005,

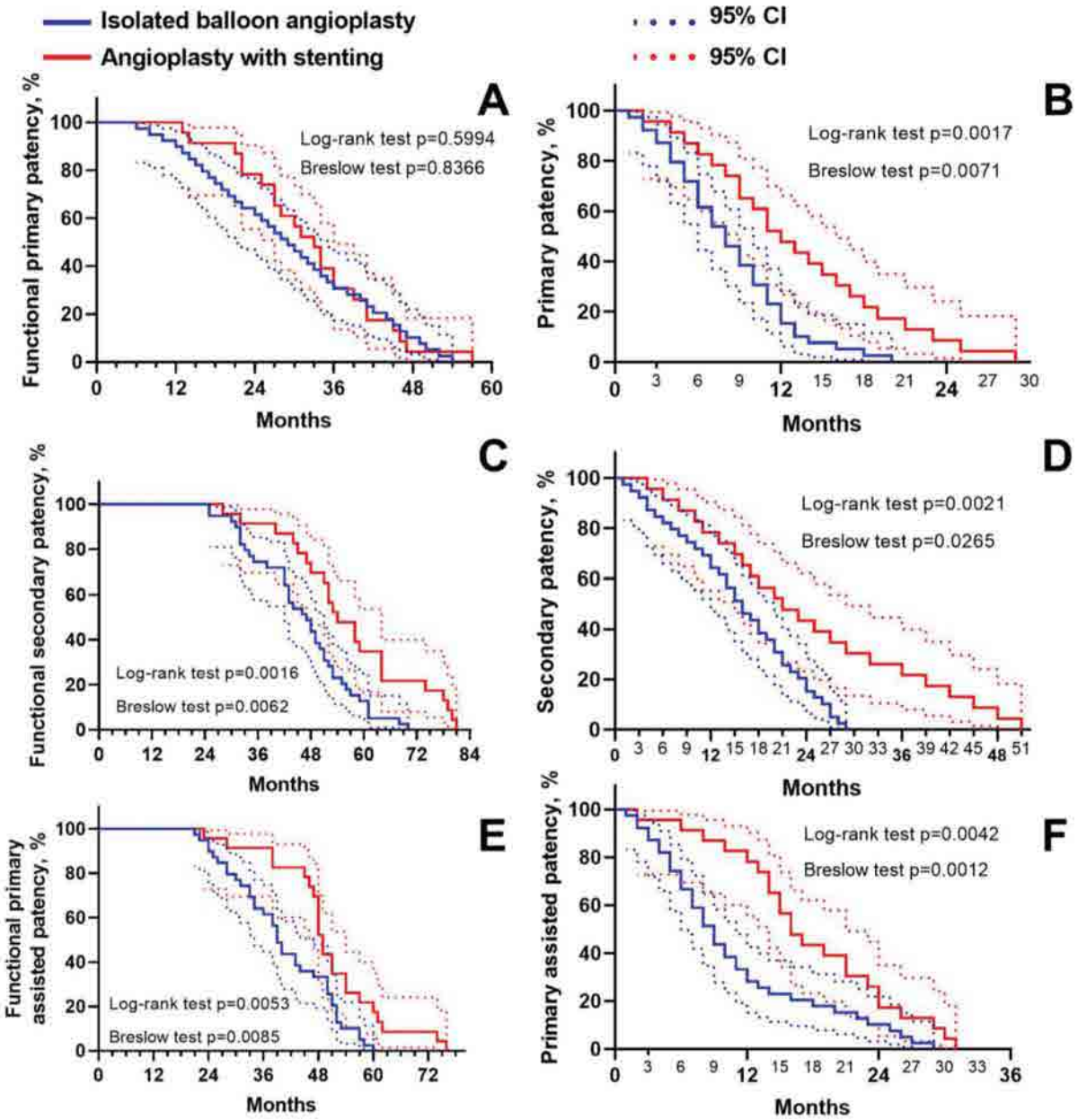


Figure 1:

respectively), but not after stenting (r = -0.351; p = 0.101 and r = -0.304; p = 0.159, respectively).

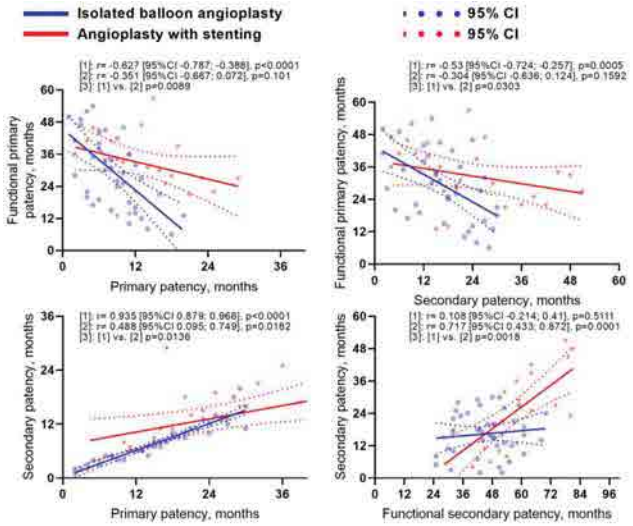


Figure 2 In a case of isolated BA, the success of the first intervention largely determines the secondary patency, which is expressed in a strong, statistically significant positive correlation of primary patency and secondary patency. In a case of BA with stenting, the correlation between these estimates is also statistically significant, but significantly lower.

Conclusion: 1. The results of balloon angioplasty without stenting are significantly influenced by the duration of the period between the start of AVF use and the manifestation of central vein stenosis. 2. The use of stents can slightly improve the results of endovascular interventions in central vein stenosis, regardless the its time of development. 3. The use of stents leads to a moderate increase in the median patency of AVF and a significant increase in the proportion of patients with functional AVF in the late postoperative period. 4. The use of stents does not reduce the need for surgical interventions

P1330 **ACCURACY OF CARDIOPULMONARY RECURCULATION ASSESSEMENT IN HD PATIENTS**

Aleksei Zulkarnaev[1], Vadim Stepanov[1], Ewgenii Strugaylo[1], Natalia Fominykh[1], Vasily Rogozin[2]

[1]Moscow Regional Research and Clinical Institute, Surgical department of transplantation and dialysis, Moscow, Russia and [2]Moscow Hospital for war veterans No. 2, Department of vascular surgery, Moscow, Russia

Background and Aims: cardiopulmonary recirculation (CRP) is one of the most informative instrumental parameters, which are widely used to predict adverse cardiovascular events. The CRP is calculated on the basis of two indirectly measured estimates. We observe a significant variability in CRP, the reason for which we have tried to explain.

Method: The prospective study included 88 patients with native AVF. At the first stage, we evaluated the inter- and inner-observer agreement of AVF volume blood flow (Qa) measurement with color duplex ultrasound. Two specialists with 5-7 years of experience measured Qa twice on the brachial artery, twice on fistula vein, after that - twice measured cardiac output before HD and one time after HD. Ultrafiltration during HD was 1.9±0,5 l.

Results: We observed good concordance between measurements on the brachial arteria by one specialist (fig 1A) and by two specialists (fig. 1B). There was poor concordance between the brachial artery and the fistula vein, even if the measurement was performed by one specialist (fig. 1C). Qa measurement on the fistula vein has a low repeatability, even if the measurement was performed by one specialist: the variance is very high (fig. 1 D).

We observed a good concordance between measurements (fig. 2A) and between specialists (fig. 2B) in CO assessment.

The main pitfalls of CPR-based cardiovascular risk stratification are related to the fact that CO changes significantly after HD (fig. 3A), while Qa values remain relatively stable (fig. 3B): the QA before and after HD difference is statistically significant, but it is minimal.

Median CO decrease was 13.4% (maximum 26.6%), while median of Qa decrease was 1.7% (maximum 6.1%).

This leads to a significant increase of the CPR value after HD, which can reach 40%(!) in some patients (absolute increase – 0.11).

Conclusion: Qa assessment should be performed on the brachial artery. After HD, there is a significant decrease in cardiac output (even with moderate ultrafiltration) with relatively stable AVF volume blood flow. This leads to a significant increase of CPR value after HD in some patients. Assessment of CPR before HD may lead to underestimation of cardiovascular risk.

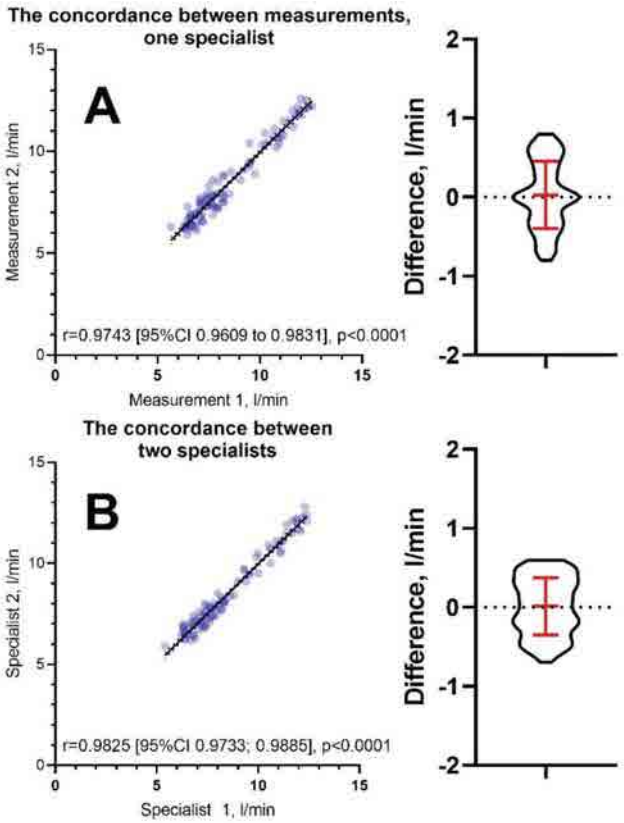


Figure: 2.

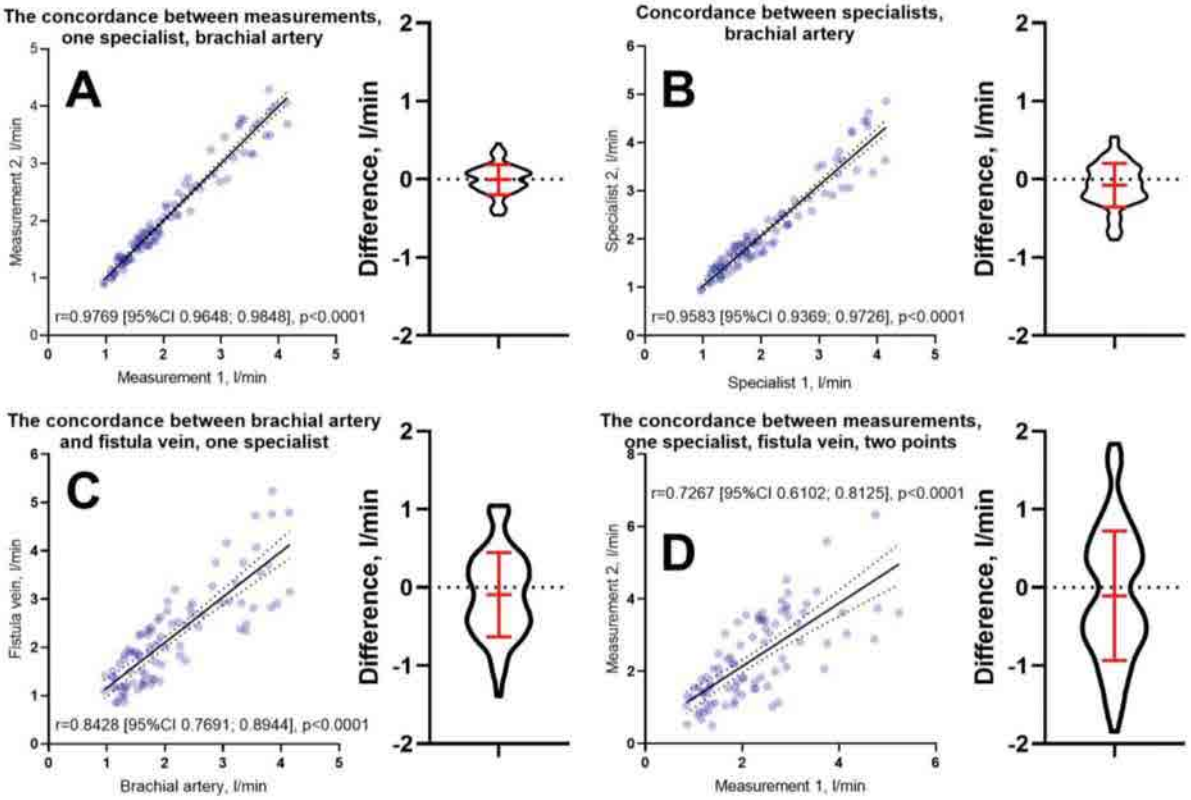


Figure: 1.

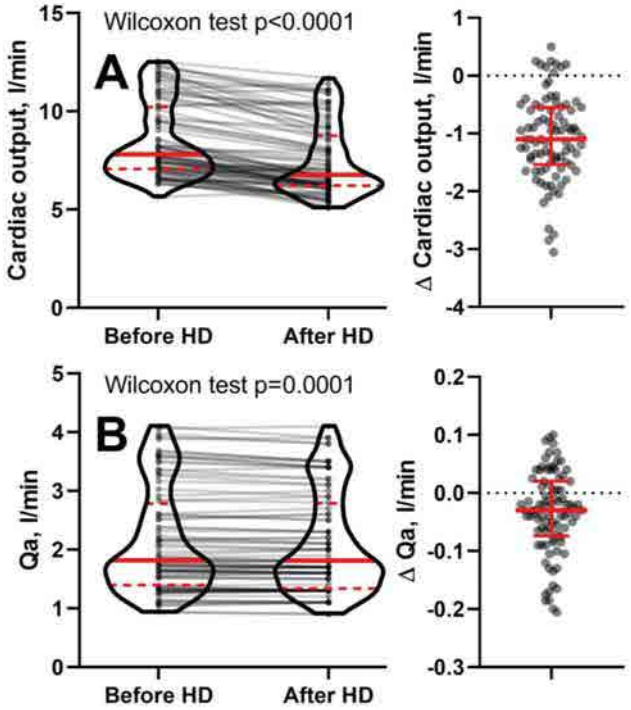

Wilcoxon test p<0.0001
A
Cardiac output, l/min
Δ Cardiac output, l/min
Before HD
After HD
Wilcoxon test p=0.0001
B
Qa, l/min
Δ Qa, l/min
Before HD
After HD

Figure: 3.

P1331 **OPTIMAL PLANNING OF VASCULAR ACCESS IS CALLED FOR IN WOMEN. AVF ARE MORE INTERVENED AND ABANDONED DESPITE LESS CO-MORBIDITY.**

Gunilla Welander[1,2], Fredrik Lundin[2], Birgitta Sigvant[2,3]

[1]Uppsala Universitetet, Department of medical sciences, Uppsala, Sweden, [2]Region Värmland, Centrum för klinisk forskning, Karlstad, Sweden and [3]Department of surgical sciences, Uppsala Universitetet, Sweden

Background and Aims: Central venous catheter (CVC) increase the risk of infection, central stenosis, hospitalizations, morbidity, mortality and later arterio-venous (AV) access failure. Vascular access planning begins in the predialysis stage of Chronic Kidney Disease (CKD). An optimal timely referral to vascular surgeon is possible since 80 % of patients are known to kidney units before initiating hemodialysis (HD). Despite this, some 71 % (75% women and 68 % men respectively) of incident patients had a CVC as vascular access when starting HD in Sweden during 2017. Some reports have shown increased risk of AVF failure in women which has been contradicted by others. The aim of this study was to determine factors of importance for achieving a functioning fistula for women and men.

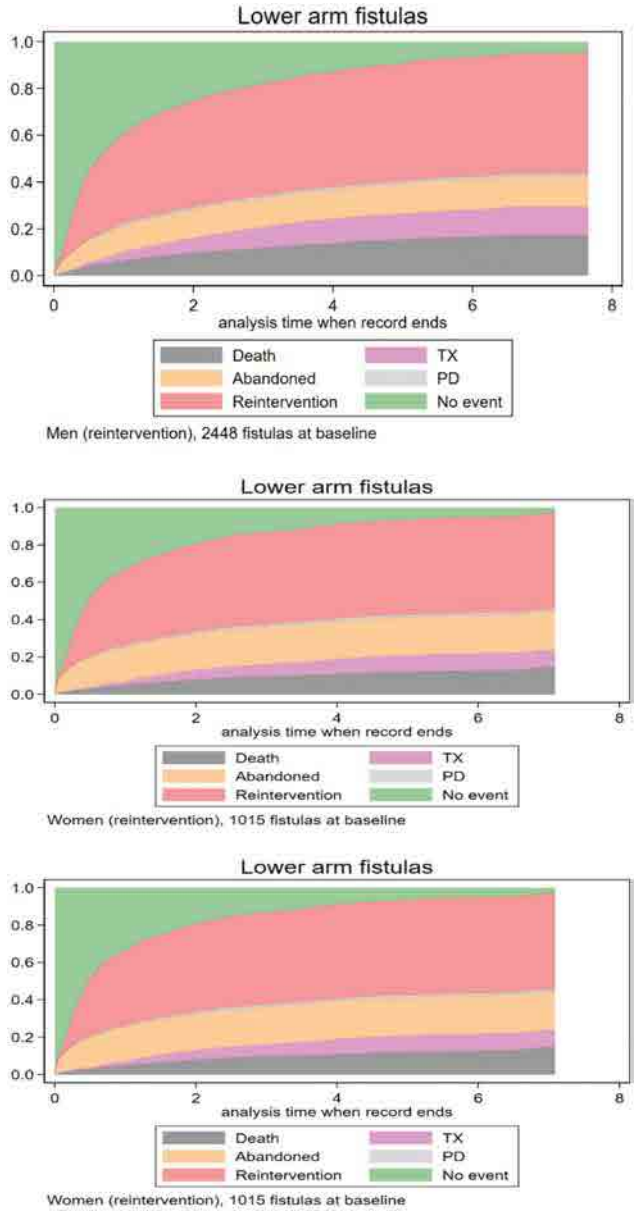


Figure 1:

Method: Data from the national Swedish Renal Registry (SRR), that covers the disease progression from CKD phase to renal replacement therapy, was used as well as mandatory national registries. Data was extracted from 2011 to 2017 for, sex, age, primary renal diagnosis, number of CVC, patient phase, co-morbidity, socio-economic factors as well as interventions and complications. A Royston-Palmer model was used for hazard ratio (HR). Cumulative incidence plots were used for fistula patency.

P value $< .005$ was considered significant

Results: The study included 5040 patients at baseline (33% women). The mean age, the time in dialysis before fistula placement and numbers of CVC did not differ between the sexes. Prevalence of polycystic kidney disease was the only primary diagnosis that differed between the sexes (10.7% among women versus 6.5% among men respectively $p<.01$). Cancer, hypertension and ischemic heart disease, was more prevalent among men (24.0 vs 19.1 $p<.001$, 80,9% vs 75.7, $p<.001$ and 25.3 vs 18.0 $p<001$). Education level were similar between the sexes whereas more men were married and born in Sweden as compared women (49.3 vs 41.6 $p<.001$ and 78.9 vs 73.0 $p<.001$). Age, diabetes and peripheral arterial disease increased the risk for reinterventions by 6% and 28% and 36% (HR 1.06 [1.03,1.15], 1.28[1.18,1.40], and 1.36[1.19,1.56] respectively. The risk for reintervention and abandonment was higher for women (HR 1.19 [95% CI: 1,09,1,56, and 1.42[1,26,1.60)]. Figure 1. shows cumulative incidence for primary patency in lower arm fistula for men and women. Incidence of secondary patency abandonment is higher for women with lower and upper arm AVF while no differences between men and women were observed for AV grafts.

Conclusion: When receiving the first fistulas, men present a higher co-morbidity as compared to women while age and time of dialysis with a CVC is similar between the sexes. Only 42% will receive an AVF in CKD phase with detriment for men. The consequence of placement in CKD phase could matter and needs to be further analysed. AVF confers a higher risk for reintervention and abandonment, particularly among women which may explain the higher use of CVC. This higher risk must be taken into account when planning for vascular access and follow up.

P1332 **VASCULAR ACCESS IN OLDER ADULTS: MOSCOW REGION REGISTER ANALYSIS**

Aleksei Zulkarnaev[1], Vadim Stepanov[1], Andrey Vatazin[1], Ewgenii Strugaylo[1], Natalia Fominykh[1], Vasily Rogozin[2]

[1]Moscow Regional Research and Clinical Institute, Surgical department of transplantation and dialysis, Moscow, Russia and [2]Hospital of war veterans No. 2, Department of vascular surgery, Moscow, Russia

Background and Aims: For many years we observed aging of HD population: the proportion older adults is increasing. These patients have extremely low kidney transplantation rate, so vascular access is not a temporary option, but an important factor until the end of life. At the same time in older adults life expectancy is lower and the risks of cardiovascular events are much higher than in the general population of HD patients. We analyzed the results of providing elderly patients with vascular access.

Method: The study included 618 patients (age ≥ 65) from the Moscow region CKD patients register.

Results: With the current practice, only about 60% of elderly patients begin HD within a year after the AVF creation (taking into account competing events) - fig. 1. The proportion of patients with brachiocephalic AVF was significantly higher than in younger patients: 41,3% vs. 16,4%. It is known that proximal AVF have a much greater tendency to increase the volume blood flow (and therefore – cardiopulmonary recirculation) than distal. Thus, elderly patients begin HD with a more adverse comorbid background. Therefore, elderly patients have an additional risk factor - the onset of HD after 65 years – fig 2. Paradoxically, but according to our data, patients who started HD after 65 years had a worse prognosis than patients who reached 65 while already on HD. At the same time, the onset of HD with CVC with the subsequent successful conversion to AVF was not associated with a significant increase in the risk of death («CVC-AVF» factor). Only if CVC remained the only vascular access («CVC» factor), the risk of death is increase significantly. This is indirect evidence in favor of the fact that in elderly patients, the AVF must be created closer to the expected start of HD.

In adjusted model, the significant risk factors also were diabetes, systemic diseases (factor «Other») and comorbidity (CIRS score), but not age.

Among patients who started HD with CVC, all patients received functional AVF or died within 11 months – fig. 3. Infections occur with the same frequency (CVC-AVF vs. AVF) and clinical manifestations of central venous insufficiency do not have time to occur during the expected life period in most patients: incidence rate ratio IRR 1.21 [0.91; 1.31] and IRR 1.11 [0.93; 1.19], respectively.

Is a conversion of AVF to CVC can improve the outcomes in older adults? In some patients probably - yes.

Since many elderly patients initially have heart failure and a reduced cardiac output (CO), the potential for compensating of AVF blood flow (Qa) is significantly less than in younger patients. We found that this leads to the fact that in the elderly, at a lower Qa value, a greater value of cardiopulmonary recirculation is noted. Even with a Qa value of 1.0-1.2 l/min, the Qa/CO value can reach ≈ 25%, which is associated with a significant risk of death. But there is good news: in the older adults some criteria are more informative than in the general population of HD patients: AUC-ROC of ejection fraction (EF), estimated pulmonary artery systolic pressure (ePASP) and Qa/CO – 0.821, 0.804 and 0.846, respectively vs. 0.654, 0.726 and 0.764. The bad news: the decision to convert from a functional AVF to a CVC is a very difficult choice. Specific indications are still not determined. We believe that it is necessary to consider the conversion from AVF to CVC in a case of decompensated heart failure, with EF<30-33% or ePASP>50-55 or Qa/CO>20-25%, *if the reduction of Qa does not improve these parameters*. In this case, conversion from CVC to AVF may improve the prognosis. Older patients require more careful monitoring than younger patients.

Conclusion: 1. The start of HD with CVC is not a problem in case of subsequent successful conversion to AVF. 2. The most important risk factors is comorbidity, starting of HD after 65 years, diabetes and only then - vascular access type. 3. Given all the facts, in the older adults we tend to create an AVF closer to start of HD than in the general HD population.

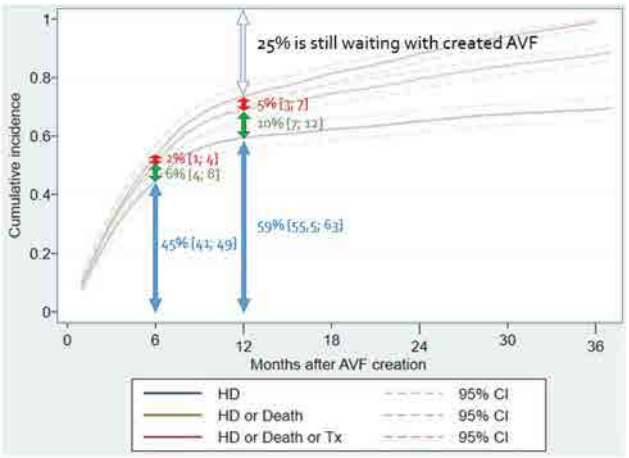


Figure:

P1333

PULSE WAVE ANALYSIS UNDER THE CONDITIONS OF HIGH ARTERIAL FLOW: ASSESSMENT OF SHUNT FUNCTION AND REACTIVE HYPEREMIA

Niklas Mueller[1], Joachim Streis[2], Sandra Müller[3], Hermann Josef Pavenstädt[4], Stefan Reuter[4], Veit Busch[2,4,5]

[1]Hospital of the Ludwig-Maximilians-University Munich, Internal Medicine III, Division of Haematology and Oncology, Muenchen, Germany, [2]University of Applied Sciences and Arts, Information technologies, biomedical engineering, Dortmund, Germany, [3]University of Vienna, Kurt Gödel Research Center, Faculty of Mathematics, Wien, Austria, [4]University Hospital Münster, Division of General Internal Medicine, Nephrology and Rheumatology, Münster, Germany and [5]Nephrovital, Kamen, Germany

Background and Aims: Fistula-creation as well as reactive hyperaemia increase local arterial blood flow. We wanted to analyse the impact of these haemodynamic changes on pulse wave (PW) morphology to assess fistula- and endothelial function.

Method: We conducted a clinical pilot study including 56 patients with functioning forearm fistula. PW morphology in the A. brachialis was assessed tonometrically at the non-fistula and fistula arm using the SpygmoCor® device. We also performed a PW analysis on the non-fistula arm under the condition of reactive hyperaemia (possible in 43 patients). Duplex-sonography was used as a complementary and reference method.

Results: In comparison to measurements under physiologic conditions, both the fistula arm (a) and the non-fistula arm with reactive hyperemia (b) showed marked differences in the pulse wave morphology (figure). The changes in PW morphology were most prominent in the area of the diacrotic notch and could be assessed as the differences of the sum of the mean slope ($\Delta\lambda$ in mmHg/ms) between the diacrotic notch and the main preceding and subsequent inflexion point. Measurement with duplex-sonography confirmed increased peak blood flow velocity in the arteria brachialis (ΔVmax in cm/s) under both conditions.

Statistical significance could be proved for $\Delta\lambda$ and for ΔVmax (table). Finally, bivariate regression analysis revealed a correlation of $\Delta\lambda$ with ΔVmax (figure; c: p=0.001 and r=-0,483 for interarm-differences of the fistula and non-fistula arm; d: p= 0.030 and r=-0.343 for the differences between the physiologic state and reactive hyperaemia at the non-fistula arm).

Conclusion: PW analysis under high flow conditions has the potential to be a new useful clinical tool in nephrology to monitor fistula- as well as endothelial function assessed by reactive hyperaemia. The findings should be verified in a trial with clinical endpoints.

Paired student T-test of key variables (95% confidence intervals)

	Mean	Standard error of the mean	Lower	Upper	p (2-tailed)
$\Delta\lambda$ (fistula) mmHg/ms	0.08956	0.01223	0.06488	0.11423	0.000
$\Delta\lambda$ (reac) mmHg/ms	0.10238	0.01079	0.08061	0.12415	0.000
ΔVmax (fistula) cm/s	69.54359	7.28719	54.79145	84.29573	0.000
ΔVmax (reac) cm/s	66.44500	4.64198	75.83429	57.05571	0.000

P1334 PREOPERATIVE VOLUME STATUS IN VASCULAR ACCESS CREATION, A DESPISED INFLUENCE?

Maria Guedes Marques[1], Pedro Maia[1], Pedro Ponce[2]

[1]Nephrocare Coimbra, Dialysis, Portugal and [2]Nephrocare Portugal

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Background and Aims: The most common causes of early primary failures of a vascular access (VA) is related to small caliber vessels. Weight gain between dialyses expands both extracellular and blood volume, which may lead to rises in intravascular filling and vessels caliber. If patients presented after weekend, their weight and probably volemia would be higher.

Dry weight concept has evolved over time and nowadays incorporates objective measures of volume status like body bioimpedance spectroscopy (BIA) and lung ultrasound.

We hypothesized that preoperative volume status may influence vascular filling and vessels diameter with a significant impact on VA outcomes.

Method: A clinical, prospective, randomized, open-label, single-center crossover trial.

Inclusion criteria: age 18-80ys, under regular hemodialysis (3/week), no heart failure (CHF) and no acute pulmonar edema (APE) on the previous year.

Exclusion criteria: >3 sessions/week, CHF or APE.

Before the last-week session, patient's clinical parameters were recorded. BIA and ultrasound vascular mapping were performed.

After this first evaluation, dry weight was increased 0,5 Kg, and after weekend, the same protocol was conducted.

Primary end point was to compare vein diameters.

Results: 126 vessels were evaluated (84 veins and 42 arteries) from 21 patients. Mean age was 69±10y and 52% female.

Primary end point was achieved (Table 1). Other than humeral arterial blood flow, every parameters evaluated through ultrasound mapping significantly increased ($p<0,05$) after dry weight adjustment (>0,5 Kg) plus weekend weight gain.

After cross over, weight, overhydration (OH), extracellular water (ECW) and OH/ECW significantly increased ($p<0,05$), however, most patients had a mild-moderate OH (86-90%). Blood pressure and total body water haven't changed significantly.

No complications were reported.

Conclusion: Some additional degree of OH comparing to midweek weight gain may be effective and safe in improving peripheral vascular conditions that are predictors of VA success.

The currently lack of evidence of vascular mapping may be due to the lack of evaluation of cofactors such as volemia. Therefore, BIA and lung ultrasound may be future tools that combined to vascular ultrasound could be a safe and effective way to optimize and evaluate preoperative conditions to improve VA outcomes.

Larger and multicentric studies are needed.

	Mean ± SD	Mean Paired Difference	p
Pre Radial Artery (mm)	2,15 ± 0,61	0,46	0,000
Post Radial Artery (mm)	2,61 ± 0,65		
Pre Distal Radiocephalic Vein (mm)	2,20 ± 0,96	0,54	0,002
Post Distal Radiocephalic Vein (mm)	2,74 ± 0,88		
Pre Medium Radiocephalic Vein (mm)	2,54 ± 0,96	0,73	0,000
Post Medium Radiocephalic Vein (mm)	3,27 ± 1,03		
Pre Cephalic Vein (mm)	2,63 ± 1,82	1,31	0,000
Post Cephalic Vein (mm)	3,94 ± 1,53		
Pre Basilic Vein (mm)	3,18 ± 1,17	1,47	0,000
Post Basilic Vein (mm)	4,65 ± 1,09		
Pre Humeral Artery (mm)	4,06 ± 0,73	0,44	0,002
Post Humeral Artery (mm)	4,50 ± 0,92		
Pre Humeral Artery Blood Flow (ml/min)	55,00 ± 45,04	3,24	0,609
Post Humeral Artery Blood Flow (ml/min)	58,24 ± 42,73		

Figure:

P1335 **MALNUTRITION, INFLAMMATION, AND ANEMIA SYNERGISTICALLY IMPACT VASCULAR ACCESS FAILURE IN PATIENTS WITH FIRST-TIME ARTERIOVENOUS FISTULA FORMATION**

Masaki Hara[1,2], Naozumi Saiki[3], Hiroki Suzuki[2], Masamitsu Ubukata[2], Rin Asao[2], Yuya Nakamura[2], Masayuki Nakamura[2], Isao Ohsawa[2], Hiromichi Gotoh[2]

[1]Tokyo Dialysis Frontier Ikebukuro Station North Clinic, Department of Nephrology, Tokyo, Japan, [2]Saiyu Soka Hospital, Department of Nephrology, Saitama-Ken, Japan and [3]Saiyu Soka Hospital, Department of Vascular Surgery, Saitama-Ken, Japan

Background and Aims: There are several reports that the initial (within one year) failure of vascular access (VA) is 2–53% in several countries. Malnutrition alone, inflammation alone, and anemia alone are factors that have a well-known relationship to VA failure. We believe that the relationship of these risk factors to VA failure is a complex one. Therefore, we evaluated whether the addition of these factors had a synergistic impact on VA failure.

Method: This longitudinal cohort study sought to confirm the effects of malnutrition, inflammation, and anemia on VA failure. We included 177 patients with chronic kidney disease (CKD) with first-time arteriovenous fistulas who were treated from January 2013 to December 2017. VA failure was defined as a new onset of VA obstruction or the need for percutaneous transluminal angioplasty. Albumin (Alb), C-reactive protein (CRP), and hemoglobin (Hb) were studied as indicators for malnutrition, inflammation, and anemia, respectively. Each highest (CRP) or lowest (Alb and Hb) interquartile range (IQR) group was assigned 1 point (as a risk score). The cumulative VA failure rate was analyzed by the Kaplan-Meier method, which stratified the study cohort into four groups according to the risk scores (0–3). We assessed whether the lowest IQR group of Hb and Alb, and the highest IQR group of CRP were associated with VA failure. To determine this, we used a univariable Cox proportional hazards regression analysis to calculate the hazard ratio (HR) and its 95% confidence interval (CI). A multivariable Cox proportional hazards regression analysis was used to evaluate the association between the risk score and VA failure, with adjustment for age, sex, presence or absence of diabetes mellitus, value of calcium phosphate products, preoperative vein diameter, and intraoperative vascular assessment scores.

Results: The average observational period was 1.6 ± 1.4 years. The incidence of VA failure was 30.5% (54 patients). Cumulative VA failure was significantly higher in patients who had more than two risk scores, as compared to the patients who did not have any risk score (Figure). The univariate Cox regression analysis showed that Alb, CRP, and Hb were significantly associated with VA failure (HR, 2.00; 95% CI, 1.08–3.71 for Alb and HR, 2.21; 95% CI, 1.15–4.13 for CRP and HR, 1.96; 95% CI, 1.02–3.63 for Hb), respectively. The presence of more than two risk scores was significantly associated with VA failure (HR, 4.68; 95% CI, 1.07–18.5 for the patients with two risk scores and HR, 4.72; 95% CI, 1.32–17.2 for the patients with three risk scores).

Conclusion: Malnutrition, inflammation, and anemia independently and synergistically affect VA failure. In clinical settings, we need to be aware of the presence of malnutrition, inflammation, and anemia to better prevent VA failure.

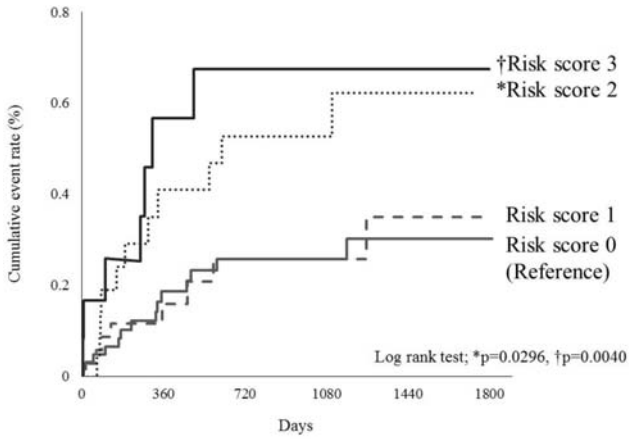


Figure:

P1335A

A NOVEL NON-INVASIVE DOPPLER ULTRASOUND GUIDED MANAGEMENT TECHNIQUE OF ACCESSORY CEPHALIC VEIN AS A CAUSE OF MATURATION FAILURE IN RADIOCEPHALIC DIALYSIS ACCESS

Moataz Fatthy abdelnaeem[1]

[1]*Cairo University, Faculty Of Medicine, Qasr Al-Ainy, Internal medicine and nephrology department, intervention section, cairo, Egypt*

Background and Aims: Background Arterio-venous fistulae (AVF) are the primary access in considerable number of patients on hemodialysis or approaching hemodialysis. A distally created AVF are preferred over proximal approach, as recommended by the guidelines. Non maturation of AVF fistulae remains a major caveat as compared to arteriovenous grafts. A consensus definition of non-maturation is not well defined; however characteristics of non-maturation include inadequate blood flow. Female gender and forearm location have been identified by previous analysis as predisposing factors for non-maturation. Patients with radiocepalic arterio-venous fistula experience the highest rate of non-maturation rates. One important cause of failed AVF maturation is the presence of collateral or veins or tributaries; this may or may not be associated with stenosis. These tributaries may reduce blood in the primary outflow vein, consequently, leading to delayed maturation of the AVF. Options to overcome this problem include coiling or embolization of the collaterals with variable success rate.

Aim To examine the efficacy of a novel non-invasive technique to manage maturation failure in radio- cephalic arteriovenous fistulae, through ultrasound guided compression obliteration of the collaterals (accessory cephalic) as identified cause of maturation failure to augment flow in the primary cephalic vein.

Method The application of this maneuver to patients according to selected criteria was approved by the institutional Ethical Review Board.

Patients' selection

Non maturation was defined by the Rule of Sixes criteria by endorsed by as follows

Flow in the fistula should be greater than 600 mL/min, 6 mm caliber, not more than 6 mm depth, discernible margins and ready for use within six weeks

Assessing non-maturation in absence of stenosis

Ultrasound and Doppler evaluation of main cephalic and accessory cephalic veins to confirm insufficient flow volume at main cephalic vein used in radio-cephalic AVF due to distributed flow to one or more accessory cephalic veins missed by vascular surgeons during surgical radiocephalic AVF creation. To be eligible for this technique, a downstream stenosis should be ruled out by ultrasound, as in such case angioplasty will offer the ideal treatment.

13 patients with failing to mature AVF were consented to this technique. The consent stated that the techniques is totally non-invasive and that, in case of failure of the technique, an endovascular management by coiling for example or a vascular surgical opinion will be sought without delay.

Technique summary: using high frequency probe linear ultrasound to perform long term compression for at least 20 minutes in short axis view over the accessory cephalic vein to obtain complete thrombosis and then examine the main cephalic vein to measure post procedure improving flow volume rate

Results: Patients' characteristics

13 patients underwent the procedure. Baseline characteristics are shown below:

The technique was successful in 9 (5 males and 4 females) out of 13 patients

Not referred to interventional radiologist or vascular surgeons

Baseline patient's characteristics

Age(years)Means63±9

SexMale5Female8

Conclusion: The novel technique as described may provide a safe non-invasive solution to patient with failing to mature radiocephalic arteriovenous fistula and may be referred for a trial of noninvasive ultrasound guided accessory cephalic vein compression obliteration to avoid invasive interventional radiology techniques or surgical repair.

A surgical option remains the ultimate solution in case of failure of this ultrasound guided maneuver.

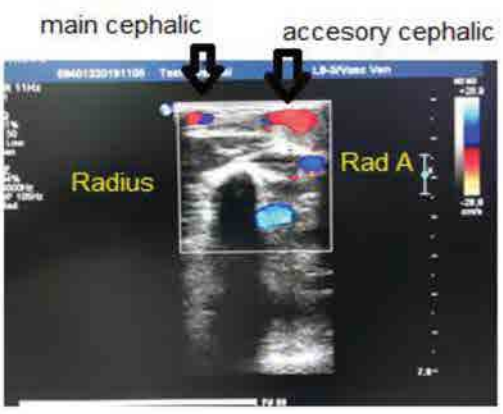


Figure:

P1336 PROPHYLACTIC CLOSING OF AV FISTULA PREVENTS HIGH OUTPUT HEART FAILURE - A SINGLE-CENTER RANDOMISED CONTROLLED TRIAL

Patrick Hetz[1], Silvana Müller[2], Lydia Posch[3], Martin Tiefenthaler[1]

[1]*Medical University Innsbruck, Nephrology and Hypertensiology, Innsbruck, Austria,*
[2]*Medical University Innsbruck, Cardiology and Hypertensiology, Innsbruck, Austria and*
[3]*University Hospital Innsbruck, Vascular Surgery, Innsbruck, Austria*

Background and Aims: AV fistulas are the favoured way ensuring a safe long-term access for patients with need for hemodialysis. Various studies, including a prior retrospective trial at our department, showed that AV fistulas are an additional burden on the cardiac-vascular system leading to frequent fistula closure in post-transplant patient. ~~In literature, there is~~ a widespread approach in dealing with high-flow fistulas in post-transplant patients with stable kidney function is reported.

Method: For this trial, patients with a stable graft function (min. 3 months post-transplant) and a brachial artery flow of min. 1,500 ml/min were recruited. Initially planned for multi-centric analysis, 28 patients were randomised in Innsbruck. Exclusion criteria were a pre-existing cardiac failure with ejection fraction less than 25%, NT-pro-BNP $>$ 1,400 ng/l and NYHA score $\geq$ III. These patients were randomised in a 1:1 ratio in intervention group with immediate fistula ligature after randomisation, and control group with no surgical intervention. Patients in the control group had fistula ligature only if at least two criteria for ligature occurred. These criteria were selected in agreement with ~~of~~ the department for cardiology and encompassed dilation of right atrium, of inferior vena cava or of pulmonary artery, left-ventricular eccentricity index $<$ 1 or a systolic pulmonary artery pressure of $>$ 35 mmHg. The main endpoint high-output heart failure was defined by min. 2 echocardiographic criteria and signs of congestive heart failure such as worsening in NYHA score. A follow-up procedure of 24 months with quarterly measurements of kidney function, NT-proBNP and lactat dehydrogenase as well as a biannual echocardiographic check-up were performed. Statistics included paired t-test and Wilcoxon-rank test for median/mean comparison and chi-quadrat test for absolute frequency.

Results: The main endpoint high-output heart failure referable to high fistula flow was reached in five of 13 control patients (38.5%), whereas in the intervention group no study patient showed a worsening in clinical and echocardiographic signs to reach criteria for ligature. Prophylactic ligature of high-flow fistulas avoided right heart failure in our patient collective (p-value 0.013, x?test). Three patients had to undergo ligature due to off-study complications such as progressive aneurysma formation and steal phenomenon. One patient with dyspnoe preferred fistula ligature but was not fulfilling echocardiographic criteria. In total nine patients in the control group were assigned to fistula ligature. Matching all conducted fistula closures median NT-proBNP was 317 ng/l pre-ligature and 223 ng/l post-ligature (p 0.003, Wilcoxon). In total, 18 of 21 patients (excluding 2 patients with lack of data) showed falling NT-proBNP values. Creatinine levels showed a decrease from 1.69 mg/l to 1.60 mg/l (p-value 0.059, paired t-test). The intervention group included 14 patients with a gender ratio of 12 men to 2 women and a mean age of 52.5 years; the same age and gender distribution was seen in the control group. Fistula flow per m?body surface did not differ significantly (980 ml/min vs. 1000 ml/min). Echocardiographic findings showed improvement in ligature patients (e.g. a drop of sPAP in 7/8 ligature patients with available data) but did not reach statistical significance.

Conclusion: A prophylactic ligature of high-flow AV fistulas can avoid high-output heart failure and a more liberal approach to closure AV fistulas may be discussed in future.

P1337 **ENDOVASCULAR REVISION OF ARTERIOVENOUS ANASTOMOSIS BY DOUBLE GUIDE TECHNIQUE**

Nicola Pirozzi[1], Jacopo Scrivano[1], Loredana Fazzari[1], Roberto Pirozzi[2]

[1]Nuova ITOR, Nefrologia Interventistica Unit, ROMA CAPITALE, Italy and [2]Nuova ITOR, Endovascular Unit, ROMA CAPITALE, Italy

Background and Aims: Juxta-anastomotic stenosis is the most frequent complication of arteriovenous fistula (AVF) for haemodialysis (HD). Treatment options are surgical bypass by creating a more proximal anastomosis or endovascular treatment by angioplasty. The available literature data show equal outcomes in term of secondary patency, but a significantly higher rate of recurrent stenosis for endovascular treatment (0.5 procedure/AVF/year). We describe the results of endovascular treatment by "double guide technique" (DGT) as to Turmel Rodrigues original description, in a series of patients referred to our centre.

Method: We describe all consecutive patients treated by DGT in the first semester of 2018 because of a *de novo* occurring juxta-anastomotic stenosis of the arteriovenous fistula for haemodialysis. The procedure was carried out as described by Turmell Rodrigues. In short: by means of a single retrograde access through the outflow vein by a 6 french valved introducer, two guide wire are navigated into both proximal and distal artery. Two consecutive dilatation of the anastomosis area are then performed including first the juxta-anastomotic vein at 6 to 7 mm (mean 6.7mm, ds 0.55), followed by the juxta-anastomotic artery at 4mm (mean 4.1mm, ds 0.33), as show in figures. Follow up was carried out at 1, 3, 6 12 month by clinical examination and ultrasound examination. Prospectively collected data was analyzed retrospectively.

Results: 25 patients were treated during the first 6 month of 2018 by a single operator. Patients data (mean): age 71years, HD vintage 31month, AVF vintage 31month. AVF distribution were: distal radio-cephalic 32%, proximal radio-cephalic 52%, distal ulnar-basilic 8%, humero-basilic 8%. Mean preoperative AVF blood flow - as measured by duplex ultrasound (US) - was 540ml/min. 32% of AVF have preoperative blood flow >600ml/min but a critical stenosis (<1.9mm of diameter). Mean juxta-anastomotic vein and juxta-anastomotic artery ballon diameter were 6.7mm (ds 0.55) and 4.1mm (ds 0.33) respectively. Overall mean blood flow at 12 month was 830ml/min. During follow up 3 patients required endovascular treatment of some new occurring stenosis, 3 patients were lost to follow up at 12 month, 1 patient died from unrelated reasons. In 52% of patients any other revision was required, while 32% required 1 further angioplasty, 4% 2 further angioplasty and 4% 4 further angioplasty of the target lesion during the following 12 month (recurrence rate: 0.28 procedure/patients/year). Assisted functional patency at 12month was 95%.

Conclusion: Endovascular treatment of juxta-anastomotic AVF stenosis by the DGT performed quite satisfactorily in our series and showed a low recurrence on the target lesion compared to data from literature. At 12 month the average AVF blood flow was below 1000ml/min. The technical advantage of the DGT consist in the single, small caliber percutaneous access, needed to complete the procedure. A larger series would confirm how this refinement of the technique compares with the improved results we preliminary observed.

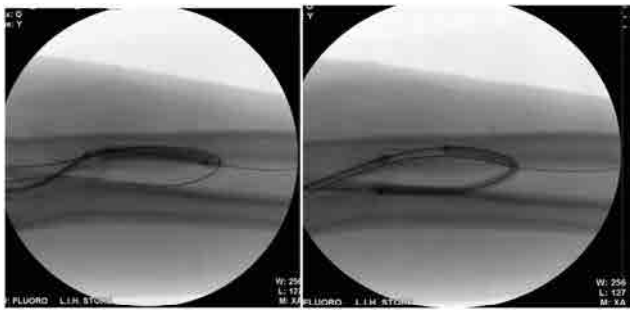


Fig 1 and 2 (vein dilatation at 6mm), (proximal artery dilatation at 4mm)

P1338 **ELDERLY PATIENTS, UPPER LIMB ISOMETRIC EXERCISES AND ARTERIOVENOUS FISTULA MATURATION**

Irati Tapia González[1], Vicent Esteve Simo[1], Sara Ibañez Pallares[2], Sandra Rubio[1], Fatima Moreno Guzman[1], Miquel Fulquet Nicolás[1], Mónica Pou Potau[1], Anna Saurina Solé[1], Verónica Duarte Gallego[1], Montserrat Yeste Campos[2], Manel Ramírez de Arellano Serna[1]

[1]Hospital de Terrassa. Consorci Sanitari Terrassa. Barcelona, Nephrology, Terrassa, Spain and [2]Hospital de Terrassa. Consorci Sanitari Terrassa. Barcelona, Vascular Surgery, Terrassa, Spain

Background and Aims: Introduction: Arteriovenous fistula (AVF) creation may be controversial in elderly population, given their comorbidities, reduced life expectancy and vascular access (VA) complications. Postoperative upper limbs isometric exercise improves AVF maturation. Nevertheless, scarce scientific evidence has been reported about their utility in elderly population until date.

Objectives: To assess the effect of a postoperative isometric exercises program on native VA maturation in our patients older than 75 years old with stages 5-5D chronic kidney disease.

Method: A 24 months prospective single-center study. After surgery, all patients were randomized to an isometric exercise group (EG) or a control group (CG). Isometric exercises protocolled programm, was performed in EG. CO received usual care. Demographical data, muscle strength using handgrip (HG) dynamometer, main Doppler ultrasound (DUS) measurements (outflow vein (OV) diameter and humeral artery blood flow rate (BFR), clinical and DUS maturation as well as medical (hematoma, stenosis, thrombosis, pseudoaneurysm, aneurysm) or surgical VA complications were assessed at 8 weeks postoperatively.

Results: 27 patients. 14 EG, 13 CO. 74,1% men. Mean age 79,9±2,8 years. 59,2% Radiocephalic AVF. Demographic data, HG and DUS measurement at baseline were similar. A significant increase in HG was observed only in EG at the end of study (19,1±7,8 vs 22,9±9,7Kg, p=0,001). DUS measurements statistically increased for both groups (OV diameter: EG 3,1 ± 0,8 vs. 5,9 ± 1,7 mm; CG 2,9 ± 0,6 vs. 5,8 ± 1,4mm; humeral artery BFR: EG 150,7± 42,7 vs. 1165,0 ± 664,5 ml/min; CG 132,9± 30,3 vs. 1310,2 ± 691,8ml/min) at the end of study. EG group obtained highest clinical (CG 46,2% vs EG 78,6%;p=0,049) and DUS maturation (CG 30,8% vs EG 71,4%; p=0,041) at 8 weeks, significantly. Despite no significant differences, the number of complications was lower in the EG, mainly hematomas and significant stenosis.

Conclusion: The upper limb isometric exercises protocolled program improved clinical and DUS maturation in our elderly patients. With our results, isometric exercises should be guaranteed in elderly patients in order to obtain a correct maturation of the performed AVF. Further studies are required to support these outcomes in this population.

P1339 **ARTERIOVENOUS FISTULA AND BASILIC VEIN TRANSPOSITION IN ELDERLY PATIENTS ON HEMODIALYSIS: AN OBSERVATIONAL STUDY**

Vinant Bhargava[1], Priti Meena[1], Ambrish Satwik[1], Apurv Srivastava[1], A K Bhalla[1], Ashwani Gupta[1], Manish Malik[1], Anurag Gupta[1], V S Bedi[1], Devinder Singh Rana[1]

[1]*Sir Ganga Ram Hospital, Department of Nephrology, New Delhi, India*

Background and Aims: With the increase in the line expectancy of chronic kidney disease in the older population (>60 years), the numbers requiring haemodialysis is progressively rising. The elderly population may be different from the younger in terms of non-suitable vessels for access creation, non-maturation, and vascular calcifications, and this may alter the outcomes of use of arteriovenous fistula (AVF). This study was conducted to analyse the outcomes of AVF in elderly patients (>60 years).

Method: Retrospective study was conducted in the Department of Nephrology at Sir Ganga Ram Hospital, New Delhi. Patients of more than 60 years of age in whom AVF was created from 1st January 2012 to 31st December 2016 were included in the study. Follow-up data of 3.5 years was analysed. The primary endpoint was to assess primary and secondary patency rates.

Results: A total of 300 patients were included in the study. The mean age was 63.8 years. Radiocephalic AVF (RCAVF) was the most common site of [69.8% (n = 210)], followed by brachiocephalic (BCAVF) in 25.2% (n = 75) and basilic vein transposition (BVT) in 5% (n = 15). At 12 months, overall survival of the AVF was 66.8%. At 42 months, the primary patency rate of RCAVF, BCAVF, and BVT was 50.6%, 52.6%, and 50.4% respectively. The commonest cause of access failure was thrombosis (20.4%) followed by non-maturation (9%). Vascular access abandonment was found least in BCAVF.

Conclusion: AVF remains the preferred vascular access for haemodialysis in the elderly population. Brachiocephalic AVF has higher primary and secondary patency rates. Thrombosis and failure of maturation are major concerns in the elderly AVF.

P1340

CATHETER-RELATED BLOODSTREAM INFECTIONS IN HEMODIALYSIS: ANALYSIS OF PATIENT- AND CATHETER-ASSOCIATED RISK FACTORS

Francesca Zanoni[1], Laura Pavone[1], Valentina Binda[1], Giovanni Luigi Tripepi[2], Graziella D'Arrigo[2], Antonio Scalamogna[1], Piergiorgio Messa[1,3]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Unit of Nephrology, Dialysis and Renal Transplantation, Milan, Italy, [2]CNR-IFC, Institute of Clinical Physiology, Reggio Calabria, Italy and [3]Università degli Studi di Milano, Department of Clinical Sciences and Community Health, Milan, Italy

Background and Aims: Tunneled central venous catheter (T CVC) use is rising among patients undergoing chronic hemodialysis (HD) and non-tunneled (NT) CVCs are often used for HD initiation in late referral chronic kidney disease (CKD) or acute kidney injury (AKI). Catheter-related bloodstream infections (CRBSI) are a major complication of CVC use. This study examines potential patient- and CVC- related factors associated with CRBSI incidence and its microbiological features.

Method: In this retrospective single-center study, 413 patients undergoing an extracorporeal treatment (HD or Plasma Exchange) between February 1st 2014 and January 31st 2017 with 561 CVCs were recruited. Clinical data at study entry and CVC type are summarized in table 1. All bloodstream infections (BSI) occurring during the observation period were recorded and classified into CRBSI or non-CRBSI (nCRBSI), and their infecting agents collected. An incidence rate ratio (IRR (95% CI)) was calculated to assess the association between CRBSI incidence rate (IR), expressed as events/1000 catheter-days, and each clinical variable or CVC type. Significant associations at the univariate analyses were investigated with multivariate cox models.

Results: During a cumulative follow-up time of 66686 catheter-days, 54 (IR: 0.81) CRBSI and 30 (IR: 0.45) nCRBSI events occurred. CRBSI had higher frequency of GRAM+ bacteria compared with nCRBSI (70% vs 33%, p<0.001). Among CRBSI, GRAM- bacteria were more frequent in patients with age <80y (16 (36%) vs 0, p=0.02), and T CVC (40% vs 18%, p=0.07).

At the univariate analysis, male sex, age <80y and AKI were associated with higher CRBSI IR (table 2). Compared with T Jugular CVC, higher CRBSI IR was associated with NT Jugular (IRR 6.45 (2.99-13.56), p<0.0001) and NT Femoral (IRR 12.90 (5.87-27.61), p<0.0001) CVC; T Femoral CVC was associated with higher non-significant IR (IRR 2.45 (0.93-5.85), p=0.07). At the multivariate analyses, factors associated with higher CRBSI IR were AKI (hazard ratio - HR 3.03 (1.38–6.67), p=0.006), NT CVC (HR 3.11 (1.30–7.41), p=0.01), and Femoral CVC (HR 2.63 (1.36–5.07), p=0.004).

Conclusion: Patients affected by AKI and use of NT or Femoral CVCs are independently associated with CRBSI risk.

Table 1. Characteristics of patients and CVCs.

Patient characteristics	N (%)
Male sex	241 (58)
Age (years) *median (IQR)*	68 (56, 78)
Age ≥ 80 years	87 (21)
Diabetes (DM)	88 (21)
Immunosuppression (IS)	114 (28)
Renal disease	
AKI	151 (36)
CKD	242 (59)
Other*	20 (5)
Vintage dialysis** m*edian (IQR)*	135 (1, 1067)
Vintage dialysis** ≥ 180 days	122 (47)
CVC characteristics	**N (%)**
NT Jugular CVC	230 (41)
T Jugular CVC	186 (33)
NT Femoral CVC	109 (19)
T Femoral CVC	28 (5)
NT Subclavian CVC	4 (1)
T Subclavian CVC	3 (0.5)
Data not available	1 (0.5)

*18 PEX, 2 HD for iodine-based contrast nephropathy prevention

**in patients affected by CKD

Table 2. CRBSI incidence rates according to characteristics of the patients and univariate analysis.

Parameter	IR	IRR	95% C.I.	P
Male/Female	1.067/0.560	1.905	1.060 - 3.527	0.03
Age <80/≥80 years	0.995/0.419	2.372	1.145 – 5.519	0.016
DM pos/neg	0.99/0.77	1.295	0.637 – 2.466	0.5
IS pos/neg	1.22/0.709	1.72	0.895 – 3.159	0.1
AKI/CKD	3.162/0.566	5.592	3.05 – 9.99	<0.0001
Vintage dialysis* ≤180/>180 days	0.459/0.328	1.398	0.508 – 3.571	0.6

*in patients affected by CKD

P1341

FACTORS AFFECTING THE ATTAINMENT OF ADEQUATE BLOOD FLOW OF ARTERIOVENOUS FISTULA FOR HEMODIALYSIS

Nikola Gjorgjievski[1], Pavlina Dzekova-Vidimliski[1], Ana Stojanoska[1], Julija Gjorgievska[2], Petar Dejanov[1], GJULSEN SELIM[1], Igor Nikolov[1], Irena Rambabova Bushljetikj[1], Zvezdana Petronijevik[1], Shqelkim Muharremi[3], Goce Spasovski[1], Ninoslav Ivanovski[4], Aleksandar Sikole[1]

[1]University Hospital of Nephrology, Skopje, Republic Of North Macedonia, [2]University Children Hospital, Skopje, Republic Of North Macedonia, [3]Institute of Nephrology, Struga, Republic Of North Macedonia and [4]Zan Mitrev Clinic, Skopje, Republic Of North Macedonia

Background and Aims: An arteriovenous fistula (AVF) remains the best choice of vascular access (VA) for hemodialysis (HD). The aim of our study was determination of factors associated with achieved adequate blood flow (BF) of AVF during 4-th week after creation

Method: : Created AVF in 63 patients with chronic kidney disease (CKD) stage 4, 5 and 5-HD were analyzed in the prospective single center study, from January 2019 to October 2019. Preoperative mapping of blood vessels by Doppler ultrasound (DUS) on the forearm was performed in all patients. All patients were undergoing surgical creation of new forearm AVF (radio-cephalic) by one doctor. The DUS was used for measuring the diameter size of artery radialis, artery brachialis and vein cephalica before creation of AVF and again on 1-st day, 2-nd and 4-th week after AVF creation. In addition the BF of AVF was also measured by DUS on 1-st day, 2-nd and 4-th week after AVF creation. The adequate BF of AVF for hemodialysis treatment was defined as $\geq$ 600 ml/min. Patient gender and age, hemodialysis vintage, diameter size of artery radialis, artery brachialis and vein cephalica before creation of AVF were analyzed as factors that were affecting the achieved BF of AVF during 4-th week after creation.

Results: : The average age of patients was 61.31 $\pm$ 12.9 years. From all patients, 60.31% (38/63) were men. The adequate BF of AVF ($\geq$600 ml/min) during 4-th week after creation was achieved in 43.54% (27/63) of created AVFs. The blood flow of AVF measured in male gender was significantly higher compared to the blood flow of AVF measured in female gender (576.03 ml/min vs 375.12 ml/min, p=0.004). The age of the patients and hemodialysis vintage were not significantly associated with achieved adequate BF of AVF during 4-th week after creation of AVF. The adequate BF of AVF was achieved in blood vessels with bigger diameter size. The diameter size of the blood vessels with achieved adequate BF was significantly higher compared to the diameter size of the blood vessels without adequate BF (artery radialis : 2.45 mm vs 2.03 mm, p=0.000; artery brachialis: 4.78 mm vs 4.06 mm, p=0.001 and vein cephalica: 3.12 mm vs 2.83 mm, p=0.018).

Conclusion: The gender and the diameter size of artery radialis, artery brachialis and vein cephalica before creation of AVF were significantly associated with achieved adequate BF of AVF ($\geq$600 ml/min) during 4-th week after creation of AVF.

P1342 OUTCOME OF ELDERLY PATIENTS AFTER PREDIALYSIS VASCULAR ACCESS CREATION

Dr Sanjay Bhat[1], Alok Srivastava[2], Nisar Ahmad[3], Priyanka Rai[1], R .P Singh[1], Rohit Srivastava[1], A K ROY[3], Jalees Fatima[4]

[1]RML Institute of Medical Sciences, Surgery, Lucknow, India, [2]RML Institute of Medical Sciences, Urology, Lucknow, India, [3]Era Medical College, Surgery, Lucknow, India and [4]Era Medical College, Medicine, Lucknow, India

Background and Aims: Guidelines to create vascular access for elderly patients is guided by a number of factors i.e. competing risk of death, high rate of arteriovenous fistula (AVF) maturation failure, and poor vascular access outcomes, influencing the outcomes in this population . Does early creation of AVF in elderly patients with advanced CKD influence dialysis outcomes needs evaluation.

Method: We conducted a retrospective study among elderly (> 65 years) who chose to create a permanent vascular access before dialysis initiation were identified between Jan 2014-Jan 2017 in Tertiary care hospital, Lucknow and assessed in 43 elderly patients (aged ≥65 years) with CKD undergoing predialysis AVF .

Results: They were observed for the frequencies of dialysis initiation, death before dialysis initiation, and dialysis-free survival for 2 years after vascular access creation. 45.6 % were diabetic, 78.9% were hypertensive, and 14.2 % had peripheral vascular disease. In all, 67% of patients with predialysis AVF initiated dialysis within 1 years of access placement, but the overall risk of dialysis initiation was modified by patient age. Only one half of patients initiated dialysis with a functioning AVF, 47.9% of AVFs were created <90 days before dialysis initiation. The primary patency rates were 42.7% at one year and 37.8 % at 2 years. Catheter dependence at dialysis initiation was more common in patients receiving predialysis AVF. In conclusion, most elderly patients with advanced CKD who received predialysis vascular access creation initiated dialysis within 1 year. As a consequence of late predialysis placement or maturation failure, almost one half of patients receiving AVFs initiated dialysis with a catheter.

Conclusion: Insertion of an AVF closer to dialysis initiation may serve as a "catheter-sparing" approach and allow delay of permanent access placement in selected elderly patients with CKD.

P1343 DOES "FISTULA FIRST" FITS TO ELDERLY?

Valerio Patri-cia[1], Elsa Soares[1], Ana Farinha[1], Teresa Furtado[1], Catarina Abrantes[1], Patrícia Domingues[1], Ana Natário[1]
[1]Centro Hospitalar De Setúbal E.P.E., Nephrology, Setúbal, Portugal

Background and Aims: The incident patients on hemodialysis (HD) are becoming older. However, the optimal type of initial permanent vascular access (VA) among the elderly is controversial. Patient comorbidities and life expectancy are important considerations in whether to place an arteriovenous fistula (AVF) or graft (AVG).

We design an observational study to compare clinical outcomes of elderly (≥65 year old) *versus* younger patients, who underwent for first VA placement before initiation of renal replacement therapy, between January 2014 and December 2018.

Method: We evaluated successful use of VA, requirement of surgical interventions before successful use, VA in use after the first and third months on HD and clinical outcomes, until December 2019. The comorbidity burden was calculated through age-adjusted Charlson Comorbidity Index (aCCI).

We also evaluated the impact of comorbidity burden on the VA type on HD start and mortality after HD initiation.

Results: We identified 252 predialysis patients who underwent for VA placement in our center. We created two groups based on age at the time of VA placement: there were 199 (79,0%) with age ≥ 65 years (the elderly group), and 53 (21,0%) younger patients.

The elderly group presented a mean age of 76,3 ± 6,4 (maximum of 92) years on first VA placement; in the younger group, the mean age was 54,5 ± 9,1 (minimum of 26) years.

The following analysis are presented for elderly *versus* younger group. On both groups there were a predominance of male gender (66,8%; 73,6%; p=0,498) and caucasian race (95,0%; 88,7%; p=0,193).

At time of referral for AV placement, both groups presented similar mean estimated glomerular filtration rate by CKD-EPI equation (11,7 ± 3,2; 11,2 ± 3,2 mL/Kg/1,72m2; p=0,391).

Elderly group presented a significant higher aCCI (7,3 ± 1,74; 9,0 ± 1,9; p<0,001). The groups were also different in smoking status (6,0%; 30,8%; p<0,001). There were no differences on kidney disease etiology between groups, with diabetes being the most prevalent (23,1%; 24,5%; p=0,856).

For all patients, the first VA placed was AVF. Only two patient placed an AVG on second and third vascular accesses.

The median number of VA placed were similar between the two groups [1,0 (1 to 4); 1,0 (1 to 2); p= 0,811], likewise the occurrence of early complications (9,5%; 5,7%; p=0,583) and the need for surgical interventions (46,7%; 47,2%; p=1,000).

In both groups, the majority of patients started HD (80,4%; 90,6%; p=0,103), with similar successful use of the VA (68,1%; 75,0%; p=0,474).

In multivariate logistic regression, proteinuria (measured at time of referral for AV placement) and heart failure (HF) were predictors to HD initiation through a central venous catheter (CVC). This model classified correctly 74,9% of cases, with an HF odds ratio (OR) of 4,149 [confident interval (CI) of 1,721 to 10,000] and a proteinuria OR of 1,148 (CI: 1,047 to 1,259).

After the first month on HD, 34,8% of elderly patients needed a CVC, a number significantly different from the younger group (15,9%; p=0,023). The same result was observed after the third month (22,2%; 7,1%; p=0,028).

During the time of follow-up, the mortality rate was higher in the elderly group who started HD (log Rank test = 0,004), with a median survival of 29,3 (0,1 to 89,8) months, when compared to the younger group [median survival of 38,3 (0,1 to 76,9) months].

Conclusion: There were no difference in the kind of VA on HD start (definitive VA *versus* CVC) between the two groups. However, elderly patients presented more fistula failure in the first three months after HD initiation. The need of CVC due to nonfunctioning AVF on the first and three months after HD initiation was higher in the elderly.

The analysis of the patients who started HD showed that the elderly group presented a significant reduced survival when compared to the youngest patients.

P1344 10 YEARS EXPERIENCE WITH HEMODIALYSIS TUNNELED CATHETERS

Paolo Ancarani[1], Marco Amidone[1], Elena Baratto[1], Antonella Matrisciano[1]

[1]*Hospital Nephrology Unit, Sestri Levante, Italy*

Background and Aims: A well functioning vascular access (VA) is vital for hemodialysis (HD) patients. To date a native arteriovenous fistula (NAVF) remains the gold standard but patients vascular characteristics are often not optimal for vascular surgery. A tunneled central venous catheter (tCVC) are becoming increasingly used as permanent dialysis access and are also competitive to NAVF for the easy and safe insertion tecnique. Our retrospective study observe, during a 10 years period, infection rate of tCVC, bacteriologic analysis and cause of removal.

Method: From January 2010 to December 2019, 176 tCVC were placed in 158 patients (mean age 74 +/- 18) . All tCVC were inserted by nephrologist in internal giugular vein (IGV), subclavian vein (SV) and femoral vein (FV) using ultasonographic guide. Standards protocols, according to European Renal Best Practice (2010) detailing all aspects of preventive care were used. Each tCVC was followed until it was removed or until the end of the study. 62110 days was the follow up period. 143 tCVC wew placed in IGV (81,5%), 22 in FV (11,5 %) and 11 in SV (7%). The diagnosis of infection was based on clinical evidence and positive blood culture or positive exit site swab, with no sign of other infection site. We considered a tCVC disfunction in case of blood flow less than 250 ml/m'. Event rates were calculated per 1000 catheters days.

Results: Mean tCVC duration was 353 days. We observed a progressive increment in CVC prevalence during the observational period (from 15% in 2010 to 39% in 2019). Catheter replacement recurred in 19 patients and the main cause of replacement was loss of patency (0,3 per 1000 catheter days). We observed 63 catheter related bloodstream infection (CRBI) and 71 exit site/tunnel infection (ESI/TI). Incidence for CRBI was 1 per 1000 catheter days and ESI/TI was 1,14 per 1000 catheter days. In CRBI the most common organism isolated were MRSA (40%) and MSSA (26%) . In ESI/TI the most common organism isolated was Staphilococcus epidermidis (39.5%) . We used systemic antibiotics, local therapy and lock therapy with a 93% resolution without removal. 12 tCVC were removed for recurrent CRBI (0,19 per 1000 catheter days).

At the end of the observation 25 tCVC were still in use.

Conclusion: Our data showed an high survival rate of tCVC in hemodialysis patients. We observed CRBI and ESI/TI rates at the lower limits of the data reported in the literature. Infections were successfully treated conservately in most cases. Careful nursing protocol may reduced the frequency of infection and an early diagnosis can facilitate the rescue of the tCVC with systemic/lock therapy or local therapy. We consider in an elderly population with many comorbidities the use on tCVC recommended especially in patients with poor native peripheral vessels, in patients with steal syndrome high risk and also with a low life expectancy.

P1345

CATHETER FAILURE AND MORTALITY IN HEMODIALYSIS PATIENTS WITH THE TUNNELLED-CUFFED CATHERTER TIP POSITIONED IN THE INFERIOR VENA CAVA

Lu Cheng[1], Shen-Ju Gou[1], Jing Yi[1], Qian Ren[1], Tian-Lei Cui[1], Ping Fu[1]

[1]West China Hospital of Sichuan University, National Clinical Research Center for Geriatrics and Kidney Research Laboratory, Division of Nephrology, Chengdu, P.R. China

Background and Aims: For patients with multiple central vein obstruction (CVO) and exhausted all options for arteriovenous accesses, how to establish a new effective vascular access is an urgent problem, and the key point to solve this problem is where to locate the tip of catheter. This study focused on these patients and investigated the safety and efficient of tunnelled cuffed catheter (TCC) with the tip placed in the inferior vena cava (IVC).

Method: Thirty-three maintenance haemodialysis patients with vascular access malfunction presented to West China Hospital of Sichuan University from March 2013 to December 2016 were included in this retrospective study and followed up until their catheter failure or death or until June 30, 2019. The short-term efficacy and safety of the procedure placing TCC tip in IVC were observed. The survival rates of TCC with catheter tip in IVC and patients were analysed.

Results: All thirty-three patients achieved adequate blood flow to complete the first session of haemodialysis after catheterization procedure and no obvious complications, such haemorrhage, arrhythmia and pulmonary embolism. The mean survival time of the TCC with catheter tip in IVC was 58.5 (95% CI 48.8–63.4) months by Kaplan–Meier analysis. The survival rates of TCC with catheter tip in IVC were 87, 83, 75, 71% in 1, 2, 3, 4 years, respectively. The highest incidence of catheter dysfunction was at 12 months after catheterization. The mean survival time of patients was 56.2 (95% CI 46.9–65.4) months by Kaplan–Meier analysis. The patient survival rates were 88, 82, 70, 67 % in 1, 2, 3, 4 years, respectively. The highest mortality was at 12 months after catheterization.

Conclusion: Our study suggested that placement of the tunnelled-cuffed catheter tip in the IVC was safety and efficacy in the end-stage haemodialysis patients who has exhausted vascular resources with CVO. The TCC with tip in the IVC was feasible to be a long-term vascular access for these patients.

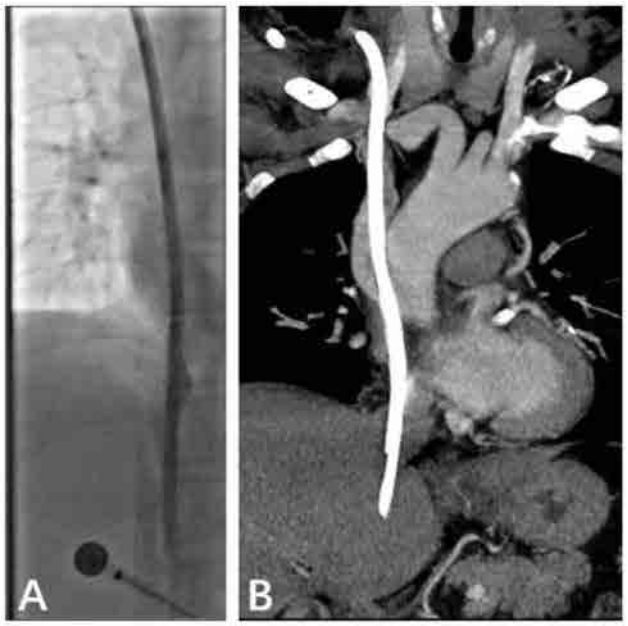


Figure 1. (A) Fluoroscopic image of a dialysis TCC with the tip of catheter placed in the IVC; (B) CT) three-dimensional reconstruction showed a TCC with the the tip of catheter past the SVC and the right atrium placed in IVC.

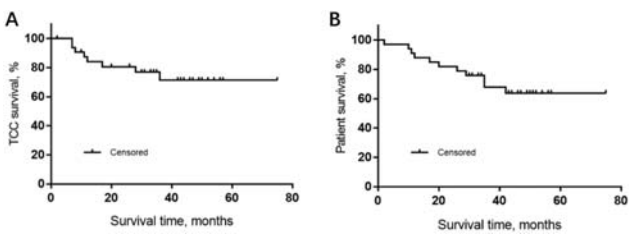


Figure 2. Survival time of TCC with catheter tip placed in the IVC (A) and patients (B).

P1346 PLANNING VASCULAR ACCESS CREATION FOR HEMODIALYSIS: IS THERE A ROLE FOR THE NEPHROLOGIST? A SINGLE-CENTER EXPERIENCE.

Ana Cunha Rodrigues[1], Luísa Lemos Costa[1], André Ferreira[1], Carolina Reis Ferreira[1], Andreia Silva[1], Jesus Garrido[1], Tânia Sousa[1], Tiago Barra[1], Sérgio Lemos[1]

[1]*Centro Hospitalar Tondela-Viseu, Nephrology, Viseu, Portugal*

Background and Aims: Vascular access planning is a crucial step in the path to dialysis treatment. Although the vascular surgeon role is of undeniable importance on vascular access creation, the nephrologist's view may be an added advantage on vascular access planning.

Method: A retrospective observational study of the vascular access appointments carried out at the Centro Hospitalar de Tondela-Viseu's nephrology department between 1/1/2017 and 13/12/2019 was performed. Of the 173 consultations reviewed, 71 patients were referred to preoperative vascular mapping, which were selected. In those selected, 38 had a vascular access built. A descriptive and statistical analysis of the population and proposed vs constructed access was performed.

Results: Of those patients referred to the vascular access appointment for vessel mapping, the median age was 70 years, the majority were men (59.2%), most of them had Chronic Kidney Disease (CKD) stage 5 (57.7%) and most frequently had Diabetic Nephropathy (38.6%) or Chronic Glomerulonephritis (14.9%) as the cause of kidney disease. The majority were Diabetic (62%), Hypertensive (91.5%), Obese (63.4%) and had a history of stroke, coronary or peripheral arterial disease (63.4%).

The vascular mapping was performed for creation of first access in 64.8% of the patients and the nephrologist most commonly proposed a radio-cephalic fistula (63.6%) as first line access creation, followed by brachio-cephalic (30.3%) and brachio-basilic (6%) fistulas. An arteriovenous graft was suggested in only 1 case and 4 patients were not referred to the vascular surgeon as they had no vascular patrimony to autologous vascular access creation. Regarding those patients who had already a vascular access at the time of this study (n=36), 58.33% coincided with the first line access suggested by the nephrologist.

We found that the nephrologist most frequently proposed a brachio-basilic fistula in older patients (median age 77.5), while younger patients had proposed other fistulas (median age 77.5 years, p=0.031). Those patients without history of stroke, coronary or peripheral arterial disease had 4.57 times more odds of being proposed to a radio-cephalic fistula (p=0.007) and those with history of atherosclerotic events had 4.36 times more odds of being proposed for a brachio-cephalic fistula (p=0.003). Patients with more vascular calcification on the vessel mapping appointment had 7 times more odds of not being proposed for a distal fistula (p=0.000) and had instead 5.56 times more odds of being proposed to a brachio-cephalic fistula (p=0.003). Gender, etiology of CKD, smoking, diabetes, hypertension, heart failure and obesity were not significantly associated with vascular access proposed by the nephrologist.

Conclusion: In light of the results of this study, we conclude that there is an important place for ultrasound preoperative mapping by the nephrologist on planning the vascular access for haemodialysis.

P1347

A DYNAMIC ULTRASOUND-IMAGING-BASED GUIDED TECHNIQUE TO TUNNELED DIALYSIS CATHETER BY MICROBUBBLES.

Erica Melo[1], Marcelo Silveira[1,2], Sérgio Souza[1], Ana Baptista[1,3], Filipe Miranda[1,3], Carolina Nascimento[1,3], Fernanda Coelho[1,2,3], Fábio Dutra[1,3], Marcel Gomes[1], Mauricio Reixeira[1], Juliana Caldas[1,2], Octavio Messeder[3], Augusto Farias[3], Paulo Benigno[1,2], Rogério Passos[1,2]

[1]Hospital São Rafael, Nephrology, Salvador, Brazil, [2]D'Or Institute for Research and Education, Rio de Janeiro, Brazil and [3]Hospital Português, Nephrology, Salvador, Brazil

Background and Aims: In patients with end-stage renal disease (ESRD), the use of cuffed, tunneled dialysis catheters (TDCs) for hemodialysis has become integral to treatment plans. Fluoroscopy is a widely accepted method for the insertion and positioning of cuffed dialysis catheters, because it is easy to use, accurate and reliable, and has a relatively low incidence of complications. The purpose of our study was to evaluate the feasibility of tunneled hemodialysis catheter placement without the use of fluoroscopy but with a dynamic ultrasound-imaging-based guided technique.

Method: From January 2015 to December 2017, we performed an observational prospective cohort study of 56 patients with ERDS who required TDC placement.

Results: The overall success rate for ultrasound-guided central access was 100%, with a mean number of 1.16 (± 0.4) attempts per patient. There were no incidences of guide wire coiling/kinking, carotid puncture, pneumothorax, or catheter malfunction. Catheter flow during dialysis was 286 (± 38) ml/min. The total number of catheter days was 7,451, with a mean of 133 days and a range of 46 to 322 days. Life table analysis revealed primary patency rates of 100%, 96%, and 53% at 30, 60, and 120 days, respectively.

Conclusion: Dynamic ultrasound-based visualization of microbubbles in the right atrium is a highly accurate method to detect percutaneous implantation of large-lumen, tunneled, central venous catheters without the need for fluoroscopic guidance technology.

P1348 EFFECT OF CILOSTAZOL ON ARTERIOVENOUS FISTULA IN HEMODIALYSIS PATIENTS

JAE WAN JEON[1], Young Rok Ham[1], Haeri Kim[1], Wonjung Choi[1], Ki Ryang Na[1], DAE EUN CHOI[1], Kang Wook Lee[1]

[1]*Chungnam National University Hospital, Nephrology, Daejeon, Korea, Rep. of South*

Background and Aims: Permanent vascular access is important in patients requiring hemodialysis. However, among patients requiring hemodialysis, even if arteriovenous fistula surgery is performed, many are unable to undergo hemodialysis with vascular access due to maturation failure.

Method: Using 194 patients who underwent arteriovenous fistula surgery, a cilostazol group (n = 107) and a control group (n = 87) were compared and analyzed for the occurrence of vascular complications.

Results: In the cilostazol group, there were less vascular complications (36.4% vs. 52.9%; p = 0.022), especially maturation failure (2.8% vs. 11.5%; p = 0.016). However, there was no significant difference between the cilostazol group and control group regarding percutaneous transluminal angioplasty (PTA) requirement nor frequency and interval to PTA after vascular surgery. The frequency of reoperations due to vascular injury after the start of hemodialysis after maturation was also significantly lower in the cilostazol group.

Conclusion: These results suggest that vascular access patients may benefit from postoperative cilostazol therapy.

P1349 **CATHETER RELATED BACTERAEMIA AND EFFECTIVENESS OF UNIVERSAL MEASURES: 11-YEAR PROSPECIVE STUDY**

Jose Ibeas[1], Carolina Rubiella[1], Oriol Gasch Blasi[2], Josep Guitart[3], Eva Criado[3], Sandy Pico[1], Tamara Lopez[1], Elena Viudes[1], Elisabeth Uroz[1], Sara Sole[3], Valle Jimeno[3], Alexis Mateos[3], Ruben Iglesias[1], Montserrat Marcet[1], Carmen Moya[1]

[1]Parc Taulí University Hospital, Nephrology, Sabadell, Spain, [2]Parc Taulí University Hospital, Infectious Diseases, Sabadell, Barcelona, Spain and [3]Parc Taulí University Hospital, Interventional Radiology, Sabadell, Spain

Background and Aims: Tunnelled catheter-related bacteraemia (BRC) of the patient in chronic hemodialysis program results in high morbidity and mortality. Antibiotic catheter lock has been suggested to reduce the incidence of BRC in clinical trials.

Aim: To demonstrate the effectiveness of universal aseptic measures in obtaining an optimal BRC rate in a long-term single-centre study.

Method: Design: Prospective cohort study, single-centre. Follow-up time: 11 years (2008-2018) Tunneled catheters: Optiflow, Hemostar, Hemosplit, Equistream, Hemoglide (Bard Access Systems, New Jersey, USA) and Palindrome (Covidien, -Medtronic, Mansfield, Massachusets, USA). Days / catheter analyzed: 207,320. Catheter placement: Ultrasound-guided interventional radiology equipment, with fluoroscopy and universal aseptic measures + 1 single dose of Vancomycin / cefazolin. Follow-up: Nursing and Nephrology and Infectious physicians. Universal aseptic measures. Heparin lock. BRC is considered to be the presence of a positive blood culture after discarding another focus and related to the negative catheter or blood culture with no other focus than the catheter. All available samples at the time of bacteraemia are analyzed: blood, sputum, urine, faeces, pleural fluid, peritoneal fluid, cerebrospinal fluid, exudates, smears etc, and their results. The BRC rate x 1000 days / catheter is evaluated

Results: Results BRC 2008 to 2018: 0.57, 0.47, 0.31, 0.1, 0.43, 0.37, 0.42, 0.16, 0.2, 0.18 and 0.04 respectively. The evaluated catheters, follow-up days, catheter-related bacteraemias, germ typing and treatment are analyzed: antibiotic vs. catheter removal in Table 1.

Conclusion: 1. The use of universal measures only, without the use in the antibiotics lock or anticoagulants other than heparin, can achieve a bacteraemia rate related to the optimal catheter, being cost / effective and avoiding possible resistance to antibiotics and side effects of other anticoagulant drugs.

2. Antibiotic sealing should be reserved for cases of difficult epidemiological control of BRC.

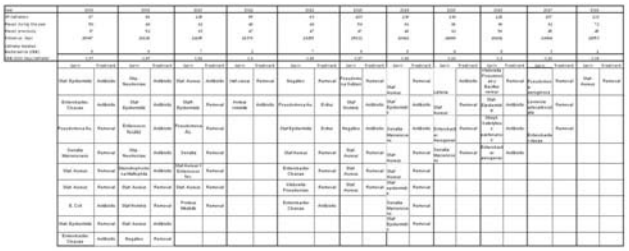


Figure:

P1350 A COMPARISON OF CENTRAL VENOUS CATHETER INFECTIONS FOR HEMODIALYSIS AND HEMATOLOGY PATIENTS

Ahmet Murt[1], Mevlut Tamer Dincer[1], Abdulkadir Ercaliskan[2], Cebrail Karaca[1], Tugrul Elverdi[2], Sinan Trabulus[1], M Cem Ar[2], Mehmet Riza Altiparmak[1], Nurhan Seyahi[1]

[1]Cerrahpaşa Medical Faculty, Nephrology, Istanbul, Turkey and [2]Cerrahpasa Medical Faculty, Hematology, Istanbul, Turkey

Background and Aims: In addition to nephrologists who use central venous catheters (CVCs) as venous access for hemodialysis, it is also a routine practice for hematologists to benefit from them for their medical applications. There may be immediate or delayed complications of CVC placement and infections are accepted as delayed complications. We aimed to compare CVC-related infections in hematology and hemodialysis patients groups both of whose CVCs were placed by interventional nephrologists. Group specific infectious agents as well as infection risk factors were analyzed in order to develop guides and practices to decrease infection rates for the future.

Method: The number of patients who were placed a CVC in bone marrow transplantation (BMT) unit was 69 (37 males, 32 females) in the year of 2019. These patients were 47,5 ± 14,3 years old. Their CVC infection numbers and rates as well as infection agents were analyzed. This group was compared with hemodialysis patients that have non-cuffed hemodialysis catheters and who were age and sex matched with the BMT group. Infection rates for 1000 catheter days were calculated separately for both groups. Catheter infections were defined as hemoculture positivity of samples obtained from catheter lumens and/or identification of any microorganism in the catheter tip. Cases were followed up from insertion day of the catheters until when infection was identified or until the day of catheter removal.

Results: Catheters remained in a central vein for a median of 25 days in hemodialysis group [range: 10-51 days] while these duration was 16 days [range:8-29 days] for BMT group. The number of cases in whom a catheter related infection was identified was 17 for BMT (24%) and nine (13%) for hemodialysis group. Infection rate was 23 for 1000 catheter days in BMT group while it was 11 for 1000 catheter days in hemodialysis patients. BMT patients have a wider range of infection agents; 78% of them being gram positives and 19% of them being gram negatives. It was noteworthy that all of the catheter related infections in hemdialysis patients were related to gram positive bacteria. Rate of infections due to extended spectrum beta lactamase (ESBL) secreting *E.coli* or *Klebsiella* was 24% and infection risk of ESBL secreting agents was directly proportional to the time spent with the catheter. Infection findings in the catheter exit site (e.g. erythema, crusts or effusions) was found as statistically significant risk factors for bloodstream infections in BMT patients while these factors were not statistically significant for hemodialysis patients.

Conclusion: Gram positive infections make up the majority of CVC-related infections both for hematology and hemodialysis patients. Infection risks due to resistant species is proportional to the time spent with catheters. Catheter exit site findings should be cautionary for probable bloodstream infections especially for immunosuppressed patients.

P1351 **MARKERS FOR AVF DYSFUNCTION; A RETROSPECTIVE ANALYSIS.**

Anna Vb Wāɒrme[1], Bernd Stegmayr[2], Salmir Nasic[3], Henrik Hadimeri[4]

[1]Institution of medicine, Department of internal medicine and clinical nutrition, Sweden, [2], Department of Public Health and Clinical Medicine,, Umeå, Sweden, [3], Research and Development Centre, FOU, Skövde, Sweden and [4]Institute of Medicine, Department of internal medicine and clinical nutrition, Gothenburg, Sweden

Background and Aims: The native Arterio venous fistula (AVF) is the recommended first choice for regular hemodialysis treatment. However, its patency is mainly limited due to stenosis and thrombosis, leading to insufficient dialysis, costly interventions, subsequent in-hospital care and follow ups.

Primary aim: To find medical or laboratory markers associated with dysfunctional AVF.

Method: Retrospective analysis of radiologic examinations and medical records was made due to clinical suspicion of AVF dysfunction (cases) from two hospitals during 2006-2014. Comparison was made with data from 52 patients without complications (controls) with repeated blood sampling during the same period. Differences between groups were calculated with Mann- Whitney test and paired statistics with Wilcoxon U test before and after examination.

Results: Mean age in both groups was 65 years. In 153 patients 473 radiological examinations were performed due to clinical suspicion of dysfunction. Angiography and PTA were made when suitable according to guidelines. In 171 of these examinations no intervention was performed. Cases versus controls had lower access flow (599±442 vs 1140±523, p<0.001), blood pump speed (291±49 vs 313±34, p<0.001), PTH (31±39 vs 39±29 pmol/L, p=0,021), Ca-phosphate product (3.9±1.1 vs 4.2±1.0, p=0.025), C-reactive protein (17±25 vs 24±38, p=0.004) and, higher in regard to recirculation (5.1±11 vs 0.5±3.4, p<0.001), HbA1c (52±16 vs 47±17, p=0.027), dose of tinzaparin (14330±8000 vs 12743±5400U/week, p= 0.025), weekly dose of erythropoietin stimulating agent (ESA, 8900±7100 vs 4900±4600U/week, p<0,001), and higher weekly iron supplement dosing (60±61 vs 41±54mg/week, p<0.001). Alfa- and Beta-blockers against hypertension were more often used among cases.

Conclusion: The reason for AVF problems in cases showed limited disturbances in Ca-phosphate hemostasis and inflammation. Instead, it seems that higher dosing of ESA and LMWH (as indicator of clotting) are factors that could be associated with development of AVF malfunction.

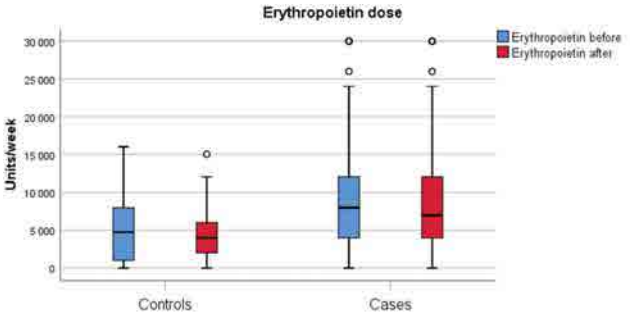


Figure:

P1352 ULTRASOUD OR LANDMARKS FOR THE PLACEMENT OF HAEMODIALYSIS CATHETERS

Nabil BELLIK[1]

[1]*University Hospital of Bab el Oued, Nephrology, Algiers, Algeria*

Background and Aims: To compare the success and immediate complication rates of the anatomical landmark method (AL) and the ultrasound guided technique (EG) in the placement of haemodialysis catheters.

Method: This was a randomized prospective study on 285 patients requiring dialysis catheter in the University Hospital of Bab el Oued between November 2016 and november 2018.

Patients were randomized into two groups: EG and AL.

The EG group had their catheters inserted under ultrasound guided technique [1], whereas the AL group had their dialysis catheter inserted by anatomical landmarks technique.

Data were collected on demography, side of insertion.

Outcome measures included successful insertion, successful insertion at the first puncture, number of attempts, and complications.

Results: A total of 285 procedures (142 EG and 143 AL) were performed during the study.

The success rate was 52.4% in the ALT group as compared with 90.1% in the EG group ($p < 10^{-6}$) in the first procedure.

First attempt success rate was 24.4% in the AL group as compared with 53.5% in the EG group (p=0.0002).

The complication rate was 45.5% in the AL group and 19.7% in the EG group ($p < 10^{-6}$).

Conclusion: The use of ultrasound guidance in the placement of haemodialysis catheters significantly improves the success rate and success rate at the first puncture and significantly decreases the incidence of catheter insertion complications.

P1353 IS AGE RISK FACTOR FOR TUNNELED VASCULAR CATHETER OUTCOMES?

Sanja Bajcetic[1], Aleksandar Jankovic[1,2], Petar Djuric[1], Bojan Stopić[1], Radomir Naumovic[1,2], Nada Dimkovic[3]

[1]Medical University Center Zvezdara, nephrology, Belgrade, Serbia, [2]Faculty of Medicine, University of Medicine, Belgrade, Serbia and [3]Academy of Medical Sciences, Serbian Medical Society, Belgrade, Serbia

Background and Aims: According to previous data, the prevalence of tunnelled cuffed vascular catheters (TCC) is more frequent in elderly as compared to younger HD patients. Still, it is not clear if elderly have decreased survival of TCC as compared with survival in younger.

Method: During the period from January 2010 to June 30, 2015, 110 permanent catheters were implanted in 64 patients (1.72 catheters per patient, 51.6% male mean age 67±12years, 20 diabetics). Out of all patients, 44 (68.7%) were older than 65 years, 12 (27.3%) were diabetic and 11 (25%) were previously treated with peritoneal dialysis. In the age-based subpopulations we compared the incidence of infections, thrombosis, chemical removal of thrombus by actilysis and TCC outcome.

Results: Reasons for TCC placement in elderly were inability of the second option and exhausted vascular approach and these reasons were found to be significantly more frequent compared to patients younger than 65 years (p = 0.020). Primary position of TCC was right jugular vein in both groups (39.1%, No = 25 vs 14.1% No = 9), more commonly in group of elderly patients, but there was no significant difference in the initial TCC position depending on the age structure of the patient (Hi square = 1.720, p = 0.886). The overall incidence of infections was 3.44 episodes per 1000 catheter days and patients' age did not affect TCC replacement, infection, thrombosis and inflammation. In the group of elderly, 27 patients had catheter infection (61.4%), 10 (22.7%) had catheter thrombosis and actilysis resolved thrombosis in 6 (13.6%) patients without significant difference as compared with younger patients. Catheter-induced bacteraemia were more common in TCC over 65 years (47 TCC vs. 12 TCC) but without statistical significance (p = 0.062). Similarly, exit site infection, was more common (14 TCC vs. 4 TCC) for those older than 65 years but also without statistical significance. Thrombosis of TCC occurred in 7 patients with TCC younger than 65 years and in 20 TCC in cohort of elderly (Hi square = 0.033, p = 0.535) (Table 1). Regarding treatment outcome, 19 (43.2%) elderly patients died while being treated with TCC, 12 patients (27.3%) changed treatment modality to peritoneal dialysis, 4 patients (9.1%) received arteriovenosus graft (AVG) and 9 patients had functional TCC at the end of follow up (20.5%) and no significant difference was found in the outcome compared to younger patients.

Conclusion: The reason for placement of TCC in elderly is the inability of other treatment options and exhaustion of vascular access. Concerning catheter related complication and outcome, there was no significant difference between the elderly and younger patient.

Table 1. Catheter related complication and outcome in elderly and in younger patients

Catheters		Age			
		<65 years	>65 years	Hi square	P
TCC in order	1	19	44	0.619	0.286
	2	11	36		
Catheter infected	No	18	33	3.089	0.067
	Yes	12	47		
Exit site infection	No	26	66	0.227	0.418
	Yes	4	14		
TCC thrombosis	No	23	60	0.033	0.535
	Yes	7	20		
TCC survival	Alive	16	51	0.994	0.218

P1354 POSTOPERATIVE MATURATION AND CHANGES IN CARDIAC FUNCTION DIFFER BETWEEN TYPES OF VASCULAR ACCESS

Koji Hashimoto[1], Taro Kanno[2], Yuji Kamijo[1], Yutaka Kanno[2]

[1]Shinshu University School of Medicine, Nephrology, Matsumoto, Japan and [2]Kanno Dialysis and Vascular Access Clinic, Matsumoto, Japan

Background and Aims: The blood flow of vascular access can be increased about tens of times after access creation. If the flow of vascular access is too low, vascular access does not provide sufficient circulation for hemodialysis and sometimes gets thrombosed. However, if the flow of vascular access is too high, it can result in high cardiac output and trigger heart failure. Although patients receiving hemodialysis require vascular access with necessary and sufficient flow, the actual change in flow after access creation is not well known. We investigated the relationships among preoperative factors, types of vascular access, clinical courses of access maturation, and changes in cardiac function.

Method: This single-center retrospective observational study included patients who underwent vascular access-related surgery, except thrombectomy, in 2016. Diameters and flow volumes of the brachial artery were examined using Doppler ultrasound before surgery and 1 week, 12 months, and 24 months after surgery. Cardiac functions were assessed using sonography at the same timepoints. Patients' background information and data related to surgery, such as anastomosis size, were extracted from medical records. The obtained data were statistically analyzed.

Results: Fifty-eight patients [37 arteriovenous fistula (AVF), 10 arteriovenous graft (AVG), and 11 partial replacement using grafts (PR)] participated in this study. Diameters of the brachial artery increased from 4.7 mm to 5.4 mm at 1 week after access surgery. Blood flows of the brachial artery also increased from 106 mL/min to 699 mL/min. Blood flow through AVG at 1week was significantly higher than that through AVF (940 ml/min vs. 589 ml/min). Although blood flow through AVF at 12 and 24 months after access creation was significantly increased than that at 1 week after access creation, blood flow through AVG at 12 and 24 months after access creation did not show significant changes, and blood flow through PR at 12 and 24 months after access creation was significantly decreased. AVG and PR required more catheter intervention for vascular access than AVF during this observational period. Preoperative blood flow of the brachial artery and cardiac outputs were positively correlated to postoperative blood flow through AVF. However, this relationship was not observed in AVG and PR cases. The amount of cardiac output increased from 4.2 L/min before surgery to 4.4 L/min and 4.6 L/min at 12 and 24 months, respectively, although not significantly. Cardiac output at 24 months after surgery significantly increased only in AVF cases.

Conclusion: The clinical maturation course after vascular access creation surgery differs between AVF and AVG cases. Because blood flow through AVF is likely to increase gradually after access creation, surgeons should consider cardiac stresses related to vascular access, especially in cases with high-flow brachial artery or high cardiac output before surgery. Blood flow through AVG is not likely to increase in the long course. However, because blood flow through AVG just after access creation is high, regardless of the brachial artery size, surgeons should consider the risk of arteriovenous access-related ischemic steal syndrome after surgery especially in cases with severe arteriosclerosis. PR is not likely to affect blood flow volume of accesses and cardiac function.

P1355 NEW SURGICAL TECHNIQUE TO CONTROL EXCESS VASCULAR ACCESS BLOOD FLOW

KIYOSHI IKEDA[1]

[1]*Ikeda Vascular Access, Dialysis and Internal Medicine Clinic, FUKUOKA-SHI, Japan*

Background and Aims: During dialysis, if blood flow rate increases above 1500ml/min. there is an increase in pulsation and a high possibility of heart failure.

In the long run, it can cause valvular disease and arrhythmia. In EDTA 2015, we presented a method of blood flow suppression for dialysis patients who had heart failure caused by excessive blood flow. However, within one year, 30% of the cases had relapsed. To solve this problem, we were able to prevent the recurrence of excess blood flow through improvement measures with a new device. Report including theoretical mechanisms.

During vascular access excessive shunt blood flow creates a heavy load on cardiac function. Performing blood flow control surgery on dialysis patients with heart failure symptoms improves said function. Depending on the surgical method, it may recur. For this reason, we devised a surgical method that theoretically considers recurrence suppression.

Method: Clinical symptoms before surgery were based on trial hemodialysis patients with significant arrhythmia and shortness of breath at the time of exertion (6 males 4 females) using EPTFE of 4mm in diameter and 4cm in length or more replaced veins extended from anastomosis. (As shown in Poiseuille's law, it is necessary to replace veins with a shunt of smaller diameter but longer length than the vein being replaced.) The point of insertion at the anastomosis portion of the artery is 4mm. In order to connect to the larger section of the vein to the other end, it is cut diagonally to make the connection secure. During the operation, blood flow was monitored using ultrasound. The central side of the tibia artery was also tied off in some cases to control blood flow.

Results: Blood flow was reduced to 787 ml/min immediately after surgery from 1970ml/min before surgery, 1007ml after 6 months, and 721 ml/min after one year. Symptoms of arrhythmia disappeared in two patients during surgery and in all cases shortness of breath during exertion disappeared the day after surgery. Cardiac index improved three months after surgery in three cases. In none of the cases did we observe the complete rekindling of blood flow after one year. The average blood flow was less than 63% of the rate before surgery.

Conclusion: Replacement of 4cm or more length sections of veins with a 4mm diameter graft was useful in improving cardiac function in dialysis patients with heart failure.

P1356 PACLITAXEL-COATED BALLOON ANGIOPLASTY FOR STENOSIS OF ARTERIOVENOUS FISTULA IN PATIENTS UNDER HEMODIALYSIS: 18TH MONTH FOLLOW-UP

IOANNIS GRIVEAS[1], GEORGIOS VOURLIOTAKIS[1], IOANNIS KANDOUNAKIS[1]

[1]417 Army Share Fund Hospital, Nephrology, Chalandri, Greece

Background and Aims: The recording of the experience of the use of paclitaxel-coated balloons in patients with End Stage Renal Disease under hemodialysis (HD) exhibiting narrowing in arteriovenous fistulas (AVF).

Method: 20 patients with ultrasonographically confirmed AVF dysfunction were subjected after angiographic screening to prosthesis with a simple angioplasty balloon, and then a balloon drug gradually released the drug paclitaxel. After the damage was restored (one-day clinic), arteriovenous communication was used immediately. The degree of vascular stenosis, blood flow to it and kt / V before and after recovery were assessed by ultrasound. At the same time, the clinical course of the patient and the vestibule of the vessel were monitored for 18 months.

Results: In the 20 patients of the study, since the damage was recovered, AVF was immediately treated without any problems. After angioplasty the degree of stenosis of the responsible vessel was statistically significantly reduced from 69.85% to 27.38% ($p < 0.05$). Flow volume increased statistically significantly from 690.47 mils / min to 942.67 mils / min ($p < 0.05$). The kt / v of patients improved from 1.25 to 1.6. During the 18th -month follow-up, the clinical course of the patients was stable, no problems related to vascular access appeared. Restenosis occurred to two patients, one of each received another successful angioplasty.

Conclusion: Drug-releasing balloons can be a useful therapeutic option for patients with AVF stenosis due to accelerated endothelial hyperplasia. The use of paclitaxel-coated balloons helps reduce the risk of restenosis of arteriovenous anastomoses and is a safe, time consuming, minimal invasive and immediate solution to AVF management.

P1357 **SODIIUM BICARBONATE CAN REPLACE THE HEPARIN AS "CATHETER LOCK SOLUTION" OF CENTRAL CATHETERS (CVC) FOR HEMODIALYSIS (HD)?**

Roberto Corciulo[1], Pierfelice Zazzera[2], Fernanda Misceo[2], Simone Corciulo[3], Carlo Lomonte[3], Pasquale Libutti[3]

[1]Policlinico di Bari, Nefrologia, Dalisi e Trapianto, Bari, Italy, [2]New Dial Srl, Ambulatorio di emodialisi, Bari, Italy and [3]Regional General Hospital "F. Miulli ", Nefrologia, Dalisi e Trapianto, Acquaviva delle Fonti, Italy

Background and Aims: The CVC often faces thrombosis and/or infection and currently there are no interventions that guarantee the efficiency of the CVC and the absence of bacterial infections. Recently Adel S. El-Hennawy et al. NDT, 2019, have shown that the use of sodium bicarbonate as "catheter lock solution" (SBCLS) in HD patients has a local anticoagulant effect and reduces the frequency of thrombosis and infections. Therefore, we wanted to use SBCLS in the management of our dialysis patients who needed HD treatment through CVC.

Method: The study included n. 15 HD patients (8M and 7F) with a CVC (see tab.1), whose CVC were previously medicated with heparin or citrate. At the time of the introduction of the SBCLS, patients showed no signs of CVC thrombosis or bacteremia; 2 patients had previously had haemorrhagic complications, 3 had malfunctioning thrombotic CVC. The observation period was 2379 days (mean 158 ± 50). Upon the conclusion of HD treatment, each port of all two-port catheters was flushed and locked with 10 mL of SBCLS (NaHCO3 at 8.4% -pH 7-8.5) and approximately 2 mL of the injected solution remained locked within the catheter. One patient who was allergic to heparin was included in the study.

Results: At the end of the study, only 3 patients had thrombotic problems with CVC and none had infections. However, none of the enrolled patients had to replace the CVC. The treatment was well tolerated by all patients who did not present complications.

Conclusion: In our short and brief experience, SBCLS has proved effective and safe in the prevention of thrombosis and infection of CVC. SBCLS appears to be an effective alternative to heparin and citrate in the management of CVC in the absence of bleeding complications. Finally SBCLS is a valid medical solution in patients allergic to heparin.

	Pts	sex	follow up/days	CVC	Malfunction	Infections
1	A.C.	M	86	tunneled in internal jugular v.	yes	no
2	L.S.	M	153	tunneled in internal jugular v.	no	no
3	L.L	M	103	tunneled in internal jugular v.	yes	no
4	S.A.	M	152	tunneled in subclavian v.	no	no
5	G.M	M	223	Tesio cath in internal jugular v.	no	no
6	I.P	M	**220**	tunneled in internal jugular v.	no	no
7	L.V.	F	204	tunneled in internal jugular v.	no	no
8	M.A.	F	205	tunneled in internal jugular v.	no	no
9	M.C.	F	174	tunneled in femoral v.	no	no
10	N.P.	M	203	tunneled in internal jugular v.	yes	no
11	P.G.	F	141	tunneled in femoral v.	no	no
12	P.P.	M	188	tunneled in internal jugular v.	no	no
13	G.A.	F	140	tunneled in internal jugular v.	no	no
14	M.N.	F	127	tunneled in internal jugular v.	no	no
15	M.G.	F	60	tunneled in internal jugular v.	no	no
		8M/7F	**2379 mean 158 SD 50**			

P1358

THE MONITORING OF FIRST LEVEL IN DIAGNOSIS OF COMPLICATION OF VASCULAR ACCESS: MULTICENTRIC STUDY ON 900 HEMODIALIZED PATIENTS WITH FOLLOW UP TO 5 YEARS.

Ersilia Satta[1], Carmine Romano[2], Carmelo Alfarone[3], Sandro Gentile[4], Domenico Russo[5]

[1]Nefrocenter research, Nyx Start up, Naples, Italy, [2]Nefrocenter research, Nyx/sturt up, Naples, Italy, [3]Nefrocenter research, Naples, Naples, Italy, [4]Nefrocenter research,, Nyx sturtup, Naples, Italy and [5]Institute of nephrology, University of Study Federico II, Naples, Italy

Background and Aims: Vascular Access (VA) is the lifeline of hemodialysis patient. The universal goal of access monitoring is to identify access stenosis and enable intervention prior to thrombosis; thereby, maximizing access longevity and minimizing morbidity. The advent and use of techniques including dynamic and static venous pressure monitoring, physical examination, access flow measurement, imagining and combined imaging and flow monitoring by duplex ultrasound demonstrate that it is possible to predict which accesses are at high risk for future thrombosis.

Currently arteriovenous fistula (AVF) and arteriovenous graft (AVF) have been recognized as the permanent access. This study takes advantage of the opportunity to utilize data from 19 associated Dialysis Clinics to examine trends in VA use, trends in patient characteristics and practice associated with VA.

Determine the status quo of the overall information related to the VA to start a five years follow up study with the aims to reduce VA complications 8stenosis and thrombosis) and related hospitalization days to improve patient's quality of life.

Method: VA data were collected for each patient at study entry. Practice pattern data from the facility medical director, nurse manager and VA surgeon were also analyzed. We have developed a mask on the management database to implement the first level monitoring of access and collected data at each treatment (Fig.1)

Results: Average age of 801 patients enrolled was 73,5 years. Native AVF was used by 79%, AVG by 2% and CVC by 19%. As the age increase as well as he use of CVC move from 6% (15-39(years) to 50,5% in patients with more than 85 years. Most frequent complications were: Thrombosis 16,5 %, Infectios 5,5%. Related VA hospitalization days are 28,7 % of total days. Average dialysis goals achieved were: QB 290 ml/Min; blood processed 69,7 L; KT/V:1,35.

Conclusion: By interpreting collecting data for specific performance measures using accurate reports allow health care professionals to highlight the VA performance/inefficiences and provide correct information to the clinical staff to support them in their daily clinical practice and decision making.



Fig.1 Shows the masks implemented on the management database in a lineAVF and in b line CVC.

P1359 PATTERNS OF CENTRAL VENOUS OBSTRUCTION AND OUTCOMES OF ENDOVASCULAR INTERVENTIONS IN CKD PATIENTS ON HAEMODIALYSIS

Rajendra Mathur[1], Dibyajyoti Kalita[1], Amar Mukund[2]

[1]Institute of Liver & Biliary Sciences, Nephrology, New Delhi, India and [2]Institute of Liver & Biliary Sciences, Interventional Radiology, New Delhi, India

Background and Aims: Central Venous Obstruction (CVO) is one of the major causes of morbidity in Chronic Kidney Disease (CKD) patients on maintenance Hemodialysis (HD).

The aim of the study was to assess the patterns of CVO and the role of Endovascular interventions to restore the patency of vascular access in patients on HD with CVO.

Method: We report 15 cases of CVO in HD patients between April 2015 to April 2018. Data regarding patients' basic information, primary disease, dialysis duration, access at initiation, number and sites of central venous catheterizations, vascular segments stenosed or thrombosed, type of endovascular interventions done and outcomes were collected from electronic record system.

Results: Out of 15 cases of CVO, 11 had the first dialysis with a temporary catheter either to Internal Jugular vein or femoral vein. The average time of presentation to our hospital from initiation of dialysis was 14.8 months. 8 patients presented with symptomatic SVC obstruction. The most common site of CVO was left Brachio-cephalic vein followed by right brachio-cephalic, right subclavian and left subclavian vein. 12 patients underwent Percutaneous Transluminal Angioplasty (PTA) and 3 required bare metal stenting (BMS) along with PTA. One patient required repeat PTA after 4 months. 11 patients did not require further procedure in the mean follow up period of 110 days. PTA was found to be successful in 11 out of 12 cases. Post PTA 9 patients underwent tunneled HD catheter insertion.

Conclusion: Patients of CKD who present late to the nephrologists require HD to be initiated through temporary catheters to central veins. Repeated central venous catheterization is associated with CVO. Endovascular intervention is an effective modality for maintaining HD access patency in such cases.

P1360 ARTERIOVENOUS FISTULA MATURATION DELAY - ENDOVASCULAR TREATMENT IS A VALID APPROACH

Rui Nogueira[1], Nuno Oliveira[1,2], Emanuel Ferreira[1,2], Ana Belmira[1], Rui Alves[1,2]

[1]Centro Hospitalar Universitário de Coimbra, Nephrology, Portugal and [2]Faculdade de Medicina da Universidade de Coimbra, Nephrology, Portugal

Background and Aims: Arteriovenous fistula is the optimal vascular access for hemodialysis as it has the best long-term patency rate and the lowest complication rate among hemodialysis vascular accesses. However, its occasional delayed maturation poses a challenge. Surgery has been advocated as the best treatment option. We proposed to evaluate the results of endovascular approach of arteriovenous fistula's maturation delay in our hospital.

Method: We conducted a retrospective study, selecting patients referenced to our diagnostic and therapeutic angiography unit due to arteriovenous fistula delayed maturation, between April 2017 and October 2019. Physical examination and echography were used to confirm arteriovenous fistula delayed maturation.

Results: Thirty patients were referenced. Nine were excluded as maturation delay was not confirmed. Three patients were excluded due to extensive outflow stenosis since they were proposed to new vascular access creation. The other 18 patients were subjected to percutaneous endovascular treatment. Mean patient's age was 65 years old. Twelve patients (66,7%) had forearm fistulas and the remaining (33,3%) had arm fistulas. Fourteen patients (77,7%) had maturation delay due to peri-anastomotic stenosis. The mean follow-up time was 14 months, (minimum - 3 months; maximum - 33 months). Seventeen fistulas (94,4%) were salvaged, although 3 (16,7%) needed a second intervention. Primary and secondary patencies at 3, 6 and 12 months were 77,8% vs. 94,4%, 69,2% vs. 92,3% and 75% vs. 100%, respectively. Arm fistulas had 83,3% of primary and secondary patencies. Forearm fistula's primary and secondary patencies were 66,7% vs. 91,6%, 57,1% vs. 100% and 60% vs. 100%, at 3, 6 and 12 months, respectively. When maturation failure was due to peri-anastomotic stenosis, primary and secondary patencies were 71,4% vs. 92,9%, 66,7% vs. 100% and 66,7% vs. 100% at 3, 6 and 12 months, respectively.

Conclusion: Even though we are still lacking consensus about the best treatment option for fistula's maturation delay, current guidelines suggest that, at least in delayed maturation due to peri-anastomotic stenosis, surgery may be the best treatment. Our results point out that endovascular treatment is a good treatment option for arteriovenous fistulas with maturation delay, mainly in the arm fistulas. Even though surgical treatment appears to have better primary patency, a step by step approach seems to be a valid approach, as our secondary patency shows.

P1361

IS THE INFLAMMATORY STATE A DETERMINING FACTOR OF THE PRIMARY PERMEABILITY OF ARTERIOVENOUS FISTULES?

LUIS GUILLERMO PICCONE SAPONARA[1], MARIA PAZ CASTRO FERNÁNDEZ[1], NANCY GIOVANNA URIBE HEREDIA[2], Agustin Carreno[1], SARA ANAYA FERNANDEZ[1], MARIA DIAZ LÓPEZ[3], PATRICIA SANCHEZ ESCUDERO[1], Diego Siedel[1], ALICIA FERNANDEZ MELERO[1], MARIA DEL CARMEN VOZMEDIANO POYATOS[4]

[1]Ciudad Real, Nephrology, Ciudad Real, Spain, [2]Guadalajara, Cardiology, Guadalajara, Spain and [3]Ciudad Real, ANGIOLOGY, Ciudad Real, Spain

Background and Aims: Clinical practice guidelines recommend an arteriovenous fistula (AVF) as the preferred vascular access for hemodialysis and are associated with a lower incidence of morbidity and mortality. However, primary vascular access (AV) failure is not uncommon. Low-grade inflammation is present in ERCT. We identify the inflammatory parameters that influence the primary permeability of vascular access for hemodialysis.

Method: Cross-sectional study; We include all the AVs performed in the HGUCR. We evaluate the initial operation after the creation of the AV. Demographic variables (age, sex), aetiology of CKD and associated comorbidity were collected. Statistical analysis with SPSS 25.0. Categorical variables are expressed as percentages and are compared using the Chi2 Test. Quantitative variables are expressed as mean ± standard deviation and the t-student was used to compare them. We performed a multivariate analysis to determine those factors involved in the primary failure of the VA. Statistical significance for a value of $p < 0.05$.

Results: 600 VA performed on 466 patients were reviewed between October 2009 and December 2019. 492 autologous VA (86.8%) and 75 prosthetic VA (13.2%) were performed. The mean age of the patients was 65.3 ± 14.2 years and 66.2% were male. The most frequent etiology of CKD was diabetic nephropathy (29.9%), followed by non-affiliated (18%) and glomerulonephritis (16.5%). 90.8% of the patients had arterial hypertension (HT), diabetes mellitus (DM) 48%. 77.2% of AV presented primary permeability. In the univariate analysis using Chi2 and T student, statistical age ($p = 0.017$), HT ($p = 0.002$), statin treatment ($p = 0.002$), antiplatelet therapy ($p = 0.001$), low ferritin levels ($p = 0.011$) and PCR ($p = 0.019$). When performing a multivariate analysis, the high CRP figures (OR: 0.64 95% CI 0.42-0.98 $p = 0.043$) and ferritinemia (OR: 1.04 95% CI 1.01-1.06 $p = 0.013$) are predictive factors of primary AV failure.

Conclusion: In our study, high CRP decreases the probability of primary functioning of AVFs by 36% and elevated ferritin levels are predictors of primary failure after adjusting for age and sex in the multivariate model.

P1362

AN EXPERIENCE WITH PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY IN ARTERIO-VENOUS FISTULA DYSFUNCTION SECONDARY TO VASCULAR STENOSIS.

Mohammed Shoeb Ahmed Khan[1], Faiz Mukthar[1], Vinod Kumar K[1], Bipi Prasannan[1], Rohit P. V Nair[2], Arjun Sadananda[2], V. Narayanan Unni[1]

[1]Aster Medcity, Nephrology, Kochi, India and [2]Aster Medcity, Interventional Radiology, Kochi, India

Background and Aims: Arterio-venous fistula (AVF) is the life line of a hemodialysis patient. Dialysis Outcomes and Practice Study (DOPPS) showed that one year patency for AVF in the USA is 68% and 83% in Europe. The maintenance of the vascular pathways are vital. Vascular stenosis in native AVF at the anastomotic sit, venous cannulation zone, outflow vein or the central vein can lead to loss of AVF. Stenosis necessitate vascular intervention or creation of a "de novo" AVF. The number of possible vascular access sites are limited.

Aim : To evaluate the outcome of percutaneous transluminal angioplasty (PTA) in arterio-venous fistula due to vascular stenosis.

Method: This is a retrospective study of two years (02.05.17 to 02.05.19). Records of patients admitted to our hospital were obtained from hospital archives and images from the hospital radiology archive system. Demographic characteristics, duration of dialysis, stenosis or occlusion level, patency rates of AVF were evaluated. All procedures were performed by interventional radiologists in a hybrid cath lab. Antegrade, retrograde, or both antegrade and retrograde punctures were used, depending on the site of the stenosis as deemed on preoperative ultrasound. A complete angiogram from the proximal arteriovenous anastomosis to the central venous outflow was performed in all cases. A successful percutaneous balloon angioplasty was defined when there was no more than 30% residual stenosis (KDOQI). Primary patency rates were assessed at six months and one year.

Results: Total number of patients studied were 16. The average age was 66.6 years. All were hypertensive and diabetics comprised 75% of study group. Coronary artery disease was established in 81.25%, and two patients were known to have chronic liver disease. Most common type of AVF was the left brachio-cephalic (62.5%), followed by radio-cephalic (37.5%). Average dialysis vintage of AVF at the time of procedure was one year. Previously failed AVF was present in two patients. There were 18 vascular stenosis in 16 patients. The most common site of stenosis was the venous cannulation zone (62.5%), followed by anastomotic site stenosis (31.5%) and central vein stenosis (18.75%). Successful PTA was done in 12 patients. There were no complications; hemodialysis was resumed within 24 hours after the procedure. The primary patency rate at three months was 100%, six months was 75% and at one year it was 37.5%. Four patients were lost to follow up. Mean follow up was 9.41 ±6.79 months. None underwent a repeat PTA.

Conclusion: Percutaneous transluminal angioplasty is effective for salvaging arterio-venous fistula in majority of hemodialysis patients.

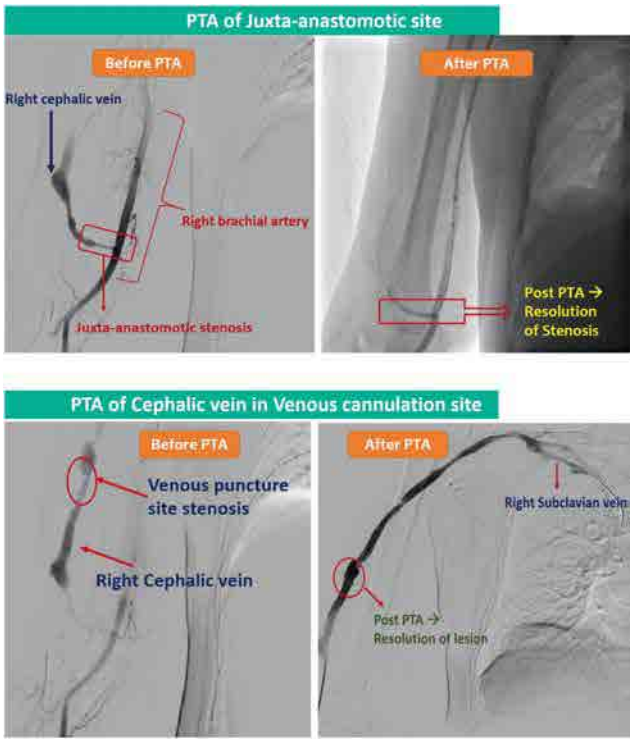


Figure:

P1363 **ON-LINE SURVEILLANCE OF ESTABLISHED HAEMODIALYSIS ARTERIOVENOUS FISTULA UTILISING FRESENIUS THERAPY MONITORING SYSTEM AND EUROPEAN CLINICAL DATA SYSTEM (EUCLID): THE SHUNT STUDY- BASELINE DEMOGRAPHICS OF PARTICIPANTS**

Richard Bodington[1], Adil Hazara[1], Sunil Bhandari[1]

[1]*Hull Royal Infirmary, Renal department, United Kingdom*

Background and Aims: The arteriovenous fistula (AVF) is well established as the preferred vascular access for haemodialysis (HD). However AVF remain prone to a number of complications, the most common of these being thrombosis, which usually occurs on the background of a developing stenosis. The development of stenosis can be detected and the lesion treated before thrombosis occurs; this forms the rationale behind monitoring and surveillance programs. Surveillance uses more resources than monitoring and has not been convincingly shown to improve outcomes such as access loss. The evidence supporting the use of the various monitoring techniques in AVF is in the main observational, under-powered, out of date and based on studies populations of predominantly arteriovenous grafts (AVG). Monitoring techniques have been shown in multiple studies to have higher utility in AVF than AVG. The modern, high efficiency dialysis machine with integrated on-line clearance monitoring (OCM) necessitates the reconsideration of the performance and utility of monitoring metrics such as Kt/V and access recirculation (AR). The lack of evidence surrounding monitoring techniques is recognised by KDOQI who recommend that further research is required to validate these indicators. In this study we aim to examine if changes in AR and Kt/V values obtained through OCM during HD can help predict AVF failure.

Method: SHUNT is a UK single-centre prospective cohort study with a 1-year follow-up of all study participants. The 100 participants are aged over 18 years receiving in-centre maintenance HD with through an established AVF. We use the Fresenius Therapy Data Monitoring System (F-TDMS) and EuCliD system to capture all dialysis treatment data from Fresenius 5008 machines. This will allow trend analysis for AR and Kt/V to assess the accuracy of these parameters in predicting access failure. The primary outcome measure is to determine whether changes in AR and Kt/V trends are able to predict AVF failure. Secondary outcome measures include assessment of the utility of AR and Kt/V alone to predict AVF failure, the comparison of AR and Kt/V trends pre- and post-intervention and the assessment of the number of patients referred for fistulograms, requiring AVF intervention and suffering access failure, VA related hospitalization and central line use.

Results: The planned 100 AVF patients have been recruited. Participants' mean and median age is 63.07 and 63.32 years respectively with a standard deviation of 14.21. The patients are 59% male and the mean BMI is 28.27kg/m^2. The mean vintage on HD is 3.41 years with a median of 2.32 years. The AVF are 37% brachiocephalic, 35% radiocephalic (65% of which are at the wrist), and 13% brachiobasilic transposition. Aetiology of primary renal disease is diabetic nephropathy in 22%, glomerulonephritis in 19%, unknown in 19%, obstructive in 15%, polycystic kidney disease in 11%, renovascular/hypertensive in 9% and assorted other pathology (eg. ATN, TIN) in 5%.

Conclusion: Our study participants are broadly representative of the UK's AVF population as a whole. We hope that the SHUNT STUDY will provide representative, up-to-date and robust evidence for the utility of these basic monitoring tools in the prediction of AVF stenosis in the age of OCM.

P1364 CATIONIC CELLULOSE BASED PAD STOPS BLEEDING WITHIN FIVE MINUTES AFTER HEMODIALYSIS.

Kazuhiko Shibata[1,2], Hirokazu Morita[3], Mitsutaka Ueda[3], Shigeru Nakai[4]

[1]Yokohama Minami Clinic, Yokohama, Japan, [2]Artisan-Lab Co.,Ltd, Tokyo, Japan, [3]NIPRO CORPORATION and [4]Fujita Health University, Department Department of Clinical Engineering School of Medicine, Japan

Background and Aims: In case of prolonged bleeding at the vascular access site after hemodialysis, a nurse must compress the bleeding site longer than usual. This situation causes the risk of intravascular thrombosis and consumes valuable time of both patients and staff. Therefore, the method that can surely stop bleeding from the puncture site in short time is desired. Nowadays, chitosan is considered as one of the strongest hemostatic substance. Nipro Corporation and Artisan-lab co.,Ltd found the cationic cellulose could clot blood faster than chitosan in the activated clotting time (ACT). After carefully examining its safety and efficacy, it was approved as medicine by the Japanese Ministry of Health, Labor and Welfare. Then, a trial to verify its clinical efficacy as a hemostat was conducted in the Yokohama Minami Clinic.

Method: 150 hemodialysis patients treated at the Yokohama Minami Clinic excluding those using catheters or having with good hemostasis were selected as candidates for this study. 127 patients (64 men and 63 women) among them agreed to participate in this study after our explanation. 547 times of 5 minutes' compression hemostasis were performed to the patients using cationic-cellulose pads for hemostasis from December 29th in 2019 to January 3rd in 2020. We checked the bleeding evidence of the puncture sites at the both timing of immediately after relieving their compression and the start of the following session. At their following session starting, we also checked the existence of adverse effects at their puncture sites, such as contact dermatitis or infection.

Results: Five of 547 cases (0.9%) had bleeding immediately after their compression relieving, and they needed to prolong their compression (the average of prolongation time was 3.0 minutes). But the other 542 cases (99.1%) successfully stopped bleeding within 5 minutes. All cases except two cases with redness at the adhesive tape attached site did not have any adverse effects such as redness, itching or pain of their hemostatic pad attached sites, including one case who forgot to remove his hemostatic pad until 48 hours later. The nurses could reduce their efforts to check the patients' hemostasis and work smoother than usual, throughout this study period.

Discussion: In most cases of this study, the cationic-cellulose pad could stop bleeding within 5 minutes without any adverse effects. This result suggests that this material has sufficient performance for clinical use. The cationic-cellulose used for the hemostatic pads in this study had already had high enough quality for clinical use and it was produced by Kao Corporation. At present, clinically available strong hemostatic agents are too expensive to be applied for every patient. But the cost to get the cationic-cellulose to make hemostatic pads may be reduced enough low to be distributed to all hemodialysis patients because this material is mass-produced for hairdressing agent.

Conclusion: The cationic cellulose pad can save precious time and efforts of both patients and staff through its quick hemostasis.

Figure: The cationic cellulose pad

P1365 **HEMODIALYSIS CATHETER-RELATED BLOODSTREAM INFECTIONS : A CASE SERIES**

Ouni Amal[1], Meriem Ben salem[1], Malek Mojaat[1], Hadj Brahim Mayssa[1], Ben salah Manel[1], Mouna Hammouda[1], Handous Insaf[1], Ltaief Ahmed[1], Hawala Fawzi[1], Ines Jaafer[1], Aloui Sabra[1], Habib Skhiri[1]

[1]*Monastir university Hospital, nephrology*

Background and Aims: the recourse to catheter among patients on hemodialysis is frequent due to many reasons. It is highly associated to a risk of infection in comparison to AVF. The aim of our study was to determine the clinical and bacteriological parameters in patients hospitalized for dialysis catheter related bloodstream infections.

Method: We conducted a retrospective descriptive study based on the data of patients hospitalized for hemodialysis catheter-related bloodstream infection in the department of nephrology in Fattouma Bourguiba University hospital between January 2013 and February 2018. Data concerning the bacteriological exams were obtained from our bacteriology laboratory.

Results: 50 patients were included with a mean-age of 56 years old. 74% were women, 30% diabetic and 18% considered immunodepressed. The indications for the placement of catheter were: 21 patients waiting for the creation of AVF, 16 patients with a dysfunction of AVF, 6 patients with AKI and 7 patients with inadequate veins for the creation of AFV. The IJV was the site of insertion in 74% of patients (with 4 % of tunneled catheters).

26 % of patients developed a septic choc, and 74 % developed a sepsis. The culture of the specimen of catheters was positive in 32 patients (64%). Staphylococcus aureus was isolated in 14 patients (28%) with MSSA among 8 patients and enterobacteria among 8 patients. Hemoculture was only positive in 13 patients. The catheter was removed in the majority of cases except in 6 patients in whom there was no other venous access. The evolution was favourable in 80 % of patients. 5 patients developed an infective endocarditis as a secondary localization.

Conclusion: The AVF remains the best vascular access for hemopadialysis patients. The recourse to catheters must be considered as a last choice because of the risk of infections which frequently necessitates the hospitalization with an increase in mortality.

P1366 **THE ROLE OF A NEPHROLOGIST IN THE CREATION OF VASCULAR ACCESS FOR HEMODIALYSIS**

Gennadii Fomenko[1]
[1]Chernihiv Regional Hospital, nephrology & hemodialysis, Chernihiv, Ukraine

Background and Aims: The creation of vascular access: has it anything to do with a nephrologist ? At first glance, the concept of vascular access is the responsibility of surgical specialists. However, a nephrologist has started executing some of the common intensive treatment methods, using the equipment and techniques, specific to the field of dialysis. In this case, a nephrology specialist sets up different kinds of vascular access, namely the AV (arteriovenous) fistula, the AV graft, and the venous catheter; he/she is, therefore, responsible for its assessment and congruent correction.

Method: the usage of statistical data, gathered by the medical specialists of the dialysis unit of the Regional Chernihiv Hospital; the analysis of the possible nephrologist's contribution to the creation of vascular access in patients with kidney diseases.

Results: During 2017-2019, 332 catheterizations were performed, during each of them vascular access was established:

- in the *vena jugularis interna dextra;*
- in the *vena jugularis interna sinistra;*
- in the *vena subclavia* or the *vena femoralis* (see Figure 1).
- Among them, 293 catheterizations were executed in patients with chronic kidney disease, the rest, 39 procedures, - in patients with acute kidney injury (see Figure 2).
- Subsequently, 190 patients with chronic kidney disease underwent AV fistula surgeries, performed by the vascular surgeons.
- Aiming to reduce the risk of possible complications, the nephrologists used real-time ultrasound guidance during catheterization. Having completed the medical procedure, the chest of a patient was x-rayed, aiming to ensure the proper position of the catheter tip and avoid pneumothorax or hemothorax.
- Permanent venous access was established in patients with chronic kidney disease whose AV fistulas couldn't mature.
- Predominantly, catheters were implanted in the internal jugular vein, the position of the distal end of the catheter was determined radiologically and placed at the level of the cavoatrial junction or deeper, which provided the blood flow rate of 300 ml / min.
- A nephrologist, performing the insertion of tunnel catheters into the central veins, took measures to prevent the infection, assessed the adequacy of blood flow rate, controlled the dose of hemodialysis, and performed the necessary manipulations.

Conclusion: 1. A nephrologist, in collaboration with a vascular surgeon, is particularly interested in the creation of vascular access in a patient with chronic kidney disease at the pre-dialysis stage;

2. In most cases, a nephrologist can set up temporary or permanent vascular access in patients with chronic kidney disease or acute kidney injury, which improves the quality of hemodialysis by making him an active participant of the treatment process.

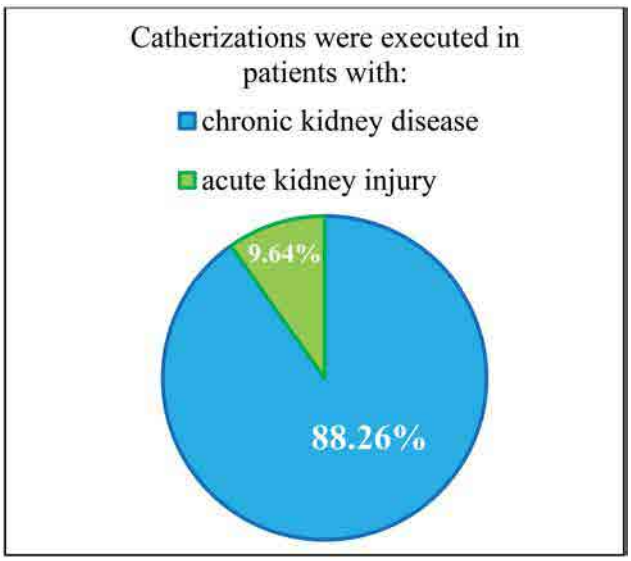


Figure 1:

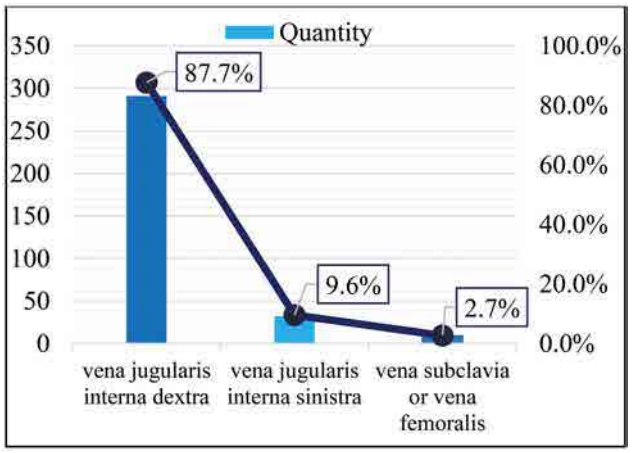


Figure 2:

P1367 **THE RELATIONSHIP OF SERUM PHOSPHORUS LEVEL AND ARTERIOVENOUS FISTULA DYSFUNCTION IN MAINTENANCE HEMODIALYSIS**

Hyung-Jong Kim[1], Mi Jung Lee[1]

[1]*CHA Bundang Medical Center, Internal Medicine, Seongnam, Korea, Rep. of South*

Background and Aims: It is known that maintenance of function of arteriovenous fistula (AVF) is very important in the management of hemodialysis (HD) patients. Therefore, identifying a risk factor for decreased vascular access flow has a clinical relevance in real world practice. Although hyperphosphatemia plays a crucial role in the pathogenesis of vascular calcification, there is lack of studies evaluating the effect of hyperphosphatemia on AVF. This study investigated the impact of serum phosphorous (P) on vascular access flow in HD patients.

Method: Sixty-two maintenance HD patients who visited dialysis unit of Bundang CHA Medical Center from November 2016 to December 2017 were included in this study. Serum P levels were determined every month and time-averaged serum P was calculated. All patients had left arm AVF (side to side anastomosis) and vascular access flow was assessed by Transonic HD 03. Decreased vascular access flow was defined as less than 600 mL/min.

Results: The mean age was 57.9 ± 12.1 years, 32 patients (51.6%) were men. The mean serum P levels were 5.1 ± 1.1 mg/dL and the vascular access flow was 1,071.4 ± 504.2 mL/min. Decreased vascular access flow was observed in 14 of 62 patients (22.6%). In univariate analysis, higher serum P was significantly associated with decreased vascular access flow (odds ratio [OR]=2.089, 95% confidence interval [CI]=1.159-3.766, P=0.014). But there was no significant association of dialysis blood flow rate, ejection fraction on echocardiography and serum calcium (Ca) levels with vascular access flow. Multivariable analysis indicated that higher serum P was independently associated with greater risk of decreased vascular access flow (OR=4.012, 95% CI=1.651-9.711, P=0.002). Old age, reduced EF, low dialysis blood flow rate and higher serum Ca was not associated with vascular access flow.

Conclusion: This study demonstrated that higher serum P was the independent risk factor for decreased vascular access flow in maintenance HD patients. Serial monitoring of serum P may be helpful to stratify the risk of vascular access dysfunction in these patients.

P1368 EVOLUTIVE PROFILE OF HEMODIALYSIS VASCULAR ACCESSES

Mechri Aya[1], Chermiti Mohamed[1], Imen Gorsane[2], Elloumi Zied[1]

[1]Tunis, nephrology, kef, Tunisia and [2]Tunis, medecine A Charles Nicolle hospital, Tunis, Tunisia

Background and Aims: Arterio-venous fistula (AVF) is considered to be the first choice vascular access for hemodialysis (HD). Hemodialysis catheter (KT) may be a temporary or permanent alternative. The aim of our work was the study of indications, and complications' contributing factors of KT, and to identify complications and predictive factors of AVF survival.

Method: It's a retrospective, descriptive, analytic, and multicentric study interesting AVF and KT created in patients with end stage renal disease and who have been treated with hemodialysis in the four hemodilysis centers of the KEF governorate in Tunisia over the period from 01/07/18 to 31/12/18.

Results: We have studied 288 AVF and 148 KT that were created in 205 patients averaging 58.14 ±15.56 years in age [25-93 years]. The sex ratio was 1.5. Diabetic nephropathy was the most common (25.9%). For the KT, the main indication was the wait of AVF creation (68.9%). The overall incidence of immediate complications was 11.5%. Dysfunction was reported in 23.6% of cases with obesity (p=0.035) and tunneled type of KT (p=0.045) as contributing factors. KT infection, occuring in 39.2% of cases, was promoted by prolonged duration of use (p=0.041) and hemoglobin level <8 g/dl (p=0.039). The use of an antiseptic lock reduces infections' risk (p=0.011). For the AVF, the most common complications were thrombosis (36.2%), aneurysm (29.9%) and stenosis (22.6%). The survival rates were 60% at 2000 days. The AVF impairing factors were diabetes (p=0.05), obesity (p=0.05), the anterior AVF creation (p=0.011), AVF grafts (p=0.016) and the use of an anticoagulant therapy (p=0.0001). An antiplatelet therapy improved AVF patency (p=0.02).

Conclusion: Despite of concerted efforts, much remained to be done to reduce the incidence of catheterization, the creation of AVF on time and the prevention of its complications.

P1369 ACUTE EXTRACORPOREAL DIALYSIS USING TWO-WAY PICC POWER INJECTABLE IN YOUNG CHILDREN

Luigi Annicchiarico Petruzzelli[1], Vittorio Serio[1], Ilaria Luongo[1], Daniela Molino[1], Bruno Minale[1], Lorenza Lepore[1], Serena Ascione[1], Carmen Lubrano[1], Gabriele Malgieri[1], Carmine Pecoraro[1]

[1]*A.O.R.N. Santobono-Pausilipon - Ospedale Santobono, Nephrology and Dialysis, Napoli, Italy*

Background and Aims: Acute extracorporeal dialysis is a short treatment, performed by a central venous catheter of large size, ensuring high flow. These devices have limitations: high caliber, excessive length, impossibility of tunneling and exit-site location in the supraclavicular region, with a subsequent high risk of dislocation and contamination. The authors report a new approach to dialytic central venous catheters selection in children.

Method: From January 2013 to December 2017, 16 children weighing less than 15 kg needed acute extracorporeal dialysis. Patients received an ultrasound guided percutaneous implantation of a two-way PICC power injectable catheter, in the right internal jugular vein or in the anonymous right vein. The device size always respected the ratio of 1/3; the catheters were cut to be adapted to child height, and subclavear tunnelizations and stabilizations were ensured. The hemodialysis was performed with the Prismaflex Gambro system. The effectiveness of treatment was evaluated by recirculation test and by measuring the KT/Vat the third hour, expressing the dialysis adequacy.

Results: Two-way power injectable central venous catheter,sized from 5 to 7 Fr and long from 8 to 15 cm were used. The recorded blood flow ranged from 4.7ml/min/kg to 7ml/min/kg; a KT/V variable from 0.5 to 1 was detected; the recycling rate was between 32% and 40%. No catheter related complications were observed.

Conclusion: In children weighing less than 15 kg, PICC power injectable have lower blood flow and higher recirculation rate compared to traditional dialysis catheters. However, the dialytic adequacy was suitable for an acute hemodialysis treatment. In addition, these catheters are available in a wide range of calibers and result more adaptable to the venous system of younger children.

Age (months)	Weigth (Kg)	Catheter (PICC)	VEIN	catheter days	KT/V	QB ml/min /kg
6	8	5 Fr, 12 cm	Anonymous vein right	10	0,7	7,5
18	12	5 Fr 10 cm	Internal jug right	10	0,6	6,66
18	10	5 Fr 8 cm	Anonymous vein right	7	0,65	4
24	12	7 Fr 15 cm	Anonymous vein right	8	0,5	5,8
40 days	5	5 Fr 15 cm	Internal jug right	6	0,5	3
72	18	7 Fr 15 cm	Internal jug right	21	0,7	3,8
18	11	7 Fr 14 cm	Internal jug right	7	0,6	6,6
18	10	7 Fr 14 cm	Internal jug right	7	0,8	7
36	13	7 Fr 12 cm	Internal jug right	8	0,6	4,6
18	19	7 fr 13 cm	Internal jug right	6	0,7	4,2
24	18	7 Fr 13 cm	Internal jug right	16	1,3	4,4
6	6	6 Fr 13 cm	Internal jug right	15	0.7	8,3
3	4	5 Fr 13 cm	Internal jug right	60	1	10
3 days	1,7	5 Fr 10 cm	Internal jug right	60	0,7	17
36	15	7 Fr 13 cm	Internal jug right	30	0,7	4
1	3	5 Fr 10 cm	Anonymous vein right	15	0,7	6

Figure:

P1370 **UNPOPULAR SOLUTIONS FOR VASCULAR ACCESS DIFFICULTIES IN HEMODIALYSIS PATIENTS: A CASE SERIES**

Ahmed Mohamed Naguib Attiya[1,1], Samar Elshahat[1], Ibrahim Galalah[1], Ahmed Elmowafy[1], Khaled Eldahshan[1], Salwa Elwasif[1], Ayman Refaie[1]

[1]*Urology & Nephrology center Mansoura university, Nephrology, Mansoura, Egypt*

Background and Aims: Vascular access remains a significant challenge for patients on chronic hemodialysis (HD) and often requires creative thinking to preserve and construct durable long-term access. While AVFs continue to remain the gold standard for vascular access, HD access remains an ongoing challenge for surgeons and patients.

The cases: This report is about 4 ESRD patients on chronic hemodialysis with multiple closed A-V fistulas (left and right radiocephalic then left and right brachiocephalic). Also, they suffered from catheter related blood stream infection (CRBSI) when central lines were inserted so the vascular sureon had to find solutions for them. ***First patient*** was 36-year old hemodialysis patient since 1995 2ry to posterior urethral valve. In 1994, he sought renal transplantation from his motivated brother who was the only available living related donor but unfortunately the surgeon discovered a congenital anomaly in the donor side during surgery. So the patient was maintained on hemodialysis. After multiple thrombosed AVF and recurrent episodes of CRBSI with central lines, the vascular surgeons inserted **a synthetic graft on left chest wall between axillary artery and axillary vein** 3 years ago and it is well functioning with efficient dialysis. ***The 2nd case*** (figure 1) is a 42-year old graft failure patient since 2005 and In view of high PRA, 2nd renal transplantation was not an option. After multiple thrombosed AVF and recurrent episodes of CRBSI with central lines, the vascular surgeons **created a new fistula in lower extremities between right great saphenous vein and common femoral artery** 2 years ago and it is still functioning. ***The 3rd case*** (figure 2) is about 14-year old child who received renal allo-transplantation from his father 8 years ago. Now, he is on chronic hemodialysis. First, he underwent peritoneal dialysis. But he suffered from recurrent peritonitis, so he was shifted to hemodialysis. Unfortunately, he suffered from CRBSI with catheters and multiple AVF were thrombosed. So, vascular surgeons performed **arterio-arterial synthetic graft using right subclavian artery** which is well functioning over 2 years. ***The 4th case*** (figure 3) is about 43-year old graft failure case on chronic hemodialysis with widespread thrombosis and difficult central line fixation. Also,AV fistulas had short survival. So, vascular surgeons decided to create **AVF in lower extremities between right greater saphenous vein and superficial femoral** artery 2 years ago. The patient after that received warfarin and the graft is functioning well till now.

Conclusion: Hemodialysis access remains an ongoing challenge for surgeons and patients lives.



Figure (1): A fistula between right great saphenous vein and common femoral artery

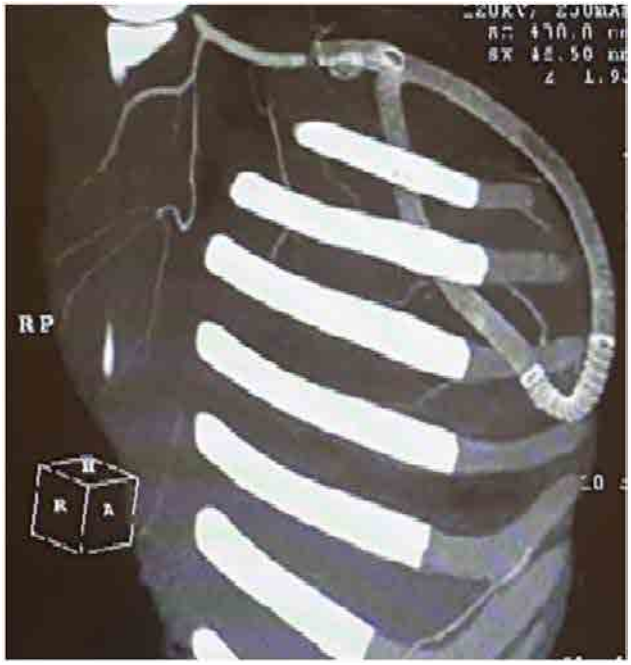


Figure (2): Arterio-arterial synthetic graft using right subclavian artery

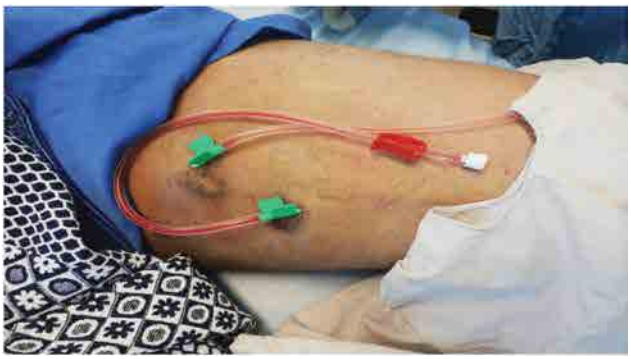


Figure (3): AVF between right greater saphenous vein and superficial femoral

DIALYSIS. ANAEMIA

P1372 **PRE-DIALYSIS HAEMOGLOBIN TARGET ATTAINMENT AND POST-DIALYSIS OUTCOMES IN PERSONS WITH RENAL ANAEMIA: A NATIONWIDE STUDY.**

Yang Xu[1], Marie Evans[2], Franz Peter Barany[2], Glen James[3], Katarina Hedman[4], Arvid Sjolander[1], Juan Jesus Carrero[1]

[1]Karolinska Institutet, Medical Epidemiology and Biostatistics, Stockholm, Sweden, [2]Karolinska Institutet, Renal Medicine, Stockholm, Sweden, [3]AstraZeneca, United Kingdom and [4]AstraZeneca, Gothenburgh, Sweden

Background and Aims:

Attaining the narrow hemoglobin range (10-12 g/dL) recommended by current ERBP renal anemia guidelines may be difficult, and whether this leads to better outcomes is not well known. This study aimed to identify patient and clinical factors associated with difficulties in maintaining hemoglobin target ranges in routine non-dialysis nephrologist care. We also evaluated whether adherence to ERBP hemoglobin recommendations during pre-dialysis care predicted early post-dialysis outcomes.

Method:

Observational study from the Swedish Renal Registry including all patients with non-dialysis dependent CKD stages 3b-5 developing renal anemia or initiating treatment (iron, ESA or both) between 2012-2016. Through multinomial logistic regression with clustered variance, we identified clinical conditions associated to serum hemoglobin values outside the ERBP recommended range (<10 and >12 g/dL) throughout all recorded patient visits until death, dialysis or end of follow-up. For those who initiated dialysis, we calculated the proportion of patient-time in which hemoglobin was maintained within range (time in range [TIR]). We then explored associations between TIR and subsequent one-year risk of death or MACE (composite of death caused by CVD and non-fatal MI, stroke, heart failure) with Cox proportional hazards regression.

Results:

A total 8106 patients with CKD 3b-5 developed incident anemia in Sweden during 2012-2016, contributing with 37422 nephrology visits during median 2 years of follow up. In multinomial logistic regression, being a man and having received iron or higher ESA doses was associated with hemoglobin values outside target range. Patients with CKD 3b and 4, ongoing transplant, history of CVD, or with higher serum calcium and albumin levels had higher odds of maintaining hemoglobin values above range. Conversely, recent bleeding or transfusions, nephrosclerosis, inflammation (CRP>5 mg/dl), and higher phosphate levels increased the odds of having hemoglobin values below range. A total 2435 patients initiated maintenance dialysis during the study period. Of those, 327 died and 701 developed MACE during the subsequent year. Their median TIR during their pre-dialysis period was 44% (IQR: 34-50). On a continuous scale (FIGURE), we observed worse outcomes for patients with poor guideline recommendation adherence (low percentage TIR), although the association was judged weak. On a categorical scale, patients that spent more than 40% of their pre-dialysis TIR had lower hazards of death (0.57, 95% CI 0.41-0.80) and MACE (0.67, 95% CI, 0.54-0.84) compared to those with <44% TIR.

Conclusion:

This nationwide study reports that greater adherence to ERBP anemia guidelines during pre-dialysis care, using existing conventional therapeutic approaches, is associated with better post-dialysis outcomes. Whether active interaction by healthcare practitioners affected the observed relationship needs to be further explored.

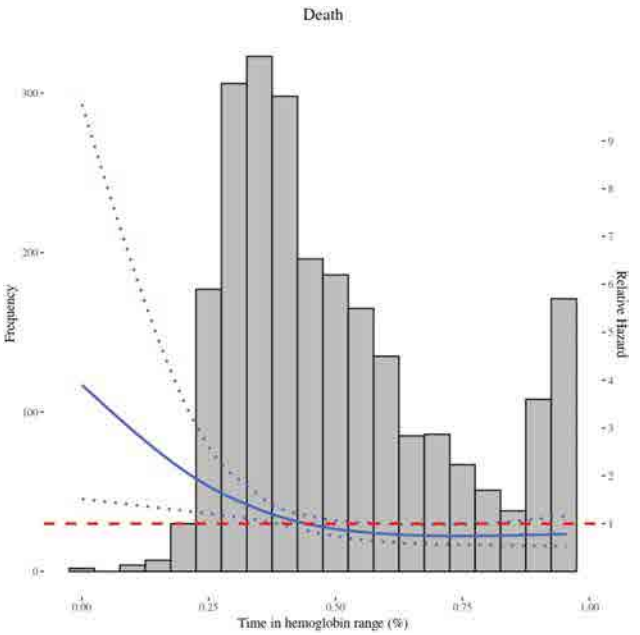


Figure. Multivariable-adjusted associations between time in haemoglobin range during predialysis care and the risk of death or MACE after initiation of dialysis. Blue straight line depicts Hazard ratios, and dashed blue lines 95% confidence intervals. The red line shows null hazards.

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P1373

ERYTHROPOETIN RESISTANCE IN PRE-DIALYSIS PERIOD AND ITS RELATION TO PROGNOSIS IN JAPANESE INCIDENT DIALYSIS PATIENTS

Takatoshi MORINAGA[1], Atsushi FUKATSU[2], Takeshi ITO[1], Hirofumi TAMAI[1]

[1]Anjo Kosei Hospital, Nephrology, Anjo, Japan and [2]Fukatsu Medical Clinic, Internal Medicine, Anjo, Japan

Background and Aims:

Erythropoiesis stimulating agents (ESA) are essential for better quality of life and longer life expectancy in end-stage kidney disease patients (ESKD). Resistance to ESA leads to worse prognosis in hemodialysis and peritoneal dialysis patients. Resistance to ESA exists in pre-dialysis period. We studied the clinical significance of pre-dialysis resistance to ESA by investigating the erythropoietin resistance index (ERI) in patients with ESKD prior to dialysis induction and its association with mortality and cause of death in three-year follow-up after dialysis initiation.

Method:

Subjects included 1,420 patients in 17 centers participating in Aichi Cohort Study of Prognosis in Patients Newly Initiated into Dialysis (AICOPP) from Oct. 2011 to Sep. 2013. ESA responsiveness was estimated by using erythropoietin resistance index (ERI) (U/kg/week/g/dL), which was calculated as weekly weight-adjusted epoetin dose divided by the hemoglobin (Hb) concentration before starting dialysis. We excluded 302 patients because ERI was not available. Thus, 1,118 subjects were enrolled. Subjects were divided into four categories of ERI; ERI < 5, $5 \leq$ ERI < 10, $10 \leq$ ERI < 15 and $15 \leq$ ERI. Cumulative survival rates from all-cause, cardiovascular disease (CVD), infection and malignancy were compared by Kaplan-Meier method according to ERI categories. Three-year mortality was analyzed by logistic regression analysis adjusted by age, gender, Charlson comorbidity index (CCI), and ERI categories.

Results:

During three-year follow-up period, 191 (17.1%) patients died. Age and female gender share were higher in proportion to ERI. Diabetes, coronary artery disease (CAD), and values of albumin (Alb) and brain natriuretic peptide (BNP) were not correlated with ERI (Table 1). Kaplan-Meier survival curve showed that patients with the highest ERI ($15 \leq$ ERI) had a higher all-cause mortality (Log rank test p=0.002, Figure 1). Concerning the cause of death, mortality from infection (p=0.023, Figure 2) and malignancy (p=0.031) were high in the highest ERI category, however there was no significant difference in each ERI category regarding CVD mortality (p=0.33). According to multivariate analysis analyses by logistic regression model, all-cause (odd ratio [OD]: 1.65, 95% confidence interval [CI]: 1.14-2.38, p=0.008) and infection-related mortality (OR: 2.13, 95% CI: 1.08-4.11, p=0.029) were significantly correlated with the highest ERI category, but unexpectedly CVD mortality was not (OR: 1.04, 95% CI: 0.59-1.75, p=0.90). Mortality from malignancy did not reach the significant level (OR: 1.92, 95% CI: 0.96-3.73, p=0.063) and may require longer observation period for analysis.

Conclusion:

Pre-dialysis ERI is a prognostic marker in Japanese dialysis patients and predicts the susceptibility to infection.

Table 1. Baseline characteristics

	ERI<5	5≤ERI<10	10≤ERI < 15	15≤ERI	p value
n	247	355	247	269	
Age year	63.7 ± 12.9	67.8 ± 12.5	68.6 ± 13.0	70.6 ± 11.9	<0.001
Female %	22.7	30.7	35.6	45.4	<0.001
Diabetes %	56.7	53.2	54.3	46.1	0.110
CAD %	14.6	15.6	15.0	17.5	0.813
Hb g/dL	9.8 ± 1.4	9.7 ± 1.3	9.5 ± 1.2	9.0 ± 1.5	<0.001
Alb g/dL	3.3 ± 0.6	3.3 ± 0.5	3.2 ± 0.6	3.2 ± 0.6	0.137
BNP pg/mL	179 [72-510]	247 [96-703]	276 [92-644]	293 [148-520]	0.055
CCI	4.7 ± 1.6	4.7 ± 1.7	4.8 ± 1.7	4.8 ± 2.1	0.980
EPO U/week	1907 ± 886	4009 ± 1254	6286 ± 1604	9409 ± 2662	<0.001
ERI	3.2 ± 1.2	7.4 ± 1.4	11.9 ± 1.4	20.9 ± 5.5	<0.001

Mean ± standard deviation, Median [interquartile range]

Figure:

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DEVELOPMENT OF HEMOGLOBIN PREDICTION AND ERYTHROCYTE STIMULATING AGENT RECOMMENDATION ALGORITHM (HPERA) USING RECURRENT NEURAL NETWORK IN END-STAGE KIDNEY DISEASE PATIENTS

Tae-Hyun Yoo[1], Hae-Ryong Yun[1], Jae Hyun Chang[2]

[1]*Yonsei University, Department of internal medicine, Seoul, Korea, Rep. of South and*
[2]*Gil Hospital, Department of internal medicine, Incheon, Korea, Rep. of South*

Background and Aims: The optimization of anemia management is a challenging task due to the complexities of underlying diseases and heterogeneous responses to erythropoiesis-stimulating agents (ESA) in patients with end-stage kidney disease (ESKD). Recent studies have shown that machine learning (ML) algorithms can be an effective tool to predict hemoglobin (Hb) levels and determine the ESA doses in these patients. However, most of the proposed ML approaches are not designed to handle multivariate longitudinal patient data. Thus, we developed Hb prediction and ESA doses recommendation algorithm (HPERA) using recurrent neural networks (RNN).

Method: A total of 466 participants, who underwent hemodialysis in 7 hospitals in the Republic of Korea, were included in the present study. We selected 15 variables from an extreme gradient boosting (XGBoost) algorithm. The outcome of the prediction algorithm was Hb levels in next month. In the recommendation algorithm, the outcome was the ESA dose for target Hb next month. Among various types of RNN families, gated recurrent units (GRU) were used to build both the prediction and recommendation algorithms. In addition to holding out a separate validation dataset, we used a Gaussian noise layer following each input layer to avoid overfitting. We also performed linear regression, multilayer perceptrons, and extreme gradient boosting with an extensive hyperparameter search to validate our GRU-based prediction algorithm. The performances of each model were evaluated in terms of the mean absolute error (MAE).

Results: The mean age of the study population was 57.8 years, 248 (53.2%) participants are male, and the mean observation period is 30.0 months. The best result of our prediction algorithm in terms of MAE was 0.59 g/dL and was obtained by two stacked GRU layers followed by a single hidden feedforward network with 6-month follow-up patient data. The best recommendation algorithm had 43.2 μg in MAE and this was obtained by one GRU layer followed by two layers of a feedforward network. The HPERA had a lower overall ESA dose (μg/months) [155 (80–240) vs. 140 (70–210), $P<0.001$], decreased Hb difference (g/dL) [0.8 (0.4–1.4) vs. 0.6 (0.3–1.0), $P<0.001$)], and had a higher success and a lower failure rates of reaching target Hb compared to those in real practice.

Conclusion: The GRU-based prediction model outperformed previous ML methodologies, though hyperparameter turning was much simpler. Using the HPERA showed the possibility of a reduced amount of ESA, decreased Hb difference, and increased the reaching rate of target Hb levels. Our study revealed a great potential direction of anemia management using ML in ESKD patients.

P1375 **ORAL VITAMIN C EFFECT ON HEPCIDIN LEVEL IN HAEMODIALYSIS PATIENTS WITH FUNCTIONAL IRON DEFICIENCY ANAEMIA**

Maha Abdelmoneim Behairy Said[1], Reem Elsharabasy[2], Ahmed Gharib[1], Mahmoud Zaki[2]

[1]Ain Shams University- Faculty of Medicine, Internal Medicine and Nephrology, cairo, Egypt and [2]Ain Shams University- Faculty of medicine, Internal medicine and Nephrology, Cairo, Egypt

Background and Aims: Hepcidin is a key regulatory peptide in iron homeostasis, inhibiting iron absorption by binding to ferroportin. Inflammatory mediated increase in hepcidin levels and reduced clearance in hemodialysis (HD) patients lead to functional iron deficiency (FID) and Erythropoiesis-stimulating agent (ESA) resistance. Ascorbic acid (Vitamin C) may be used as adjuvant therapy in FID anemia through its anti-inflammatory and anti-oxidant nature, but there was limited studies investigating the direct relation between vitamin C and hepcidin level in HD patients. We Aimed to test the reducing therapeutic effect of oral vitamin C supplement on hepcidin level among hemodialysis patients with functional iron deficiency anaemia.

Method: This study is an open label randomized controlled clinical trial that was conducted in hemodialysis units of Ain Shams University hospitals, 48 prevalent HD patients with mean age of 46.48 ± 15.57 years were included ,Group 1 (study group) :31 patients [13(41.9%) males & 18(58.1%) females] who received the conventional treatment of erythropoietin stimulating agents together with oral supplementation of vitamin C 500 mg every other day dose for 3 months. Group 2 (control group): included 17 patients [8(47.1%) males and 9 (52.9%) females] who received only the conventional therapy of erythropoietin stimulating agents according to their Hb levels. The patients enrolled in the study were patients on regular conventional HD for more than 6 months with functional iron deficiency anemia, defined as: hemoglobin level <11 gm/dl, ferritin level >200 ng/ml and TSAT >20 %. Patients with history of non-renal causes of anemia including malignancy, end-stage liver disease, or chronic hypoxia, patients with evidence of active or occult bleeding, patients who received blood transfusion within the last 4 months, history of recent hospitalization or infection requiring antibiotics within the last 4 weeks and patients with evidenced iron deficiency anemia were all excluded from the study .Laboratory parameters including serum hepcidin level, highly sensitive CRP (hsCRP) titer, CBC, kidney function tests and iron indices were measured at baseline and after 3 months .

Results: Oral vitamin C supplementation in Group 1(study group) resulted in statistically significant reduction in Hepcidin levels in the study group [mean 2506.45± 1320.53 pg/ml to 1748.39 ±1432.28 pg/ml](P=0.03), and highly significant reduction in hsCRP level [mean 8603.23 ±2547.77 ng/ml to 5611.29 ±2829.27 ng/ml](P=0.001) after 3months of treatment. On comparing the two groups regarding changes in Hepcidin levels during follow up, illustrates that vitamin C together with time resulted in significant reduction of hepcidin levels in the study group (P<0.05) by repeated measure ANOVA test (Figure 1). Comparison between the two groups regarding change in hsCRP levels during follow up showed there was a highly significant change in the mean hsCRP over time, and the mean hsCRP differed significantly between the two groups (Figure 2). A significant reduction in serum iron and ferritin levels was observed in study group after treatment vitamin C but the change of the mean of S. ferritin level didn't differ significantly in comparison to control group . Decreased EPO requirements and elevation of hemoglobin level were observed in the study group but without a statistical significance compared to the control group, this might be attributed to the short period of vit C supplementation. There was a highly significant correlation between serum hepcidin and hsCRP (r=0.46, P<0.01) .

Conclusion : Oral Vitamin C may be promising therapy in decreasing serum hepcidin and hsCRP in prevalent hemodialysis patients with functional iron deficiency anemia.

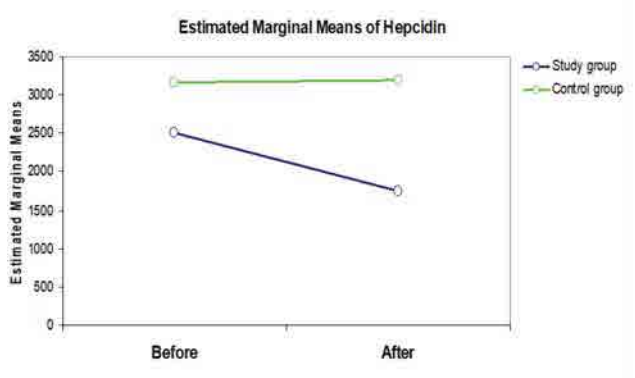


Figure:

P1376 IRON MANAGEMENT IN A HAEMODIALYSIS POPULATION POST-PIVOTAL

Rosiane Kenou Djotsa[1], Iain C. Macdougall[1], Martin Ford[1]

[1]King's College Hospital, United Kingdom

Background and Aims: IV iron plays a critical role in the management of anaemia in haemodialysis patients. The PIVOTAL trial recently generated new insights in this context, and suggested potential harm associated with under-treatment with IV iron.

To perform a prospective cross-sectional survey of iron management in a single-centre haemodialysis population in light of the results from the PIVOTAL trial.

Method: During June 2019, we prospectively measured haemoglobin, serum ferritin and transferrin saturation in a prevalent haemodialysis population at a tertiary renal centre. The current dose of IV iron sucrose was also recorded. Extrapolating from the PIVOTAL trial results (best outcomes in the high-dose group with a mean ferritin of around 650 ng/ml and a TSAT of around 26%), we arbitrarily and conservatively defined under-treatment with iron as a ferritin level $\leq$500 ng/ml and a TSAT $\leq$25%.

Results:

A total of 587 patients were identified, 581 of whom had a ferritin result available. Of these, 358 (62%) had a ferritin level $\leq$500 ng/ml and 295/527 (56%) had a TSAT $\leq$25%. For the 527 patients in whom both ferritin and TSAT measurements were available, 204/527 (39%) were defined as under-treated. Of the 587 patients, 111/582 (19%) were not receiving IV iron. 71/582 (12%) were on 100 mg monthly, 48/582 (8%) were on 200 mg monthly, 339/582 (58%) were prescribed 400 mg iron sucrose/month and 14/582 (2%) were on $\geq$ 400 mg. The iron dose was not available in 5 patients. Of the 204 undertreated population, 22 (11%) were not on IV iron. 17/204 (8%) were on 100 mg/month, 16/204 (8%) on 200 mg/month, 137/204 (61%) on 400 mg/month, and 11/204 (2%) on $>$ 400 mg monthly. Of the patients defined as undertreated, the haemoglobin ranged from 63 to 151 g/l with a mean of 109.8 g/l and a median of 111 g/l. 30 patients had a haemoglobin less than 100 g/l and 92 patients had a haemoglobin less than 110 g/l. 24/204 patients were not on an ESA (one patient was on Daprodustat) with a mean dose of 12,200 U/week.

Conclusion:

Our current iron protocol is under-dosing a significant proportion of patients. This protocol requires review in light of the PIVOTAL study since it is likely significant cost savings could be achieved as a result of using lower doses of ESA therapy, along with the cardiovascular benefits seen in the higher dose arm of the trial.

P1377 **ANEMIA MANAGEMENT IN DIALYSIS PATIENTS IN SWITZERLAND**

Rebecca Winzeler[1], Patrice Max Ambühl[1]

[1]*Institute of Nephrology, Waid and Triemli City Hospital, Zurich, Switzerland*

Background and Aims: Anemia is highly prevalent in dialysis patients and is associated with increased morbidity and mortality. The purpose of the present analysis is to evaluate current anemia management in dialysis patients in Switzerland collected from the Swiss Dialysis Registry (srrqap), which covers all dialysis patients in Switzerland.

Method: All medical establishments in Switzerland (both public and private; N=92) providing chronic treatment by either hemo- and/or peritoneal dialysis, had to provide relevant data for the year 2018. All individuals being on chronic dialytic therapy in the year 2018 were enrolled (N=4646). To calculate survival probabilities, all deaths from incident dialysis patients between 2014 and 2018 were analyzed.

Results: 65 percent of all dialysis patients receive iron and EPO. Regardless of anemia management, 82% of patients reach target hemoglobin levels 10 g/dL. In 18% of patients inadequate management to reach Hb targets may be suspected.

The distribution of iron and EPO substitution is similar in all age groups. However, 26% of the age group 20-44 years receive EPO, but no iron, compared to only 15% in the other age groups.

Survival analysis by Cox regression adjusted for age, Charlson score and treatment modality revealed that patients with Hb levels equal or greater than 11 g/dl have the best survival (reference group). In comparison, patients in the Hb categories below 9, 9-9.9 and 10-10.9 g/dl have an odds ratio of 3.9, 2.0 and 1.3, respectively, to die.

Conclusion: Anemia management to reach Hb target levels following KDIGO guidelines seems to be adequately implemented among dialysis patients in Switzerland. In 18% of patients treatment might be optimized to achieve Hb targets. As expected, patients with Hb levels equal or greater than 11 g/dl have better survival rates compared to patients with lower Hb values.

Table 1: Overview of iron and EPO substitution in dialysis patients, stratified by hemoglobin concentration

	All	Hemoglobin (Hb), g/dL			
Iron / EPO-Substitution		**≤ 8.9**	**9-9.9**	**10-10.9**	**≥ 11.0**
Iron no / EPO no, %	8.5	2.6	8.3	20.2	69.0
Iron no / EPO yes, %	16.6	9.3	13.6	28.7	48.4
Iron yes / EPO no, %	9.8	0.7	3.8	17.2	78.3
Iron yes / EPO yes, %	65.1	7.3	13.0	26.3	53.4

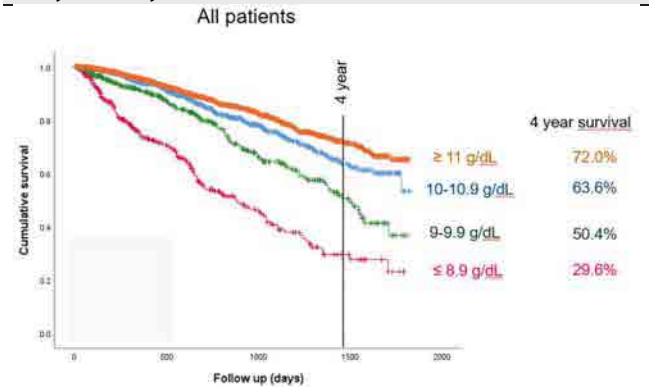


Figure 1:

P1378 **PROCESS NORMALIZATION AND CLINICAL OUTCOMES FOLLOWING IMPLEMENTATION OF THE ANEMIA CONTROL MODEL FOR PERSONALIZED ANEMIA MANAGEMENT**

Luca Neri[1], Isabella Cattinelli[1], Elena Bolzoni[1], Carlo Barbieri[1], Rosa Ramos Sanchez[1], Stefano Stuard[1]

[1]*Fresenius Medical Care, Bad Homburg, Germany*

Background and Aims: Anemia management is still challenging in a large share of dialysis patients. ESA resistance show wide variations across patients as well as fluctuations along time within the same patient. The Anemia Control Model (ACM) is a software application which can be integrated in electronic health record systems. ACM is based on an artificial neural network system trained on 1 million health records which simulates patient's personalized dose-response relationship to ESA and Iron. Based on patients' response forecast, ACM suggests the optimal drug dose recommendations to reach or maintain the hemoglobin level within target and to minimize the drug consumption. The ACM has earned medical device certification and it is currently used in 13 countries within the EMEA FMC network. Effectiveness and safety of ACM has been demonstrated in previous real-world evidence studies. We report ACM use and its clinical outcomes among hemodialysis patients registered in the Spanish FME Network

Method: We recorded all medical prescriptions and their clinical outcome for which an ACM recommendation was computed (ACM prescription). prescription occurred in 9 clinics located in Catalunya (Spain) from September 2017 to September 2018. We report dynamics of ACM suggestion acceptance rate, ESA consumption and Hb target achievement in the study period.

Results: There were 1189 active patients per month during the study period on average. ACM suggestion acceptance rate was 73,3%. ESA monthly consumption ranged from 234:7±281:9 – 310.2 ± 310:8 UI/Kg; 86% of patients receiving ESA doses according to ACM recommendations achieved or remained within Hb target range; on the contrary, when physicians rejected ACM recommendations and prescribed a different dosage, only 77% of patients reached or maintained the Hb level on target ($p<0.05$).

Conclusion: Our study demonstrated that ACM suggestions were frequently accepted by physicians. Acceptance of ACM suggestion was associated with higher Hb target achievement.

P1379 **PLATELET/LYMPHOCYTE RATIO AS A MARKER OF ERYTHROPOIETIN RESPONSIVENESS IN END-STAGE RENAL DISEASE**

Sonja Golubović[1,2], Tijana Azasevac[1], Siniša Živković[1], Bojana Ljubiäiä‡[3], Violeta Knezevic[1,2], Dejan Celic[1,2]

[1]Clinical Center of Vojvodina, Department of Nephrology and Clinical Immunology, Novi Sad, Serbia, [2]University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia and [3]Clinical Center of Vojvodina, Emergency Center, Novi Sad, Serbia

Background and Aims: Neutrophil/Lymphocyte Ratio (NLR) and Platelet/Lymphocyte Ratio (PLR) are closely associated with increased inflammation in end-stage renal disease, which often contributes to the severity of anemia in these patients. Erythropoiesis stimulating agents (ESA) have become a standard treatment of anemia in hemodialysis patients. Since some patients do not respond well to erythropoietin therapy (EPO) the aim of this study is to investigate if NLR and PLR as markers of increased inflammation, could be associated with resistance to EPO therapy.

Method: A total of 90 patients (36 females, 54 males; mean age 60,45 ±11,58) undergoing maintenance hemodialysis and who received recombinant human EPO therapy were examined. Patients' clinical characteristics, laboratory data, dialysis adequacy and the applied doses os EPO were examined in a period of 3 months. EPO hyporesponsiveness index (EHRI) was calculated as the weekly dose of EPO divided by kilograms of body weight divided by the hemoglobin level.

Results: Obtained results show a statistically significant correlation of moderate-intensity between EHRI and NLR ($r = 0.497$, $p < 0.01$) as well as a negative correlation of moderate-intensity between EHRI and hemoglobin levels (Hgb) ($r = -0.403$, $p < 0.01$). When it comes to the connection of NLR and PLR with logarithmically converted EHRI values, the results show that there is no statistically significant correlation between NLR and EHRI. Comparison of PLR among 25th, 50th and 75th percentile of EHRI showed that PLR levels increased going from the 25th towards the 75th percentile ($p < 0.01$). Post hoc analysis indicated that there is also a statistically strong connection for the 25th i 50th percentile (<0 .05) and furthermore for the 50th and 75th percentile (< 0.05).

Conclusion: PLR was found to be superior to NLR in terms of evaluating ESA therapy resistance. PLR could be used as a predictor of ESA therapy response.

P1380 A SYSTEM FOR FORECASTING OF DRUG DOSAGE FOR ANEMIA CORRECTION IN PATIENTS ON CHRONIC DIALYSIS

Dmitriy Zinovev[1], Vladimir Novitskiy[1,2], Andrey Malkoch[1,3,4]

[1]Nephrology Expert Council, Moskva, Russia, [2]Moscow State University of Food Production, Informatics and computing technology of food production, Moskva, Russia, [3]Moscow State University of Food Production, Therapy and children diseases, Moskva, Russia and [4]Russian Medical Academy of Continuous Professional Education, Nephrology and Hemodialysis, Moskva, Russia

Background and Aims: Anemia is a most common complication of CKD in patients on chronic dialysis. Adequacy of anemia correction directly affects both patient's life quality and patient's long-term survival. The most important aspect of anemia correction is drug therapy. In this work, we present a system for forecasting of iron supplements and ESA (Epoetin alfa) dosage, that is based on logical rules and artificial intelligence (AI) models.

Method: As an input dataset, system uses patient's anthropomorphic parameters, results of laboratory studies, and information on previous drug therapy. The output of the system are dosages of ESA an iron supplements that have to be administered in order to bring the patient's hemoglobin as close as possible to target range of values (100-120 g/l). The system consists of two sequentially triggering forecasting models (for ESA and for iron supplements), where each model is a combination of logical rules and artificial neural network, that has been trained on a data, collected in more than 20 "Nefrosovet" hemodialysis clinics for the period of 3 years.

The effect of system usage was examined for the group of 356 hemodialysis patients with median follow-up time of 4 month. The primary end-point was a number of patients in target range of hemoglobin values (100-120 g/l).

Results: During the study we determined that as a result of using the dose forecasting system, number of patients in target range of hemoglobin values significantly increased from 239 patients at the beginning of system employment to 266 patients at the end of the study (p=.0318). Furthermore, we observed that there was a concomitant effect of system usage – significant reduction of average monthly ESA dosage from 14300 IU at the beginning of system employment to 13900 IU at the end of the study (p=.0331).

Conclusion: Employment of automated drug dosage forecasting system based on logical rules and AI models, allows to improve the efficiency of anemia correction in hemodialysis patients and reduce the dosage of administered ESA, which, in turn, reduces the risk of possible complications and treatment cost.

P1381

SWITCHING FROM IRON GLUCONATE TO FERRIC CARBOXYMALTOSE CAN BE ASSOCIATED WITH A BETTER CONTROL OF IRON STATUS AND ANEMIA IN HEMODIALYSIS PATIENTS?

Massimiliano Martone[1], Massimiliano Tosto[1], Piero Luigi Mattei[1], Dorina Berbecar[1], Manuela Bosco[1], Emanuela Boer[1], Neva Milutinovic[1]

[1]*Azienda Sanitaria Universitaria Giuliano Isontina ASUGI, SOC Nefrologia e Dialisi, Gorizia, Italy*

Background and Aims: Before evaluating any ESA treatment, International guidelines (NICE-2015, KDIGO-2012, ERBP–2013) suggest to administer iron first to patients with iron deficiency anemia and not still on ESA therapy. Moreover anemic CKD patients treated with ESA should be iron supplemented (unless ferritin is> 800 mcg/l) to maximize the benefits of ESAs.

A recent retrospective study of switching iron sucrose to ferric carboxymaltose (FCM), conducted by Hofman et al., showed a better control of iron status in hemodialysis (HD) patients. New generation drugs, like carboxymaltose, may change the iron administration methods on dialysis, due to their different properties: therefore more experience is needed. In the following evaluation we report the results of switching from iron gluconate (our previous standard therapy) to FCM in HD patients.

Primary Endpoint: switching effects on iron parameters (TSAT, ferritin) and hemoglobin.

Secondary Endpoints: switching effects on iron and ESA doses administered

Method: Study design: retrospective review of data from 106 HD patients from 2 Italian different dialysis centers, who were switched from iron gluconate to ferric carboxymaltose in a 1: 1 ratio.

Study duration: 9 months (3 months pre-switch, 6 months post-switch)

Treatment schedule: -ferritin <100 ng/ml and/or TSAT <20%: 100 mg of iron/weekly

-ferritin <200 µg/l, or TSAT<20%: 100 mg of iron/weekly

-ferritin 200–500 µg/l, and/or TSAT 20–30%: 100 mg of iron/every 2 weeks

-ferritin 500–800 µg/l and/or TSAT 30–50%: 100 mg of iron/monthly

-ferritin> 800 µg/l and/or TSAT>50%: no iron.

Hb, TSAT, Ferritin and PCR evaluation every 4 weeks.

Results: after switching from iron gluconate to FCM, Hb levels were stable or improved, reaching a significantly higher percentage of target patients (from 60% to 80% with Hb > 10,5 g/l). The switch was also associated with a significant improvement of iron status, unrelated to iron dose: the percentage of patients with a target TSAT (TSAT >=20%) has doubled after six months, moving from 30% to 70%, while the average consumption trend of FCM decreasing over time (-48% after six months). It was also shown a marked reduction in ESA consumption: the ESA dose was decreased on average by -1907 IU per patient/month.

Conclusion: The switch from iron gluconate to FCM is associated with a better control of iron status and iron anemia in CKD patients on hemodialysis. The treatment schedule proposed has guaranteed to reach the primary and secondary endpoints, underlining the importance and the effectiveness of a tailored therapeutic protocol.

P1382 **RED CELL DISTRIBUTION WIDTH - A POTENTIAL MARKER FOR IRON OVERLOAD DIAGNOSIS IN CHRONIC HEMODIALYSIS PATIENTS**

Radulescu Daniela[1,2], Simona-Daniela Onofrei[1,2], Brinzea Mihaela Madalina[2], Vacaroiu Ileana Adela[1,2], CRISTIANA DAVID[1,2]

[1]„Carol Davila" Medicine and Pharmacy University, Clinical Department no.3, Nephrology, BUCHAREST, Romania and [2]Clinical Emergency Hospital "Sf. Ioan", Nephrology and Dialysis, BUCHAREST, Romania

Background and Aims: The indication for starting iron supplementation in chronic hemodialysis patients is precisely stipulated in all guidelines, while the criteria for stopping or reducing iron administration are still a subject of debate. Inflammatory status is a characteristic of chronic dialysis patients and it increases ferritin levels in this population; therefore iron overload is difficult to diagnose. The aim of this study was to investigate the relationships between red cell distribution width (RDW) and ferritin levels in stable maintenance hemodialysis patients, in order to help differentiating iron overload-induced increased ferritin from inflammation-induced causes.

Method: In a retrospective analysis, we studied the biochemical parameters in the last 9 months in 88 patients on maintenance hemodialysis (59.09% males) from 2 dialysis centers, mean age and dialysis duration 66.94 years, and 56 months respectively. Patients with active infections or history of neoplasia, hematologic diseases (other than CKD-associated anemia) or immunosuppressive use were excluded, and also patients having less than 3 months dialysis. Mean values (expressed as average value ± standard deviation) for ferritin, RDW (reference interval 10-15%) and C-reactive protein - CRP (reference interval 0-0.5 mg/dL), assessed every 3 months, were analyzed, and Spearman bivariate correlation test was applied to assess each pair of variables using IBM SPSS 20 for Windows.

Results: 65 patients were qualified as eligible. Mean values of ferritin, RDW and CRP were 638.57± 530.84 ng/mL, 16.15±2.09 %, and 2.04±5.43 mg/dL respectively. We found a strong positive correlation between RDW and CRP values (p=0.002; rho=0.357; 1-tailed), but no relationship between CRP and ferritin (p=0.273; rho=0.076) or between RDW and ferritin (p=0.329; rho=0.056) at the entire cohort of studied population.

According to RDW values, we then divided the patients into two groups: group A with high RDW (≥15%), 48 patients (73.84 %) and group B with normal RDW (10-15%), 17 patients (26.15%), and analyzed correlations between the study parameters. There was no relationship between RDW and ferritin in group A (p=0.286; rho=0.075), and neither between RDW and CRP (p=0.092; rho=0.174). In group B, there was a highly significant correlation between RDW and ferritin levels (p=0.018; rho=0.414), and also between RDW and CRP levels (p=0.037; rho=0.357), pointing out an inflammatory state.

Conclusion: Elevated levels of RDW are usually associated with iron deficiency, and in dialysis population also with increased CRP as inflammatory marker.

We found in the present study that the RDW values used in conjunction with ferritin level may be useful in differentiating between inflammation-caused increased ferritin levels and iron-overload-caused increased ferritin levels. The inflammatory state is a common finding in chronic dialysis patients and it often produces increases in ferritin levels, making RDW a handy and helpful marker in monthly iron prescriptions, additional to CRP.

P1383

ECONOMIC BENEFITS OF SWITCHING FROM INTRAVENOUS TO SUBCUTANEOUS ERTHROPOIESIS-SIMULATING AGENTS THERAPY FOR MANAGEMENT OF ANEMIA IN HEMODIALYSIS PATIENTS

Bhanu Prasad[1], Maryam Jafari[2], Joanne Kappel[3], Julie Toppings[1], Linda Gross[3]

[1]Regina General Hospital, Saskatchewan Health Authority, Medicine, Regina, Canada, [2]Dr. T Bhanu Prasad Medical Prof Corp, Regina, Canada and [3]St. Paul's Hospital, Saskatchewan Health Authority, Medicine, Saskatoon, Canada

Background and Aims: Erythropoiesis stimulating agents (ESA's) were introduced in the treatment of anemia in 1989 and it immediately led to a marked decline in the number of blood transfusions and improved quality of life in patients across the spectrum of chronic kidney disease. Several studies from the mid 1990s have shown that the required doses of Epoetin alpha were lower when administered subcutaneously (SQ). These studies led to guidelines by NKF (1997) and KDOQI (2001) recommending the use of SQ over intravenous (IV) as considerable cost savings could be achieved without compromising care. The rise in the reported cases of pure red cell aplasia (PRCA) led to a change in guidelines in 2006 and led to units changing exclusively to IV route. It was subsequently identified that polysorbate 80 from uncoated rubber stoppers in pre-filled syringes rather than the route of administration was the most plausible cause of PRCA. However, higher doses of ESAs, have been associated with adverse health outcomes across all hematocrit categories in hemodialysis patients. While the current practice is to administer ESAs to patients through IV route, SQ ESAs achieve the same target hemoglobin level at a reduced dose and cost. Given the dose -sparing advantages of SQ Epoetin alpha administration, we decided to gradually transition our patients to SQ and examined the cost of IV versus SQ treatment. The objective of our study was to determine the economic benefit of the change in the route of administration from IV to SQ ESA in hemodialysis patients.

Method: We conducted a retrospective cohort study in 215 hemodialysis patients who transitioned from IV Epoetin alfa to SQ at four hemodialysis sites in the province of Saskatchewan, Canada from September 2014 to July 2017. The dose and cost of different routes of Epoetin alfa administration per patient per month was calculated. Also, blood hemoglobin, markers of erythropoiesis (transferrin saturation and Ferritin), IV iron dose and cost were determined in relation to route of Epoetin alfa administration. The dependent t-test was used to compare mean variables between pre-switch and post-switch period. Differences in variables across three serum hemoglobin ranges (<95, 95-115, >115 gram/liter) were assessed using the independent t-test.

Results: The mean Epoetin alfa doses per patient per month (47,327.9±33,133.0 international unit) during pre-switch (IV) period were greater than of post-switch (SQ) period (34,253±24,858.1), a decrease of 27.62% ($p<0.001$). The mean hemoglobin concentration for patients in both periods remained stable (103.3±9.2 versus 104.3±13.3, $p=0.34$) and within the target range. The reduction in the dose of Epoetin alfa per patient per month (IU± standard deviation) upon conversion remained similar (IV versus SQ) in all the subcategories: hemoglobin <95 g/L (65,941 versus 52,717), hemoglobin 95-115g/L (42,120 versus 29,619) and (35,289 versus 17,651) for hemoglobin >115 g/L. There were no significant differences in transferrin saturation, Ferritin and IV iron dose and cost between the two study periods. The mean cost (CAD± SD) of Epoetin alfa per patient per month decreased from 674.4±477.4 pre-switch to 484.8±354.3 post-switch ($p<0.001$), a decrease of 28.11%; whereas, the cost of IV iron remained similar in pre- and post-switch period.

Conclusion: The (mean) cost of Epoetin alfa per patient per year in our study when given IV was $ 8,088 (CAD) and once converted to SQ was $ 5,817 (CAD) while achieving equivalent hemoglobin levels, a saving of $ 2271 (CAD) per year. Based on these values, if we extrapolate our savings to 900 prevalent patients to SQ Epoetin alfa we can realize a cost saving of $2,043,900 per year. Conversion of Epoetin alfa from IV to SQ led to substantial cost savings at our hemodialysis units.

P1384 EFFECT OF ANEMIA ON EFFICACY AND SAFETY OF CHRONIC HEPATITIS C TREATMENT AMONG RENAL PATIENTS USING DIRECT ACTING ANTI-VIRUS

Ahmed Elmowafy[1], Mohamed Abbas[1], Han Elmaghrabi[2], Reham Soliman[3], Salwa Elwasif[1], Hussein Sheashaa[1], Gamal Shiha[4], Lionel Rostaing[5,6], Mohammed Bakr[1]

[1]Urology & Nephrology center Mansoura university, Nephrology, Mansoura, Egypt, [2]College of Medicine, University of Port Said, Nephrology, Port Said, Egypt, [3]College of Medicine, University of Port Said, Tropical, Port Said, Egypt, [4]Egyptian Liver Research Institute and Hospital, Hepatology, Sherbin, Egypt, [5]Chu Grenoble Alpes, Nephrology, Hemodialysis, Apheresis, and Kidney Transplantation, La Tronche, France and [6]Université Grenoble Alpes, Grenoble, France

Background and Aims: With the advance of new direct acting antiviral, treatment of HCV became safer and easier. Renal impairment makes treatment of HCV more difficult due to poor drug tolerability. Anemia is a common side effect occurring in renal patients. Effect of anemia on the efficacy and safety of these drugs in those particular populations is a point of interest.

Method: This is a single center cohort study was held in Urology and Nephrology Center, Mansoura, Egypt, including 235 renal patients who were divided into 2 groups according to presence/absence of anemia; hemoglobin below 10.5 g/dL is considered cut-off value: 70 chronic kidney disease patients (CKD) (42 anemic and 28 non-anemic), 40 hemodialysis patients (HD) (24 anemic and 16 non-anemic) and 125 kidney-transplant recipients (KTRs) (40 anemic and 85 non-anemic). Hemodialysis patients received ritonavir-boosted paritaprevir and ombitasvir±ribavirin (OMV/PTV/RTV), KTRs received sofosbuvir and daclatasvir. CKD with eGFR >30 ml/min/1.73m^2 received sofosbuvir and daclatasvir. CKD with eGFR <30 ml/min/1.73m^2 received OMV/PTV/RTV. All patients were followed-up for 6 months after completing HCV treatment.

Results: ***Demographics:*** Mean age was 49.17y for CKD, 43.2y for HD and 45.2y for KTRs. Most of them were males with body mass index around 23.8. Out of 235, 22 patients had been previously treated with interferon-IFN- (14 patients showed relapse after primary response on IFN and 8 patients could not tolerate IFN due to severe anemia, leucopenia and recurrent infection) and 7 patients had been co-infected with hepatitis B virus (all patients were cleared from the virus prior to HCV treatment).

Efficacy: Rapid virologic response was achieved in all groups. 12-week sustained viral response (SVR-12) among CKD patients was 92.86% in anemic group and 96.42% in no-anemic group (p=91%). SVR-24 was lower in both groups. There were 16 relapse cases among CKD patients (11 in anemic group and 5 in non-anemic group; p value=0.69). Relative Risk for relapse incidence among anemic CKD patients was 1.4 with 95% CI 3.58 to 8.58 (p value: 0.42). Among HD patients, there was only 1 relapse case and it was in anemic group. All KTRs achieved SVR-12 and SVR-24.

Safety: Deterioration of kidney function within 1 month from starting DAAs was the major side effect in both groups among CKD patients but it was more profound in anemic group (59.5%) (p value: 0.024). Deterioration of creatinine clearance was more obvious in anemic group (26.7±11.8mL/min, 21.28±12.97mL/min; p value: 0.014). More cases needed hemodialysis either temporary (3 cases) or permanently (13 cases) in anemic group (p value: 0.03 for temporary hemodialysis and 0.005 for permanent hemodialysis). Relative Risk for A/CKD incidence with anemia among CKD patients was 1.85 with 95% CI from 22.94 to 1.98 (p value: 0.04). Anemia was associated with rise of serum creatinine among kidney transplant recipient also. Graft impairment among anemia group was 30% (12 out of 40 patients) in comparison to 3.5% in no-anemia group (3 out of 85 patients); p value: 0.0002. Relative Risk for graft impairment with anemia among KTRs was 8.5 with 95% CI 6.95 to 2.64. Subsequently, drug interruption was more frequent among anemia group in both CKD and KTRS as treatment was suspended during AKI period.

Regarding hemodialysis patients, the only difference was that worsening of anemia was more frequent among no-anemia group (p value: 0.0002). Ribavirin resulted in this this difference as no-anemia group received ribavirin while the other group did not receive it.

Conclusion: Direct-acting anti viral drugs are considered advance in treatment of hepatitis C infection and it is well tolerated by kidney disease patients. However, this particular population needs special care. Correction of anemia before starting DAAs may improve the outcome. Hemoglobin levels below 10.5 g/dL prior to DAAs are associated with rise of serum creatinine among KTRs and CKD patients.

P1385

BOLUS FERRIC CARBOXYMALTOSE ADMINISTRATION COULD BE A GOOD OPTION FOR IRON MAINTENANCE THERAPY IN HD FACILITIES WITHOUT REGULAR MEDICAL ASSISTANCE

Chiara Brunati[1], Denise Vergani[1], Francesca Gervasi[1], Alberto Montoli[1], Enrico Minetti[1]

[1]*ASST Grande Ospedale Metropolitano Niguarda, Nephrolgy and dialysis, Milano, Italy*

Background and Aims: In 2013, the European Medicines Agency (EMA) claimed that iron preparations should be exclusively given in an environment where resuscitation facilities are available and, therefore, the iron administration was highly discouraged without the presence of a doctor. What this means is that in dialysis centres without regular medical presence the dose of iron administered might be inadequate. Ferric carboxyimaltose (FCM) allows to administer high single doses of iron with an excellent safety profile.

Method: We compare the effect of a *maintenance iron therapy* in two groups of prevalent and clinical stable hemodialysis patients; the former (A; n=19pts) was treated with iron gluconate (FG) in low refracted doses (i.e. 60 mg one or two times a week) while the latter (B;n=20 pts) was treated with FCM in high doses (i.e. 200 mg once or twice a month). The groups have been followed up for one year. All treated patients in the two groups had similar and "adequate" basal iron parameters according to European Clinical Guideline (Serum Ferritin(SF) ≥200 mic/l and transferrin saturation(TS) ≥20%) (see Table 1). The therapy was administered in order to maintain SF between 200-500 mic/l and TS between 20-40%. Erythropoietin dose (Epo) was evaluated considering the erythropoietin resistance index (ERI =EPO/weight/Hb).

Results: Table 1 show the results at the start and end follow up. The mean monthly iron dose was similar between the two groups at the end of follow up (144±100 mg group A vs 157±81 mg group B). In group A there was a more significant increase in the TS with a non-significant trend to an increase in SF. Six pts of group A had an overshooting of SF (1164±360mc/L) vs 3 pts in group B (SF 830±30 mc/L).

No significant differences in pre and post therapy ERI could be recorded.

Conclusion: A therapy with a high single doses of FCM could be a positive solution to treat patients in dialysis centres without regular medical presence.

Table 1

	Group A	Group B	P*
Hb pre	10,8±0,9	10,9±1	ns
Hb post	11,1±1,3	10,8±1	ns
p**	ns	ns	
SF pre	452±260	486±280	ns
SF post	662±432	452±233	0,059
p	0,053	ns	
TS pre	23±9	26±8	ns
TS post	31±10	26±9	ns
P**	ns	<0,05	
ERI pre	7,6±5	7,6±5	ns
ERI post	5,5±4,3	8,0±6,9	ns
P**	ns	ns	

*Between the two groups (unpaired T test)

**Between pre and post therapy (paired T test)

DIALYSIS. BONE DISEASE

P1387

IRON CITRATE BLOCKS THE PROGRESSION OF CALCIUM DEPOSITION BY REVERTING APOPTOSIS AND AUTOPHAGY IN VSMCS

Paola Ciceri[1], Monica Falleni[2], Delfina Tosi[2], Carla Martinelli[2], Mario Gennaro Cozzolino[2]

[1]Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Nephrology, Dialysis and Transplant, Milano, Italy and [2]University of Milan, Health of Sciences, Milano, Italy

Background and Aims: Cardiovascular disease is the first cause of mortality in chronic kidney disease (CKD) induced by vascular calcification. Since, in advanced CKD, iron based phosphate binders have been proposed to treat hyperphosphatemia, we studied, in high-phosphate (Pi) calcified VSMC, the effect of iron citrate (iron) on the progression of calcium deposition.

Method: We treated VSMCs with 5 mM Pi and iron citrate to evaluate Ca deposition by Alizarin Red destaining, DNA fragmentation by ELISA, gene expression by RT-PCR and protein expression by Western blot.

Results: High-Pi calcification was blocked when iron was added from day 7 to 15 (1.30 ± 0.03 *vs* 0.61 ± 0.02; OD/mg protein; day 15; Pi*vs*Pi+Fe, $p<0.01$). Since iron added prophylactically prevented apoptosis and potentiated autophagy we studied the role of these two processes in the therapeutic protocol. Adding iron from day 7 to day 11 decreased apoptotic cell number (17.3 ± 2.6 *vs* 11.6 ± 1.6; Annexin V; % positive cells; day 11; Pi*vs*Pi+Fe; $p<0.05$, figure). To confirm the effect of iron on apoptosis, we demonstrated its action in blocking the H_2O_2-induced increase in calcification when added from day 7 to day 14 (1.37 ± 0.03 vs. 0.96 ± 0.05; H_2O_2+Pi day 7-14 vs Fe+H_2O_2+Pi day 7-14; day 14; OD/mg protein; $p<0.01$). We then investigated the mechanism of the anti-apoptotic effect by studying the pro-survival axis GAS6/AXL, finding that iron treatment from day 9 to day 14 counteracted the protein down-regulation, and induced their *de-novo* synthesis. Supporting the effect of therapeutic added iron on apoptosis we found a decrease in apoptotic nuclei both in VSMCs and aortic rings after iron treatment from day 7 to 15 (3.8 ± 0.2 *vs* 2.3 ± 0.3 and 4.0 ± 0.3 *vs* 2.2 ± 0.2; apoptotic nuclei; arbitrary score; day 15; Pi*vs*Pi+Fe; VSMCs and aortic rings; $p<0.05$). Moreover, iron added from day 9 to day 15 potentiated autophagic flux and increased the number of autophagosomes with damaged mitochondria.

Conclusion: Iron exerts an anti-apoptotic and pro-autophagic effect on established calcified VSMC when simil-osteoblastic transformation was already occurred.

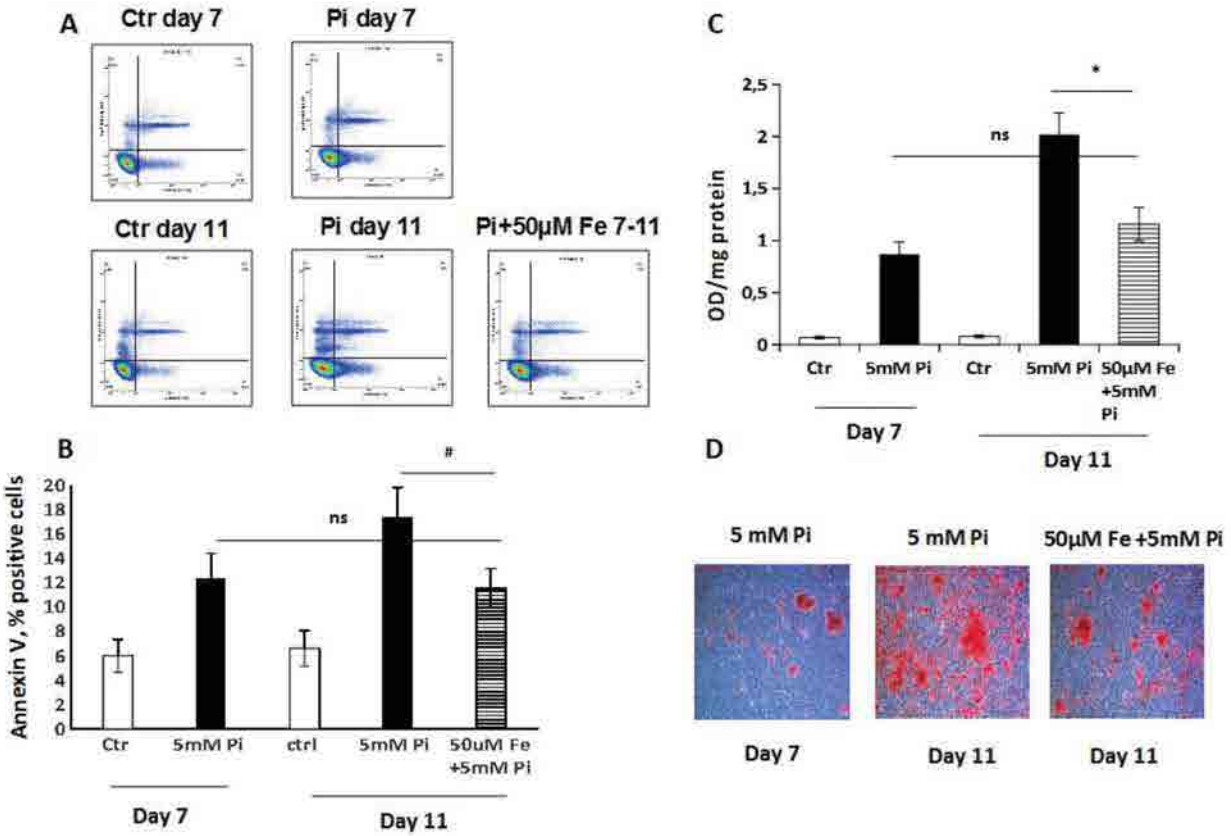


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P1388 **ASSESSING BONE TURNOVER IN CHRONIC KIDNEY DISEASE: SHOULD WE MEASURE NON-OXIDIZED PTH**

Stan Ursem[1], Annemieke Heijboer[1], Patrick D'Haese[2], Geert Behets[2], Marc Vervloet[3], Pieter Evenepoel[4]

[1]Amsterdam UMC, Vrije Universiteit Amsterdam and University of Amsterdam, Endocrine Laboratory, Department of Clinical Chemistry, Amsterdam Gastroenterology & Metabolism, Amsterdam, Netherlands, [2]University of Antwerp, Department of Biomedical Sciences, Laboratory of Pathophysiology, Antwerp, Belgium, [3]Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Nephrology, Amsterdam Cardiovascular Sciences (ACS), Amsterdam, Netherlands and [4]University Hospitals Leuven, KU Leuven, Department of Nephrology and Renal Transplantation; Department of Microbiology and Immunology, Laboratory of Nephrology, Leuven, Belgium

Background and Aims: Parathyroid hormone (PTH) is a key regulator of bone turnover. PTH can be oxidized in vivo, which impacts biological activity. Variable PTH oxidation may be hypothesized to contribute to the rather poor correlation of PTH with indices of bone turnover. Non-oxidized PTH may better reflect the hormonal function than currently measured intact PTH (iPTH). Therefore, we investigated whether n-oxPTH would be superior compared to iPTH as indicator of bone turnover in ESRD.

Method: Thirty patients with a wide range of bone turnover, as assessed by bone histomorphometry (BHM), were selected from an ongoing, prospective observational study in patients with ESRD (NCT01886950), that underwent bone biopsy. Both iPTH (Cobas, Roche Diagnostics, Rotkreuz, Switzerland) and n-oxPTH (A1112; Immundiagnostik AG, Bensheim, Germany) and in addition bone turnover markers (bone-specific alkaline phosphatase (BSAP), P1NP and tartrate-resistant acid phosphatase 5b (TRAP5b)) were assessed in blood samples taken at the time of the bone biopsy. Descriptive statistics, Pearson correlation, regression analysis and ROC curves were used to assess the discriminative ability of n-oxPTH vs iPTH to detect bone turnover.

Results : n-oxPTH and iPTH were strongly correlated ($r=0.96$; $p<0.001$) and n-oxPTH values were on average 87% lower than iPTH values. Bone turnover, assessed by BHM (both static and dynamic measures) were strongly correlated with n-oxPTH and iPTH, e.g. bone formation rate $r=0.65$; $p<0.001$ and $r=0.69$; $p<0.001$, respectively. Bone turnover markers (BSAP, P1NP and TRAP5b) were also strongly and similarly associated with n-oxPTH and iPTH. The AUROC values for discriminating between low/non-low turnover for n-oxPTH and iPTH were 0.81; $p<0.01$ and 0.86; $p<0.01$, respectively (Figure 1A). For high/non-high turnover the AUROC was 0.88; $p<0.01$ and 0.90; $p<0.01$, respectively (Figure 1B).

Conclusion: n-oxPTH was not superior compared to iPTH in discriminating between high/non-high and low/non-low turnover and also showed no stronger correlation to biomarkers of bone turnover. Therefore, we conclude that there is no added value of n-oxPTH for evaluating bone disease in ESRD patients receiving dialysis, using the currently available method. Since this method cannot distinguish partially form completely oxidized PTH, we cannot definitely rule out the possibility that oxidation of PTH has impact on bone turnover.

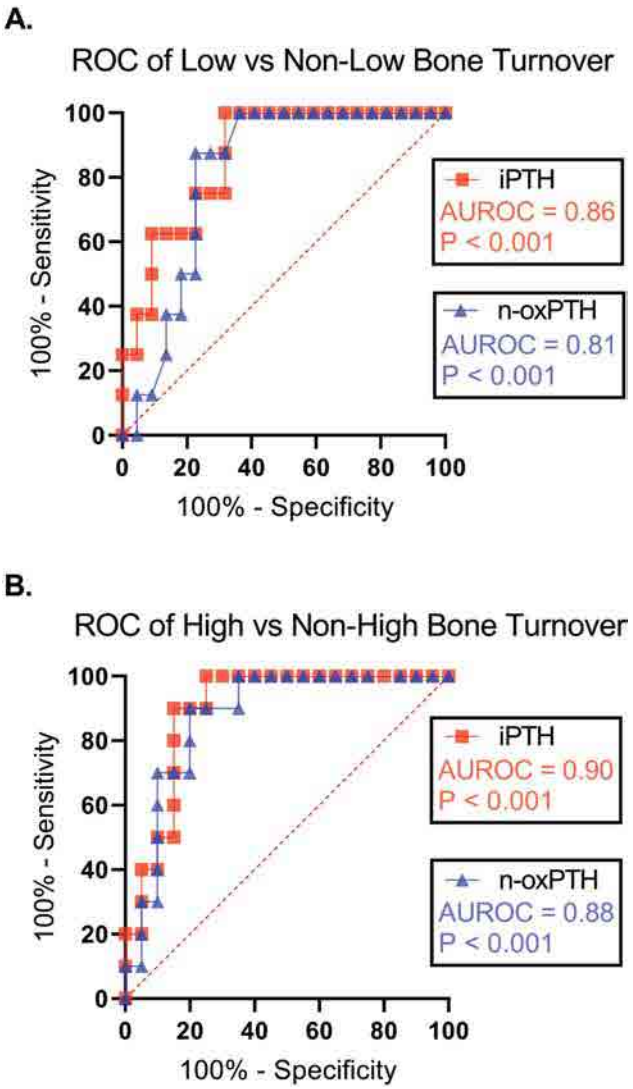


Figure 1.

P1389 **MAJOR OSTEOPOROTIC FRACTURES AFTER INITIATION OF DIALYSIS: INCIDENCE, PREDICTORS AND ASSOCIATION WITH MORTALITY**

Ken Iseri[1,2], Juan Jesus Carrero[3], Marie Evans[1], Li Felländer-Tsai[4], Hans Berg[4], Björn Runesson[1], Peter Stenvinkel[1], Bengt Lindholm[1], Abdul Rashid Tony Qureshi[1]

[1]Karolinska Institutet, Divisions of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Sweden, [2]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Tokyo, Japan, [3]Karolinska Institute, Department of Medical Epidemiology and Biostatistics and [4]Karolinska Institutet, Division of Orthopaedics and Biotechnology, Department of Clinical Science, Intervention and Technology

Background and Aims: Major osteoporotic fractures (MOF) are common in dialysis patients. We investigated incidence, predictors and clinical outcomes associated with first MOF occurring after initiation of dialysis (MOF_{first}).

Method: In Swedish Renal Registry of 9714 incident (2005 -2016) dialysis patients (median age 68 years, 67% men), we identified all MOF_{first} in hip, spine, humerus and forearm. Using flexible parametric hazard models and Fine-Gray analysis, we estimated incidence, mortality rates and predictors of MOF_{first}, and, in time-dependent analysis, risk of all-cause and cardiovascular disease (CVD) mortality following MOF_{first}.

Results: During median follow-up of 2.2 years, the crude incidence rate of MOF_{first} (n=835) was 24/1000 patient-years (pt-yrs) and that of hip fractures (n=470) 13/1000 pt-yrs. The multivariate-adjusted fracture incidence rates increased gradually after dialysis initiation and were 47% higher among women. Female sex, higher age, presence of comorbidities, and previous history of MOF ($MOF_{previous}$) were associated with increased risk for MOF_{first}, whereas peritoneal dialysis as compared to hemodialysis was associated with decreased fracture risk. The adjusted fracture incidence rate of MOF_{first} during the first 90 days following dialysis initiation was higher in patients with $MOF_{previous}$ than in those without $MOF_{previous}$. MOF_{first} independently predicted increased all-cause mortality (sub-distribution hazard ratio, sHR, 1.67(95%CI 1.47-1.91) and CVD-related mortality (sHR 1.49 (95%CI 1.22-1.84). Adjusted mortality rate following hip fractures was higher than for other types of MOF. Spline curves showed that mortality following MOF_{first} was highest during the first 6 months of follow-up.

Conclusion: Major osteoporotic fractures are common and associated with increased mortality in incident dialysis patients.

P1390

METHOD FOR AN EFFECTIVE INTRAOPERATIVE IDENTIFICATION OF PARATHYROID GLANDS IN HEMODIALYSIS PATIENTS WITH SEVERE HYPERPARATHYROIDISM FOR ADEQUATE PARATHYROIDECTOMY

Renata Vakhitova[1], Sergey Zinchenko[2]

[1]Kazan Federal University, Hemodialysis, Kazan, Russia and [2]Kazan Federal University, Sergery 2, Kazan, Russia

Background and Aims: Secondary and tertiary hyperparathyroidism (HPT) in patients undergoing chronic hemodialysis is one of the most important problems of clinical nephrology.

The removal of altered parathyroid glands has a number of difficulties: the detection and

accurate allocation of the entire volume of the parathyroid glands due to their small size, similar structure to the surrounding tissues (thyroid gland, lymph nodes and adipose tissue) and complex anatomical location.

Usually parathyroid glands are located directly on the posterior surface of the thyroid lobes, but in some cases they can be located atypically. In addition, the parathyroid glands are often "immersed" in the tissue of the thyroid gland, which also makes their visualization difficult.

Isolation and differentiated intraoperative visualization of the parathyroid glands is extremely important for an adequate amount of surgical intervention.

Method: Seven dialysis patients with severe hyperparathyroidism were operated on using oral administration of 5-aminolevolenic acid for intraoperative imaging of the parathyroid glands. Secondary and tertiary hyperparathyroidism ware diagnosed in patients with C5D stage CKD by a significant increase in the level of intact parathyroid hormone (iPTH) and increased parathyroid glands detected by ultrasound. In all patients, the level of iPTH before surgery was more than 1500 pg / ml. At the prehospital stage, in all patients, according to the results of ultrasound, enlarged parathyroid glands were revealed (the number of parathyroid glands in one patient was 4 +/- 2). For intraoperative identification of changed parathyroid glands in these patients, the oral administration of a solution of 5-aminolevulinic acid was used (given in 180 minutes before the start of surgery at a dose of 10 -15 mg / kg body weight). Then the surgical field was irradiated with polarized blue light with a wavelength of 395–405 nm to record fluorescence. If fluorescent formations were detected in the area of irradiated tissues, they were removed with subsequent reimplantation of a less altered part of the hyperplastic parathyroid gland into the forearm region.

Results: Specific bright red fluorescence and luminescence of the parathyroid glands caused by special external sources of polarizing blue light during the operation were observed in all 7 patients. In each patient from 3 to 6 light portions of parathyroid glands were detected.

These lightning portions were isolated, removed, and in 3 patients the most unchanged areas of the parathyroid glands were autotransplanted into the forearm. In the postoperative period, all patients showed the decrease in the level of iPTH less than 300 pg/ml, a syndrome of "hungry" bone, which was corrected by the administration of calcium and vitamin D preparations. Histologically all the found tissues were characterized as tissue of the parathyroid glands. The duration of operations was 48 +/- 12 minutes.

Patients did not have any side effects indicated in the annotation to the drug.

Conclusion: Intraoperative fluorescence diagnostics of the parathyroid glands with preoperative oral use of 5-aminolevolenic acid is a simple and effective method of their visualization.

This method promotes adequate parathyroidectomy and allows to reduce the time of surgical intervention in hemodialysis patients.

P1391 **PROGRESSION OF CALCIFICATION AND ITS RISK FACTORS IN CHINESE DIALYSIS PATIENTS**

Zhihong Liu[1]

[1]National Clinical Research Center of Kidney Disease, Jinling Hospital, Nanjing University School of Medicine, Department of Nephrology, Nanjing, P.R. China

Background and Aims: The China Dialysis Calcification Study (CDCS) aims to investigate prevalence and progression of vascular calcification (VC) as well as predictive values of VC in Chinese dialysis patients. This abstract reports VC progression and its risk factors during 4-year follow-up.

Method: The CDCS is a nationwide, multicenter observational study. 1497 dialysis patients from 24 centers in China were enrolled from 2014-2015 and continuously followed up for 4 years. Coronary artery calcification (CAC), abdominal aortic calcification (AAC) and cardiac valve calcification (CVC) were assessed at baseline and 4-year follow-up. CAC was assessed by Agatston score measured by electron beam computed tomography or multi-detector computed tomography. AAC was assessed by Kauppila score measured by plain lateral lumbar radiograph. CVC was measured by echocardiography. Progression was defined by comparing VC images at baseline with those at 4-year. When CAC/AAC scores at 4-year were greater than baseline, CAC/AAC were considered progressed; when there were more cardiac valves involved at 4-year than baseline, CVC was considered progressed. Logistic progression model was used to investigate the risk factors for calcification progression.

Results: 711 patients completed 4-year follow-up and 680 of them had calcification tests. Patients had the same type assessments (CAC, AAC or CVC) at both baseline and 4-year were included in analysis. At the 4-year follow-up, 89.4% (608/680) patients had at least one site vascular calcification (CAC, AAC or CVC), CAC affected the highest proportion of patients. Prevalence of CAC, AAC and CVC were 81.0% (517/638), 79.3% (310/391) and 45.6% (308/675), respectively. Progression of CAC was observed in 93.9% (368/392) patients with presence of baseline CAC, and 51.3% (123/240) patients without baseline CAC. CAC progression at 4-year follow-up was stratified by baseline CAC score (Figure1). Progression of AAC was observed in 96.5% (165/171) patients with presence of baseline AAC, and 63.8% (139/218) patients without baseline AAC. AAC progression at 4-year follow-up was stratified by baseline AAC score (Figure2). Progression of CVC from single to double cardiac valve calcification was observed in 33.3% (40/120) patients, and cardiac valve calcification occurred in 33.4% (162/485) patients without baseline CVC after 4-year follow-up. Multivariate logistic regression analysis results are showed in Figure3. Variables significantly increased the risk of calcification progression were baseline calcification score, abdominal obesity, hypertension, and calcium, phosphorous, iPTH during 4-year follow-up.

Conclusion: In the 4 years follow-up, progression of calcification is common among dialysis patient, and is associated with higher baseline severity, medical history and disease management.

Baseline CAC score	#CAC progression (% of ITTC patients)	CAC Progression		Number (%) of patients with CAC progression stratified by change of CAC score			
		Mean (SD)	Median Q1-Q3	0-100	100-400	400-1000	1000
0	123/240 51.3%	91.23(300.82)	0.65 0.00-63.65	70/123 (56.9%)	43/123 (35.0%)	6/123 (4.9%)	4/123 (3.3%)
0-100	141/150 94.0%	436.94(737.95)	165.95 57-388.1	49/141 (34.8%)	55/141 (39.0%)	18/141 (12.8%)	19/141 (13.5%)
100-400	107/112 95.5%	820.56(851.73)	643.60 205.5-1167.85	13/107 (12.1%)	25/107 (23.4%)	33/107 (30.8%)	36/107 (33.6%)
400-1000	53/55 96.4%	1619.76(1561.51)	1126.65 407-2342.2	1/53 (1.9%)	10/53 (19.2%)	11/53 (21.2%)	30/53 (55.7%)
>1000	67/75 89.3%	2324.61(2474.09)	1953.95 694.1-3300.55	1/68 (1.5%)	3/68 (4.4%)	13/68 (19.1%)	50/68 (75.0%)

Figure 1: CAC progression at 4-year follow-up stratified by baseline CAC score

Baseline AAC score	#AAC progression (% of ITTC patients)	AAC Progression		Number (%) of patients with AAC progression stratified by change of AAC score			
		Mean (SD)	Median Q1-Q3	0-3	3-6	6-12	>12
0	139/218 63.8%	6.2(5.38)	4.0 2.0-9.0	60/139 (27.5%)	31/139 (14.2%)	25/139 (11.5%)	23/139 (10.6%)
0-5	75/80 93.8%	7.0(4.66)	6.0 4.0-10.0	18/75 (22.5%)	20/75 (25.0%)	28/75 (35.0%)	9/75 (11.3%)
5-16	83/84 98.9%	8.0(4.07)	8.0 5.0-11.0	13/83 (15.5%)	18/83 (21.4%)	40/83 (47.6%)	12/83 (14.3%)
>16	7/7 100%	2.9(1.35)	3.0 2.0-4.0	5/7 (71.4%)	2/7 (28.6%)	0	0

*ITTC: patient with both baseline and 4-year follow-up calcification images for a same site

Figure 2: AAC progression at 4-year follow-up stratified by baseline AAC score

Calcification	Factors	Factor value	OR (95%CI)	p
CAC	Baseline CAC score stratification	<100 vs. 0	22.69 (8.83-58.30)	<0.0001
		≥100 vs. 0	15.40 (5.96-39.80)	<0.0001
		≥400 vs. 0	17.92 (4.19-76.63)	<0.0001
		≥1000 vs. 0	5.17 (2.18-12.22)	0.0002
	Abdominal obesity	Yes vs. No	2.77 (1.56-4.91)	0.0005
	Average serum Ca		5.90 (1.29-27.01)	0.0222
AAC	Baseline CAC score stratification	<5 vs.0	6.11 (2.21-16.86)	0.0005
		≥5 vs. 0	60.47 (5.37-681.18)	0.0009
	Serum phosphorous SD in 7 visits*		20.49 (2.95-142.39)	0.0023
	Hypertension	Yes vs. No	3.07 (1.36-6.96)	0.0074
	Abdominal besity	Yes vs. No	1.95 (1.04-3.67)	0.0386
CVC	Average serum iPTH		1.13 (1.06-1.21)	0.0001
	Baseline hyper sensitive CRP		1.02 (1.00-1.05)	0.0256
	Phosphate binders	Use vs. Without use	0.52 (0.35-0.78)	0.0014
	Dyslipidemia	Yes vs. No	2.39 (1.24-4.59)	0.0091
	Serum iPTH SD in 7 visits		0.94 (0.87-1.01)	0.0909

*7 visits were baseline, 6 month, 12 month, 18 month, 24 month, 36 month and 48 month

Figure 3: Multivariable logistic regression of factors related to calcification progression

P1392 **ANALYSIS OF CALCIFYING POTENTIAL OF UREMIC SERUM FROM HAEMODIALYSIS PATIENTS TREATED WITH A MEDIUM CUT-OFF (THERANOVA) DIALYSER: A PROSPECTIVE, CROSS-OVER STUDY.**

Paola Ciceri[1], Andrea Galassi[2], Nicolas Fabresse[3], Jean-Claude Alvarez[3], Ziad Massy[4], Mario Gennaro Cozzolino[2]

[1]Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Renal Research Laboratory, Department of Nephrology, Dialysis and Renal Transplant, Milan, Italy, [2]University of Milan, Health Sciences, Milan, Italy, [3]Raymond Poincare University Hospital, APHP, Division of Pharmacology, Paris, France and [4]Ambroise Pare University Hospital, APHP and Inserm U1018 Team 5, Division of Nephrology, Paris, France

Background and Aims: The retention of a large number of solutes that are normally excreted or metabolized by the kidney is responsible for the classical symptoms of haemodialysis (HD) patients. These molecules are defined as uremic toxins and can be classified into three groups: small water-soluble molecules, middle molecules and protein-bound toxins. Recently, efforts were put in order to develop dialysis membranes that allow the removal of large-middle molecules without clinically relevant albumin loss. These dialysers are the medium cut-off (MCO) membranes, which allow the removal of middle molecules up to approximately 50,000 Da. We performed a prospective, open-label, controlled, cross-over pilot study comparing expanded HD (HDx) with MCO membrane Theranova and conventional HD in 20 patients.

Method: Ten patients underwent conventional HD high-flux dialyser and 10 patients underwent HDx for 3 months, later the patients switched and received the other treatment for a further 3 months. We then analyzed the pro-calcifying effect of patient uremic serum in a model of high-phosphate (Pi) induced calcification in vascular smooth muscle cells (VSMCs).

Results: In this study each patient was the control of himself and, interestingly, we found a tendency of less pro-calcifying potential of serum from patients when treated with HDx, in comparison with HD (6.6 ± 1.1, 5.6 ± 0.6 and 6.7 ± 1.0, OD/mg protein, baseline HD, 0-3 HDx and 3-6 HD, months, respectively; and 4.7 ± 0.7 vs 3.2 ± 0.2, OD/mg protein, 0-3 HD vs 3-6 HDx, months, respectively) (Figure). Investigating the major mechanisms involved in high-Pi induced calcium deposition, we found that serum from patients when treated with HDx induced less necrosis in VSMCs, compared with HD (3.2 ± 0.8 vs. 0.9 ± 0.1, necrosis enrichment factor, 0-3 HD vs. 3-6 HDx, months, respectively). Nevertheless, no differences were found between the different dialysis treatment in the serum potential to induce apoptosis and to modulate the expression of a panel of genes involved in VSMC osteoblastic-differentiation such as BMP2, RUNX2, osteocalcin, MGP, OPN, and elastin. In the effort to characterize the difference in uremic toxin profile during the two different dialysis treatments, we measured a panel of protein-bound uremic toxins which have been shown to promote vascular calcification and /or bone loss and shown a significant increased removal by HDx of 3-indoxyl sulfate (30.6 ± 13.2 vs -17.1 ± 10.2 Δ%; 0-3 HD vs 3-6 HDx, months; $p<0.05$; and -21.1 ± 11.4 vs 54.4 ± 33.2 Δ%; 0-3 HDx vs 3-6 HD, months; $p<0.05$), indole 3-acetic acid (43.1 ± 16.9 vs -2.3 ± 10.9 Δ%; 0-3 HD vs 3-6 HDx, months; $p<0.05$), CMPF (61.8 ± 27.6 vs -16.1 ± 9.6 Δ%; 0-3 HD vs 3-6 HDx, months; $p<0.05$), and kynurenine (44.2 ± 12.9 vs -0.2 ± 6.8 Δ%; 0-3 HD vs 3-6 HDx, months; $p<0.05$).

Conclusion: These preliminary data suggest a role for HDx in reducing the calcifying potential of uremic serum. Our findings are promising and they need to be confirmed in larger studies.

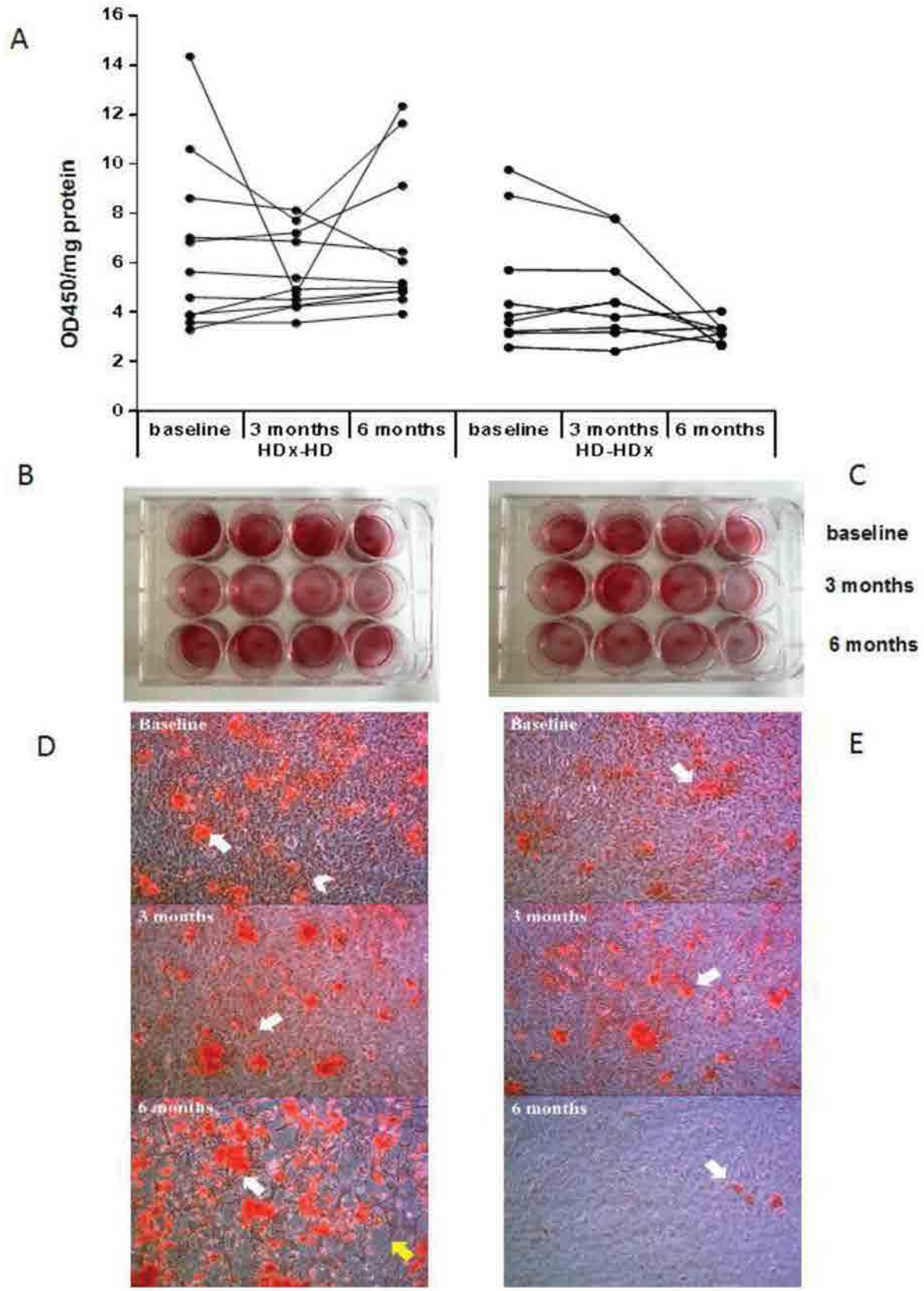


Figure legend: Calcification in VSMCs coultered with 10% uremic serum and challenged with 3.3 mM Pi for 3 days. Panel A left, B and D 0-3 months HDx and 3-6 months HD. Panel A right, C and E 0-3 months HD and 3-6 months HDx. **A:** Quantification of calcium deposition by Alizarin Red destaining. **B-C:** Representative pictures of Alizarin Red staining in wells. **D-E:** Ca deposition was visualized at light microscopic level (Alizarin Red staining). Magnification x200.

P1393

A SYSTEM FOR FORECASTING OF DRUG DOSAGE FOR BONE MINERAL DISORDERS CORRECTION IN PATIENTS ON CHRONIC DIALYSIS

Dmitriy Zinovev[1], Vladimir Novitskiy[1,2], Andrey Malkoch[1,3,4]

[1]Nephrology Expert Council, Moskva, Russia, [2]Moscow State University of Food Production, Informatics and computing technology of food production, Moskva, Russia, [3]Moscow State University of Food Production, Therapy and children diseases, Moskva, Russia and [4]Russian Medical Academy of Continuous Professional Education, Nephrology and Hemodialysis, Moskva, Russia

Background and Aims: Bone and mineral disorders (BMD) is a common complication of CKD in patients on chronic dialysis. Timely and adequate correction of BMD is the most important aspect of patient's treatment. This work presents a system for forecasting of phosphate-binding agents (PBA) dosage and vitamin D receptor activators (VDRA) dosage. The system consists of sequentially triggering artificial neural network forecasting models (separate model for each drug type).

Method: As an input dataset, system uses patient's results of laboratory studies (blood calcium, phosphate and PTH) for the period of 6 months, information on previous drug therapy and data on adequacy of patient's dialysis therapy. The output of the system are dosages of PBA an VDRA that have to be administered in order to bring the patient's parameters as close as possible to target range of values (2.1-2.5 mmol/l for calcium, 0.87-1.5 mmol/l for phosphate and 150-300 pg/ml for PTH). The system consists of two sequentially triggering forecasting models (for PBA and for VDRA), where each model is an artificial neural network, that has been trained on a data, collected in more than 20 "Nefrosovet" hemodialysis clinics for the period of 3 years.

The effect of system usage was examined for the group of 356 hemodialysis patients with median follow-up time of 3 month. The primary end-points were a number of patients in target range of values With respect to calcium (2.1-2.5 mmol/l), phosphate (0.87-1.5 mmol/l) and PTH (150-300 pg/ml).

Results: During the study we determined that as a result of using the dose forecasting system, number of patients in target range of values significantly increased with respect to calcium (from 178 to 209, p=.0196), phosphate (from 99 to 152, p=.0000), and PTH (from 83 to 109, p=.0281).

Conclusion: Employment of automated drug dosage forecasting system based on artificial neural network models, has a positive effect on BMD correction quality, which, in turn, reduces the risk of possible complications.

P1394 **ASSOCIATION BETWEEN PARATHYROID HORMONE AND MORTALITY IN HAEMODIALYSIS: THE DIABETES MAKES THE DIFFERENCE**

José Luis Fernandez-Martin[1], Beatriz Martín-Carro[1], Cristina Alonso-Montes[1], Jürgen Floege[2], Markus Ketteler[3], Gérard London[4], Francesco Locatelli[5], Jose Luis Gorriz[6], Manuel Anibal A. Ferreira[7,8], J. Emilio Sanchez-Alvarez[9], Miguel Ángel Suárez Hevia[10], Jesús María Fernández Gómez[11], Carmine Zoccali[12,13], Jorge B. Cannata-Andia[1,14]

[1]Hospital Universitario Central de Asturias., Bone and Mineral Research Unit, REDinREN del ISCIII. Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain, [2]RWTH Aachen University, Department of Nephrology and Clinical Immunology, Aachen, Germany, [3]Klinikum Coburg, Division of Nephrology, Coburg, Germany, [4]Centre Hospitalier FH, Manhes, France, [5]Alessandro Manzoni Hospital, Department of Nephrology, Dialysis and Renal Transplant, Lecco, Italy, [6]Hospital Clinico Universitario, Department of Nephrology. Department of Medicine, Health Research Institute INCLIVA, University of Valencia., Valencia, Spain, [7]Hospital Curry Cabral, Nephrology Department, Lisboa, Portugal, [8]Universidade NOVA de Lisboa, Faculdade de Ciências Médicas, Lisbon, Portugal, [9]Hospital Universitario de Cabueñes, Department of Nephrology, Gijón, Asturias, Spain, [10]Hospital Universitario Central de Asturias, UGC of Urology, Oviedo, Spain, [11]Hospital Universitario Central de Asturias, UGC of Urology. Universidad de Oviedo., Oviedo, Spain, [12]Ospedali Riuniti, Clinical Epidemiology and Physiopathology of Renal Disease and Hypertension and Renal and Transplantation Unit, Italy, [13]CNR National Research Council, Italy and [14]Universidad de Oviedo, Department of Medicine, Oviedo, Spain

Background and Aims: Diabetes is the most common cause of chronic kidney disease (CKD) stage 5 and a relevant risk factor for mortality. The available CKD-MBD guidelines do not make differences between diabetics and non-diabetics regarding the optimal targets of the serum bone and mineral biochemical parameters. Thus, the objective of this analysis of COSMOS was to compare the association between the main serum bone and mineral biochemical parameters (calcium-Ca, phosphorus-P and parathyroid hormone-PTH) and mortality in diabetic and non-diabetic patients in haemodialysis.

Method: COSMOS is a 3-year, observational, prospective, open-cohort study that includes 6797 patients from 227 dialysis centres that were randomly selected from 20 European countries. Cox proportional hazard regression models with penalized splines smoothing were used to analyse the association between relative risk of mortality vs. Ca, P or PTH. Hazard ratios were adjusted by demographics, comorbidities, treatments and biochemical parameters. Interaction analysis was used to analyse if diabetes can influence the association between relative risk of mortality and Ca, P and PTH.

Results: The present analysis includes 6306 patients with follow-up data and accurate information on diabetes status. The mortality rate in COSMOS was 13.3 deaths per 100 patient-years (17.8 in diabetics and 11.4 in non-diabetics). At baseline, diabetic patients were older (66.7 ± 11.7 vs. 62.8 ± 15.3 years, $p < 0.001$), had a higher body mass index (27.3 ± 5.6 vs. 24.5 ± 4.5 kg/m2, $p < 0.001$) and more frequent history of cardiovascular disease (83.1% vs. 67.2%, $p < 0.001$). The percentage of patients prescribed drugs to correct the bone and mineral biochemical parameters such as, phosphate binding agents, vitamin D receptor activators and calcimimetics was lower in diabetics (82.3% vs. 86.4%, 45.4% vs. 48.5% and 4.6% vs. 6.9% respectively, $p < 0.03$). There were no significant differences in serum P (5.3 ± 1.3 vs. 5.4 mg/dL ± 1.5, $p = 0.3$) and haemoglobin (11.4 ± 1.4 vs. 11.4 ± 1.4 g/dL, $p = 0.5$) but diabetic patients showed significant -but not clinically relevant- lower levels of Ca (9.0 ± 0.7 vs. 9.1 ± 0.8 mg/dL, $p < 0.001$), PTH (median [interquartile range]: 199 [109, 335] vs. 216 [108, 396] pg/mL, $p = 0.001$) and albumin (3.7 ± 0.5 vs. 3.8 ± 0.5 g/dL, $p < 0.001$). No significant interaction was found between diabetes and serum Ca or P and their association with relative risk of mortality. However, diabetes and PTH showed a marginal significant interaction in their association with mortality ($p = 0.050$). The slopes of the curve of relative risk of mortality vs. PTH were more pronounced in diabetics (see figure). High serum PTH was significantly associated with a higher relative risk of mortality in diabetics but not in non-diabetics. The range of serum PTH where the minimum risk of mortality was observed (defined as serum PTH with a HR<1.1, i.e. less than 10% increase in the relative risk of mortality) was narrower in the diabetics compared with non-diabetics (204-546 vs. 166-757 pg/mL, figure)

Conclusion: These results suggest for the first time a differential effect of diabetes on the association between relative risk of mortality and serum PTH. High serum PTH predicts death only in diabetics. These findings could have relevant implications for the diagnosis and treatment of CKD-MBD in diabetic and non-diabetic patients in haemodialysis.

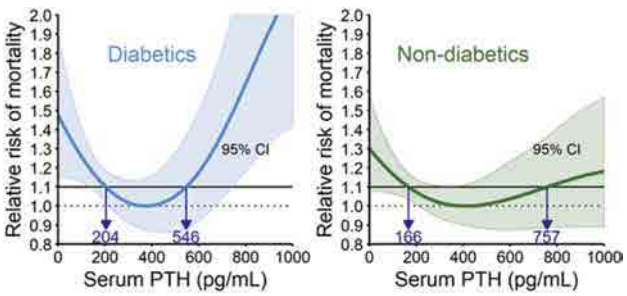


Figure:

P1395

FIBROLAST GROWTH FACTOR 21 CORRELATES POSITIVELY WITH AND PREDICTS TO OSTEOPOROSIS IN HEMODIALYSIS PATIENTS

Lili Zhu[1], Bin Wang[1], Bicheng Liu[1]

[1]*Nephrology, Zhong Da Hospital, Nanjing, P.R. China*

Background and Aims: Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) has been recognized as a common complication and arises early in the course of CKD. Osteoporosis can be one form of renal osteodystrophy, one component of the bone abnormalities of CKD-MBD. Fibroblast growth factor 21 (FGF21) is increased progressively with a decline of renal function and higher FGF21 levels predict high all-cause mortality in hemodialysis patients. In recent studies, FGF21 has been approved to exert an inverse effect on bone mineral density. Hence, our study was performed to investigate the relationship and role of FGF21 in osteoporosis in our hemodialysis (HD) patients cohort.

Method: We screened HD patients in Nanjing Zhongda Hospital and The First People's Hospital of Changzhou according to a strict inclusion criteria and exclusion criteria. We recorded demographic information, blood data before dialysis and serum FGF21, FGF23 levels and measured the CT-attenuation values (in Hounsfield units (HU)) of trabecular bone in L1 on axial images to evaluate the severity of osteoporosis. We used univariate analyses to compare the differences between two groups. Meanwhile, bivariate correlation analyses were performed to assess the correlation of L1 attenuation with serum FGF21, FGF23 and other clinical parameters. Stepwise multivariate linear regression analyses were employed to evaluate variables independently associated with attenuation values. We constructed ROC curves to calculate the AUC and compared the prognostic value of every independently associated factor or united factor to osteoporosis. All analyses were two-tailed, and a $P < 0.05$ was considered to be statistically significant. SPSS Software, version 18.0 was used for all statistical analyses.

Results: 339 HD patients from two big HD centers in China that met our standards were screened. The mean age of HD patients was 56.79 ± 15.60 years. 339 HD patients were divided into two groups osteoporosis (n = 98) and non-osteoporosis (n = 241) on the basis of HU level (L1 attenuation ≤ 135 HU). Remarkably, serum FGF21 were higher in osteoporosis compared to non- osteoporosis in HD patients (median 640.86 pg/ml vs. 245.46 pg/ml, $P < 0.01$). We also divided HD patients into two groups according to tertiles of serum FGF21 levels. Moreover, attenuation levels were negative associated independently with serum FGF21 ($r=-0.136$, $P<0.05$). To evaluate the different values of independent associated or united factors in predicting osteoporosis, receiver operating characteristic (ROC) curves was constructed. The area under the curve (AUC) for FGF21 combined with age yielded a marked increment (AUC=0.836, P=0.000) with a good sensitivity (93.8%).

Conclusion: In conclusion, elevated FGF21 level has a positive relationship with the incidence of osteoporosis in HD patients. Simultaneously, FGF21 in combination with age can be a predictive parameter of osteoporosis in HD patients.

Table 1. Comparison of clinical characteristics and laboratory data between osteoporosis and non- osteoporosis group in HD patients.

	All HD patients	osteoporosis	non-osteoporosis	*P* value
Number	339	98	241	
General data				
Age(years)	56.79 ± 15.60	66.45 ± 13.28	52.86 ± 14.77	**0.000**
Sex(male %)	193(56.93%)	60(61.22%)	133(55.19%)	0.309
Dialysis vintage(years)	4.33 ± 4.91	4.63 ± 4.87	4.21 ± 4.94	0.469
Body mass index(BMI)	22.99 ± 4.01	22.93 ± 4.03	23.01 ± 4.01	0.868
Systolic BP(mmHg)	145.78 ± 24.40	145.94 ± 24.37	145.72 ± 24.46	0.940
Diastolic BP(mmHg)	82.32 ± 14.60	78.51 ± 14.55	83.87 ± 14.36	**0.002**
Blood data				
Hemoglobin(g/L)	97.57 ± 20.14	98.47 ± 20.94	97.20 ± 19.84	0.601
Albumin(g/L)	35.89 ± 6.13	35.36 ± 6.41	36.11 ± 6.02	0.309
Uric acid(mmol/L)	378.64 ± 125.83	368.83 ± 120.70	382.63 ± 127.89	0.361
Triglycerides(mmol/L)	1.81 ± 1.37	1.75 ± 1.45	1.84 ± 1.33	0.438
Total cholesterol(mmol/L)	4.13 ± 1.12	4.06 ± 1.00	4.16 ± 1.17	0.605
Dicarbonate(mmol/L)	22.65 ± 3.76	22.63 ± 3.87	22.66 ± 3.72	0.943
Calcium(mmol/L)	2.26 ± 0.24	2.28 ± 0.25	2.26 ± 0.24	0.548
Phosphate(mmol/L)	1.70(0.19,4.16)	1.69(0.28,4.16)	1.76(0.19,3.35)	0.305
Parathormon(pg/ml)	374.07 ± 418.87	347.02 ± 385.80	385.07 ± 431.87	0.449
FGF21(pg/ml)	185(1,3176)	641(2,3176)	245(1,1764)	**0.000**
FGF23(pg/ml)	5695(25,48663)	6686(25.47491)	5408(30,48663)	0.804
Comorbidity				
Diabetes(%)	112(33.04%)	45(45.92%)	67(27.80%)	**0.001**
Hypertension(%)	298(87.91%)	87(88.78%)	211(87.55%)	0.754
CVD(%)	94(27.73%)	48(48.98%)	46(19.09%)	**0.000**
Medicine usage				
Vitamin D(%)	151(44.54%)	31(31.63%)	120(49.79%)	**0.002**
Calciu supplements(%)	86(25.37%)	22(22.45%)	64(26.56%)	0.431
Cinacalcet(%)	52(15.34%)	11(11.22%)	41(17.01%)	0.180
ACEI/ARB(%)	94(27.73%)	28(28.57%)	66(27.39%)	0.825
FRAX(30%)				
Major Osteoporosis	3(0.9,14)	4.0(1.0,13.0)	2.55(0.9,14)	**0.000**
Hip fracture	0.8(0.0,10.0)	1.95(0,10)	0.5(0,10)	**0.000**

HD, haemodialysis; FGF21, fibroblast growth factor 21; FGF23, fibroblast growth factor 23; CVD, cadiocerebrovascular disease; ACEI, angiotensin converting enzyme; ARB, Angiotensin receptor II antagonist; FRAX, fracture risk assessment tool.

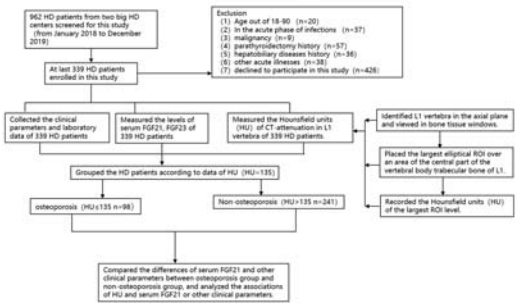


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P1396

EFFECT OF MIXED VERSUS ANIMAL-BASED LOW PHOSPHORUS DIETS IN DIALYSIS PATIENTS ON INTACT FGF23 LEVELS: A RANDOMIZED CLINICAL TRIAL

Juan C. Ramirez-Sandoval[1], Ximena Atilano-Carsi[1], Jorge Sánchez-Silva[1], Celene Arce-Santander[1], Cristino Cruz[1], Pamela Basulto-Sosa[1], Luis Tamez-Pedroza[1], Miguel García de León[1], Ángeles Espinosa-Cuevas[1], Ricardo Correa-Rotter[1]

[1]*Salvador Zubirán National Institute of Health Sciences and Nutrition, Nephrology and Mineral Metabolism, Ciudad de México, Mexico*

Background and Aims: The FGF23-lowering effect of different phosphate-sources (vegetable versus animal) in low-phosphorus diets are scarcely known. In this trial, we assess the effect on intact FGF23 (iFGF23) of two low-phosphorus diets, animal versus mixed (vegetable + animal), in dialysis patients.

Method: A randomized, two-center, open-label, clinical trial was performed. Subjects on stable dialysis for >6 months with P>4.5 mg/dL were randomized into a mixed-based (3 ounces equivalent of animal protein + 3 ounces equivalent of legumes) vs. animal-based (6 ounce equivalent of animal protein) low phosphorus diet with equivalent nutrients (phosphorus <1000 mg/day; protein=1.3 g/kg/day). The primary outcome was the difference in serum iFGF23 change (ELISA) after 12 wks. We excluded patients who modified their dialysis dose, phosphate binder, or vitamin D prescription during trial.

Results: 556 subjects were screened, only 57 subjects (37 hemodialysis[HD] and 18 peritoneal dialysis[PD]) were randomized. Age, sex, phosphate-binders use, and other baseline characteristics were similar between groups. Baseline iFGF23 levels were 7394 (IQR 2379-16629) and 6859 (1543-17521) ng/mL in mixed-based and animal-based groups respectively (p=0.62). Both groups had a significant decrease in iFGF23 after 12 weeks of intervention (iFGF23 change: -285 [IQR -3002 to 227] ng/mL, p<0.001, and -182 [IQR -9323 to 228] ng/mL, p<0.001); there were not significant differences in iFGF23-decrease between both diets (Figure, p:0.78). Serum phosphorus in the mixed-based and the animal-based declined by -0.66 (95% confidence interval [95% IC], -1.39 to -0.04] mg/dL and -0.21 (95% IC -0.81 to 0.38) respectively (p=0.14). There was a trend between the decrease in observed phosphorus and iFGF23 (rho = 0.265, p=0.058). There were no differences between groups in the change of serum Ca, albumin, PTH, and other biochemical parameters.

Conclusion: Dietary phosphorus restriction for 12 weeks with animal-based or mixed-based phosphorus sources similarly decreases iFGF23 concentration in HD or PD patients.

P1397 LONG-TERM EFFICACY AND SAFETY OF ETELCALCETIDE IN HEMODIALYSIS PATIENTS WITH SEVERE SECONDARY HYPERPARATHYROIDISM

Carlo Massimetti[1], David Micarelli[1], Sandro Feriozzi[1]

[1]*Ospedale Belcolle, Nefrologia e Dialisi, Viterbo, Italy*

Background and Aims: Currently the therapeutic strategies most frequently used in the treatment of secondary hyperparathyroidism (SHPT) are represented by vitamin D receptors activators (VDRAs) and cinacalcet. However, both drugs have side effects that limit their use. Recently, in the treatment of SHPT has been introduced the etelcalcetide, a second generation calcimimetic given intravenously (i.v.). This new route of administration could improve adherence to therapy and reduce gastrointestinal side effects. The aim of the study was to evaluate the efficacy and safety of the etelcalcetide in hemodialysis (HD) patients with SHPT inadequately controlled with traditional therapy (cinacalcet and/or VDRAs), or who had side effects with cinacalcet, or that were not adherent to cinacalcet therapy.

Method: For this purpose we have selected 28 HD patients with inadequate control of SHPT (PTH $>$ 500 pg / ml; range 502-2148 pg/ml). Serum albumin-corrected calcium (sCa), phosphate (P), calcium–phosphate product (Ca x P), and PTH were assessed monthly. Baseline 19 patients were taking stable doses of active vitamin D analogs and all patients were taking phosphate binders. Etelcalcetide was administered three times a week after each hemodialysis session. The starting dose was 2.5 or 5.0 mg and then adjusted between 2.5 and 10.0 mg according to sCa and PTH levels. Treatment was temporarily withheld for sCa $<$7.5 mg/dl, or symptomatic hypocalcemia and was subsequently resumed at a lower dose. The primary endpoint was a PTH reduction $>$ 30% compared to baseline levels.

Results: At present 12 months have passed since the beginning of etelcalcetide therapy. In most patients PTH levels were reduced immediately after the start of therapy. After 12 months we observed a reduction $>$ 30% in 82% of patients, meanly -54% with a range between – 22% and – 81%. On average PTH levels decreased from 1167$\pm$444 to 558$\pm$310 pg/ml (P$<$.001). Serum calcium significantly reduced already after one month of therapy settling on stable levels from the third month onward, sCa decreased from 9.7$\pm$0.4 to 9.2$\pm$0.5 mg/dl (P$<$.01). However, the percentage of patients treated with calcium salts rose from 21% at baseline to 44% at F-U, mean dose at F-U 1.8 $\pm$ 0.9 g/d, while the percent of patients treated with VDRAs increased from 68% to 91%. Serum phosphate decreased from 6.4$\pm$1.4 to 4.6$\pm$1.3 mg/dl (P$<$.001), Ca x P decreased from 60$\pm$13 to 42$\pm$12 mg^2/dl^2 (P$<$.001). The median average dose of etelcalcetide at F-U was 6.2 $\pm$ 1.7 mg/HD, with a range of 2.5-10.0 mg/HD. Throughout the study, the only side effect was asymptomatic hypocalcemia that required the use of calcium salts. There were no gastrointestinal adverse effects.

Conclusion: Our results confirm that in hemodialysis etelcalcetide therapy is effective and safe in the control of SHPT refractory to conventional therapy over a 1-year treatment period.

P1398 EFFECTS OF CONVERTING FROM CINACALCET TO ETELCALCETIDE

Sofia Homem Melo Marques[1], Pablo Alija[1]

[1]*Uninefro by B.Braun*

Background and Aims: Secondary hyperparathyroidism is a common problem in patients undergoing chronic hemodialysis and its treatment includes vitamin D analogs and calcimimetics which act upon the calcium-sensing receptor. Etelcalcetide was introduced as an intravenous calcimimetic easy to administer at the end of the hemodialysis session with improved adherence. Hypocalcemic episodes have raised some concerns although this side effect is not unanimously described.

As an institutional policy most patients from 2 hemodialysis units were switched from cinacalcet to etelcalcetide between July 2017 and January 2018. We aimed at evaluating the impact of this conversion upon laboratory values and ongoing medication.

Method: We collected data from patients in 2 hemodialysis units including monthly serum values of calcium, phosphorus, hemoglobin and albumin, quarterly parathormone (PTH) values from 3 months previous to conversion until 3 months post-conversion as well as the calcimimetic dose during the same time frame. Descriptive statistics concerning mean and median values of the previous 3 and next 3 months following conversion were used. A paired sample t-test was performed to compare values before and after conversion.

Results: Of the approximately 200 patients, 22 were on cinacalcet and were switched to etelcalcetide. These had a mean age of 66.9 years and included 9 women and 8 diabetics. Mean PTH value before conversion was 728±391 (range 371-1900pg/mL) and did not differ significantly from that after conversion 717±330 (p=0.9). No significant statistical difference between values before and after conversion was found for serum calcium (9.3±0.5 vs 9.2±0.6; p=0.43), phosphorus (5.4±0.8 vs 5.1±1.0; p=0.15), albumin (4.1±0.2 vs 4.1±0.2; p=0.83) and hemoglobin (11.3±0.8 vs 11.4±0.9; p=0.50). The mean number of hypocalcemic values during the 3 months before and after conversion was identical (0.6±1 vs 0.6±0.9; p=0.86). The median cinacalcet dose on the month before conversion was 30mg/day (IQR 22.5) and the median etelcalcetide dose at conversion was 2.5mg three times per week (IQR 1.9). The conversion factor was 27mg cinacalcet: 1mg etelcalcetide, because even patients on high cinacalcet doses were initially started at low etelcalcetide doses. However, at 3 months following conversion, the median etelcalcetide dose was 8.75 (IQR 7.5). The doses of erythropoiesis-stimulating agents (ESA), vitamin D analogues and phosphorus binders were not significantly affected.

Conclusion: Switching from cinacalcet to etelcalcetide in all patients on hemodialysis in a particular institution did not change laboratory values or increased the number of hypocalcemic measurements. The etelcalcetide dose was adjusted up for the first 3 months and the mean PTH value did not change significantly. Treatment with ESA, vitamin D analogues and phosphorus binders remained unchanged after conversion. Secondary hyperparathyroidism is a chronic condition and etelcalcetide provides a useful means to control it with an easy administration regimen.

P1399

SPARING EFFECT OF PERITONEAL DIALYSIS VS HEMODIALYSIS ON CHANGE OF BONE MINERAL DENSITY EVALUATED BY WHOLE-BODY DXA AFTER INITIATION OF DIALYSIS THERAPY AND ITS IMPACT ON CLINICAL OUTCOME

Ken Iseri[1,2], Longkai Li[1], Abdul Rashid Tony Qureshi[1], Xin Li[1], Jonaz Ripsweden[3], Olof Heimbürger[1], Franz Peter Barany[1], Ingrid Bergstrom[4], Peter Stenvinkel[1], Torkel Brismar[3], Bengt Lindholm[1]

[1]Karolinska Institutet, Divisions of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, [2]Showa University School of Medicine, Division of Nephrology, Department of Medicine, [3]Karolinska Institutet, Division of Medical Imaging and Technology, Department of Clinical Sciences, Intervention and Technology and [4]Karolinska Institutet, Division of Endocrinology, Metabolism and Diabetes, Karolinska University Hospital

Background and Aims: Bone loss is associated with progression of cardiac calcification and increased mortality in end stage renal disease (ESRD) patients but the relations and underlying causes are unclear. We investigated factors associated with changes of bone mineral density (BMD) during the first year after initiation of dialysis and the association between BMD changes and subsequent mortality in ESRD patients.

Method: In a prospective study of 242 ESRD patients (median age 55 years, 61% men) starting dialysis, total BMD and BMD at specific bone sites (including seven subregions: head, arms, legs, trunk, hip, pelvis and spine) was assessed by whole body dual-energy X-ray absorptiometry (DXA) at baseline and one year after dialysis start. Framingham cardiovascular disease (CVD) risk score, body composition, nutritional status, handgrip strength, various biochemical biomarkers (white blood cell, hemoglobin, albumin, creatinine, calcium, phosphate, intact parathyroid hormone, triglyceride, cholesterol, HDL cholesterol and high-sensitivity C-reactive protein) were recorded. We used multivariate linear regression analysis for BMD change analysis. We followed patients from 12 months after initiating of dialysis until renal transplantation, death or end of 60 months follow-up. During follow-up, 59 patients (24%) died due to CVD (n=33) or other causes (n=26) and 95 patients (39%) underwent renal transplantation. Fine and Gray competing risk analysis was used to ascertain associations of BMD changes with all-cause and CVD-related mortality.

Results: From baseline to one year after initiation of dialysis, there was a significant decrease of BMD_{total} and $BMD_{leg,\ trunk,\ rib,\ pelvis\ and\ spine}$ in hemodialysis (HD) patients, whereas no difference was seen in peritoneal dialysis (PD) patients. In multivariate linear regression analysis adjusting for several confounders, HD therapy - compared to PD therapy - was significantly associated with negative changes in $BMD_{total\ (\beta=-0.15)}$, $BMD_{head\ (\beta=-0.14)}$, $BMD_{leg\ (\beta=-0.18)}$ and $BMD_{trunk\ (\beta=-0.16)}$. The direction and extent of changes in BMD, i.e. increase of BMD, associated with statistically significant lower all-cause mortality risk for BMD_{total} (sHR, 0.91), BMD_{head} (sHR 0.91) and BMD_{leg} (sHR 0.92), while for CVD-mortality a significant association with BMD changes was found only for changes in BMD_{head} (sHR 0.92).

Conclusion: In patients starting on dialysis, PD therapy appeared to have a beneficial effect on BMD changes as compared to HD during the first year of dialysis therapy. This difference may have implications for clinical outcomes as the degree of bone loss was associated with subsequent mortality. Changes towards increased BMD_{total}, BMD_{head} and BMD_{leg} associated with lower all-cause mortality. For head region – which is known as a cortical bone rich site – positive BMD change associated also with lower CVD mortality suggesting that increase or maintenance of BMD of cortical bone rich sites may have stronger association with clinical outcome in ESRD than BMD of trabecular bone.

P1400

ASSOCIATION BETWEEN MEAN SERUM MAGNESIUM LEVEL DURING THE FIRST 3 YEARS OF HEMODIALYSIS AND THE RISK OF SUBSEQUENT BONE FRACTURES

Takayuki Fujii[1], JUNYA KOSHIZAKA[1], NOBUAKI YAMAUCHI[1], MAYU MORIMOTO[1], NORIKO TERASAKI[1], HIROAKI TANAKA[1], SATOSHI SUZUKI[1]

[1]*Seirei Sakura Citizen Hospital, Kidney center, Sakura city, Japan*

Background and Aims: Serum magnesium levels are an important factor associated with vital prognosis, cardiovascular disease, and vascular calcification in hemodialysis patients. Moreover, low serum magnesium levels are reportedly associated with an increased risk of hip fractures. Previously we reported that mean magnesium level during the first 3 years of hemodialysis was associated with all-cause mortality in ERA-EDTA 2018. Here, we investigated whether mean magnesium level during the first 3 years of hemodialysis can predict fracture risk.

Method: A retrospective cohort study was conducted in 283 patients who started hemodialysis at our hospital between March 2004 and the present and who could be followed for at least 3 years or had a fracture within 3 years. To assess the association between mean serum magnesium level during 3 years after the start of hemodialysis or until fracture and fracture risk, a multivariate analysis was performed using the Cox proportional hazard model with factors related to fractures as covariates, with all fractures such as hip fracture and spinal compression fracture as the outcome.

Results: The mean follow-up period was 6.1 years, and the mean age of patients was 64 years, with women accounting for 31%. Of all 283 patients, 62 developed fractures. A univariate analysis of factors associated with fractures revealed that high serum magnesium level was a significant fracture suppressor (hazard ratio [HR]: 0.31 [0.12–0.73]). Multivariate analysis conducted with significant factors in univariate analysis (mean serum albumin level, serum phosphorus level, hemoglobin level, C-reactive protein level, age, history of heart disease, history of bone fractures, and use or nonuse of phosphate binder during the 3 years) as the covariates revealed that the serum magnesium level was not significantly associated with bone fractures (HR: 0.95 [0.33–2.78]), whereas, old age, history of fractures, low albumin level, high CRP level, and nonuse of phosphate binder were significantly associated with fractures.

Conclusion: Serum magnesium levels during 3 years after the initiation of hemodialysis did not predict the risk of subsequent fractures, whereas a high level of inflammatory response, malnutrition, and nonuse of phosphate binder did.

P1401 THE REMOVAL EFFICIENCY OF PHOSPHATE FROM INTRACELLULAR FLUID DURING HEMODIALYSIS

Hiroshi Kikuchi[1], Hisaki Shimada[2], Ryo Karasawa[1], Masashi Suzuki[2]

[1]Toyosaka Hospital, Internal medicine, Nligata city, Kita-ku, Japan and [2]Shinraku-en Hosppital, Kidney center, Niigata city, Nishi-ku, Japan

Background and Aims:

In hemodialysis (HD) patients without residual renal function, almost all of phosphate (P) absorbed through intestine is eliminated with HD. To avoid hyperphosphatemia, which is major risk for mortality in HD patients, reduced P absorption and /or improved P removal efficiency should be required. The P elimination during HD from intracellular fluid (ICF) remarkably differs from that from extracellular fluid (ECF). Because the total P removal is too complicate to analyze, few studies about P removal efficiency have been performed. In this study, we tried to separately estimate the amount of P removal from ICF and ECF.

Method:

Fifty-eight patients undergoing 4-hour HD with BMI 22±3 were enrolled this study. ECF and ICF volumes were considered respectively as 20% and 40% of body weight (BW). The amount of urea nitrogen (UN) removal (Run) was calculated using the values of serum UN concentration (UN_0, UN_4) and total body fluid (60% of BW) at pre and post HD as 0.6(UN_0 x pre BW – UN_4 x post BW). The amount of intradialytic total P removal (Rp) was calculated using the formula previously reported. At starting phase of HD, P is considered to be removed only from ECF, and from ECF and ICF at later stage. In initial hours, when P is removed only from ECF, serum P concentration change exponentially ($P = Kp^tP_0$) as serum UN concentration ($UN = Kun^tUN_0$). (Where, Kun and Kp are exponential coefficient of UN and P respectively, t is time (min), P_0 is serum P concentration before HD). If P outflow from ICF is disregarded, the exponential change in P persists, and serum P concentration at the end of 4-hour HD is $Kp^{240}P_0$. Consequently, the amount of P removal from ECF ($Rp_{(ex)}$) was calculated as 0.2(P_0 x preBW - $Kp^{240}P_0$ x postBW). The exponential coefficient in P change was reported to be 0.997788 times of that in UN. The amount of P removal from ICF ($Rp_{(in)}$) was calculated as difference between Rp and $Rp_{(ex)}$. Each removal efficiency was calculate as Run/UN_0, $Rp_{(ex)}/P_0$ or $Rp_{(in)}/P_0$. Intradialytic removal of P from ECF and ICF were compared with that of UN. Regression analysis was performed on 24 factors which might affect the efficiency. The relationship between drug administration and the removal efficiency was investigated as for 22 drugs.

Results:

UN removal and P removal from ECF were closely related. Run and $Rp_{(ex)}$ had positive correlation (0.564, $p<0.001$). And Run/UN_0 also correlated positively to $Rp_{(ex)}/P_0$ ($R=0.970$, $p<0.001$). $Rp_{(ex)}/P_0$ and P_0 had a positive correlation ($R=0.334$, $p<0.01$) as well as Run/UN_0 and UN_0 ($R=0.382$, $p<0.01$). P removal from ICF showed different pattern. In comparison between P removal from ECF and ICF, removal amount showed positive correlation ($R=0.634$, $p<0.001$), but removal efficiency showed no correlation($R=0.006$, ns). Notably, $Rp_{(in)}/P_0$ and P_0 had negative correlation ($R=0.315$, $p<0.02$). $Rp_{(in)}$ accounted for 44.6±6.2% of Rp. On regression analysis concerning the 24 factors, only P_0 and its confounding factors showed correlation with $Rp_{(ex)}$, $Rp_{(in)}$, $Rp_{(ex)}/P_0$ or $Rp_{(in)}/P_0$. $Rp_{(ex)}/P_0$ or $Rp_{(in)}/P_0$ were not affected with administration of 22 investigated drugs. To exclude the influence of P_0 on $Rp_{(in)}/P_0$, adjusted $Rp_{(in)}/P_0$ (removal efficiency of P from ICF not affected by P_0) was calculated. Investigation on iron containing P binders and ion exchange resins revealed each drug groups ameliorated adjusted $Rp_{(in)}/P_0$.

Conclusion:

This is the first report to analyze separately P removal from ECF and ICF during HD. Increased UN removal efficiency results in increased the removal efficiency of P from ECF, but did not improved that from ICF. $Rp_{(in)}$ accounts for about half of Rp. For improving total P removal efficiency, removal efficiency of P from ICF should be increased. Some drugs were suggested to increase removal efficiency of P from ICF.

P1402 USE OF ROMOSOZUMAB FOR OSTEOPOROSIS IN HEMODIALYSIS PATIENTS

Rie Kiyosumi[1], Naofumi Ikeda[2]

[1]SEKISHINKAI SAYAMA RENAL CLINIC, Department of nephrology, Saitama, Japan and [2]SEKISHINKAI SAYAMA RENAL CLINIC, department of nephrology, Saitama, Japan

Background and Aims: Recently, the importance of osteoporosis and chronic kidney disease-mineral bone disorder (CKD-MBD) has been highlighted as a cause of increased fracture risk in dialysis patients. However, many osteoporosis drugs require careful administration or are contraindicated in dialysis patients, and evidence for their use in dialysis patients is scarce. Here, we administered the new human anti-sclerostin antibody preparation romosozumab to hemodialysis patients with osteoporosis, and examined changes in bone density, bone metabolism markers and other values.

Method: Romosozumab was administered once per month to 12 hemodialysis patients (mean age: 72.6 ± 9.4 years old; 4 males, 8 females) who were diagnosed with osteoporosis while visiting our hospital and who had no history of cardiovascular complications in the preceding year. Bone density YAM value was measured every 3 months by dual energy X-ray absorptiometry (DXA). TRACP-5b, BAP, P1NP and whole-PTH values were measured every month as bone metabolic markers. Values at the start of observation were regarded as pre-dosing values and the mean values during the 6 months after administration were measured as post-treatment values. The results were then compared.

Results: At 6 months after the start of treatment, no change was seen in bone density of the proximal femur compared to the pre-dosing value. In contrast, lumbar spine bone density YAM value (%) was significantly improved, from 63.8% ± 9.4% to 70.9% ± 5.2% ($P = 0.012$). Regarding bone metabolism markers, mean value of bone resorption marker TRACP-5b after the start of administration did not significantly differ from that at the start of observation. BAP value increased significantly from 16.2 ± 8.7 to 25.2 ± 11.0 ($p < 0.01$) while whole-PTH significantly increased from 103.5 ± 52.8 to 236.1 ± 100.8 ($p < 0.01$). In addition, serial time changes for each bone metabolic marker, whole-PTH value, and corrected Ca value during the observation period are also reported.

Conclusion: Romosozumab may improve bone density in dialysis patients with osteoporosis.

P1403 **PLASMA OSTEOPONTIN LEVELS DIRECTLY CORRELATE WITH INTACT PARATHYROID HORMONE AND ALKALINE PHOSPHATE LEVELS IN END STAGE RENAL DISEASE**

Vinod Bansal[1], Aleksander Druck[2], Emily Bontekoe[2], Dimpi Patel[2], Debra Hoppensteadt[2], Jawed Fareed[2]

[1]Loyola University Medical Center, Nephrology, Maywood, United States of America and [2]Loyola University Medical Center, Pathology, Maywood, United States of America

Background and Aims: Bone turnover disorders and reduction in bone mineral density are commonly observed in end stage renal disease (ESRD) patients. Osteopontin (OPN) is a glycol-phosphoprotein that stimulates osteoclast adhesion to bone. OPN may play a significant role in the pathways involved in bone turnover disorders. The objective of this study was: (1) to identify plasma levels of OPN in ESRD and normal populations, and (2) to elucidate if relationships exist between OPN and iPTH, and OPN and alkaline phosphatase.

Method: Plasma levels of OPN were measured via commercially available enzyme linked immunosorbent assays (ELISAs) in ESRD patients (n=92). A chart review was conducted on these patients to identify levels of intact parathyroid hormone (iPTH) and alkaline phosphatase at time of plasma draw. Additionally, levels of total calcium, albumin, calcium corrected for albumin, phosphorus, ferritin, white blood cell count (WBC), and platelet count (PLT CT) were identified at time of plasma draw via the chart review. OPN levels were also measured in normal control patient plasma (n = 49) purchased from George King Bio-Medical, Inc., Overland Park, KS.

Results : The ESRD cohort showed a statistically significant elevation of OPN plasma levels ($p < 0.0001$, Mann-Whitney t-test) compared to the normal group. Spearman correlation tests revealed a significant positive correlation of OPN with iPTH ($p < 0.0001$; $r = 0.5606$, 95% confidence interval = 0.3968 to 0.6898) and OPN with alkaline phosphatase ($p < 0.0001$; $r = 0.4381$, 95% confidence interval = 0.2494 to 0.5948) in the ESRD cohort. No statistically significant correlations were identified between OPN and total calcium, calcium corrected for albumin, albumin, phosphorus, ferritin, WBC, and PLT CT ($p > 0.05$).

Conclusion : OPN levels are significantly elevated in ESRD patients. Furthermore, OPN levels were also found to be positively correlated with the bone turnover biomarkers iPTH and alkaline phosphatase. These studies suggest that hyperparathyroidism secondary to ESRD increases circulating iPTH, stimulating osteoblast and osteoclast activation and differentiation that increases alkaline phosphatase and OPN production, ultimately resulting in increased bone turnover.

P1404

A PHASE 2 OPEN-LABEL, SINGLE-ARM, FIRST JAPANESE STUDY OF TENAPANOR, A NOVEL PHOSPHATE ABSORPTION INHIBITOR, FOCUSING ON PILL BURDEN DECREASE IN PATIENTS WITH HYPERPHOSPHATEMIA UNDERGOING HEMODIALYSIS

Tadao Akizawa[1], Hironori Kanda[2], Masayuki Takanuma[3], Jun Kinoshita[4], Masafumi Fukagawa[5]

[1]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Tokyo, Japan, [2]Kyowa Kirin Co., Ltd., Nephrology R&D Unit, R&D division, Tokyo, Japan, [3]Kyowa Kirin Co., Ltd., Biometrics Department, R&D division, Tokyo, Japan, [4]Kyowa Kirin Co., Ltd., Clinical Development Center, R&D division, Tokyo, Japan and [5]Tokai University School of Medicine, Division of Nephrology, Endocrinology, and Metabolism, Department of Internal Medicine, Kanagawa, Japan

Background and Aims:

Phosphate binders (PB) are usually prescribed to dialysis patients with hyperphosphatemia. Several studies have reported that higher PB pill burden may reduce adherence and lead to insufficient phosphorus control. Tenapanor is an investigational, minimally absorbed, orally administered, non-binder, small-molecule that inhibits the sodium/hydrogen exchanger isoform 3 (NHE3) in development for the control of serum phosphorus. A previous Ph3 study sponsored by Ardelyx, Inc. (NCT02675998) showed a significant phosphorus decrease compared to the placebo in patients with hyperphosphatemia undergoing hemodialysis (HD) in the US. Tenapanor was expected to reduce PB pill burden since it is administered as one small pill, taken twice a day. This was the first study in Japanese HD patients, which aimed to confirm whether tenapanor reduces the pill burden of PB.

Method:

This was a multicenter, open-label, single-arm Ph2 study. The study consists of a screening period, a 3-week observation period, and a 26-week treatment period. Patients whose serum phosphorus level was $\geq$ 3.5 and $\leq$ 7.0 mg/dL, taking at least two PB pills three times a day were enrolled. The patients started to receive 30 mg of tenapanor twice daily. The tenapanor dose could be reduced in a step-wise manner (60, 40, 20 and 10 mg/day) at the investigator's discretion, based on GI tolerability. PB treatment was continued according to individual regimens, however, the dose could be adjusted appropriately to maintain serum phosphorus level within $\pm$0.5 mg/dL from the baseline. The primary endpoint was an achievement of at least a 30% decrease in the mean of the total number of PB and tenapanor pills compared to the number of PB pills at baseline. The proportion of patients who achieved at least a 30 % decrease were tested using binomial test with a threshold level of 20% and a one-sided significance level of 0.025. The analysis was conducted using the data as of Dec25, 2019.

Results:

The primary endpoint was met. Of 67 enrolled patients at the timing of analysis, 48 patients (71.6%, [95% CI: 59.3% - 82.0%], $p<0.001$) achieved a 30% decrease in the total number of PB and tenapanor pills, and of those, 35 patients (52.2%, [95% CI: 39.7% - 64.6%]) achieved a 50% decrease and 18 patients (26.9%) no longer required the use of any PB at week 26. Mean phosphorus levels were maintained during the study from 5.2 mg/dL at the baseline to 4.7 mg/dL at week 26. The most frequent adverse event was diarrhea (76.1%), which was mostly mild to moderate. Only four patients discontinued the study due to diarrhea. Serious adverse events were reported in five patients, only two of which were related to tenapanor (diarrhea and acute myocardial infarction).

Conclusion:

Tenapanor was able to provide phosphorus control with significantly fewer pills compared to PB. AE profile was similar to previous US studies. This result suggests that tenapanor, a non-binder, phosphate absorption inhibitor that provides a novel approach to the management of hyperphosphatemia, could potentially improve drug adherence by reducing PB pill burden while maintaining effective phosphorus control.

P1405 ETELCALCETIDE USE IN HEMODIALYTIC PATIENTS: A SINGLE CENTER EXPERIENCE

Bianca Covella[1], Luigi Rossi[1], Pasquale Libutti[1], Simone Corciulo[1], Elisabetta Manno[1], Carlo Lomonte[1]

[1]*Miulli General Hospital*

Background and Aims: Etelcalcetide is an injectable calcimimetic, utilized to treat secondary hyperparathyroidism. Recently introduced as alternative to cinacalcet, it acts on a different CaSR (Calcium Sensor Receptor) binding site. Outlined advantages are the intravenous formulation, which solves non adherence, the lower gastrointestinal side effects incidence. The main limitation is iatrogenic hypocalcemia. We show our experience to evaluate findings of our initial fieldwork in order to optimize drug efficacy, safety and tolerability

Method: We included 27 patients during 2018 (15 M and 12 F, Caucasian, mean age 60,7 ± 13,7 years), followed for at least 6 months. Initial etelcalcetide dose was 15 mg in all patients. PTH, Calcium, Phosphorus monitoring was done every month. Concomitant drugs as phosphorus binders, Vitamin D or analogues, Calcium and the switch from cinacalcet were considered. Therapeutic variations and side effects were recorded. Data are registered at the beginning and the end of follow up.

Results:

Starting values are: PTH 1298 ± 545 pg/ml, Calcium 9,1 ± 0,9, Phosphorus 5,1 ± 1,4. 14 patients already took phosphorus binders, 10 paricalcitol. 12 patients were switched from Cinacalcet because of non-adherence or inefficacy, the other 15 patients never took calcimimetics. Mean values after 6 months are: PTH 661 ± 469 pg/ml, Calcium 8,2 ± 0,5 mg/ml, Phosphorus 4,1 ± 1,6 mg/ml. These data point out a mean decrease in PTH value of 49%, reaching the therapeutic target in 18 patients, that is the 75% of the total population studied.

It have been necessary dose modifications in 15 patients (62.5%): 9 etelcalcetide dose variations (37,5%), 6 vitamin D and Calcium supplementation, both the changes in 5 of them. Side effects were hypocalcemia (14), pruritus (1), diarrhea (1), low platelet count (1), registered in 17 patients (63%), 3 of them withdrew therapy and then refused to start it again. It has to be said that thrombocytopenia, occurred after the follow up time (at 7th month), solve after etelcacetide withdrawal. Subgroup analysis pointed out a statistically significant correlation between drug efficacy and switch from cinacalcet, both in terms of extent of iPTH reduction (65% vs 42% - p value $< 0,05$) and of achievement of the therapeutic target (89% vs 66% - p value $< 0,05$), and between concomitant paricalcitol therapy at zero-time and lower hypocalcemia incidence (10% vs 76% - p value $< 0,05$).

Conclusion: Results confirm etelcalcetide efficacy and suggest a correlation between concomitant paricalcitol therapy at baseline and lower hypocalcemia incidence and between greater efficacy and switch from cinacalcet. These data, if confirmed in larger sample, could be useful to guide the starting approach and the maintaining treatment with etelecalcetide.

P1406

A CASE-CONTROL STUDY ON RISK FACTORS OF CALCIPHYLAXIS: DATA FROM CHINESE HEMODIALYSIS PATIENTS

Yuqiu Liu[1], Xiaotong Xie[1], Canlin Yang[1], Xin Yang[1], Xiao liang Zhang[1]

[1]*Institute of Nephrology, Zhong Da Hospital, Southeast University School of Medicine, Nanjing, P.R. China*

Background and Aims: Calciphylaxis (CUA) is a rare but potentially fatal disease that is commonly occurred in dialysis patients. Since there is no data based on Chinese population, the study is aimed to investigate risk factors of CUA in Chinese hemodialysis patients.

Method: We retrospectively evaluated medical records of 20 hemodialysis patients who were newly diagnosed with CUA by skin biopsy admitted to Zhongda Hospital Southeast University from Oct.2017 to Dec.2018. Non-CUA dialysis patients with the same age and duration of dialysis were randomly selected as controls (Ratio=1:2).

Results: Most of CUA patients were male (80%) and elderly (55%), while 50% had a body mass index higher than 24. The mean time interval since start of dialysis to CUA diagnosis was 114.65±81.32 months, and the median time from appearance of skin lesion to diagnosis was 6 (2, 15) months. The incidence of hyperparathyroidism was higher in patients with CUA (80% vs 62.5%), but the differences of duration of elevated serum intact parathyroid hormone (iPTH) and its highest value were not significant compared with the controls. Warfarin therapy had no significant difference between two groups (15% vs 5%). Univariate logistic regression analysis indicated that male (OR 3.619, 95%CI 1.027-12.748), each 1 point increase in score of use of vitamin D and its analogues (OR 1.505, 1.029-2.201), each 1 mmol/L increase in corrected serum calcium level (OR 24.486, 1.570-381.873), each 1 mmol/L increase in serum phosphate level (OR 5.382, 1.767-16.389), each 1 pg/mL increase in iPTH level (OR 1.002, 1.000-1.003), each 1 g/L decline in serum albumin level (OR 1.181, 1.041-1.340), each 1 IU/L increase in serum alkaline phosphatase (ALP) level (OR 1.005, 1.000-1.009) and each 1 mg/L increase in hypersensitive c-reactive protein level (OR 1.029, 1.000-1.059) were significantly associated with CUA. Serum phosphate, albumin and ALP were still significant risk factors after multivariate analysis.

Conclusion: This is the first report of risk factors of CUA based on Chinese population. The results show that high levels of serum phosphate and ALP, low level of serum albumin are independent risk factors of CUA in Chinese hemodialysis patients. Unlike previous research from western countries, warfarin therapy didn't show an increased risk in this study, propably because of the low exposure rate of it in China.

P1407 **LIVER, HEART AND BONE: THE PATH OF IRON OVERLOAD IN HEMODIALYSIS PATIENTS**

Lucas Acatauassu Nunes[1,2], Luciene Reis[1], Hanna Machado[1], Rosse Osório[3], Rosa Moyses[1], Hilton Leão-Filho[4], Rosilene Motta[1], Carlos Rochitte[3], Vanda Jorgetti[1], Melani Custodio[1]

[1]Faculty of Medicine - USP, LIM 16, São Paulo, Brazil, [2]Faculdade de Medicina - FAMED - UFPA, Medicina, Belem, Brazil, [3]Heart Institute, University of São Paulo, São Paulo, Brazil and [4]InRad, São Paulo, Brazil

Background: Chronic kidney disease (CKD) is associated with several comorbidities, including anemia, since with decreased renal function there is a decrease in erythropoietin (EPO) production and changes in iron (Fe) metabolism. In hemodialysis patients, prescription of Fe is indicated to supplement the needs of this element by maintaining ferritin levels above 100 mg/dl and transferrin saturation greater than 20%. However, the excess of Fe can generate free Fe not bound to transferrin, and deposit in organs such as liver, heart, and bone marrow, with consequent impairment of their function. In hemodialysis patients, the diagnosis of Fe overload, its clinical significance and therapeutic decision have been poorly studied, unlike thalassemia patients. **Aims**: To assess whether hemodialysis patients with ferritin levels equal to or greater than 1000 mg/l also have Fe overload in liver, heart, and bone marrow, as well as compromise bone density and remodeling.

Method: This is a cross-sectional analysis that included 28 adult patients on regular conventional hemodialysis. Inclusion criteria were serum levels of ferritin $\geq$ 1000 mg/l, and ESRD treated by regular hemodialysis for at least 6 months. We excluded patients with HIV, cancer, hepatic disease, patients who received desferroxamine in the latest year, and those previously submitted to a kidney transplant. All patients underwent dual-energy X-ray absorptiometry (DXA), serum ferritin, transferrin saturation index (STI), Fe, C reactive protein (CRP), Calcium(Ca), phosphorus (P), parathyroid hormone (PTH) and alkaline phosphatase (AP) levels were recorded. T2* image acquisition of Magnetic Resonance Imaging (MRI) 1,5 Tesla, were used for the assessment of Fe of liver, and heart. R2* and R2* Water were used of liver and bone (iliac crest). Bone biopsy was also performed.

Results: We evaluated 28 hemodialysis patients with a mean age of 55.8$\pm$13.1, hemodialysis time of 42.5$\pm$26.5 and iron use in the year prior to study enrollment of 311.5$\pm$179.8 mg/month. Biochemical analysis showed 3 patients with Hb below 9.0 mg/dl and 14 with values above 11.5 mg/dl; 6 patients with SatFe $<$30% and 12 patients with ferritin $>$1500mg/dl; 16 patients with PTH $<$300pg/ml and eight with $>$600pg/dl. MRI revealed Fe overload in the liver and bone tissue (figure 1) of all patients but not in the heart. Serum ferritin levels correlated with liver and bone overload (figure 2). Densitometry and bone biopsy results were not affected by Fe overload, however, serum Fe levels were associated with lower bone remodeling and mineralization suggesting an effect of this element on osteoblast activity.

Conclusion: High serum ferritin is associated with liver and bone marrow Fe overload, but not heart, as well as with low bone remodeling and mineralization. We must be aware of these side effects of high doses of Fe that are commonly used in these patients.



Figure 1. Illustrative magnetic resonance imaging of the heart and the iliac crest.

(A)

(B)



Figure 2. Correlations between serum ferritin and magnetic resonance parameters.

P1408 **PAIN MANAGEMENT IN CALCIPHYLAXIS: A KNOWLEDGE,ATTITUDE AND PRACTICE SURVEY AMONG PHYSICIANS**

Rajkumar Chinnadurai[1], Mary Miller[2], Aoife Lowney[3], Smeeta Sinha[1]

[1]Salford Royal NHS Foundation Trust, Department of Renal Medicine, Salford, United Kingdom, [2]Oxford University Hospitals, Department of palliative medicine, Oxford, United Kingdom and [3]Oxford University Hospitals, Renal Supportive and Palliative Care, Oxford, United Kingdom

Background and Aims:

Calciphylaxis is a rare disease usually seen in patients with end-stage renal disease. Pain is a hallmark of this disease and can be extremely difficult to control. Anecdotal data suggests that pain management in calciphylaxis is unsatisfactory with differing practice, variable across the United Kingdom (UK) and also around the world. This knowledge, attitude and practice (KAP) survey aims to gather information on the current practice in the management of pain in patients with calciphylaxis.

Method:

A pre-tested online questionnaire was circulated among physicians (renal and palliative care) involved in the management of pain in calciphylaxis. (https://www.gmann.co.uk/website/calciphylaxis-pain-management-survey.cfm). The questionnaire included a mix of open-ended questions and questions with drop down options.

Results:

One hundred and six clinicians responded to the survey of which 60 (57%) respondents were from palliative medicine and the remainder 46 (43%) were from renal medicine. There were 31 (30%) respondents, across both specialties who had not encountered any patients with a diagnosis of calciphylaxis (renal-2, palliative care-29). 18% of renal physicians refer patients to palliative care team, 32% refer to pain team and 50% refer to both. Only 3% of the palliative medicine respondents indicated that they'd received a referral from the renal team at the time of diagnosis. Opioids were the preferred initial drug of choice for the management of all types of pain although the preferred drug varied with the specialities (Fig–1). Paracetamol was universally selected as the preferred first-choice adjuvant agent for management of all types of pain. Additional procedures to aid pain management (epidural analgesia and nerve blocks) were used by 6.6% of respondents. A majority (83%) felt the presence of infection impacts on the effectiveness of pain control. The importance of advanced care planning was also highlighted with 72% undertaking advanced care planning discussions often or most of the times.

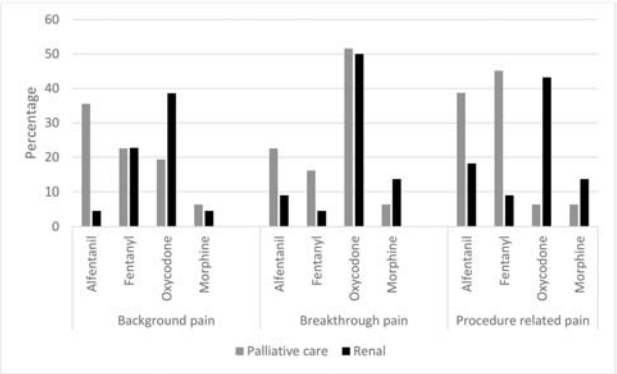


Figure 1: Opioid preference based on speciality

Conclusion:

In conclusion, there was wide variation in the current practice of management of pain in calciphylaxis, with variation between renal specialists and palliative care specialists. Referral to pain specialists is not universal despite the severe nature of the pain experienced by patients with calciphylaxis. The data generated will enable to us to develop practice guidelines to support complex pain management in a group of patients with multiple comorbidities.

P1409 HIP FRACTURE TRENDS IN SWEDISH GENERAL POPULATION AND DIALYSIS PATIENTS

Ken Iseri[1,2], Juan Jesus Carrero[3], Marie Evans[1], Li Felländer-Tsai[4], Hans Berg[4], Björn Runesson[1], Peter Stenvinkel[1], Bengt Lindholm[1], Abdul Rashid Tony Qureshi[1]

[1]Karolinska Institutet, Divisions of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, [2]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Japan, [3]Karolinska Institutet, Department of Medical Epidemiology and Biostatistics and [4]Karolinska Institutet, Division of Orthopaedics and Biotechnology, Department of Clinical Science, Intervention and Technology

Background and Aims: Hip fracture incidence rate is higher in dialysis patients than in general population. We investigated and compared temporal changes in age-standardized hip fracture incidence rate ($ASR_{hip\ fracture}$) 2007-2016 in men and women in the dialysis population and in the general population.

Method: We used the population-based Swedish national database of fractures and the Swedish Renal Registry of ESRD patients to retrieve data on $ASR_{hip\ fracture}$ in the general population and among dialysis patients. The average annual percent change of the hip fracture incidence trend was evaluated by join-point regression analysis according to gender in the two databases.

Results: $ASR_{hip\ fracture}$ was about three times higher in Swedish dialysis patients as compared to the Swedish general population. In dialysis patients, rates have steadily declined during the recent decade when assessed in both sexes combined, and when analysed in women and men separately. A similar trend was also seen in the general population; however, the rate of decline was steeper in dialysis patients than in the general population. The most recent data on $ASR_{hip\ fracture}$ (for 2016) show that $ASR_{hip\ fracture}$ was similar among female and male dialysis patients whereas $ASR_{hip\ fracture}$ in the general population was higher in women than in men.

Conclusion: Hip fracture incidence is declining in the general population and even more so in dialysis patients. In contrast to the general population where hip fracture incidence in 2016 is higher among women than in men, there was no such difference between the two sexes among dialysis patients.

P1410 IMPACT OF VITAMIN D SUPPLEMENTATION ON CKD-MBD HEMODIALYSIS PATIENTS - A PROSPECTIVE STUDY

Cátia Raquel Figueiredo[1], Ana Rita Valerio Alves[1], Hernâni Gonçalves[1], Karina Lopes[1], Flora Sofia[1], Ana Vila Lobos[1]

[1]*Hospital Rainha Santa Isabel - Torres Novas (Centro Hospitalar Médio Tejo, EPE), Nephrology, Torres Novas, Portugal*

Background and Aims: There are evidences suggesting that 50-90% of hemodialysis (HD) patients are vitamin D deficient [25(OH) D level <20 ng/mL] or insufficient (between 21 to 29 ng/mL). Recent guidelines recommend evaluation and supplementation low serum vitamin D levels in HD patients. However the effects of supplementation remains uncertain. Our aim was to evaluate the effect of supplementation on phosphocalcic metabolism and secondary hyperparathyroidism in HD patients of a hospital unit.

Method: Prospective study with an 18 months follow-up period. HD patients were supplemented with 12000 IU cholecalciferol 3 times a week if vitamin D level under 30ng/mL and 4000 IU if above. Every 6 months (3 time points) vitamin D, bone alkaline phosphatase (AF), calcium (Ca^{2+}), phosphorus (P^{+}) and intact parathyroid hormone (iPTH) blood levels were measured. Demographic, analytical and clinical data, including diabetic status, were analyzed. Categorical variables are presented as frequencies and percentages, continuous variables as means and standard deviations, or medians and interquartile ranges (IQR) for variables with skewed distributions. Statistical analysis was performed using SPSS version 21 for Windows.

Results: Sixty patients completed the follow-up period. The average was 74.70±1.43 years, 65% (n=39) were male and 41.7% (n=25) were diabetic. The average HD time at point 3 (18 months) was 3.15±3.62 years.

A repeated measures ANOVA with a Greenhouse-Geisser correction showed that cholecalciferol supplementation significantly changed vitamin D blood levels along time ($F(2.492;144.54)=26.832$; $p<0.001$), with a statistically significant increase in vitamin D blood levels from time point 0 to point 3 (+8.27 ng/mL, $p<0.001$). There was also a significant reduction of phosphorus (-0.53mg/dL, p=0.017) and iPTH blood levels (-144.09 pg/nL $p<0.001$) in the same period. Seric calcium had a statistically significant increase from point 0 to 2 (+0.22 mg/dL, p=0.038). Using Pearson's correlation, from point 0 to 3, we found a negative correlation between vitamin D and iPTH blood levels variation (Rs= -0.303, p=0.018) and a positive correlation between vitamin D and AF blood levels variation (Rs= 0.043, p=0.002).

Conclusion: Oral cholecalciferol supplementation increases significantly vitamin D blood levels and can be a good option in the management of secondary hyperparathyroidism and hypocalcemia. However, one of the limitations of our study was not to evaluate the use of medication such as P+ chelating agents and the small sample size. Therefore, large randomized clinical trials with clinically meaningful endpoints (fracture, hospitalization, parathyroidectomy, death) are still required to assess the usefulness of different vitamin D compounds for CKD and dialysis patients.

P1411 **THE EFFICACY AND SAFETY OF THE SUCROFFERRIC OXYHYDXIDE IN HEMODIALYSIS PATIENTS : RESULTS OF A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL**

Evgeny Shutov[1,2], Galina Kotlyarova[2], Ksenia Lysenko[2], Galina Ryabinskaya[2], Sergey Lashutin[2]

[1]Russian Medical Academy of Continuous Professional Education, nephrology and dialysis, Moscow, Russia and [2]Botkins Clinical City Hospital, dialysis, Moscow, Russia

Background and Aims: The treatment of hyperphosphatemia is the main goal in the treatment of mineral and bone disorders in patients with CKD. However, the results of the correction of hyperphosphatemia remain unsatisfactory. This is due to the absence of effective and safe medicines. In our prospective randomized controlled trial were evaluated the effects of a 16-week treatment with new phosphate binder - sucroferric oxyhydroxide and a sevelamer carbonate ("sevelamer") on CKD-MBD parameters in patients on hemodialysis with hyperphosphatemia.

Method: After a 2-4-week washout period from previous phosphate binders, 50 stable patients with hyperphosphatemia (P > 5.5 mg / dl) were randomized at a 1: 1 ratio to receive sucroferric oxyhydroxide (n = 25) or sevelamer (n = 25) for treatment up to 16 weeks. In all patients were evaluated levels of P, Ca, PTH, ferritin, transferrin saturation, Hb, FGF-23, soluble Klotho, CRP - monthly. The dose of both medications was adjusted according to serum phosphate.

Results: Phosphate binder therapy of sucroferric oxyhydroxide was associated with a significant decrease in serum phosphate from 6.8 ± 1.5 to 5.27 ± 0.99 mg/dl (p <0.01); however, treatment with sevelamer did not decrease in the level of P: 6.32 ± 1.5 vs 6.35 ± 1.9 mgl/dl. The number of tablets was lower in the sucroferric oxyhydroxide group (mean ± SD 2.0 ± 1.5 tablets / day) compared with sevelamer (mean ± SD 6.1 ± 3.2 tablets / day). The average intact fibroblast growth factor-23 (FGF-23), PTH, transferrin saturation and ferritin did not significantly change in both groups. Klotho changed only in patients received sucroferric oxyhydroxide, an increase of 25% (p < 0.05) and we also noted in this group an increase in Hb level from 105.6 ± 15.7 to 111.9 ± 22.3 g/l (p <0.05) by the end of the study, simultaneously level of CRP significantly decreased (P < 0.01) by 50% . During the study, 6 patients in the group with sucroferric oxyhydroxide and 5 in the sevelamer group dropped out due to dyspeptic symptoms.

Conclusion: Sucroferric oxyhydroxide is a new effective phosphate binder with a comparable safety profile to a sevelamer. Treatment with this drug can significantly increase the level of Hb, and Klotho and reduce level of inflammation.

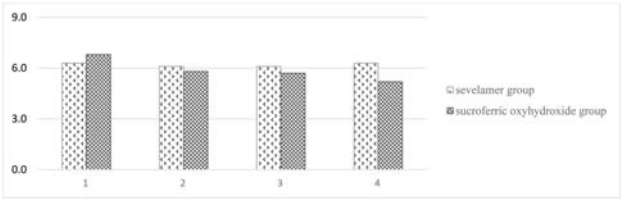


Figure: Changes in P levels (mg/dl) in the compared groups

P1412 CARDIO PULMONARY AND CKD-MBD INTERACTIONS IN HEMODIALYSIS PATIENTS

Nooshin Dalili[1]

[1]MD, Assistant Prof. of Nephrology, Division of Nephrology, Shahid Labbafinejad Medical Center, Chronic Kidney Disease Research Center (CKDRC), Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Aims: Emerging evidence suggests that pulmonary hypertension (PHT) is closely associated with cardiac, pulmonary, and mineral bone diseases in hemodialysis patients. Previous results indicated that extra osseous calcifications might be a risk factor for PHT although results in human studies about this association have been conflicting. Multiple factors including abnormal calcium phosphate levels, uremia and inflammation are known to be important in vascular calcification development. In hemodialysis patients' vascular calcifications may be evaluated by different techniques. The utilization of plain X-ray for screening vascular calcifications has been suggested by KDOQI and KDIGO .In this study, we examined the association between PHT, peripheral vascular calcification by plain X-Ray score, and echocardiographic parameters in hemodialysis patients.

Method: Chronic (> 6 months) hemodialysis patients (150) on a three times per week dialysis schedule were studied. Two-dimensional trans thoracic echocardiography was performed before dialysis. Global systolic function was evaluated by left ventricular ejection fraction (LVEF). Systolic pulmonary arterial pressure (SPAP) was recorded. Pulmonary hypertension was defined as, pulmonary artery pressure (PAP) greater than 35 mm Hg based on European Society of Cardiology Guideline. Vascular calcification score is evaluated in plain X-ray of pelvis and hands. Each film is divided into four sections. Any vascular calcification either in an irregular or linear pattern is considered. The presence of vascular calcifications in each section is rated as 1 and its absence as 0. Final score is the sum of all sections and ranges from 0 to 8.Demographic data and lab results including Calcium (Ca), Phosphorous (P), Ca X P product, 25OH-vitD and iPTH were collected for all enrolled patients. The effects of different peripheral vascular calcification scores in plain X-Ray, structural heart abnormalities in echocardiography and Ca-P-iPTH- vit D axis disorders on the development of pulmonary hypertension were evaluated to elucidate cardio, pulmonary and CKD-MBD interactions.

Results: Hemodialysis patients had a high prevalence of PHT (30%), which warrants special attention to this important complication in hemodialysis population. Severe peripheral VCs (VCs >3) were independent risk factor for PHT. In addition to the old age, duration of hemodialysis, and mitral valve disease, the presence of higher Ca- P product was another independent predictor of PHT in chronic hemodialysis patients.

Conclusion: Prevalence of PHT in dialysis patients seems to be high, and is closely associated with peripheral VC, mineral bone disorders and structural heart abnormalities suggesting further a strong cardio pulmonary renal interaction.



Echocardiographic and laboratorial data in groups of hemodialysis patients with(PAP>35 mmHg) and without pulmonary hypertension

	Pulmonary Hypertension (n=14)	No pulmonary Hypertension (n=36)	p
LA (mm)	46.2±4.29	41.9±5.68	**0.002**
Mitral Reg(mod-severe)	8 (55%)	3 (8.3%)	**0.001**
PTH (pg/ml)	241(117-491)	257(128-481)	**0.726**
Creatinine(mg/dl)	10.7±3.16	10.9±3.07	**0.811**
Albumin (g/dl)	3.6±0.36	3.8±0.41	**0.082**
Calcium (mg/dl)	9.5±0.80	9.0±0.72	**0.056**
Phosphorus(mg/dl)	5.8±1.74	5.1±1.57	**0.04**
Ca x P	47.5±16.94	41.3±14.33	**0.04**
SVCS ≥ 3	6 (39.7%)	8 (21.1%)	**0.013**
Hgb	10.6±1.6	11.2±1.7	**0.071**

Figure:

P1413

EFFECT OF PULSE ORAL VERSUS INTRAMUSCULAR VITAMIN D REPLACEMENT IN HEMODIALYSIS PATIENTS WITH VITAMIN D DEFECIENCY

Abdelbassit Shaarawy[1], Waleed Anwar[1], Maha Abdelmoneim Behairy Said[1], Lina Khedr[1], Reem Elsharabasy[1], Zinab Mahmoud[1]

[1]*ain shams university, faculty of medicine, Cairo, Egypt*

Background and Aims: Low 25-hydroxyvitamin D (25(OH)D) level is common in patients with chronic kidney disease and hemodialysis (HD) patients . It has been associated with high bone turnover, secondary hyperparathyroidism (SHPT), and decreased bone mineral density (BMD). We aimed to investigate the efficacy of equivalent doses of pulse oral cholecalciferol (25,000 IU weekly for 12 weeks) versus single intramuscular cholecalciferol (300,000 IU) in correcting serum 25 (OH) D levels in HD patients.

Method: Prospective randomized open label Clinical trial. 40 prevalent HD patients with vitamin D deficiency were enrolled. Serum 25 hydroxy-vitamin D (25 (OH) D) level $<$ 20 ng/m and Serum parathyroid hormone level (iPTH) $>$100 pg/ml. Exclusion Criteria were serum calcium $>$ 10 .5mg/dl, Calcium phosphorus product $\geq$ 55, tertiary hyperparathyroidism and Parathyroidectomy among others. Patients were randomized equally into two groups. 36 patients were compliant and completed the study. Group I :17 HD patients received oral cholecalciferol 25000 IU weekly of (Vidrop® 2800 IU/ml) for 12 weeks. Group II: 19 HD patients received a single intramuscular injection (IM) of cholecalciferol 300,000 IU (Devarol® 200000 IU/ ampoule). Vitamin D supplements were stopped if serum calcium $>$10.5mg/dl or 25(OH) D level $>$ 100 ng /ml (toxic level) during study. Serum calcium (albumin-adjusted), phosphorus, 25(OH) D by ELISA, Alkaline phosphatase (ALP) and intact parathyroid hormone (iPTH) were monitored at baseline, 6 and 12 weeks of intervention. Both groups were maintained on their regular medications used to control mineral bone disorder as: alfacalcidol, sevelamer or a calcium-based chelator.

Results: Significant increase in serum 25(OH) D level in group II patients who received single dose IM Cholecalciferol after 12 w. Means of 25 (OH)D levels basal and 12 w of study were (10.54$\pm$5.14 and 13.45 $\pm$5.72) ng/ml respectively. There was a significant increase in the mean of serum calcium basal and at 12 w (8.19$\pm$0.69 and 8.42 $\pm$0.54) mg/dl respectively. No significant reduction in the iPTH level or any significant change in the serum phosphorus level was noticed.

compared to group I with oral vitamin D, there was an insignificant change in the mean of serum 25(OH) D basal and at 12 w were (11.91$\pm$6.13 and 9.30$\pm$5.29) ng/ml respectively, associated with insignificant increase in serum calcium and an insignificant change in either the level of phosphorus or iPTH level.

Conclusion: Cholecalciferol 300,000 IU IM single dose showed better response on serum 25 (OH) D and calcium levels as a treatment of hemodialysis patients with Vitamin D deficiency compared to weekly oral dose for 3 months.

P1414 THE PREDICTORS OF PARATHYROID HORMONE VARIABILITY IN HEMODIALYSIS PATIENTS

Vasilije Tomanoski[1], Gordana Gjorgjievska[1], Vasiliki Krecova[1], Aleksandar Andonoski[1], Margarita Nakovska[1], Katerina Ristoska[1], Jasminka Zvezdakovska[1], Sintia Kepeska[1], Angela Kachakova[1], Tode Klisheski[1], Bejane Ferati[1], Liljana Vasileva[1], Koco Cakalaroski[1]

[1]*Sistina Nefroplus, Hemodialysis centers, Skopje, Republic Of North Macedonia*

Background and Aims: KDIGO Clinical Practice Guidelines suggest in hemodialysis (HD) patients using a dialysate calcium concentration between 1,25 and 1,5 mmol/L and maintaining serum intact parathyroid hormone (sPTH) levels in the range of approximately 2 to 9 times the upper normal limit for the assay. The aim of the study was to evaluate the predictors of PTH variability in HD patients over a 12 months period.

Method: The multicenter restrospective study encompassed 398 patients (256M and 142F) with the average age 59,64±13,29 years and the average HD vintage 78,63±64,26 months. Over a 12 months (M0-M12) period: serum calcium (sCa), serum phosphorus (sPi), serum alkaline phosphatase (sAPh), oral calcium-carbonate daily dose, oral calcitriol weekly dose, and dialysate Ca concentration (dCa) were monitored monthly, and sPTH at 6 months. According to PTH assay reference level (18,4-80,1 pg/ml) 3 groups of patients were categorized: patients with low sPTH<160, with target range sPTH =160-721, and with high sPTH>721. For statistical analysis chi-square test, analysis of variance with repeated measures and logistic regression analysis were performed by softver SPSS.

Results: Over a 12 months period the number of patients with low sPTH significantly decreased, but the number of patients with target range sPTH and high sPTH increased (Chi square=269,45; p<0.001). On the basis of overall pattern of sPTH fluctuation over a 12 months period six subgroups of patients were observed: consistently low in 20,6% of patients, consistently within the target range in 22,1%, consistently high in 14,07%, low-amplitude fluctuation with low and target range sPTH levels (LAL) in 31,4%, low-amplitude fluctuation with target range and high sPTH levels (LAH) in 10,55%, and high-amplitude fluctuation (HA) subgroup with low, target range and high sPTH levels in 1,25%. In 35 patients constantly hemodialyzed over a 12 months period with dCa=1,25 mmol/L due to high sCa the significant increase of sPTH (M0=797±657 vs M12=1030±740 pg/ml; p=0.001) and no significant changes of sCa (M0=2,44± vs M12=2,34± mmol/L; n.s.), sPi (M0=1,81±0,49 vs M12=1,68±0,49 mmol/L; n.s.), Ca-carbonate daily dose (M0=1,88±1,54 vs M12=2,22±1,53 g/d; n.s.) and calcitriol weekly dose (M0=0,84±1,38 vs M12=1,1±1,41 ucg/w; n.s.) were observed. In 24 patients constantly hemodialyzed with dCa=1,75 mmol/L due to low sCa the significant decrease of sPTH (M0=518±582 vs M12=391±530 pg/ml; p=0.037) and no significant changes of sCa (M0=2,17±0,19 vs M12=2,18±0,17 mmol/L; n.s.), sPi (M0=1,3±0,34 vs M12=1,36±0,52 mmol/L; n.s.), Ca-carbonate daily dose (M0=2,53±1,58 vs M12=2,1±1,91 g/d; n.s.) and calcitriol weekly dose (M0=1,33±1,23 vs M12=1,42±1,69 ucg/w; n.s.) were observed. In 195 patients constantly hemodialyzed with dCa=1,5 mmol/L no significant changes of sPTH (M0=388±421 vs M12=434±459 pg/ml; n.s.), sCa (M0=2,29±0,18 vs M12=2,27±0,15 mmol/L; n.s.), sPi (M0=1,48±0,41 vs M12=1,52±0,41 mmol/L; n.s.), Ca-carbonate daily dose (M0=2,42±1,4 vs M12=2,57±1,2 g/d; n.s.) and calcitriol weekly dose (M0=0,47±0,72 vs M12=0,38±0,68 ucg/w; n.s.) were observed. By model of logistic regression analysis dCa=1,75 (OR=8,33), increased sCa (OR=7,7), and presence of diabetes mellitus (OR=2,44) were the most significant predictors of low sPTH<160 (Chi square=116,27; p<0.001), but the increased sCa (OR=6,88), dCa=1,25 (OR=5,08), and the increased sPi (OR=2,72) were the most significant predictors of high sPTH>721 (Chi square=72,475; p<0.001).

Conclusion: The prolonged use of dCa=1,25 in patients with high sCa led to significant sPTH increase likely due to net negative calcium balance, but prolonged use of dCa=1,75 in patients with low sCa led to significant sPTH decrease likely due to net positive calcium balance.

P1415 PARATHYROIDECTOMY IMPROVES MUSCULAR FUNCTION BUT NOT MUSCLE MASS IN HEMODIALYSIS PATIENTS WITH SEVERE HYPERPARATHYROIDISM

Shirley Crispilho[1], Eduardo J Duque[2], Carla Avesani[3], Rosa Maria R Pereira[4], Ana Lúcia De Sá-Pinto[4], Vanda Jorgetti[2], Peter Stenvinkel[3], Bengt Lindholm[3], Rosilene Motta[1,2], Rosa Moyses[2]

[1]UNINOVE, São Paulo, Brazil, [2]Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Nephrology Division, São Paulo, Brazil, [3]Karolinska Institute, Renal Medicine and Baxter Novum, Sweden and [4]Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Reumathology Division, São Paulo, Brazil

Background and Aims: Increased levels of parathyroid hormone (PTH) are associated with a negative impact on the bone-muscle axis including sarcopenia with muscle weakness and muscle atrophy and osteoporosis, and it is possible that treating hyperparathyroidism (HPT) can ameliorate these disturbances. However, the effects of parathyroidectomy (PTX) on muscle mass, strength and performance, and physical activity have not been thoroughly investigated. This study aims to evaluate the impact of PTX on muscle (mass, strength, and performance), physical activity, body fat and resting energy expenditure (REE) in patients on hemodialysis with severe HPT.

Method: We are prospectively evaluating muscle mass strength, performance and physical activity of 30 patients before and after 6 months of PTX by using Actigraph GT3X accelerometer, timed-up-and-Go (TuG), Sit-to-Stand-to-Sit (STS) and muscle strength tests [handgrip (HGS), supine (SP) and leg press (LP)]. Body composition changes were assessed by dual-energy x-ray absorptiometry (DXA), and REE was examined by indirect calorimetry.

Results: At 6 months after PTX, 11 patients who already completed the protocol, showed a significant drop in PTH [1445 (1363-1937) vs. 54 (23-132) pg/mL; p = 0.002] and alkaline phosphatase [306 (235-744) vs. 77.5 (52-100] U/L); p = 0.002], a significant increase of number of steps/day [4321 (3384 – 6317) vs. 5950 (3918 – 7159); p = 0.04] and improvements of strength tests: HGS (27 ±14 vs. 31 ±15 kg; p = 0.01); SP (27 ±15 vs. 31 ±17 kg; p = 0.01] and LP [27 (2-36) vs. 36 (24-89) kg; p 0.04]. In addition, there was a significant reduction of TuG [10 (8-15) vs. 8 (7-11) seconds; p = 0.01], and a tendency towards STS improvement [6 (0-7) vs. 8 (7-11); p = 0.06]. A significant increase in body weight (66 ± 12 vs. 68 ± 14 Kg; p = 0.02), body mass index [24 (21–26) vs. 26 (21–28) kg/m^2; p 0.001], and bone mineral content (BMC) [1.8 (1.3-2) vs. 2.1 (1.7-2.7); p=0.002] was seen. However, lean body mass (LBM) decreased [40.4 (38-55) vs. 39 (37-51) Kg; p=0.001], whereas fat mass (FAT) increased [18 (17-28) vs. 24 (17–30) kg; p = 0.02]. No change was noted in skeletal muscle index (SMI) and in REE [1580 (1193–1988) vs. 1473 (1326 - 1786) kcal/day; p = 0.7). We noticed a tendency toward an increase in IGF-1 levels [180 (141-207) vs. 223 (151-281) µg/L; p = 0.08], but no significant variation was found in serum albumin, insulin and HOMA index.

Conclusion: In hemodialysis patients with secondary hyperparathyroidism undergoing PTX, there were marked improvements of muscular function and bone mass, but not of muscle mass. Our findings suggest that PTH-associated sarcopenia is mediated not only by a decrease in muscle mass but also by muscle dysfunction. The long-term effect of PTX on muscle status remains to be further examined.

P1416

EFFECT OF SWITCH FROM CINACALCET TO ETECALCETIDE IN HEMODIALYSIS PATIENTS WITH A POOR CONTROL OF SECONDARY HYPERPARATHYROIDISM

Karen Rivero Garcia[1], Sebastian Tamayo Arroyo[1], Sebastian Tamayo[2], Jesus Martin-Centellas[1], Alejandro Rodríguez Campón[1], Pilar Fraile Gómez[1], Luis Correa Marcano[1], Guadalupe Tabernero Fernandez[1], Alberto Martin Arribas[1], Jose Luis Lerma Marquez[1], Gabriela González Zhindon[1], Jose Antonio Menacho Miguel[1], Manuel Heras Benito[1]

[1]Complejo Asistencial Universitario de Salamanca, Nephrology, Salamanca, Spain and [2]Dyalisis Center Burgos, Neprhology, Burgos, Spain

Background and Aims: Patients on hemodialysis (HD) show a high incidence of secondary hyperparathyroidism (SHPT). An inadequate control of this condition increases morbidity and mortality, most of the times due to lack of adherence to the treatment. There is currently an available intravenous calciomimetic drug that could be an alternative to improve the prognosis and management of SHPT. **Objectives:** To analyze the switch from cinacalcet to etelcalcetide in patients with a poor control of SHPT.

Method: : A descriptive observational study was carried out with patients on HD with iPTH levels over 400 pg/mL who had previously been treated with cinacalcet for at least 6 months and then with etelcalcetide for a year. The analysis assessed their basal characteristics, the evolution of their analytical parameters (calcium/phosphorus/iPTH) and their comorbidity, and a questionnaire was completed to observe their adherence to treatment.

Results: The study included 34 patients; average age 65±15 years (58% men); hemodialysis time 84±69 months. The main comorbidities were: 97% hypertension; 44% diabetes; and 47% heart disease. The average basal dose of cinacalcet was 62±26 mg/session, and the average dose of etelcalcetide was 2.8±2.6 mg/session. Over the 12 months of treatment with etelcalcetide a better control of iPTH was observed (from 681±279 to 291±190, p=0.004), with a decrease of iPTH by >50% in 79% of the patients. There were no significant changes in the levels of albumin, calcium or magnesium, but a significant decrease was observed in the levels of phosphorus, Ca x P product and alkaline phosphatase. 44% of the patients showed hypocalcemia after 6 months of treatment, which was asymptomatic in all cases and was corrected with an increase in the oral administration of calcium (44%) or with a change of dialysate [Ca] concentration (50%). None of the patients reported clinical intolerance with etelcalcetide. Table 1:

Conclusion:

- Etelcalcetide achieves an effective decrease of iPTH in patients on hemodialysis with a poor control of HPT.
- The decrease in hyperphosphatemia and alkaline phosphatase could be considered a positive effect of the drug.
- A common secondary effect is mild asymptomatic hypocalcemia, which requires a higher administration of calcium to disappear.

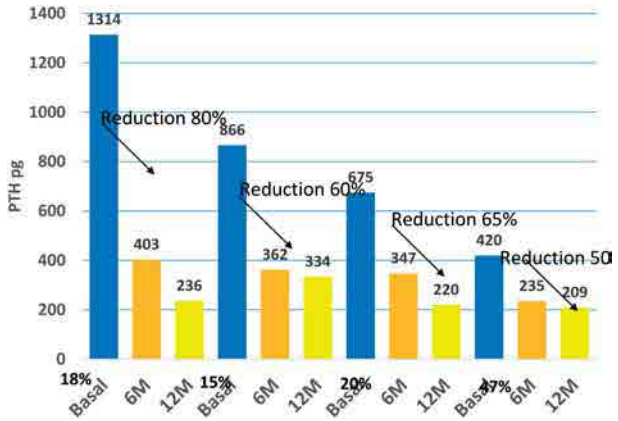


Figure:

P1417 **ALTERED CATHEPSIN-K LEVELS REFLECT SEVERITY OF MINERAL BONE DISEASE AND INFLAMMATION IN CHRONIC HEMODIALYSIS PATIENTS**

Giuseppe Coppolino[1], Marta Greco[1], Giuseppe Leonardi[1], Michele Provenzano[1], Omar Tripolino[1], Valentina Arcidiacono[1], Cinzia Donato[2], Salvatore Chiarella[2], Emilio Russo[1], Daniela Foti[1], Giorgio Fuiano[1], Michele Andreucci[1], Davide Bolignano[1]

[1]Magna Græcia University, Health Sciences, Catanzaro, Italy and [2]Hospital Pugliese Ciaccio, Catanzaro, Italy

Background and Aims: Mineral bone disease (MBD) and chronic inflammation are key triggers of the exceeding cardiovascular risk that characterizes dialysis patients. Cathepsin-K (Cts-K) is a lysosomal cysteine protease involved in bone remodeling and resorption, whose expression is promoted particularly by inflammation and whose involvement in bone and cardiovascular disorders has previously been demonstrated. We set out to undertake an exploratory, observational study to assess the possible clinical significance of Cts-K in dialysis patients.

Method: Eighty-five chronic HD patients (mean age 67±12, median dialysis vintage 3.2 yrs) with stable dry weight were studied. Cts-K was measured in peripheral blood samples before a mid-week dialysis session together with standard biochemical parameters. Twenty-six healthy subjects, matched with HD patients for age and gender, served as controls.

Results: Cts-K was statistically higher in HD patients than in controls (median 340, IQR 170-835 vs. 190 IQR 20-120 pg/mL, $p<0.0001$). At univariate analyses, Cts-K levels were significantly associated with ALP ($r=0.50$, $p<0.001$), CRP ($r=0.46$, $p<0.001$), PTH ($r=0.24$,$p=0.02$), presence of diabetes ($r=0.28$,$p<0.001$),peripheral vasculopathy ($r=0.20$, $p=0.05$) and dialysate calcium concentration ($r=-0.28$,$p<0.001$). In a multivariate model including all univariate predictors ($R2=61\%$, $p<0.001$) only ALP ($\beta=0.70$,$p<0.001$), CRP ($\beta=0.49$,$p<0.001$) and dialysate calcium concentration (β -0.40,$p=0.04$) remained significantly associated with Cts-K levels. Interestingly, Cts-K levels were significantly higher among individuals who were under active calcimimetic therapy ($n=28$; $p<0.001$) but significantly lower among those who previously underwent parathyroidectomy ($n=8$; $p<0.001$) (**Figure 1**).

Conclusion: Cathepsin-K is a biomarker at the crossroads of bone and inflammatory disorders in chronic hemodialysis patients. Future research is needed to clarify the exact pathophysiological role of this protein and to test its potential usefulness as a marker for managing MBD therapy and complications.

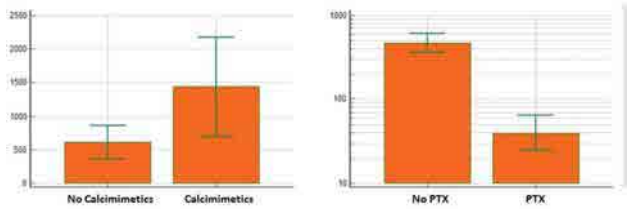


Figure:

P1418 **BONE-DERIVED HORMONES, MINERAL METABOLISM, CARDIOVASCULAR DISEASE AND PATIENT OUTCOME IN END-STAGE RENAL PATIENTS**

Ana Carina Ferreira[1,2], Marco Mendes[1,2], Cecília Silva[1], Patrícia Cotovio[1], Inês Aires[1,2], David Navarro[1], Fernando Correia Caeiro Pereira[1], Rute Salvador[3], Bruna Correia[3], Guadalupe Cabral[3], Fernando Nolasco[1,2], Manuel Anibal A. Ferreira[1,2]

[1]Hospital Curry Cabral, Nephrology, Lisboa, Portugal, [2]Nova Medical School, ., Lisboa, Portugal and [3]CEDOC, Tissue Repair and Inflammation Lab, Lisboa, Portugal

Background and Aims: Chronic kidney disease-mineral and bone disorder (CKD-MBD) is frequent in end-stage renal disease ESRD (ESRD) patients, increasing morbid-mortality. The aim of this study was to analyse the associations between the new CKD-MBD players [alpha-klotho, fibroblast grow factor (FGF) 23, sclerostin] and the usual markers of the disease [parathyroid hormone (PTH), bone alkaline phosphatase (bAP), vitamin D (vitD), phosphorus (Pi), Calcium (Ca) and Magnesium (Mg)], as well echocardiographic findings [left ventricular mass index (LVMI) measured by Devereux formula, valvular calcifications], vascular calcifications and patients outcomes.

Method: We performed a prospective cohort study of a sample of ESRD patients listed for renal transplant. All patients were submitted to renal transplant and were followed for 12 months. Patient and graft survival were recorded. At inclusion, demographic and clinical data were collected, laboratorial evaluation, bone biopsy and X-ray of the pelvis and hands (Adragão score) were performed. Continuous variables are presented as medians and categorical variables as frequencies. Associations between variables were performed using Wilcoxon rank sum test and Spearman correlation test. STATA software was used and $p < 0.05$ was considered statistically significant.

Results: We included 85 patients. Mean age 50.1±12.7 years, 59 men (69.4%), 66 caucasian (77.6%). The median LVMI was 108.5 (92 – 129) g/m^2, with 32 patients presenting LVH and 19 valvular calcifications. Median Adragão score was 1 (0 – 2). At the end of 12 months, 4 patients died and 5 had graft failure (non-primary function).

Alpha-klotho correlated with bAP (p=0.0006) and marginally with PTH and absence of valvular calcifications (p=0.05). FGF23 correlated with Pi (p<0.001), Ca (p=0.004), PTH (p=0.003), Mg (p=0.002), and inversely with bAP (p=0.003). There was a marginal association with Adragão score (p=0.06). We didn't found correlations between FGF23 and alpha-klotho or dialysis vintage or echocardiographic characteristics.

Sclerostin correlated negatively with bAP (p=0.007) and PTH (p=0.04). The 3rd sclerostin tertile was associated with high scores of vascular calcifications (p=0.02). Lower levels of sclerostin were associated with patient survival at the end of 12 months (p=0.02).

Conclusion: From these 3 new bone-derived hormones, sclerostin, a bone formation inhibitor, seems to act as a risk factor for vascular calcifications and worse outcomes.

P1419

U- SHAPED ASSOCIATION OF SERUM PARATHYROID HORMONE AND COGNITIVE DYSFUNCTION IN MAINTENANCE HAEMODIALYSIS PATIENTS

Yaser Ammar[1]

[1]*Alexandria University, Medical Research Institute, Internal Medicine, Alexandria, Egypt*

Background and Aims: Primary hyperparathyroidism (HPT) is linked with several cognitive and affective disorders in the general population that tend to improve following parathyroidectomy. Most end- stage renal disease (ESRD) patients treated with maintenance haemodialysis (MHD) have 2ry/3ry HPT encompassing a broad range of serum intact parathyroid hormone (S. iPTH) values. They commonly suffer some degree of cognitive dysfunction (CODY) that impairs medication adherence and quality of life. This CODY results from the interplay of multiple factors, including HPT. However, relative hypoparathyroidism may as well cause CODY in the setting of adynamic bone disease and increased cerebrovascular calcification. Therefore, the relationship between S. iPTH and CODY in MHD patients needs to be clearly characterized across the whole spectrum of iPTH values.

Method: Seventy two stable ESRD patients (39 males, median age 50y) treated with thrice weekly low flux MHD for $>$ 6 months underwent Montreal cognitive assessment- basic version (MoCA-B) and pre-dialysis assessment of S. iPTH, vitamin D3, alkaline phosphatase, urea, creatinine, calcium, phosphorus and haemoglobin (Hb).

Results: CODY, defined by a MoCA-B score $<$ 24/30, occurred in 37/72 (51%) patients. MoCA-B score had a statistically significant positive correlation with Hb level. A quadratic inverted U-shaped curve provided the best estimate for the relation between S. iPTH and MoCA-B score (P = 0.019, Figure). Among patients in the highest S. iPTH tertile, S. iPTH has a statistically significant negative linear correlation with MoCA-B score (r = - 0.565, P = 0.004). This correlation was attenuated but persisted after controlling for Hb level (r = - 0.516, P = 0.012).

Conclusion: Anaemia and HPT are important contributors to the high prevalence of CODY in MHD patients. Both markedly high and relatively low (still above normal) S. iPTH levels are associated with lower MoCA-B scores, indicating a U- shaped relation between S. iPTH and CODY. Contrary to other populations, some degree of mild (permissible) HPT is most compatible with near normal cognitive function in MHD patients. Our results emphasize the recommendation of avoiding overzealous suppression of PTH secretion in these patients.

P1420 IS THE CHANGE FROM CINACALCET TO ETELCALCETIDE SAFE AND EFFECTIVE IN PATIENTS ON HEMODIALYSIS WITH SECONDARY HYPERPARATHYROIDISM?

Fernando Hadad Arrascue[1], Alicia Araque[1], Ruth Amair[1], Florentina Rosique[2], Antonio Perez Perez[2], Alberto Andreu Muñoz[2], Juan Cabezuelo-Romero[3]

[1]Clínicas de Diálisis RTS, Murcia, Spain, [2]Hospital General Universitario Reina Sofía, Murcia, Spain and [3]Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain

Background and Aims:

Vitamin D analogues stimulate the absorption of calcium and phosphorus, while calcimimetics reduce parathyroid hormone (PTH) without calcium and phosphorus elevation, which reduces the risk of vascular calcification.

However, the biggest problem of first-generation calcimimetics is the lack of adherence due to abandonment or non-compliance due to side effects and the high load of tablets taken by our patients.

Method:

A prospective and exploratory 24-week study, which included 54 adult patients on chronic hemodialysis (3 times per week) with secondary hyperparathyroidism (PTH >=150 pg/ml). Thirty-three patients were converted from cinacalcet to etelcalcetide, due to the lack of adherence to cinacalcet treatment and the inability to increase the dose due to the side effects of cinacalcet. The remaining 21 patients started etelcalcetide without previously taking cinacalcet.

The dose of etelcalcetide was done according to the baseline PTH value. PTH >150 and <=300 pg/ml, started with 5 mg of etelcalcetide per week, PTH >300 and <=500 pg/ml with 7,5 mg/week, PTH > 500 and <= 800 pg /ml with 10 mg/week, PTH >800 pg/ml with 15mg/week.

Results:

In the first four weeks, calcium decreased significantly, but subsequently remained stable for the rest of the study. From the baseline to the 24-week, serum calcium 8.85 $\pm$ 0.85 vs. 8.43 $\pm$ 0.83 mg/dl ($p < 0.05$), serum phosphorus 4.64 $\pm$ 1.46 vs. 4.51 $\pm$ 2.2 mg/dl ($p > 0.05$).

PTH decreased significantly at the end of the study (718.4 $\pm$ 450 vs. 391.3 $\pm$ 232.7 pg/ml, $p = 0.03$). PTH was reduced by 42% in the group that changed cinacalcet to etelcalcetide, and 50% in the group that did not take calciomimetics before the study.

At the beginning of the study, 61.1% of our sample also maintained paricalcitol as a treatment for secondary hyperparathyroidism. At the end of week 24, 51.8% maintained paricalcitol but with a significant reduction of 36.8% of the dose of paricalcitol (3.22 $\pm$ 3.78 mg/week), without significant changes in the dose of etelcalcetide at the end of the study (9.5 $\pm$ 1.3 mg/week) . No symptomatic hypocalcaemia was recorded throughout the study.

At week 12, the dose of etelcalcetide was reduced in 11% of patients and 7% at the end of week 24 due asymptomatic hypocalcemia.

Conclusion:

Etelcalcetide showed a significant reduction in PTH with the optimization of therapeutic compliance.

In our population, the use of paricalcitol was reduced by 30% due to a progressive increase in the dose of etelcalcetide, keeping calcium levels stable and safe.

Asymptomatic hypocalcemia was the most observed side effect, but it is claimed that etelcalcetide has an even better safety profile than cinacalcet, with respect to digestive side effects.

It is advisable to use Etelcalcetide by individualizing the dose in each patient, depending on their levels of PTH and calcium.

P1421 SERUM OSTEOPROTEGERIN LEVEL IS NEGATIVELY ASSOCIATED WITH BONE MINERAL DENSITY IN PATIENTS UNDERGOING HEMODIALYSIS

Chia-Wen Lu[1], Jia-Sian Hou[1], Bang-Gee Hsu[1,2]

[1]Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Division of Nephrology, Hualien, Taiwan, R.O.C. and [2]Tzu Chi University, School of Medicine, Hualien, Taiwan, R.O.C.

Background and Aims: Osteoprotegerin, a potent osteoclast activation inhibitor, decreases bone resorption and positively affects bone mineral density (BMD). Our aim was to evaluate the relationship between BMD and fasting serum osteoprotegerin concentration in hemodialysis patients.

Method: Fasting blood samples were obtained from 75 chronic hemodialysis patients. BMD was measured by dual energy X-ray absorptiometry in lumbar vertebrae (L2-L4). Serum osteoprotegerin levels were measured using a commercial enzyme-linked immunosorbent assay.

Results: A total of 7 patients (9.3%) had osteoporosis and 20 patients (26.7%) had osteopenia in hemodialysis patients. Older age ($p = 0.023$), increased serum osteoprotegerin ($p < 0.001$), urea reduction rate (URR, $p = 0.021$), Kt/V ($p = 0.027$), while decreased height ($p < 0.001$), body weight ($p < 0.001$), body mass index (BMI; $p < 0.001$), and logarithmically transformed triglyceride (log-triglyceride, $p = 0.020$) was significantly correlated with low lumbar T-score cut-off points between groups (normal, osteopenia, and osteoporosis) in hemodialysis patients. Female patients had lower lumbar BMD than male hemodialysis patients ($p = 0.002$). Univariate linear regression analysis indicated lumbar BMD were positively correlated with height ($p < 0.001$), body weight ($p < 0.001$), BMI ($p < 0.001$), log-triglyceride ($p = 0.004$), creatinine ($p = 0.016$), while negatively correlated with age ($p = 0.001$), alkaline phosphatase ($p = 0.016$), URR ($p = 0.012$), Kt/V ($p = 0.013$), and osteoprotegerin ($p < 0.001$) among the hemodialysis patients. Multivariate forward stepwise linear regression analysis of the significant variables revealed that female hemodialysis patient (adjusted R^2 change = 0.040; $p = 0.003$), body weight (adjusted R^2 change = 0.126; $p = 0.001$), kt/V (adjusted R^2 change = 0.024; $p = 0.034$) and osteoprotegerin (adjusted R^2 change = 0.332; $p < 0.001$) were the independent predictors of lumbar BMD values in the hemodialysis patients.

Conclusion: Our study results revealed that increased serum osteoprotegerin levels were independently associated with decreased BMD in the lumbar spine, and with increased risk of osteoporosis in hemodialysis patients.

P1422 **CATHEPSIN-K IS A POWERFUL DIAGNOSTIC BIOMARKER IN PARATHYROIDECTOMIZED DIALYSIS PATIENTS**

Davide Bolignano[1], Marta Greco[1], Michele Provenzano[1], Omar Tripolino[1], Caterina Vita[1], Giuseppe Leonardi[1], Salvatore Chiarella[2], Cinzia Donato[2], Emilio Russo[1], Giorgio Fuiano[1], Daniela Foti[1], Michele Andreucci[1], Giuseppe Coppolino[1]

[1]Magna Græcia University, Health Sciences, Catanzaro, Italy and [2]Hospital Pugliese Ciaccio, Catanzaro, Italy

Background and Aims: Cathepsin-K (Cts-K) is a lysosomal cysteine protease mainly involved in bone remodeling and resorption. Although it is largely released by lung cells, osteoclasts and macrophages, increasing current evidence suggests that the parathyroids may somewhat regulate Cts-K balance. We therefore analyzed Cts-K in a cohort of 85 chronic HD patients (mean age 67+/-12, median dialysis vintage 3.2 yrs), also including some individuals who were previously parathyroidectomized.

Method: Cts-K serum levels were measured before a mid-week dialysis session together with standard biochemical parameters. Twenty-six healthy subjects matched for age and gender served as controls. Patients were further stratified according to whether they were parathyroidectomized or not.

Results: Cts-K levels were statistically higher in HD patients than in controls (median 340, IQR 170-835 vs. 190 IQR 20-120 pg/mL, $p<0.0001$) and significantly associated with ALP ($r=0.50$, $p<0.001$), CRP ($r=0.46$,$p<0.001$) and PTH ($r=0.24$,$p=0.02$). Patients with previous parathyroidectomy (n=8) had significantly lower levels of Cts-K (942.3 vs 46.2 pg/mL, $p<0.0001$). At ROC analyses, Cts-K showed an excellent diagnostic profile in distinguishing parathyroidectomized patients (AUC 0.977, best Cts-K cutoff< 100 pg/mL; sens. 100%, spec. 93%; **Figure 1**). Of note, although slightly inferior, the AUC of Cts-K was not statistically different to that of PTH ($p=0.11$ for comparison of ROC curves).

Conclusion: Cathepsin-K may represent a potential candidate biomarker for diagnosing and managing MBD complications, particularly those related to parathyroid dysfunction. Its exact biological role in these conditions deserves further examination.

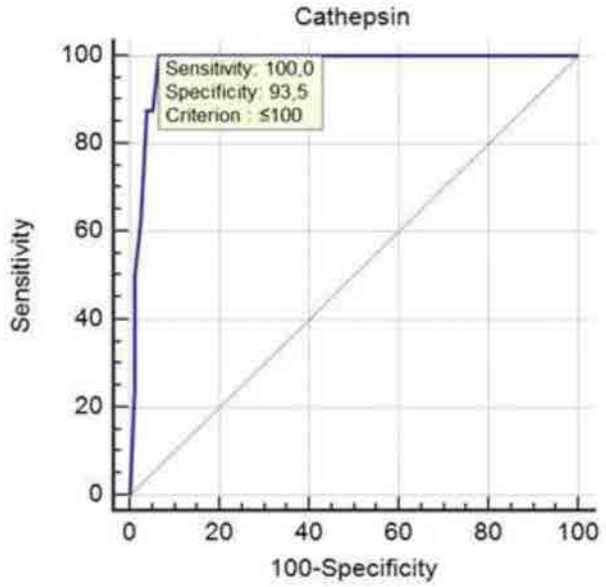


Figure:

P1423

INCREASED BLOOD FLOW RATE IN HIGH-FLUX HAEMODIALYSIS - IS IT RELEVANT FOR PHOSPHORUS REMOVAL IN HAEMODIALYSIS PATIENTS?

Nikolina Smokovska[1], Olivera Stojceva-Taneva[1], Mence Nedelkoska[1], Nadica Misovska[2], Nikola Josimovski[2], Aleksandra Vangelova[2]

[1]Diaverum, dialysis, Skopje, Republic Of North Macedonia and [2]Diaverum, dialysis, Kumanovo, Republic Of North Macedonia

Background and Aims: High-flux haemodialysis (HD), beside other uremic solutes harmful for patients, controls the level of phosphorus, major factor for HD-related morbidity and mortality. First line in phosphorus control in HD patients is dietary phosphorus intake reduction, whereas its' removal is undervalued by hemodialysis. The primary objective was to analyse whether change in the rate of blood flow is relevant in phosphorus removal in HD patients. Second objective was to evaluate other variables impacted by higher blood flow rates.

Method: Retrospective study was conducted enrolling 80 patients from a single center in a period of 12 months. In the first six months, all patients were on lower blood flow rate (LBFR group) than the same patient group was switched to a higher blood flow rate in the following six months (HBFR group). Demographic, clinical and laboratory variables were collected and intra/inter-patient group analysis was performed.

Results: Forty-seven patients were male, and 41.3% were female. Mean age of the study population was 61.2±13.47 years (males 60.3±13.38, females 62.4±13.68). Mean dialysis vintage was 63.31±66.57 months. The average real blood flow rate in LBFR group was 290.75±19.65 ml/min (median 285.34 ml/min), 344.87±9.12 ml/min in HBFR group (median 339 ml/min), p=0.0002. The level of phosphorus in LBFR group was 1.52±0.03 mmol/L, and 1.45±0.04 in HBFR group, p=0.007. Other variables that significantly showed improvement following the increase of blood flow rate were eKT/V (p=0.0006), urea clearance (p=0.02) and transferrin saturation (p=0.04). The level of post-HD urea (p=0.02) and body surface area (p=0.04) were decreased. Weekly EPO dosage decrease in HBFR group (p=0.02) was not correlated with increased iron sucrose administration (LBFR group 59.99±36.18 mg/wk, HBFR group 65.8±28.7, p=0.45). There were no significant changes related to cardiac function; systolic (p=0.44) and diastolic pressure (p=0.36), mean arterial (p=0.43) and pulse pressure (p=0.26) remained in reference range. Also, the average dose of calcium-based phosphate binders did not change significantly (p=0.34).

Conclusion: This study showed that increased blood flow rate in HD patients reduces phosphorus and EPO consumption, improves urea clearance without significant impact on cardiac function and calcium overload with calcium-based phosphate binders.

P1424 IMPACT OF DIRECTLY OBSERVED TREATMENT OF ONE ALFACALCIDOL ON MINERAL BONE DISORDER PROFILE IN DIALYSIS PATIENTS-A SINGLE UNIT PILOT STUDY

Mirza Yasar Baig[1], Rajkumar Chinnadurai[2], Tina Chrysochou[1]
[1]Salford Royal NHS Foundation Trust, Renal Medicine, United Kingdom and [2]Salford Royal NHS Foundation Trust, Manchester, United Kingdom

Impact of directly observed treatment of one-alfacalcidol on mineral bone disorder profile in dialysis patients- A single unit pilot study

Background and Aims: Secondary hyperparathyroidism (SHPT) is a common mineral bone disorder observed in patients with end-stage renal disease. Management of SHPT can be challenging mainly due to poor medication compliance. Directly observed treatment (DOT) has shown to improve management outcomes in other conditions like tuberculosis. We conducted a pilot study to investigate the impact of DOT with one alfacalcidol for SHPT in our cohort of dialysis patients.

Method: This prospective observational study was conducted on 21 end stage renal disease patients on dialysis from a single centre who were commenced on one alfacalcidol on dialysis days under direct observation .All patients had not shown any improvement in PTH despite increase in one alfacalcidol either admitted to or were suspected to have medication non-adherence. Serum bone mineral profile including parathormone (PTH), corrected calcium, phosphate and alkaline phosphatase were recorded before and after initiation of DOT. Treatment outcome was measured by comparing the mean change in the biochemical profile prior DOT initiation and at the lowest PTH value achieved on DOT. Data was analysed by paired t test using SPSS software.

Results: The mean age of our sample at the time of commencing DOT therapy was 52 years. Our sample had a predominance of males (67%) and Asian ethnicity (62%). 71% had a history of hypertension and 43% were diabetic. DOT one alfacalcidol therapy produced a significant reduction in the mean PTH value (pre-DOT- 92.2 vs post DOT-36.1 pmol/L, $p<0.001$). There was a significant rise in the corresponding mean corrected calcium levels (pre-DOT- 2.22 vs post-DOT-2.45 mmol/L, $p=0.001$) (table–1). Over a mean follow up of 8 months, a significant reduction in the one alfacalcidol dose requirement was observed in 52.38% of our cohort.

Table 1 Comparison of biochemical profile immediate pre-DOT and at lowest PTH level post DOT one-alfacalcidol treatment

Parameter	Pre-DOT	Post-DOT	p-value
Alkaline phosphatase (U/L)	172.19 (104.5)	121.1 (63.9)	0.063
Calcium (mmol/L)	2.22 (0.166)	2.45 (0.216)	**0.001**
Haemoglobin (g/L)	108.4 (19.1)	109.7 (19.5)	0.825
Phosphate (mmol/L)	1.83 (0.58)	1.75 (0.56)	0.65
Parathormone (pmol/L)	92.22 (45.3)	36.1 (36.9)	**<0.001**

Values expressed as mean (SD) and p-value by paired t test.

Conclusion: DOT one alfacalcidol therapy produced a significant improvement in the mineral bone profile in our cohort of dialysis patients. DOT approach can help to improve the outcomes in dialysis patients with poor compliance.

P1425 EFFICACY AND SAFETY OF INTRAVENOUS PARICALCITOL TREATMENT IN CHINESE HEMODIALYSIS PATIENTS WITH SECONDARY HYPERPARATHYROIDISM: A REAL-WORLD DATABASE ANALYSIS

Niansong Wang[1], Gengru Jiang[2]

[1]The Sixth People's Hospital Affiliated to Shanghai Jiao Tong University, nephrology, shanghai, P.R. China and [2]Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Nephrology, Shanghai, P.R. China

Background and Aims: The aim of this retrospective, real-world data based observational study was to evaluate the efficacy, safety profile of paricalcitol in Chinese hemodialysis (HD) patients with secondary hyperparathyroidism (SHPT) under routine clinical practice.

Method: From the Zemplar Engagement Program (ZEP) database, a total of 668 Chinese hemodialysis patients from 104 dialysis centers between January 2015 and May 2019 were included in the analysis set. Intact parathyroid hormone (iPTH), total serum calcium (Ca), phosphate (P), dosage of intravenous (IV) paricalcitol (Zemplar®) were analyzed and discussed via retrospective analysis of the database during the treatment. The comparison between baseline and end of treatment was made to reveal the fluctuation trend of each biomarker and reflected us with clues of IV paricalcitol's algorithm in real-world practice.

Results: Patients were divided into five groups according to the duration of follow-up, which includes Month 0.5-3 (Day 14–90), Month 3-6 (Day 91–180), Month 6-12 (Day 181–360), Month 12-24 (Day 361–720) and Month 24-48 (Day 721–1440). Median iPTH levels decreased from 1183.05 pg/ml at baseline to 676.03 pg/ml at last visit by 30.88% ($p < 0.0001$). 56.14% of patients had a $\geq$30% decrease and 29.34% of patients had a $\geq$50% decrease in iPTH. The proportion of patients achieving the Chinese CKD-MBD Guideline target range (<600 pg/ml) increased from 9.88% at treatment initiation to 40.12% at last observation. Serum Ca levels remained within the normal range throughout the study with only a slight but statistically significant increase in the group of Month 12-24 (P=0.0479). Serum phosphate remained stable in all follow-up groups (P>0.05). Subgroup analyses of 221 patients with hyperphosphatemia at baseline >1.78 mmol/l showed a rapid phosphate reduction from 2.00±0.20 mmol/l to 1.76±0.34mmol/l by 11.64% (P< 0.0001), within the first few weeks, along with the reduction of iPTH. Of all patients, 62.72% experienced a 30% decrease in iPTH within a median time of 16.86 weeks (95% CI, 15.57-17.86), 38.17% experienced a 50% decrease in iPTH within a median time of 21.29 weeks (95% CI, 19.86-23.14). The average weekly dose of paricalcitol was 19.69±8.99ug/week. Total dose of paricalcitol used and baseline iPTH were negatively correlated with the decrease in iPTH.

Conclusion: This is the first national retrospective real-world observational study since IV paricalcitol is available in China since 2014. It proves that up to 20ug weekly IV paricalcitol treatment is safe and effective in China HD patients with higher iPTH level. Physicians and patients could expect significantly iPTH decrease within 16-21 weeks when IV paricalcitol is initiated. This study also encores the pre-published results of paricalcitol trials and high-quality cohorts, from the real-world perspective. In summary, IV paricalcitol is well tolerated and serves as an effective approach to treat SHPT in Chinese HD patients.

Figure.1 Mean iPTH values from baseline to last measurement (pg/ml)

Figure.2 iPTH changes compared with baseline stratified by baseline iPTH values (%)

Figure.3 Proportion of patients with a >=30% or 50% decrease in parathyroid hormone (%)

Figure.4 Changes of iPTH and P from baseline to last measurement in the subgroup of hyperphosphatemia (Mean ± SD); (Hyperphosphatemia, defined as P>1.78 mmol/l)

P1426

EFFECTIVENESS AND SAFETY OF ETELCALCETIDE IN THE LONG TERM IN CLINICAL PRACTICE IN HEMODIALYSIS PATIENTS WITH SECONDARY HYPERPARATHYROIDISM

Rosa Diaz Campillejo[1], Rosa María Ruiz Calero Cendrero[1], Lilia Olivera Azevedo[1], Jorge Alberto Rodriguez Sabillon[1], Belen Ruiz Jimenez[2], Maria Antonia Fernandez Solis[3], Maria Josefa Galan Gonzalez[4], Barbara Cancho Castellano[1], Maria Victoria Martín Hidalgo Barquero[1], Sergio Barroso-Hernandez[1]

[1]Infanta Cristina Hospital, Nefrología, Badajoz, Spain, [2]Fresenius Medical Care - Centro de diálisis, Mérida, Spain, [3]Fresenius Medical Care, Villanueva de la Serena, Spain and [4]Clinica Dialisis de Badajoz, Badajoz, Spain

Background and Aims: : Secondary hyperparathyroidism (HPT) is a frequent complication in hemodialysis (HD) patients. Until now we had oral Vit / D analogues and oral Cinacalcet for treatment. The appearance of Etelcalcetide brings new treatment possibilities. Apart from clinical trials there are few long-term results in usual practice. Our goal is to evaluate results with the use of Etelcalcetide after more than a year of treatment in clinical practice of HD.

Method: We carry out a prospective descriptive study for 15 months with patients with HPT-HD, the ones who were with Cinacalcet and had not responded or had intolerance were changed to Etelcalcetide. Patients without prior treatment with calcimimetics were also included. Treatment with Vit D analogues and phosphate binders is treated according to usual clinical practice.

Results: We studied 25 HD patients, 12 men and 13 women with a mean age of 59.5 ± 13.6 years, 11 began de novo calcimimetic treatment and in 14 Cinacalcet was modified to Etelcalcetide due to lack of response or poor oral tolerance. Starting dose 2.5 mg post-dialysis, mean final dose 7.5 mg. We observed a reduction of PTH ≥30% in 80% of patients and a decrease ≥50% in 52%, Figure 1 shows the decrease over 15 months. The calcium corrected to albumine (Cac) decreased 4.8% ± 8 compared to baseline. The majority of patients present mild hypocalcemia (Cac between 7.5 and 8.3 mg / dl) and asymptomatic. There are no differences with P. Patients with PTH in range according to KDIGO went from 8% to 63%. No serious clinical manifestations of hypocalcemia or symptoms of digestive intolerance or other side effects appeared. **Conclusion:** Etelcalcetide in the long term significantly improves the control of HPT in HD with a high safety profile. IV administration facilitates compliance without having followed serious side effects in 15 months of follow-up.

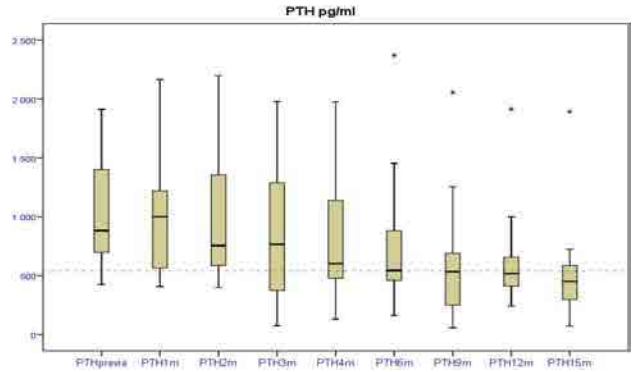


Figure 1: Median PTH evolution in15 months

P1427 **ROLE OF ETECALCETIDE IN THE MANAGEMENT OF SECUNDARY HYPERPARATHYROIDISM**

Candela Moliz[1], Elisabeth Canllavi[1], Beatriz Redondo[1], Maria Fernandez-Vidal[1], Teresa Bada Bosch[1], Hernando Trujillo[1], Lucia Aubert[1], Justo Sandino[1], Elena Gutiérrez Vilchez[1], Evangelina Mérida[1]

[1]*Univerity Hospital 12 de Octubre, Nephrology, Madrid, Spain*

Background and Aims: Secondary Hyperparathyroidism (SHPT) is a complication of chronic kidney disease (CKD). Etelcalcetide is the first intravenous calcimimetic authorized for the treatment of SHPT in haemodialysis (HD). It has proven to be effective in lowering parathyroid hormone (PTH), with an acceptable and comparable safety profile. The aim of this descriptive study was to evaluate the results of using etelcalcetide in patients on HD with SHPT.

Method: Thirty patients on HD received etelcalcetide were enrolled (figure 1). The minimum observation period was 6 months. Fifteen (50%) were previously with cinacalcet (group 1) and 15 (50%) received etelcalcetide at onset (group 2). We analyzed change of serum iPTH, calcium (Ca) and phosphorus (P) in both cohorts; as well as the dosage of calcium carbonate, non-calcium (phosphate binders) and / or vitamin D analogs. The presence of adverse effects were also recorded.

Results: Thirty patients on HD received etelcalcetide were enrolled (figure 1). The minimum observation period was 6 months. Fifteen (50%) were previously with cinacalcet (group 1) and 15 (50%) received etelcalcetide at onset (group 2). We analyzed change of serum iPTH, calcium (Ca) and phosphorus (P) in both cohorts; as well as the dosage of calcium carbonate, non-calcium (phosphate binders) and / or vitamin D analogs. The presence of adverse effects were also recorded.

In global, serum iPTH levels were significantly decreased during therapy compared to baseline levels. When comparing both groups, we found a significant decrease of Ca, P and iPTH in group 2. However, we only found significant decrease of Ca in group 1 (figure 2). When we analyzed the reducton of PTH >30% in both groups, we observed that 46.6% of patients treated with etecalcetide compared to 33.3% of patients treated with cinacalcet, achieved this reduction in PTH. The dosage of calcium binders (33.3% pretreatment vs 56.7% at the end of follow-up, p 0.054), non-calcium binders (40% pretreatment vs 63.3% at the end of follow-up, p 0.02) and vitamin D analogues (56,7% pretreatment vs 66,7% at the end of follow-up, p 0,3) were increased when etelcalcetide treatment was started. No changes were made in dialysate calcium concentration. Six patients, presented hypocalcemia (Ca < 7.5 mEq/l).

Conclusion: In our cohort, etelcalcetide has shown to be effective in reducing serum iPTH. In addition, etecalcetide was noninferior to cinacalcet reducing PTH>30%. An increase in the use of vitamin D analogues, calcium binders and non-calcium binders has been observed, probably due to the hypocalcemia.

Variable	
Edad en años (años)	55.5±18,2
Sex (n, %)	
• Women	17 (56,7)
• Men	13 (43,3)
Observation period (months)	6.7±2.1
Vascular Access (n, %)	
• Permanent venous catheter	16 (53,3)
• Arteriovenous fistula	14 (46,6)
Dialysate calcium concentration (n, %)	
• 2,5 mEq/L	20 (66,7)
• 3 mEq/L	10 (33,3)
Lost tracking	2
Parathyroidectomy	1
Parathyroidectomy	1
Starting etecalcetide dose	5-10 mg/weekly
Etecalcetide maintenance dose	15-30 mg/weekly

Figure 1

	GLOBAL	GROUP 1	GROUP 2
Calcio pretreatment	8.8 +/- 0.8*(p 0.0007)*	8.8 +/- 0.9*(p 0.026)*	8.9 +/- 0.7*(p 0.01)*
Calcio end of follow- up	8.3 +/- 0.5*(p.0.0007)*	8.7 +/- 0.5*(p 0.026)*	8.4 +/- 0.4*(p 0.01)*
Fósforo pretreatment	4.8 +/- 1.1*(p 0.065)*	4.5 +/- 0.9*(p 0.95)*	5.1 +/- 1.1*(p 0.02)*
Fósforo end of follow- up	4.5 +/- 0.7*(p 0.065)*	4.5 +/- 0.7*(p 0.95)*	4.4 +/- 0.7*(p 0.02)*
PTH pretreatment	784 +/-707*(p 0.0077)*	827 +/- 607*(p 0.26)*	741 +/- 814*(p 0.006)*
PTH end of follow- up	671 +/- 680*(p 0.0077)*	717 +/- 546*(p 0.26)*	518 +/-798*(p 0.006)*

Figure 2

P1428

PERSISTENT HUNGRY BONE SYNDROME AND HYPOPARATHYROIDISM AFTER PARATHYROIDECTOMY FOR SECONDARY HYPERPARATHYROIDISM: ARE THERE RISK FACTORS?

Ekaterina Parshina[1], Aleksei Zulkarnaev[2], Konstantin Novokshonov[3], Pavel Kislyy[1], Alexey Tolkach[1], Roman Chernikov[3]

[1]Saint Petersburg State University Hospital, Dialysis department, Saint-Petersburg, Russia, [2]M.F. Vladimirsky Moscow Regional Research Clinical Institute, Surgical Department of Transplantology and dialysis, Moscow, Russia and [3]Saint Petersburg State University Hospital, Endocrine surgery department, Saint-Petersburg, Russia

Background and Aims: Hungry bone syndrome (HBS) and postoperative hypoparathyroidism both are important postoperative complications after parathyroidectomy (PTx) for severe secondary hyperparathyroidism (SHPT). There is still a lack of data in the literature concerning associated risk factors of the prolonged HBS and hypoparathyroidism after PTx. We aimed to explore the risk factors for HBS and postoperative persistent hypoparathyroidism development in a long-term period after surgery.

Method: We performed a retrospective analysis of 55 severe SHPT patients who underwent subtotal PTx or total PTx+AT in our clinic between 2011 and 2015 with follow-up period not less than 12 months. A general cohort was divided into subgroups according to their laboratory parameters in a year after PTx. Prolonged HBS was defined as a total serum calcium concentration less than 2,1 mmol/l after 1 year from surgery. Postoperative hypoparathyroidism was defined as a iPTH value less than 10 pg/mL after one year from surgery.

Results: In terms of prolonged HBS persistence a general cohort of 55 patients was divided into two subgroups: a HBS group of 27 patients (49,1%) with mean age of 45,6 ± 9,02 years and a non-HBS group of 49,6 patients (50,9%) with mean age of 45,6 ± 10,8 years. Mean dialysis vintage for HBS and non-HBS groups was 107,8 ± 52,4 and 97,4± 54,5 months, respectively. The PTH level dropped significantly in both groups on the 1st day after surgery when compared with preoperative values: from 134 [92,7-186] to 5,0 [2,1–17,7] pmol/l in non-HBS group ($p<0,001$) and from 126 [101-223] to 4,1 [1,5-14,5] pmol/l in HBS group ($p<0,001$). The immediate ionized calcium levels also decreased significantly in both groups: from 1,26 [1,2-1,3] to 0,89 [0,79-1,09] in non-HBS group ($p<0,001$), and from 1,2 [1,11-1,29] to 0,88 [0,8-1,0] in HBS group ($p<0,001$). In univariate analysis the postoperative iPTH showed no significant difference between the HBS and non-HBS groups ($p= 0,614$) as well as ionized Ca level ($p= 0,5653$), difference of PTH before/after surgery (ΔPTH) ($p= 0,9133$), age ($p= 0,2575$) and dialysis vintage ($p= 0,6165$). Neither gender (RR 0,75 [0,44; 1,277]; $p = 0.4088$), nor type of surgery (RR 0,81 [0,45; 1,456]; $p = 0.5815$) were associated with the long-term HBS persistence.

For 51 patients data of iPTH level in a 1 year after PTx were available; 21 patients (41,2 %) were included in the postoperative persistent hypoparathyroidism-positive group (hypoPT-positive), and 30 patients (58,8%) were included in the postoperative persistent hypoparathroidism-negative (hypoPT-negative) group. In both hypoPT-positive and hypoPT-negative groups postoperative iPTH levels were decreased after surgery with significant difference being compared between groups (1,0 [0,8-2,5] vs 12,6 [3,7-17,7] pmol/l, respectively; $p= 0,0001$). We observed a moderate positive correlation between iPTH levels on the 1st postoperative day and in a 1 year after PTx ($\rho=0,548$ [95% CI 0,314; 0,72]; $p<0,0001$). Type of surgery was not associated with increased risk of prolonged hypoparathyroidism (RR=1.03 [0,569; 1,866]; $p=0.922$).

Conclusion: Prolonged persistence of HBS and postoperative hypoparathyroidism are common after PTx in patients with SHPT regardless the type of surgery. Neither laboratory (postoperative iPTH, ΔPTH, ionized Ca), nor demographic (gender, age, dialysis vintage) factors were not associated with HBS persistence in a long-term period after PTx. Only serum iPTH level on the 1st day after PTx is associated with prolonged hypoparathyroidism after surgery.

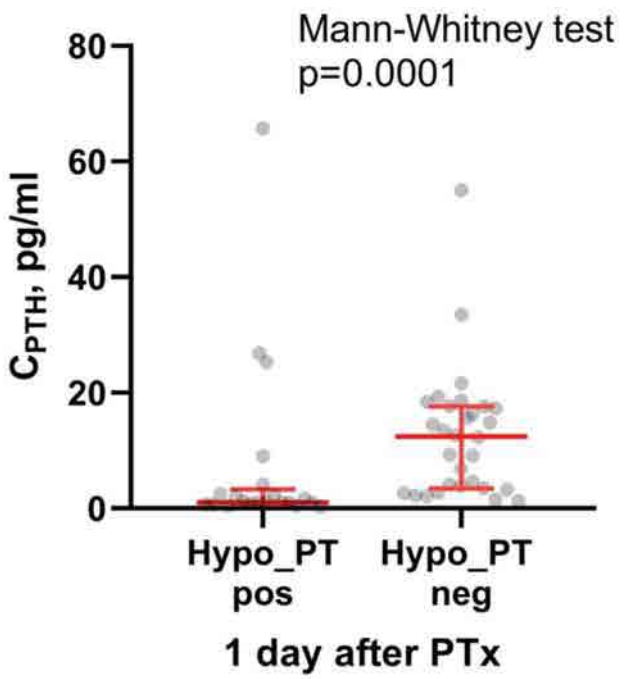


Figure:

P1429 **EVALUATION OF PARATHYROIDECTOMY IN PERSISTENT HYPERARATHYROIDISM AFTER RENAL TRANSPLANTATION: A SINGLE-CENTER RETROSPECTIVE STUDY**

Ping Zhang[1], Hulin Lu[2], Jianghua Chen[3]

[1]the First Affiliated Hospital, College of Medicine, Zhejiang University, Kidney Disease Center, P.R. China, [2]the First People's Hospital of Huzhou, Department of Nephrology, P.R. China and [3]the First Affiliated Hospital, College of Medicine, Zhejiang University, kideny disease center, P.R. China

Background and Aims: To investigate the efficacy of parathyroidectomy (PTX) in the treatment of persistent hyperparathyroidism (PHPT) after renal transplantation and the effect of PTX on renal allograft function.

Method: This single-center retrospective study enrolled 31 patients who underwent PTX for the treatment of PHPT after renal transplantation in the Kidney Disease Center of the First Affiliated Hospital of Zhejiang University from May 2010 to Oct. 2018. The changes of serum calcium, serum phosphorus, alkaline phosphatase, parathyroid hormone(PTH), serum creatinine, and estimated glomerular filtration rate (eGFR) in the preoperative and postoperative periods (1w, 1m, 3m, 6m,12m) were compared. The operative successful rate (12 m) and postoperative complications were calculated.

Results: The serum calcium before PTX was (2.78±0.18) mmol/L, which decreased significantly to (2.19±0.34) mmol/L at 1 week postoperatively ($P<0.01$). The serum phosphorus before PTX was (0.76±0.16) mmol/L, which decreased significantly to (0.97±0.26) mmol/L at 1 week postoperatively ($P<0.01$). The PTH before PTX was (276.00±200.60) pg/mL, which decreased significantly to (46.62±104.36) pg/mL at 1 week postoperatively ($P<0.01$). The alkaline phosphatase before PTX was (261.59±236.95) U/L, which decreased significantly to (154.90±117.37) U/L at 3 months postoperatively ($P<0.01$). No significant difference was found in postoperative serum creatinine or eGFR levels compared with the baseline. The operative successful rate was 90.3% at 12 months postoperatively. The incidence rates of postoperative transient hypocalcemia, persistent hypoparathyroidism, and hoarseness were 35.5%, 3.2% and 3.2% respectively. No persistent hypocalcemia, incision hemorrhage, incision infection, or surgery-related death happened.

Conclusion: PTX can quickly and effectively alleviate high calcium, low phosphorus, high PTH and high alkaline phosphatase after renal transplantation. PTX is effective and safe in the treatment of PHPT after renal transplantation, and has no effect on renal allograft function.

P1430

BETA C-TERMINAL TELOPEPTIDE OF TYPE I COLLAGEN: CORRELATIONS WITH MINERAL METABOLISM PARAMETERS AND CARDIAC VALVULAR CALCIFICATIONS IN A COHORT OF HEAMODIALYSIS PATIENTS

Anna Regalia[1], Silvia Malvica[1], Simone Vettoretti[1], Laura Pavone[1], Elisabetta Margiotta[1], Claudia Castelnovo[1], Antonio Scalamogna[1], Piergiorgio Messa[1,2]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Nephrology, Dialysis and Renal Transplant Unit, Milano, Italy and [2]Università degli Studi di Milano, Department of Clinical Sciences and Community Health, Milano, Italy

Background and Aims: Beta-carboxyterminal telopeptide of type I collagen (beta-CTx) is considered a marker of bone resorption in patients affected by osteoporosis. Nevertheless, its role in mineral bone disorder (MBD) of CKD patients is not clear. The aim of this study was to explore in a group of haemodialysis patients (HDp): 1) The levels of beta-CTx; 2) The correlation between beta-CTx levels and other mineral metabolism (MM) parameters; 3) The association between beta-CTx and CKD-MBD specific therapy 4) The relation between beta-CTx and cardiac valvular calcifications (VC).

Method: We studied a group of 21 HDp (F/M 9/12, age 68[54-78] years) randomly selected from the HDp actually followed-up in our Department. Dialysis vintage was 52[23-80] months. All HDp were on a three-weekly hemodialysis schedule, with a prescribed dialysate calcium of 1.5 mmol/l. Before the first dialysis session of the week, after the long interdialytic interval, the levels of beta-CTx, total and ionized calcium (tCa and iCa), Phosphorus (P), Magnesium (Mg), intact PTH (iPTH), total and bone isoform of alkaline phosphatase (tALP and bALP), 25-hydroxyvitamin D (25OHVD), 1,25-dihydroxyvitamin D (1,25OH_2VD), and other general biochemical parameters were measured (Figure 1). At the same time, data concerning MM therapies were recorded. In all the studied patients, the presence of VC was searched in the the most recent echocardiographic study.

Figure 1 Results:

1. The mean levels of beta-CTx in our cohort were 1828[1136-2214] ng/L. These value are similar to those reported in literature in HDp and significantly higher than those reported in general population.

Beta-CTx levels showed a significant positive correlation with tALP (r 0.92, p <0.0001), bALP (r 0.89, p <0.0001) and iPTH (r 0.87, p<0.0001) and a negative correlation with tCa (r – 0.43, p=0.05) and iCa (r – 0.52, p=0.01). No significant correlation was found with the other MM and general biochemical parameters and with the general features of the studied cohort.

1. 18 patients (85.7%) were taking P binders (72.2% Ca-based and 27.8% Ca-free). In 20 patients (95.2%) vitamin D therapy, either in the natural, active or both natural and active form (35%, 15% and 50%, respectively) was prescribed. 6 patients (28.6%) were in therapy with Cinacalcet.

No difference was found in beta-CTx levels according to the presence and the type of each of the above mentioned therapies.

1. VC were found in 38% of patients. Beta-CTx levels did not differ between VC positive and negative patients (2400±1406 ng/L and 1935 ±1339 ng/L, respectively, p=0.49)

Conclusion: Taking into account the limitations of this preliminary small size observational study, our data showed that beta-CTx levels are high in HDp. Beta-CTx correlates with iPTH, tALP and bALP. The negative correlation with tCa and iCa probably might be influenced by the negative correlation between iPTH and serum Calcium. Beta-CTx levels are not associated with CKD-MBD specific therapy or with cardiac valvular calcifications. Further prospective and randomized studies, including a higher number of HDp and possibly bone histology are needed to elucidate the possible role of beta-CTx as a marker of bone disease in HDp.

	Mean	Standard deviation	Median	Minimum	Maximum	25th – 75th percentile
Age, years	66	15	68	24	89	54 - 78
Dialytic vintage, months	55	35	52	7	132	23 - 80
Beta-CTx, ng/L	2113	1466	1828	503	6000	1136 - 2214
Ca, mg/dl	8,5	0,7	8,5	7,3	10,1	7,9 - 8,8
iCa, mmol/L	1,11	0,10	1,07	0,93	1,36	1,03 -1,18
P, mg/dl	4,9	1,4	4,9	2,2	7,5	3,9 -5,7
Mg, mg/dl	2,1	0,3	2,1	1,4	2,5	1,9 - 2,3
iPTH, pg/ml	304	409	134	22	1400	57 - 285
tALP, U/L	160	171	105	46	655	76 - 129
bALP, U/L	51	67	22	10	225	14 - 46
1,25OH$_2$VD , pg/ml	21	13	19	5	54	12 to 27
25OHVD, ng/ml	21	9	21	4	41	15 - 29
Bicarbonates, mmol/L	22,5	2,9	23,7	17,1	27,1	19,8 - 24,6
Albumin, g/dl	3,7	0,4	3,8	2,8	4,5	3,7 - 4,0
Haemoglobin, g/dl	10,9	1,2	11,3	8,2	13,0	9,8 - 11,7
C-reactive protein, mg/dl	0,28	0,25	0,22	0,03	0,99	0,08 - 0,40

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DIALYSIS. EPIDEMIOLOGY AND OUTCOME

P1437

RELATIONS BETWEEN IMPLEMENTATIONS OF EVIDENCE-BASED TREATMENTS AND IMPROVED OUTCOMES IN PATIENTS STARTING HEMODIALYSIS DURING THE LAST 10 YEARS: EXPERIENCES FROM THE SWEDISH RENAL REGISTRY 2006-2015

Marie Evans[1], Hong Xu[2], Maria Stendahl[3], Helena Rydell[1], Juan Jesus Carrero[4]

[1]Karolinska Institutet, CLINTEC, Stockholm, Sweden, [2]Karolinska Institutet, Neurobiology, Care Sciences and Society, Stockholm, Sweden, [3]Ryhov County Hospital, Internal Medicine, Jönköping, Sweden and [4]Karolinska Institutet, Medical epidemiology and biostatistics, Stockholm, Sweden

Background and Aims: Although few randomized controlled trials have been able to demonstrate benefits of single treatments in improving outcomes of patients undergoing hemodialysis (HD), the last decades have witnessed significant therapeutic advances. This relates both to the HD treatment itself and to the management of patient complications. We here evaluated temporal changes in the use of evidence-based treatments and survival rates in incident HD patients.

Method: We included all patients initiating HD in Sweden between 2006-2015 and followed them until the end of 2017. Data were linked to national registries to retrieve information on date of death, cardiovascular events, comorbidity, and drug prescriptions. We first evaluated trends in the use of different HD related therapies and selected key therapeutic targets and medications in 2-year blocks. We then evaluated the incidence of death and major cardiovascular events (MACE) within one and two years from start of dialysis through standardized incidence rates via logistic regression models to account for differences in patient characteristics over time. Via Cox regression models, we explored whether adjustment for implementation of evidence-based treatments (e.g. hemodiafiltration (HDF), frequent HD, working fistula, drugs to control CKD-MBD, anemia) modified the observed survival and MACE risks. Finally, survival trends were also compared against an age-sex-calendar year-matched general Swedish population using standardized incidence ratios.

Results: We identified 6,612 patients starting HD in Sweden during the study period. There was no difference in mean age or proportion of women over time, but body mass index, serum parathyroid hormone levels and the proportion of patients with cerebrovascular disease, atrial fibrillation and cancer increased. Conversely, mean serum hemoglobin, phosphate and albumin values decreased over time. The proportion of patients who underwent HDF, had more than three HD sessions/week, and had a working fistula increased progressively, as well as the use of phosphate binders (particularly non-calcium), cinacalcet, and vitamin D3. After standardization for differences in demography and comorbidities, the one-year risk of mortality or MACE risk decreased by 7% and 16%, respectively, in 2014/15 compared to 2006/07. Similarly, the two-year risk of death or MACE decreased by 16 and 21%. In multivariable Cox models, we explored the linear association between calendar year blocks and study outcomes. Per 2-year period, the risk of death within one year decreased by 6% (HR 0.94, 95% CI 0.92-1.00), and of MACE by 5% (0.94, 95% CI 0.92-0.98). Adjustment for changes in the evidence-based treatments over time abrogated these associations (HR 1.00, 95% CI 0.91-1.09 for death and 1.00, 95% CI 0.94-1.06 for MACE). Similar results were obtained for 2-year outcomes. Compared with the general population, the one-year risk of death for a HD patient was 6 times higher in 2006/2007 [standardized incidence rate ratio, SIR 6.05 (5.30–6.91)], but decreased to 5.5 times higher in 2014/15 [SIR 5.57 (4.82–6.44)], corresponding to a SIR reduction of 8%.

Conclusion: In patients initiating HD therapy in Sweden, there has been a gradual implementation of new and established evidence-based treatments during the last 10 years, which was associated with a parallel reduction in the risk of death and MACE.

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P1438 **IMPACT OF HOSPITALIZATION ON BODY COMPOSITION OF DIALYSIS PATIENTS**

Adrian Guinsburg[1], Alejandro Kohn Tuli[2], Eurfronio Dalmeida[3], Ana Beatriz Barra[3], Eduardo Machuca[4], Orlando Olivares[5], Javier Arango[5], María Ines Gomez Canabal[5], Leonor Briones[6], Maria Lopera[7], Maria Mercedes Resk[8], Mauro Caseiro[1], Juan Carlos Berbessi[1]

[1]Fresenius Medical Care, LatinAmerica, Argentina, [2]Fresenius Medical Care Argentina, Buenos Aires, Argentina, [3]Fresenius Medical Care, Brasil, Rio de Janeiro, Brazil, [4]Fresenius Medical Care, Chile, Chile, [5]Fresenius Medical Care, Colombia, Bogota, Colombia, [6]Fresenius Medical Care, Ecuador, Quito, Ecuador, [7]Fresenius Medical Care, Perú, Peru and [8]Fresenius Medical Care, Caricam, Panama City, Panama

Background and Aims:

Patients with CKD are at higher risk of hospitalization (hosp) and this event is a known marker of prognosis. In this study we aim to describe hospitalizations in LatinAmerica and the impact on body composition as measured by multifrequency bioimpedance.

Method:

All hospitalizations from Fresenius Medical Care clinical database (EuCliD®) registered in dialysis patients from Argentina, Brasil, Chile, Colombia, Ecuador and Perú during calendar year 2018 were included into the analysis. For each hospitalization we reviewed main reason (ICD10 code), duration and outcome (discharge or death). Body composition was measured using multifrequency bioimpedance (BMC®). On patients with BCM data available in the 30 days prior to hospitalization and before 15 days after discharge values pre and post hospitalization were recorded (BCM data, lab data, treatment data). Pre and post data were compared using Student t test for paired samples. All values expressed as mean ± standard deviation (SD).

Results:

During all calendar year 2018, a total of 23,347 hospitalizations from 44,228 patients were recorded. Mean age was 61.4 ± 16.1 / Male 56.4% / diabetes 38.7%. Accounting for time at risk, hosp rate was 0.74 hosp/pt-year at risk. Mean stay at hospital was 10.9 ± 14.4 days (7.6 days/pt-yr). 35.24% of patients suffer at least one hosp during the year.

Reasons for hospitalization are indicated in table 1:

*Table 2: Differences pre and post hosp. BCM values only considered if measurement available between 30 days pre hosp and 15 days after discharge

	Pre Hosp	Post Hosp	Change	n	p
Post dialysis weight (kg)	65,79	65,22	-0,56	3165	< 0.0001
Overhydration (liters)	2,53	3,06	0,53	3598	< 0.0001
Muscular mass (kg)	32,28	31,75	-0,53	3277	< 0.0001
Fat mass (kg)	23,48	22,75	-0,73	3277	< 0.0001
LTI (kg/m2)	12,37	12,17	-0,20	3277	< 0.0001
FTI (kg/m2)	12,44	12,05	-0,73	3277	< 0.0001
Hb (g/dl)	10,31	9,65	-0,67	18234	< 0.0001
Ca (mg/dl)	8,77	8,73	-0,04	18115	< 0.0001
P (mg/dl)	4,61	4,41	-0,19	18159	< 0.0001
Albumin (g/dl)	3,75	3,68	0,08	16963	< 0.0001
eKt/V	1,38	1,39	0,01	13023	NS
Effective treat time (min)	223,9	232,09	8,2	17596	< 0.0001

Conclusion:

Hospitalization in dialysis patients is a frequent event. It has a significant impact on Hb, Ca, P and Albumin levels. Although net patient's weight is significantly reduced, real decrease in muscular and fat mass may be masked by increase in excess water (overhydration) as shown in our results. An early BCM measurement and dry weight adjustment after discharge may be a helpful tool for patient management optimization.

Table 1: Hosp reason according to ICD10 group

Reason	Percent	n
Cardiovascular	17,4%	4071
Vascular access related	15,3%	3582
Symptons not specified	13,6%	3171
Respiratory	11,8%	2762
Urogenital	9,2%	2155
Digestive	8,3%	1937
Infections	7,0%	1638
Endocrine	5,8%	1359

Continued

Continued

Reason	Percent	n
Cardiovascular	17,4%	4071
Vascular access related	15,3%	3582
Symptons not specified	13,6%	3171
Respiratory	11,8%	2762
Urogenital	9,2%	2155
Digestive	8,3%	1937
Infections	7,0%	1638
Endocrine	5,8%	1359
Others	5,3%	1245
Blood	2,4%	567
Skin	2,1%	494
Neoplasms	0,9%	211
Unknown	0,7%	155

P1439 DO PATIENTS ON DIALYSIS AGE FASTER THAN HEALTHY ADULTS BASED ON TELOMERE LENGTH; A BIOLOGICAL MARKER OF AGEING AND MORTALITY?

Vasantha Muthuppalaniappan[1], Kieran McCafferty[1], Muhammad Yaqoob[1]

[1]*WIlliam Harvey Research Institute, Queen Mary University of London, London, United Kingdom*

Background and Aims: Telomere length (TL) is an emerging novel biomarker of ageing and survival. Telomere shortening to a critical limit is associated with replicative senescence and cell death; a process accelerated by oxidative stress and chronic inflammation. This process is often observed among patients with end stage kidney disease (ESKD). This predisposes them to increased morbidity and mortality in comparison to their normal counterparts when matched for age and gender. The exact reason for premature ageing in this cohort remains poorly understood and there is a need for further investigations into biomarkers of ageing to help understand the process. The aim of the study was to investigate if patients with ESKD in comparison to healthy controls had an increased biological age based on telomere length measurements.

Method: This was a single centre prospective, observational, cohort study among eligible dialysis patients and healthy controls. The healthy control group consisted of potential living donors. Patients were recruited as per the study protocol. Recruited patients on HD had their blood sampled prior to their mid-week dialysis session while potential live donors and PD patients had their blood sampled at outpatient clinics. Whole blood was immediately isolated for peripheral blood mononuclear cells (PBMC). Genomic DNA was extracted from PBMC to measure relative telomere length (rTL) by quantitative real-time polymerase chain reaction according to the modified Cawthon protocol. Baseline demographic data and 1-year mortality were obtained from electronic patient records.

Results: A total of 336 patients (125 patients on HD, 114 patients on PD and 100 healthy controls) had their baseline rTL measured between the period of December 2015 to July 2018. Inter assay CV for rTL assay was 4.86%. Mean age of the dialysis cohort was 54.3 with an age range between 23-83 years. Mean age of control cohort was 44.5 with an age range between 20-75years. There were 87 and 56 females in the dialysis and control cohort respectively. Age was significantly associated with TL in a multivariate regression model in both the dialysis ($p<0.001$) and control group ($p<0.001$). There was no significant difference in mean TL between gender in the healthy cohort in our study p=0.778. However, mean TL was higher in females than in males among dialysis patients, p=0.007. Mean TL of control and dialysis group was 2.23 ± 0.33 and 2.11 ± 0.34 respectively. The difference in TL between the groups was significant, p=0.006. However, a multivariate analysis of TL adjusted for age and gender was not significant, p=0.875. This was due to the control cohort consisting of younger recruits in comparison to the dialysis cohort. TL was not significantly different between HD and PD patients. There were 10 deaths in 365 days with no loss of follow up throughout the study period. All the deaths were in the dialysis cohort. There was no significant association found between TL and mortality outcomes but the direction of effect i.e shorter TL was associated with increased risk of death.

Conclusion: This study failed to show any difference between TL between dialysis patients and controls to demonstrate that patients on dialysis age faster. This does not preclude current evidence suggesting that dialysis patients do have an accelerated ageing in comparison to healthy cohort but merely that our study has shown that TL may not be the ideal biomarker of ageing to demonstrate this difference. In fact, increasing animal studies have found that the rate of change in TL over a period of time is a better representation of ageing. The study also identified no association between TL and 1-year mortality as there were only 10 deaths within the 1 year of follow up. This may be largely due to a short duration of follow up and it may be interesting to evaluate TL and 5-year mortality data in this cohort in future.

P1440

ASSOCIATION BETWEEN THE USE OF DRUGS FOR CONSTIPATION AND MORTALITY IN HEMODIALYSIS PATIENTS; FROM JAPAN-DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY (J-DOPPS)

Seiji Itano[1], Yu Honda[2], Eiji Kubo[3], Yosuke Yamada[4], Tatsuyoshi Ikenoue[5], Miho Kimachi[6]

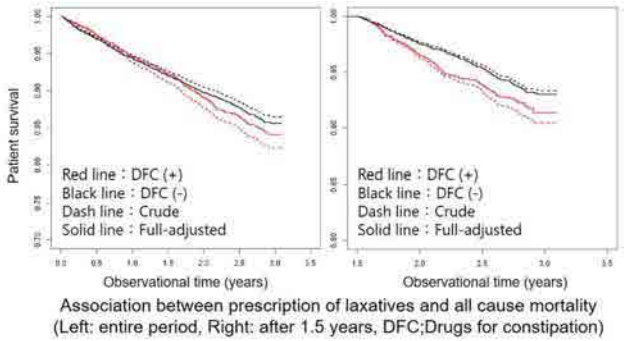
[1]Kawasaki Medical School, Department of Nephrology and Hypertension, Kurashiki, Japan, [2]The Jikei University School of Medicine, Division of Nephrology and Hypertension, Department of Internal Medicine, Tokyo, Japan, [3]Ageo Central General Hospital, Department of Nephrology, Ageo, Japan, [4]Shinshu University School of Medicine, Department of Nephrology, Matsumoto, Japan, [5]Kyoto University Graduate School of Medicine, Human Health Science, Kyoto, Japan and [6]Kyoto University Graduate School of Medicine, Department of Healthcare Epidemiology, Kyoto, Japan

Background and Aims: Hemodialysis patients have a high prevalence of constipation related to medication use, water restriction, insufficient dietary fiber intake, and reduced physical activity. Thus, these patients use drugs for constipation (DFC) more than five times that used by healthy individuals. In hemodialysis patients, two pathological factors, namely, reduced defecation function and DFC use itself, occur. These factors could be related to deteriorating life prognosis resulting from altered intestinal microbiota, gastrointestinal complications, or declining quality of life. In the general population, some reports have suggested that constipation and DFC use are risk factors of coronary artery disease, cardiovascular death, or all-cause death. However, whether such risk factors are appropriate for hemodialysis patients has not been clarified. This study aimed to investigate the association between DFC use and risk of death in hemodialysis patients.

Method: In this prospective cohort study based on the Japan-Dialysis Outcomes and Practice Patterns Study (J-DOPPS), we used J-DOPPS phase 1-5 (1998-2015) data. Hemodialysis patients enrolled in the J-DOPPS whose dialysis vintage was >3 months (n=12,217) were divided into two groups according to usage (DFC group;n=3,721) and non-usage (non-DFC group;n=8,496) of DFC. The primary endpoint was all-cause death. Secondary endpoints were deaths from infection, malignancy, and cardiovascular causes. Hazard ratio (HR) was calculated using multilevel Cox regression analysis with facility level. Potential confounders were adjusted by the inverse probability of treatment weighting using the propensity score. Rubin's rule was used for combined data. Sensitivity analysis was conducted using instrumental variable method to assess the effect of unmeasured confounders. Missing data were imputed using multilevel multiple imputation repeated 20 times.

Results: DFCs were prescribed in 30.5% of patients at baseline. Over a median follow-up of 730 [418, 974] days, 1,240 deaths from any cause were noted. Overall data were analyzed first. Although DFC use was associated with increased mortality risk (adjusted HR, 1.12; 95% confidence interval [CI] 1.03, 1.21), proportional assumptions were not met (Figure). Then, we only analyzed data of patients with observation period >1.5 years. In this study, 8,345 patients had an observation period >1.5 years, DFCs were prescribed in 31.0% of patients at baseline, and 389 patients died from any cause. Marked difference was observed after 1.5 years from baseline (adjusted HR, 1.35; 95% CI, 1.17, 1.55). Risks for deaths from infections (adjusted HR 1.62; 95% CI 1.14, 2.29) and malignancy (adjusted HR 1.60; 95% CI, 1.08, 2.36) were higher in the DFC group, but no difference in cardiovascular death risk was found (adjusted HR 1.11; 95% CI, 0.91, 1.36).

Conclusion: In hemodialysis patients, DFC use was associated with an increased risk of death. Thus, it may be important to manage defecation habit without using DFC by modulating intake of dietary fibers, exercise, or use of medications that are less likely to cause constipation.



Association between prescription of laxatives and all cause mortality
(Left: entire period, Right: after 1.5 years, DFC;Drugs for constipation)

Figure:

P1441 **SURVIVAL AND RESIDUAL KIDNEY FUNCTION IN HEMODIALYSIS PATIENTS TREATED WITH HIGH DOSES OF FUROSEMIDE. A PROSPECTIVE LONG TERM STUDY**

Esteban Siga[1], Romina Alcuaz[2], Eduardo Nozzi[2], Eugenia Melon Gil[2], Nora Vivas[1], David Aiziczon[1]

[1]Dialisis Madariaga, Hemodialysis, General Juan Madariaga, Argentina and [2]General Juan Madariaga, Internal Medicine, General Juan Madariaga, Argentina

Background and Aims: Many patients (PTS) starting dialysis have significant residual kidney function (RKF), with 45 % having an estimated glomerular filtration rate $\geq$10 mL/min/1.73 m2 . Preservation of this residual kidney function has been associated with improved outcomes, and nephrologists should try to preserve this residual kidney function as long as possible. In this setting, furosemide (FURO) could play an important role but there are no guidelines for its use and, given the need of high doses, there are safety concerns which limit its use. Besides, its long term utility has not been established. In this study, our first aim was to determine an effective and safe dose for incident PTS; and the second was to evaluate its effects on the RKF in the first year and the survival of these PTS in the long term.

Method: *Protocol I:* cross-over, single blind study, consisting of three weekly periods. During the first week (W1), after signing an informed consent, PTS were randomly assigned to receive 250 (F250) or 500 (F500) mg.of oral FURO once a day. W2 was a washout period and patients received placebo (F0). During the third week, the remaining dose was prescribed. At the end of each W, total urinary volume and Natriuresis of 24 hours was measured. All Capsules were identical, made by the Hospital's Pharmacist, and PTS were not aware of their content.

Protocol II: prospective, open label, long term study. Daily diuresis was measured In all Incident PTS from 01/01/11 to 01/06/19. Those PTS with daily diuresis lower than 200 ml. were the control sample. Those with higher than 200 ml.day, after signing an informed consent, received 500 mg. of oral FURO once a day. At the beginning and the end of the FURO period, 24 hours diuresis was colected to measure volume and Na, K y P. In some PTS, Beta 2 seric microglobulin (B2M) was also measured. All PTS (n = 101) were followed until their obitus, or were censored by transplant, change of centre or completion of the follow up period = 4 years.

Results: P*rotocol I*: n= 34. Basal diuresis (F0) was 970 ml.day. Effect of F250 and F500 on diuresis was similar. Both increased 24 hs urinary volumen by 30%. By contrast, the increase of Sodium excretion was significantly higher with F500 than with F250: 56 vs 7%, P =0.000

Protocol II: The table shows the long term effect (11.8 +/- 4.7 months) of 500 mg. once a day of oral FURO in *33* incident PTS (8 DBT, 8 women). Data are presented as median and interquartil range (IR).

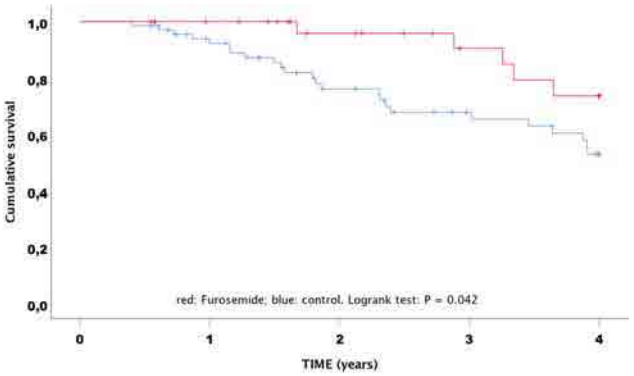
	Volumen	Sodium	Phosphorus	Potasium
Basal Urine	1180 ml	95 mEq	175 mg	32 mEq
	865-1710	68-180	120-278	17-41
Final Urine	1050 ml	123 mEq	140 mg	26 mEq
	699-1665	71-198	100-197	14-39

In the first year of HD, FURO was able to maintain the basal diuresis and the median excretion of P. Noteworthy, Natriuresis increased by 29%. Seric B2M was asociated with diuresis: r = -0.59, and was significantly lower than B2M measured in control PTS: 36.7 vs. 48.1 mg.dl (P = 0.011).

FURO and Control PTS were followed up to four years. Kaplan Meier analisis (Figure) ilustrated that survival in FURO PTS was 96, 90,5 and 73,5 % at 2, 3 and 4 years, respectively, whereas In control PTS it was 76, 65 and 53 %. (P = 0.042, logrank test).

Four PTS stopped FURO ingestion before six months and were excluded. One due to cramps and three by cutaneous manifestations. All symptoms remitted when Furosemide was suspended. No patient reported hearing impairments

Conclusion: Results of this long term prospective study suggest that Furosemide is effective to maintain RKF in the first year of HD, without major adverse effects. Furthermore, survival was significantly higher in those PTS that ingested Furosemide



Figure

P1442 **CAN THE ASSESSMENT OF ULTRASOUND LUNG WATER IN HEMODIALYSIS PATIENTS BE SIMPLIFIED?**

Claudia Torino[1], Rocco Tripepi[1], Maurizio Postorino[2], Giovanni Luigi Tripepi[1], Charalampos Loutradis[3], Panteleimon Sarafidis[4], Francesca Mallamaci[2], Carmine Zoccali[1]

[1]CNR, IFC, [2]GOM Bianchi-Melacrino-Morelli, Nephrology Unit, Reggio Calabria, Italy, [3]University Hospital of Birmingham and [4]Aristotle University of Thessaloniki

Background and Aims: Lung Ultrasound (US) reliably estimates lung water and it is increasingly applied in clinical practice in dialysis patients. Lung water is currently measured by applying a semi-quantitative US score summing up the US-B lines (an equivalent of B lines in standard X-rays of the thorax) detected in 28 lung intercostal spaces (LIS) (Jambrik Z et al., Am J Cardiol 2004; 93:1265-70). A simplified assessment restricted to 8 LIS only (Gutierrez M et al., Arthritis Research & Therapy, 2011;13:R134) has been proposed. However, the agreement among this simplified score and the reference score has not been studied and the prognostic value of the simplified score (8-LIS) has not been face to face compared with the 28-LIS score.

Method: We included in the analysis in a cohort of 303 hemodialysis (HD) patients in which the pre-dialysis US-BL score was measured at baseline with both the semi-quantitative by Jambrik and the simplified Gutierrez method. The time needed for performing the 28-LIS and the 8-LIS score by six independent assessors with various experience -from low to high- on lung US assessment was accurately measured and recorded. Patients were divided into 4 categories, according to pre-established cut-offs specific for the two methods (28-LIS score: <5; 6-15; 16-30; >30 US-BL; 8-LIS score: <10; 11-20; 21-50; >50 US-BL) The prediction power of these scores for death and fatal and non-fatal cardiovascular events was assessed by the explained variance (R2).

Results: The 28-LIS score and the 8-LIS score were highly inter-related (Spearman's $\rho=0.93$, $P<0.001$). During a mean follow-up of 3 years, 112 patients died and 129 experienced a CV event. At univariate and multivariate analysis, both scores were associated to the study outcomes (Tab.1). The explained variance (R2) of the 28-LIS score for death was 4.1% and that for CV events 4.6%. The corresponding R2 of the 8-LIS score were 5.4% (death) and 4.7%, (CV events), to values close to those of the 28-LIS score. Accordingly, when the two scores were separately added to a clinical model including easily available clinical variables (age, gender, smoking, diabetes, cardiovascular comorbidities, cholesterol, arterial pressure, BMI, anti-hypertensive treatment, NYHA class as well as dialysis vintage, hemoglobin, albumin, phosphate and CRP) the R2 of the model including the 28-LIS score (death: 31.1%; CV events: 23.9%) were again very similar to those of the 8-LIS score (30.7% and 23.1%, respectively). The median time needed to perform the examination was 3:05 min (IQR 2:22 – 5:00 min) for the 28 LIS score and 1:35 min (IQR 1:16 – 2:00 min) for the 8 LIS score.

Conclusion: The simplified Gutierrez 8-LIS score is tightly related to the classical Jambrik 28 LIS score and the two scores hold an almost identical predictive power. Even though the 28-LIS score demands less than 5 minutes, the 8-LIS score can be done in only about 90 sec. and it is therefore better suited for application in everyday clinical practice in hemodialysis units.

Tab.1 Cox Regression analysis showing the association of semi-quantitative and simplified score with the considered outcomes

	Univariate analysis HR (95%CI), P	Multivariate analysis HR (95%CI), P
Outcome: death		
Semi-quantitative score	1.24 (1.04-1.47), P=0.01	1.23 (1.02-1.49), P=0.03
Simplified score	1.38 (1.12-1.69), P=0.002	1.33 (1.06-1.67), P=0.02
Outcome: CV events		
Semi-quantitative score	1.26 (1.07-1.47), P=0.004	1.23 (1.03-1.46), P=0.02
Simplified score	1.34 (1.11-1.62), P=0.002	1.23 (1.00-1.52), P=0.05

Figure:

P1443 **USE OF WRIST-BASED MONITORING DEVICE AMONG HEMODIALYSIS PATIENTS - A FEASIBILITY STUDY**

Maggie Han[1], Priscila Preciado Rojas[1], Ohnmar Thwin[1], Xia Tao[1], Leticia Tapia[1], Lemuel Rivera-Fuentes[1], Mohamad Hakim[1], Amrish Patel[1], Nadja Grobe[1], Stephan Thijssen[1], Peter Kotanko[1,2]

[1]Renal Research Institute, Research Department, New York, United States of America and [2]Icahn School of Medicine at Mount Sinai, Nephrology, New York, United States of America

Background and Aims:

Pervasive sensing technologies allow healthcare providers to gain additional insights into patient's status outside the clinical setting. In order to adopt widespread use of remote monitoring devices we must first study the feasibility of their use. We aim to quantify how long patients will use a wearable device before requiring an intervention to maintain the use of the device.

Method:

In-center hemodialysis (HD) patients were enrolled from 4 clinics in New York City starting in May 2018 and followed for a period of up to 1 year. Patients $\geq$18 years, on HD $\geq$3 months, able to walk, owning a smartphone, mobile tablet or PC were enrolled. They were provided with a wrist-based monitoring device (Fitbit Charge 2). Participants were instructed on how to use the device, and sync data to their smartphone, mobile tablet, or PC. If a patient failed to sync data for 7 consecutive days, a text message or email reminder was sent from the research staff. We evaluated time to first notification using Kaplan Meier time-to-event analysis. Predictors of time to first intervention was assessed via univariate Cox Regression. Patients were censored at the end of the observation period (January 6, 2020). Socio-economic parameters such as living situation, marriage status, employment status, race, and education level were collected at the beginning of the study.

Results:

125 patients were enrolled into our study. 7 patients were screen-failed after enrollment. At enrollment patients were 54$\pm$12 years old with a dialysis vintage of 5.6$\pm$5.8 years. 37% lived alone, 56% were single, 59% unemployed, 64% were African-American, and 42% had an education level of some college or higher. 82% of the patients required a text message reminder to continue wearing/syncing the device. Mean and median time to first reminder were 101 days (95% CI 80 to 123) and 50 days (95% CI 35 to 70 days), respectively. The probability of being on the study without intervention is shown in Figure 1. Predictors of time to first intervention were chosen a priori and included gender, age, living situation, and education level. None of these parameters were significant predictors of time to first intervention.

Conclusion:

We found that most patients will require at least some intervention or counseling to maintain the use of a wrist-based wearable device for remote patient monitoring. While most patients require an intervention before approximately 2 months into wear, the patients who can maintain use independently after that point are likely to do so for longer.

Figure 1. Kaplan Meier curve of time to first intervention

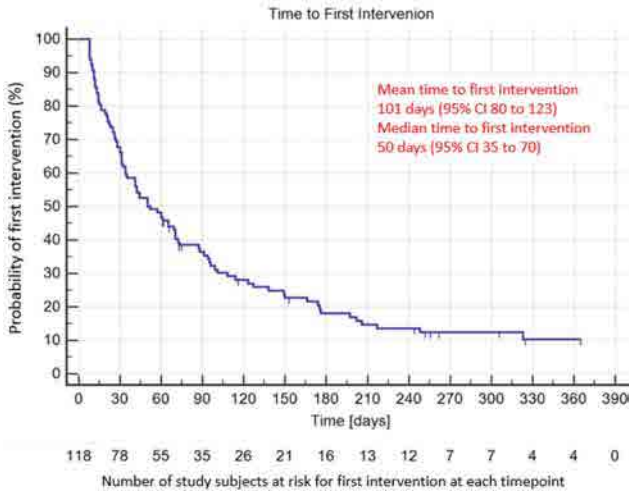


Figure:

P1444 CHANGES IN TREATMENTS AND OUTCOMES OF PATIENTS INITIATING PERITONEAL DIALYSIS DURING THE LAST 10 YEARS: DATA FROM SWEDISH RENAL REGISTRY

Hong Xu[1], Juan Jesus Carrero[2], Bengt Lindholm[3], Maria Stendahl[4], Helena Rydell[5], Marie Evans[5]

[1]Karolinska Institutet, Div of Clinical Geriatrics, Dept of Neurobiology, Care Sciences and Society, Stockholm, Sweden, [2]Karolinska Institutet, Dept of Medical Epidemiology and Biostatistics, Stockholm, Sweden, [3]Karolinska Institutet, Renal unit and Baxter Novum, CLINTEC, Stockholm, Sweden, [4]Ryhov County Hospital, Dept of Internal Medicine, Jönköping, Sweden and [5]Karolinska Institutet, Renal unit, CLINTEC, Stockholm, Sweden

Background and Aims:

The recent years have witnessed several therapeutic improvements regarding both peritoneal dialysis (PD) treatment itself and the prevention and management of complications. We evaluated trends in implementation of therapeutic improvements and their relationship with survival and other relevant clinical outcomes in PD patients from Sweden.

Method:

Using the Swedish Renal Registry (SRR), clinical data from all patients initiating PD in Sweden between 2006 and 2015 were linked to other national healthcare registries to obtain information on vital status, hospitalization and diagnoses during in and outpatient care, along with information on all dispensed drugs, from inclusion to the end of 2017. We first evaluated trends in the use of PD-related treatments and of selected key medications within 2-year blocks. We then evaluated the incidence of death, major cardiovascular events (MACE), technique failure, transplantation and peritonitis episodes within one and two years from PD initiation using standardized incidence rates via logistic regression to account for differences in patient characteristics over time. In subsequent Cox regression models, we studied whether adjustment for implementation of these therapeutic changes modified observed trends in clinical outcomes. Finally, patient survival was compared against the age-sex matched general Swedish population using standardized incidence ratios (SIR).

Results:

3,312 patients (mean age 63±15 years; 34% women) initiated PD in Sweden during the study period. Across 2-year time blocks, there was no difference over time in the distribution of age, sex or comorbidities with the exception of an increased proportion of patients with chronic pulmonary disease. The proportion of patients undergoing automated peritoneal dialysis and using icodextrin increased over time, while mean standard Kt/V and weekly creatinine clearance did not change. The use of non-calcium phosphate binders, cinacalcet and calcium-channel blockers increased, and the use of angiotensin-converting enzyme inhibitors /angiotensin receptor blockers, erythropoietin, iron, and calcium supplements showed decreasing trends.

After standardization for differences in demography and comorbidities, the one-year incidence of peritonitis decreased by 13% and the rate of kidney transplantation increased by 52% in 2014/15 compared to 2006/07. The rates of death, MACE or technique failure did not show differences over time. Similar results were observed with 2-years of follow up and when applying Cox models; Per 2-year period, the risk of peritonitis within one year decreased by 8% (HR 0.92, 95% CI 0.87-0.98) regardless of age, sex, comorbidity and the abovementioned therapeutic changes. The risk of death for PD patients was in 2006/2007 4 times higher [SIR 4.08 (3.15–5.29)] and in 2014/15 3.7 times higher [SIR 3.65 (2.70–4.94)] than the general population, corresponding to a reduction of SIR by 11%.

Conclusion:

During the last 10 years, there has been a gradual implementation of new and established evidence-based treatments in patients starting PD in Sweden. Although survival rates are improving compared to the general population, there were no clear differences in the rates of technique failure, MACE or death across PD patients over time. We observed, however, consistent improvements in peritonitis frequency and access to transplantation.

P1445 ESPECIALLY HYPOKALEMIA IS A RISK FACTOR FOR ALL-CAUSE MORTALITY IN INCIDENT HEMODIALYSIS PATIENTS

Esther De Rooij[1,2], Friedo W. Dekker[1], Saskia Le Cessie[1], Johan W. De Fijter[2], Ellen K. Hoogeveen[1,2]

[1]Leiden University Medical Center (LUMC), Clinical Epidemiology, Leiden, Netherlands and [2]Leiden University Medical Center (LUMC), Nephrology, Leiden, Netherlands

Background and Aims:

Both hypo- and hyperkalemia can potentially induce fatal cardiac arrhythmias in the general population. However, little is known about the effect of potassium as a modifiable risk factor in hemodialysis (HD) patients. Therefore, we investigated the relation between serum potassium level and all-cause mortality in incident HD patients and whether there is an optimum serum potassium level to pursue.

Method:

All incident HD patients (>18 y) from the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD), a prospective multi-center cohort study, were included. These patients were followed from the start of their first dialysis treatment until death, transplantation or a maximum of 2 years. Serum potassium levels were obtained at fixed 6-month time intervals and divided into six categories: ≤ 4.0, > 4.0 - ≤ 4.5, > 4.5 - ≤ 5.0, > 5.0 - ≤ 5.5 (reference), > 5.5 - ≤ 6.0 and > 6.0 mmol/L. Using a Cox proportional-hazards model with serum potassium category as a time-dependent variable, hazard ratios (HR) for all-cause mortality were calculated, adjusted for baseline age, sex, current smoking, diabetes and residual kidney function.

Results:

In total, 1278 HD patients were included. At baseline, mean ($\pm$SD) age was 64 ($\pm$14) years, 60% were men, 23% were current smokers, 21% had diabetes and the median (interquartile range) residual kidney function was 3.0 (1.5-4.8) ml/min/1.73m^2. Mean ($\pm$SD) serum potassium level was 4.8 ($\pm$0.8) mmol/L. The prevalence of the six potassium categories was: 10%, 19%, 26%, 22%, 15% and 8%, respectively. A total of 298 (23%) deaths was observed during 2 years of follow-up. After multivariable adjustment the HR (95% CI) for any death according to the six potassium categories were: 2.5 (1.5-4.3), 1.9 (1.2-3.0), 1.6 (1.0-2.5), 1 (reference), 1.3 (0.8-2.2) and 1.7 (1.0-3.0).

Conclusion:

We found a U-shaped relation between serum potassium and all-cause mortality in incident hemodialysis patients. Especially, low serum potassium was a 2.5-fold stronger risk factor for all-cause mortality compared to normal serum potassium. Our results indicate an optimum serum potassium level between 5.0 - 5.5 mmol/L, emphasizing that potassium lowering therapy should be used with caution in hemodialysis patients.

P1446 DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS IN PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS

Masamitsu Ubukata[1], Masaki Hara[1], Hiroki Suzuki[1], Rin Asao[1], Yuya Nakamura[1], Masayuki Nakamura[1], Kosaku Nitta[2], Isao Ohsawa[1], Yoshikazu Goto[1], Hiromichi Gotoh[1]

[1]Saiyu Soka Hospital, Department of Internal Medicine, Saitama, Japan and [2]Tokyo Women's Medical University, Department IV, Internal Medicine, Tokyo, Japan

Background and Aims: Diffuse idiopathic skeletal hyperostosis (DISH) is an idiopathic degenerative disease characterized by ossification of spinal ligaments and entheses, especially in the anterior longitudinal ligament. The ankylosed spine is prone to fracture with minor trauma and may result in spinal cord injury. It is usually asymptomatic and often diagnosed incidentally by computed tomography or other imaging methods. Several reports have revealed DISH as a risk factor for stroke, cardiovascular disease, and metabolic disorders, such as diabetes mellitus, hyperinsulinemia, obesity, dyslipidemia, and hyperuricemia. However, there are few reports of DISH in patients with end stage kidney disease (ESKD) requiring hemodialysis. Epidemiology, etiology and risk factors of DISH in patients with ESKD are unknown. We aimed to examine the prevalence and predictors of DISH in maintenance hemodialysis patients.

Method: This was a case-control study using patients who received maintenance hemodialysis in our hospital in December 2018. The prevalence of DISH at enrollment was evaluated according to Resnick and Niwayama criteria by computed tomography (CT). The criteria is defined as follows: (1) Flowing ossification along the anterolateral aspect of at least four contiguous vertebral bodies, (2) Relative preservation of intervertebral disc height in the involved segment, (3) Absence of apophyseal joint bony ankylosis and sacroiliac joint erosion. We excluded patients who could not receive chest CT or with a history of thoracic spine surgery. Fisher exact tests were used to evaluate the relationships between categorical variables, and Kruskal-Wallis or Mann-Whitney U tests were used to evaluate continuous variables. We performed logistic regression analyses to identify variables that had a statistically significant association with DISH, as measured by the estimated odds ratio (OR) with the 95% confidence interval (CI).

Results: A total of 395 consecutive patients were treated with maintenance hemodialysis in our hospital in December 2018. After excluding 4 patients who could not receive chest CT and 2 patients with a history of thoracic spine surgery, the remaining 389 patients were analyzed. The median age was 70 years, and 61.2% of patients were men. One hundred and twenty-three (31.6%) patients were diagnosed with DISH. We assigned them to the DISH group and other 266 patients to the control group. The patients with DISH were significantly more likely to have advanced age, male sex, high body weight, high bone mineral density, prior vertebral fracture, and diabetic nephropathy. Multivariate analysis showed that having DISH was significantly associated with advanced age (OR 1.06, 95%CI 1.03-1.09, $P<0.001$), high bone mineral density (OR1.02, 95%CI 1.00-1.03, P=0.03), prior vertebral fracture (OR3.22, 95%CI 1.23-8.41, P=0.017), diabetic nephropathy (OR 2.00, 1.03-3.90, P=0.041).

Conclusion: The prevalence of DISH in maintenance hemodialysis patients was high. Advanced age, male sex, high body weight, high bone mineral density, prior vertebral fracture, and diabetic nephropathy were identified as a risk factor for DISH. Physicians involved in hemodialysis treatment should be aware of the existence of DISH as one of the comorbidities in the elderly ESKD patients.

P1447

EARLY MORNING ACCELERATION AND NOCTURNAL DECELERATION IN HEART RATE ASSOCIATE WITH LVH AND THE RISK OF DEATH AND CARDIOVASCULAR EVENTS IN HEMODIALYSIS PATIENTS

Francesca Mallamaci[1], Rocco Tripepi[2], Claudia Torino[2], Giovanni Luigi Tripepi[2], Marianna Bellantoni[3], Elvira Puntorieri[1], Rocco Truglia[4], Gaetana Porto[2]

[1]Grande Ospedale Metropolitano, Nephrology, Dialysis and Transplant Unit, Reggio Calabria, Italy, [2]National Research Council, Insitute of Clinical Physiology, Reggio Calabria, Italy, [3] Presidio Ospedaliero Centrale - SS. Annunziata, Nephrology, Taranto, Italy and [4]Azienda Ospedaliero-Universitaria, Policlinico Vittorio Emanuele - Catania, Catania, Italy

Background and Aims: Cardiovascular deaths cluster in the early morning hours and studies in the general population documented that an exaggeration of the early morning increase in BP, a phenomenon accompanied by a parallel rise in heart rate (HR), is a marker of high cardiovascular risk. The circadian profile of BP and HR in hemodialysis patients is notoriously altered but the early morning changes in these parameters and the nocturnal profile of HR have not been investigated in this population.

Method: BP and HR were registered at 15 min intervals by ambulatory monitoring (24hABPM, Spacelab) during the day after hemodialysis in a series of 64 patients. We measured the early morning (the average of the 2 hours after awakening minus the average of the 2 hours pre-awakening) changes in BP and HR and the nocturnal decline in BP and HR and tested the relationship of these parameters with the left ventricular mass index (LVMI) and with the risk of all-cause and cardiovascular death over a median follow up of 40 months (Interquartile range 21-81)

Results: The rise in HR after awakening was strongly related in an inverse fashion with the LVMI (Spearman ρ=-0.61, P<001) suggesting that patients with a more pronounced increase in HR after awakening may be protected from LVH .Both, the decline in HR (ρ =-0.38, P=0.002) and in systolic BP (ρ =-0.31, P=0.01) during night-time associated inversely with LVMI. These associations remained significant also when they were reciprocally adjusted (P<0.01) in a model including also age, gender and simultaneous changes in BP. In contrast, the rise is systolic BP upon awakening had no relationship with the LVMI (ρ =0.18, P=0.18). Thirty-two deaths (16 cardiovascular) occurred during follow up. The early morning rise in HR was an inverse predictor of all cause death (HR=0.95; 95%CI 0.92-0.98 P=0.004) and of cardiovascular death (HR=0.95; 95%CI 0.91-0.98) in analyses adjusted for the simultaneous rise in systolic BP which per se failed to predict the same outcomes. Again, in similarity with analyses looking at LVMI, the nocturnal dipping in HR associated inversely with all cause and cardiovascular death (p=0.003).

Conclusion: The analysis of the nocturnal decline in HR and of the rise in HR increase upon awakening In hemodialysis patients reveals stronger links among these parameters and LVMI than the corresponding BP parameters. The protective effect on the left ventricle of a more pronounced HR rise upon awakening and of a more pronounced decline in HR during night time underscore the relevance of preserved autonomic function for cardiovascular protection in this population. These associations seem to go along with a reduced risk for all-cause and cardiovascular death. Analysis of the HR profile provides unique information for the risk of cardiomyopathy and cardiovascular events in the hemodialysis population.

P1448

FACTORS ASSOCIATED WITH INCREASED MORTALITY AFTER DIALYSIS INITIATION. RESULTS OF THE PERIDIALYSIS STUDY

James G. Heaf[1], Maija Heiro[2], Aivars Petersons[3], Baiba Vernere[3], Johan Vestergaard Povlsen[4], Anette Bagger Sørensen[4], Naomi Clyne[5], Inge Bumblyte[6], Alanta Zilinskiene[6], Else Randers[7], Niels Løkkegaard[8], Mai Ots-Rosenberg[9], Stig Arne Kjellevold[10], Jan Dominik Kampmann[11], Björn Rogland[12], Inger Karin Laegreid[13], Olof Heimbürger[14], Bengt Lindholm[14]

[1]Zealand University Hospital, Roskilde, Denmark, [2]Turku University Hospital, Turku, Finland, [3]P. Stradins University Hospital, Riga, Latvia, [4]Aarhus Univeristy Hospital, Aarhus, Denmark, [5]Lund University and Skåne University Hospital, Lund, Sweden, [6]Lithuanian University of Health Sciencs, Kaunas, Lithuania, [7]Viborg Hospital, Viborg, Denmark, [8]Holbaek Hospital, Holbaek, Denmark, [9]University Hospital of Tartu, Tartu, Estonia, [10]Vestfold Hospital, Tønsberg, Norway, [11]Hospital of Southern Jutland, Sønderborg, Denmark, [12]Kristianstad Hospital, Kristianstad, Sweden, [13]St. Olav University Hospital, Trondheim, Denmark and [14]Karolinska Hospital, Clinical Science, Intervention and Technology, Stockolm, Sweden

Background and Aims: Home dialysis with peritoneal dialysis (PD) or home hemodialysis (HD) has medical and socioeconomic benefits but home dialysis is generally underutilized. While many factors determine choice of initial dialysis modality, starting patients on home dialysis requires timely planning, educational activities and an active program to promote home dialysis. Here we investigated factors including patient suitability, pre-dialysis preparations and institutional factors determining choice of dialysis modality among patients initiating dialysis.

Method: Choice of dialysis modality was investigated in 1588 consecutive patients (age 63.8 ±15.3 years. 35.8% female; diabetic nephropathy 24.4%) participating in the Peridialysis study, a multinational multi-centre prospective study of causes and timing of planned and unplanned dialysis initiation (DI) over a 3-year period in 15 Nordic and Baltic nephrology departments. All dialysis modalities were available and free of charge to patients. All centres offered pre-dialysis education programs to patients with timely referral. Clinical and biochemical data during the pre-dialytic period, centre data, and reasons for DI and choice of dialysis modality were registered.

Results: 516 (32.4%) patients were not offered home dialysis because they were judged to be unsuitable (**384**; 24%): PD was contraindicated in 338 (21.2%) patients - for physical (142; 8.9%), mental (80, 5.0%) or abdominal (116; 7.3%) reasons and HD was contraindicated in 46 (2.9%) patients. In addition, **106** (6.7%) were not offered home dialysis for various reasons; and deaths before modality choice occurred in **26** (1.6%) patients. Factors associated with unsuitability were high age, comorbidity, late referral (risk ratio, RR, 1.9), inflammation (C-reactive protein >50 mg/L (RR 2.6) and rapid loss of renal function (RR 2.0). Patients who were not assessed for home dialysis comprised mainly patients with late referral (RR 5.8) and/or unplanned DI (RR 9.6). Of the remaining **1072** (67.6%) patients, who had a free choice of modality, **700** (65.3%) chose home dialysis, either PD (**661**; 61.7%) or home HD (**39**: 3.6%) while **372** (34.7%) patients chose centre HD. Factors associated with choice of centre dialysis were late referral (RR 1.8), suboptimal DI (RR 2.0), symptomatic uraemia (RR 1.6) and p-urea >30 mM (2.6). Somatic differences between patients choosing home dialysis and centre dialysis were minor. Independent institutional factors reducing information about home dialysis were treatment at a university hospital (RR 4.3) and absence of an active preference for home dialysis, "home dialysis first" policy (RR 3.0).

Conclusion: The results of the Peridialysis study indicate that the incidence of home dialysis could be increased by a "home dialysis first" department policy and by efforts to reduce the incidence of late referrals and unplanned DI. Acutely ill patients and patients with unplanned DI may be candidates for home dialysis if assessment of home dialysis suitability and dialysis educational program are performed after their clinical condition has improved. Given a free choice, most patients (65%) choose home dialysis.

P1449 **MORTALITY RISK ASSOCIATED WITH ACETIC ACID BASED AND CITRIC ACID BASED BICARBONATE HEMODIALYSIS: A HISTORICAL COHORT STUDY**

Luca Neri[1], Francesco Bellocchio[1], Bernard Canaud[1], Stefano Stuard[1], Charles Chazot[1]

[1]*Fresenius Medical Care, Bad Homburg, Germany*

Background. Citric Acid Based Bicarbonate Dialysate (CiD) is increasingly used in hemodialysis to improve hemodynamic tolerance and hemocompatibility associated with Acetic Acid Based Bicarbonate dialysis (AcD). We sought to evaluate the mortality risk associated with different dialysate acidifiers.

Methods: We conducted a multicenter, historical cohort study; all adult incident hemodialysis patients registered in EMEA Fresenius Medical Care network since January 1st 2014 to October 31st 2018 were enrolled. We recorded dialysate acidifier composition for each dialysis session. In the primary analysis (intention-to-treat population), patients were assigned to the exposed group if they received CiD in more than 70% of sessions during the first three months (CiD70%), whereas non-exposed received no CiD at all. In the secondary analysis, exposure was assessed on a monthly basis for the whole duration of the follow up.

Results: We enrolled 10,121 incident patients during the study period. Of them, 371 met criteria for inclusion in CiD70%. After propensity score matching mortality was 11.43 (95%CI: 8.86 - 14.75) and 12.04 (95%CI: 9.44 - 15.35) deaths/100 person-years, in the CiD0% and CiD70% groups respectively (p=0.80). A similar association trend was observed in the secondary analysis.

Conclusions: We did not observe evidence of increased mortality among patients exposed to CiD in a large European cohort of dialysis patients despite physicians were more inclined to prescribe CiD to subjects with worse medical conditions.

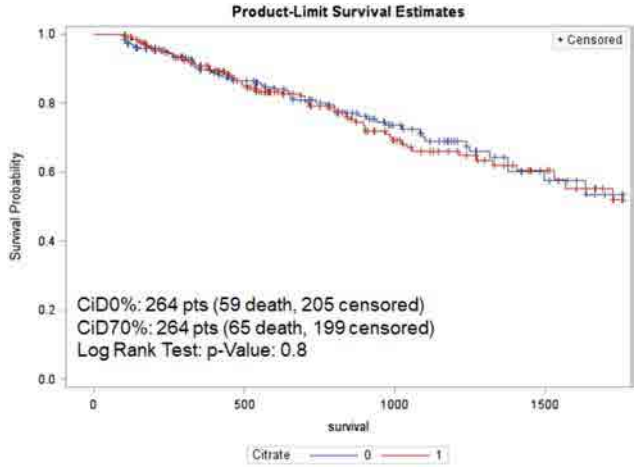


Figure:

P1450 **UREMIC PRURITUS IN MAINTENANCE HEMODIALYSIS PATIENTS: ASSOCIATED FACTORS AND OUTCOME**

Albana Gjyzari (Velaj)[1], Alma Idrizi[1], Alketa Koroshi[1], Margarita Gjata[1], Merita Rroji (Molla)[1], Erjola Lika[1], Denada Haxhiu[1], Myftar Barbullushi[1], Ilirjan Gjyzari[2]

[1]University Hospital Center Nene Tereza, Albania and [2]Health Insurance Institute, Albania

Background and Aims: Uremic pruritus (UP) is a frequent problem in hemodialysis patients. Despite the strong impact in the quality of life, its pathogenesis is not completely understood. Multiple factors are found associated with UP in several studies. The aim of this study was to evaluate the frequency and severity of pruritus in maintenance hemodialysis (MHD) patients, associated factors and outcome.

Method: This observational study was performed between January 2016 and December 2019. A total of 85 adult (age >18 years) MHD patients were included in this study. Data were collected using a questionnaire. The severity of pruritus was scored according to the localization and the disturbance in usual work and sleep during the previous month. Mild: Episodic and localized pruritus without disturbance in usual work and sleep; Moderate: Generalized and continuous pruritus without sleep disturbance; Severe: Generalized and continuous pruritus with sleep disturbance. Some relevant demographic, clinical and laboratory parameters were evaluated. During follow up 2 patients underwent transplantation and 3 patients lost follow up. Mortality was the recorded outcome. We investigated whether demographic, clinical, biochemical parameters and outcome were correlated to UP.

Results: Pruritus was present in 61 % of the hemodialysis patients. Pruritic patients were older: median years 57.5(48.5-66.5) vs. 52(45-59) non pruritic; p=0.046 and male patients were significantly more affected (76.9% male vs. 23.1% female; p=0.015). Pruritic patients had shorter time on HD (mean years 5.2±3.4 vs. 7.8±4.2 non pruritic; p=0.003). The intensity of itching was mild, moderate and severe, in 35.3%, 20% and 5.9% of patients, respectively and severe pruritic patients had a significantly shorter time on HD (3.3±1.7 years; p=0.17). Xerosis was present in 84.6% of pruritic patients vs. 66.7% of non-pruritic; p=0.053. We didn't find association with marital status, level of education, employment, presence of neuropathy, history of atopy, Diabetes Mellitus (DM). Urea redaction ratio (URR) was significantly lower in our pruritic patients: median 67(63-71) vs. 72(66-74) non-pruritic; p=049. Among biochemical parameters phosphorus (mg/dl) was significantly higher between pruritic patients: median 5.6(5.0-6.6) vs. 5.0(3.9-6.0) non-pruritic; p=0.051.

Univariate logistic regression analysis showed significant factors associated with UP: male gender OR=3.1, 95% CI: 1.2-8.0, p=0.017; time on HD OR=0.8, 95% CI: 0.73-0.95, p=0.006; phosphorus level OR=1.4, 95% CI: 1.0-2.0, p=0.034. Multivariate logistic regression analysis adjusted for confounders (age, DM) identified as independent factor associated with UP: male gender OR=3.9, 95% CI: 1.3-11.7, p=0.017 During 4 years follow up 29 (36.3%) patients died. Cox Regression analysis showed moderate pruritus as independent factor for mortality (64.7% dead vs. 35.3% survived within moderate pruritic patients) OR=3.2, 95% CI: 1.4-9.0, p=0.027 (fig. 1).

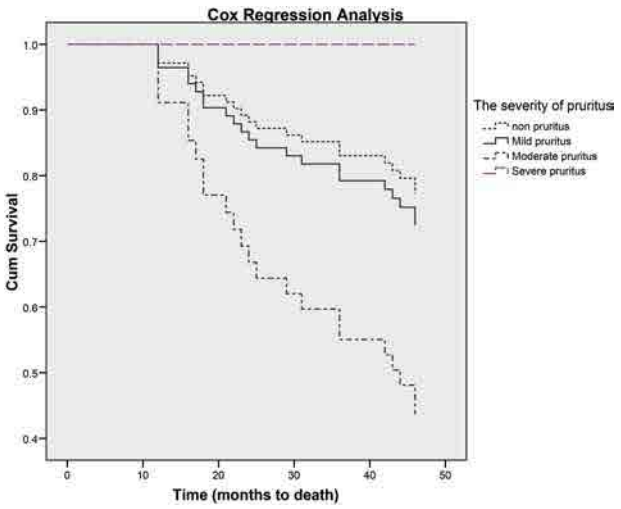


Figure:

Conclusion:

UP was a frequent complication in the first years of MHD patients and associated with a worse outcome. A multidimensional approach should be adapted for pruritic MHD patients. Data regarding the possible risk factors of male pruritic MHD patients must be followed closely.

P1451

MONOCYTE/NEUTROPHIL: LYMPHOCYTE RATIO, C-REACTIVE PROTEIN IN THE LAST YEAR BEFORE DEATH IN DIFFERENT VINTAGE GROUPS - RESULTS FROM THE MONDO INITIATIVE

Xiaoling Ye[1], Rupert Bright[2], Kevin Woollard[2], Charles Dickson Pusey[2], Neill Duncan[2], Peter Kotanko[1,3]

[1]Renal Research Institute, New York, United States of America, [2]Imperial College Renal and Transplant Centre, London, United Kingdom and [3]Icahn School of Medicine at Mount Sinai, Nephrology, New York, United States of America

Background and Aims:

Both experimental and clinical evidence have indicated the relationship between chronic inflammation and adverse outcomes in dialysis patients. It is also well know that higher white blood cell counts and their subtypes including monocyte and neutrophil counts, as well as higher neutrophil to lymphocyte ration (NLR) and monocyte to lymphocyte ration (MLR), and C-reactive protein (CRP) are related to inflammation, and higher risk of access failure, hospitalizations and death in dialysis patients. However, little has been done to explore the characteristics for each of these markers for patients with different dialysis vintage in a large sample of cohorts.

Method:

Four time periods were identified: a) acute phase - patients who died within the 1 years on dialysis, b) early-stable phase - patients who died within the 2nd year on dialysis, c) mid-stable phase – died on the 3rd year on dialysis, and 4) late-stable phase – died on the 4th year on dialysis. All-cause mortality was recorded during the 4 studied periods. Patients with at least one monocyte count, neutrophil count, and lymphocyte count during each of the study period were included. Cubic spline functions were applied to plot the trends of neutrophil counts, monocyte counts, lymphocyte counts, MLR, NLR and CRP with month 0 being the month of the event death and counting backward until the 12 months preceding to death for the 4 studied phases. Rate of change functions were also built to study the accelerating and decelerating changes of the trends within the 12 months preceding death for each of the inflammatory markers.

Results:

A total of 2,504 patients were included in acute phase analysis; 1,696 in the early-stable phase analysis, 1,462 patients in the mid-stable analysis, and 1,305 patients in the late-stable phase analysis (Figure 1). The rising trends in NLR and MLR started to happen around 6 months before patient death with a dramatic acceleration approximately 3 months before death. This is accompanied by a rise in CRP. There is an apparent ordered inflammatory response with dialysis vintage with trends being more marked in acute phase patients versus late-stable phase patients (Figure 2). Patients who died within the 1st year on dialysis had the highest neutrophil and monocyte counts, lower levels of lymphocyte count, and consequently higher levels of NLR and MLR in all months preceding to death.



Figure 1:

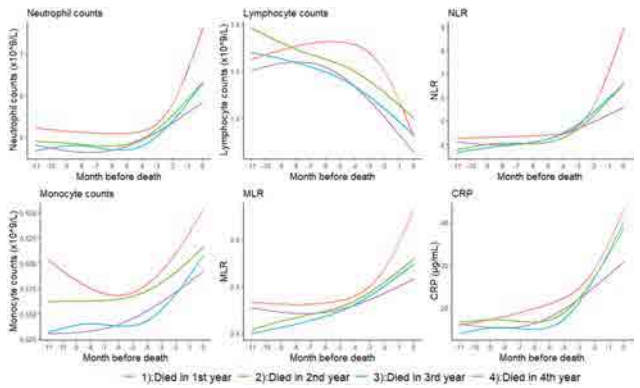


Figure 2: Conclusion:

The consistent observation of this large observational study that all the inflammatory markers show a similar trajectories in the 6 months anticipating death is remarkable. There is an apparent ordered inflammatory response by era across 4 dialysis vintage groups (acute, early-stable, mid-stable and late-stable phases) which might indicate a pathogenic role for these cell types or be an observed epiphenomena related to survivor advantage for example. This is the first detailed description of increased neutrophil and monocyte counts and notably decreased lymphocyte counts several months before death and possible mechanisms are under investigation.

P1452 **PATIENT SURVIVAL ON HOME DIALYSIS MODALITIES**

Wisam Bitar[1], Jaako Helve[1,2], Virpi Rauta[1], Eero Olavi Honkanen[1], Patrik Finne[1,2]

[1]University of Helsinki and Helsinki University Hospital, Nephrology, Helsinki, Finland and [2]Finnish Registry for Kidney Diseases

Background and Aims:

Many studies have compared survival of patients on peritoneal dialysis and hemodialysis, but knowledge on survival differences between various types of home dialysis is limited. Therefore, our study aimed to assess the associated survival in CAPD, APD and home HD.

Method:

During 2004 to 2017, 1640 patients aged 18 years or older started RRT in Helsinki University Hospital. Patients who were on one of the home dialysis modalities at 90 days (n=536), have been studied. The follow up endpoint was either death or the end of 2019. A research database was established and extensive data were systematically collected from the patient files, comprising 35 different comorbidities, laboratory results, primary renal disease, and renal replacement therapy-related factors. Study design was intention-to-treat, and patients were analyzed in the home dialysis modality group they were at 90 days after onset of RRT. Patient survival was compared between patients on CAPD, APD, and home HD using Kaplan-Meier curves and Cox regression.

Results:

Characteristics of home HD and APD patients at the start of dialysis and proportion of patients who received a kidney transplant during follow-up were similar (Table), whereas patients on CAPD had higher median age, more comorbidities, and received a kidney transplant less frequently. The probability of surviving 5 years was 56% for CAPD, 88% for APD, and 90% for home HD patients (Figure). Relative risk of death associated with APD was 0.96 (95% CI 0.60–1.5), and that of CAPD was 3.7 (2.4–5.7) as compared to home HD. After adjustment for age and number of comorbidities, the relative risks were 0.82 (0.39–1.7) and 2.5 (1.2–5.0), respectively. Additional adjustments for other possible confounding factors listed in the Table did not change the results. Censoring for kidney transplantation did not alter the conclusion.

Conclusion:

APD and home HD patients had similar characteristics and comparable survival. CAPD patients were older, had more often comorbid conditions, and their prognosis was worse even after adjustment for confounders.

Table: Patient characteristics

Home dialysis modality	CAPD	APD	Home HD
Number of patients	162	229	145
Median age (years)	65	50	50
At least 3 comorbidities (%)	65	56	56
Transplantation received (%)	37	73	81
S-Albumin (g/L)	35.9	35.7	36.0
B-Hemoglobin (g/L)	114	111	109
Body mass index (kg/m^2)	25.8	24.9	26.4

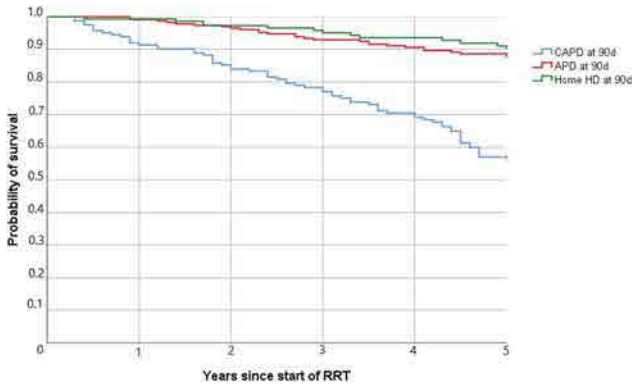


Figure: Patient survival according to home dialysis modality

P1453 **THE DEVELOPMENT OF A NEW PATIENT-REPORTED OUTCOME MEASURE TO EVALUATE THE QUALITY OF DIALYSIS THERAPY**

Ikuto Masakane[1], Minoru Ito[2]

[1]Yabuki Hospital, Global CKD Management Division, Yamagata, Japan and [2]Yabuki Hospital, Department of Nephrology and Dialysis center, Yamagata, Japan

Background and Aims: There is a growing interest in Patient-Reported Outcome Measures (PROMs) as evaluation tools of medical care globally, including dialysis therapy. We developed our original PROM for patients undergoing maintenance hemodialysis (MHD), which was named the Ai-POD (Ai means love in Japanese, POD stands for Patients Oriented Dialysis). The Ai-POD is composed of 20 items relating to physical symptoms (joint pain, itching, frustration, weakness, shortness of breath, constipation, difficulty getting to sleep, asleep condition), complaints during dialysis therapy (pain of cannulation, headache, drop of blood-pressure, leg crumps, fatigue after dialysis session), dietary conditions (appetite, food enjoyment, sore or dry mouth), mental health (depressive feeling, life enjoyment) and comprehensive life satisfaction. All items are rated on a Likert scale from 0 (best) to 4 (worst) except mental health. The mental health questions are yes-no closed questions converting 0 (excellent) or 4 (bad). The sum of all 20 components ranges from 0 to 80, denoting increasing of severity. We have been collecting the data of Ai -POD from all patients in our facilities for over ten years. We examined the associations between the score of Ai-POD and prospective mortality in our patients undergoing hemodialysis therapy to assess the usefulness of the Ai-POD score.

Method: Three hundred ninety-six patients (262 men, 134 women; age 66 ± 12years) on MHD therapy for at least three months were evaluated with Ai-POD in October 2013 and followed up for three years. We categorized the patients into the four groups according to the quartile of the Ai-POD score and compared anthropometric measurements and laboratory measurements among the groups. The four groups are as below: Grop1 (Score: 0 ∼ 10), Group 2 (11 ∼18), Group 3 (19 ∼29), and Group 4 (29 ∼). A Cox regression analysis was used to evaluate the association between the severity of the Ai-POD score and mortality risk adjusting with several factors. Kaplan-Meire analysis and Log-rank test assessed the mortality rate for comparison among the four groups.

Results: The average of Ai-POD score of all patients was 19.6 ± 11.7, following a normal distribution. Among the four quartile groups, we found no differences in age, dialysis vintage and diabetes ratio, but found the statistic difference in gender ratio and serum-albumin. Compared with Group 1, the multivariable-adjusted hazard ratio for mortality was significantly increased to 2.51 (95% CI 1.03 – 7.02) and 3.00 (95% CI 1.25 – 8.46) in Group 3 and Group 4, respectively. Kaplan-Meier analysis showed higher mortality in Group 3 and 4 (16.7% and 19.1% respectively) compared with Group 1 and 2 (5.6% and 6.5% respectively) significantly (p=0.0033) (Figure). Subanalysis with each Ai-POD item indicated that frustration, appetite, food enjoyment, and overall life satisfaction were strong independent predictors of prognosis.

Conclusion: The score of PROM is a significant prognostic factor, suggesting the Ai-POD score could be one of the useful tools to estimate the quality of dialysis therapy. The strategies to improve the score in each item could enhance the quality of dialysis therapy.

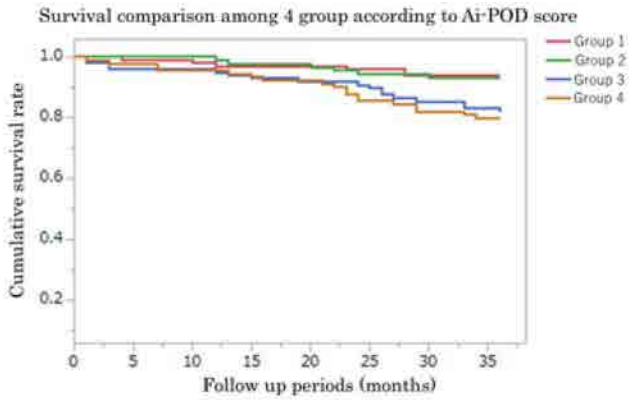


Figure:

P1454 **CIRCULATING ENDOTOXIN AND MARKERS OF INFLAMMATION: ASSOCIATES WITH PHYSICAL ACTIVITY AND THE EFFECT OF A SIX MONTH PROGRAMME OF CYCLING DURING DIALYSIS (INTRADIALYTIC CYCLING)**

Daniel March[1,2], KB Lai[3], Patrick Highton[4], Darren Churchward[1], Hannah Young[2,5], Maurice Dungey[2,4], Matthew Graham-Brown[1,2], Alice Smith[5], Nicolette Bishop[2,4], CC Szeto[3], James Burton[2,4,5]

[1]University of Leicester, Department of Cardiovascular Sciences , [2]University Hospitals of Leicester NHS Trust, NIHR Leicester Biomedical Research Centre, [3]The Chinese University of Hong Kong, Department of Medicine and Therapeutics, [4]Loughborough University, School of Sport Exercise and Health Sciences and [5]University of Leicester, Department of Health Sciences

Background and Aims:

Individuals with end-stage kidney disease receiving haemodialysis have elevated levels of circulating endotoxin as a result of changes to the intestinal barrier. These elevated levels are believed to play a role in the high levels of inflammation in this population. Programmes of cycling during dialysis (Intradialytic cycling (IDC)) can provide benefits to individuals receiving haemodialysis, but it is unclear how they may effect circulating levels of endotoxin. Therefore, the primary aim of this study is to investigate the effect of a 6-month programme of IDC on circulating endotoxin. Further aims are to investigate the associations between levels of physical activity and levels of circulating endotoxin and markers of inflammation in haemodialysis patients.

Method:

This is a secondary analysis of the CYCLE-HD randomised controlled trial (ISRCTN11299707). Participants were randomised to either a 6-month programme of IDC (thrice weekly, moderate intensity cycling at RPE 12-14) in addition to usual care (n=46), or usual care (n=46) only. At baseline and 6 months blood samples were collected from the arterial needle immediately prior to haemodialysis therapy and following centrifugation stored at -80°C. Endotoxin, interleukin (IL)-6, IL-10, tumour necrosis factor-α (TNF-α) and high sensitivity C-reactive protein (Hs-CRP) were quantified using immunoassays. Levels of physical activity were measured using an accelerometer. Participants were instructed to wear the accelerometer for 7 days at baseline, and steps per day were calculated by dividing total steps by number of days worn .

Results:

Steps per day data and endotoxin and inflammatory data was available for n=81 participants at baseline. There was a significant negative association between number of steps per day and IL-6 (P=0.001, R=-0.361), Hs-CRP (P<0.0001, R=-0.450) and Endotoxin (P=0.032, R=-0.238) levels. The effect of a 6-month programme of IDC on endotoxin levels and the inflammatory markers are presented in Table 1.

Conclusion:

Higher levels of physical activity were associated with lower levels of circulating endotoxin, IL-6 and Hs-CRP in individuals receiving haemodialysis. A 6-month programme of IDC did not result in increases in circulating endotoxin, indicating that this physiological stress does not result in changes to the intestinal barrier in haemodialysis patients. Lastly, IDC did not appear to increase circulating markers of inflammation.

Table:

	IDC Group		Usual Care Only Group		
Marker	Baseline	6 Months	Baseline	6 Months	ANOVA interaction P value
Il-6 (ng/L)	3.12 ± 2.75	3.17 ± 2.73	3.02 ± 3.18	3.11± 2.31	P=0.641
IL-10 (ng/L)	0.55 ± 0.54	0.46±0.24	0.51 ± 0.27	0.54 ± 0.37	P=0.152
TNF-α (ng/L)	6.73 ± 2.05	6.11 ± 1.37	6.44 ± 1.77	6.24 ± 2.00	P=0.458
Hs-CRP (mg/L)	13.93±31.02	15.76±33.30	13.10 ± 18.61	13.80 ± 18.39	P=0.277
IL-6/IL-10	7.15 ± 6.56	9.02 ± 10.13	6.63 ± 5.86	6.93 ± 6.06	P=0.707
Endotoxin	0.34 ± 0.08	0.34 ± 0.08	0.34 ± 0.09	0.37 ± 0.07	P=0.218

P1455

PRIORITIZATION BY MEDICAL DIRECTORS OF NUTRITIONAL PROTEIN VERSUS DIETARY PHOSPHORUS CONTROL IN HEMODIALYSIS PATIENTS: ASSOCIATION WITH MORTALITY IN THE DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY (DOPPS)

Suguru Yamamoto[1], Brian Bieber[2], Hirotaka Komaba[3], Hiroki Kitabayashi[4], Takanobu Nomura[5], Aleix Cases[6], Christian Combe[7], Ronald Pisoni[2], Bruce Robinson[2], Masafumi Fukagawa[3]

[1]Niigata University Graduate School of Medical and Dental Sciences, Division of Clinical Nephrology and Rheumatology, Niigata, Japan, [2]Arbor Research Collaborative for Health, United States of America, [3]Tokai University School of Medicine, Division of Nephrology, Endocrinology and Metabolism, Isehara, Japan, [4]Kyowa Hakko Kirin Co. Ltd., Medical Affairs Department, Japan, [5]Kyowa Hakko Kirin Co. Ltd., Medical Affairs Department, Isehara, Japan, [6]Universitat de Barcelona, Barcelona, Spain and [7]Université de Bordeaux, France

Background and Aims: Patients undergoing dialysis for end-stage kidney disease (ESKD) have poorer nutritional status than the general population, and worse nutritional status is associated with poor clinical outcomes. Hyperphosphatemia is common in dialysis patients owing to abnormal mineral and bone metabolism. Nephrologists manage hyperphosphatemia by prescribing phosphate binders and/or recommending restriction of dietary protein intake; the latter may, however, adversely affect nutritional status. In this analysis, we address the hypothesis that, even in the presence of hyperphosphatemia, liberalizing dietary protein leads to better patient outcomes.

Method: The analysis includes 11,628 hemodialysis (HD) patients in 12 countries in DOPPS phase 4 (2009-2011), from 254 facilities where the medical director completed a survey reporting facility practices. Demographic data, comorbid conditions, laboratory values, and medications were abstracted from patient records. Mortality was assessed during study follow-up. The primary exposure variable was response to the following question: "For patients with serum albumin 3.0 g/dL and phosphate 6.0 mg/dL, do you typically recommend to (A) increase or (B) not change or decrease dietary protein intake?" The primary outcome was all-cause mortality, analyzed by Cox regression, stratified by country, accounting for facility clustering using robust sandwich covariance estimators, and adjusted for case-mix and laboratory values. Linear regression was used to model the associations between the exposure variable and intermediate nutritional markers including serum albumin, creatinine, and phosphorus. We used multiple imputation to replace missing values for model covariates.

Results: Median follow-up was 1.4 years. In the case scenario, 91% of medical directors in North America recommended to increase protein intake compared to 58% in Europe (range=36-83% across 7 countries) and 56% in Japan (Figure). Advice to increase dietary protein intake was associated with 0.33 mg/dL higher serum creatinine levels (95% CI: 0.08-0.57) after adjustment for case mix, while clinically meaningful associations were not observed for serum albumin and phosphorus. Advice to increase dietary protein intake was weakly associated with lower mortality [HR (95% CI): 0.89 (0.77-1.03)]. The association with survival was stronger in patients with age 70+ years [HR (95% CI): 0.81(0.68-0.96), P=0.08 for interaction] and for those without diabetes [HR (95% CI): 0.81(0.66-0.98), P=0.20 for interaction]

Conclusion: In this large international cohort study, the medical director's stated preference to recommend an increase in dietary protein intake for HD patients with low albumin and high phosphorus levels was most common in North America and was associated with higher patient serum creatinine levels and potentially lower all-cause mortality. Additional research into the possible benefits of protein intake liberalization for HD patients, even in the presence of hyperphosphatemia, is warranted.

This abstract was directly supported by Kyowa Kirin Co.,Ltd..

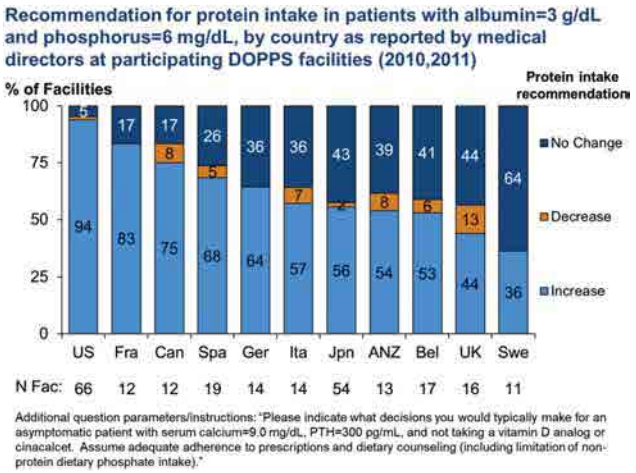


Figure:

P1456 PREVALENCE OF HEPATITIS B CORE ANTIBODY AND OCCULT INFECTION AMONG HAEMODIALYSIS PATIENTS

Nandakumar Mooppil[1], Seema Aithal[1], Rajiva Ibakkanavar[1], Tripti Singh[1]
[1]NKF Singapore, Medical, Singapore, Singapore

Background and Aims:

Haemodialysis (HD) patients are highly susceptible to blood borne virus infections and prevention strategies include surveillance, segregation, vaccination and strict implementation of standard precautions. As per new guidelines it is mandatory for all HD patients to be tested for hepatitis B core antibody at the beginning of renal replacement therapy. In the present study we sought to determine the prevalence of core antibody positivity and occult HBV infection as evidenced by viraemia in hepatitis B surface antigen (HBsAg) negative patients on maintenance haemodialysis.

Method:

All HD patients (aged$\geq$ 18 years) who were dialyzing in 2019 were included in this cross-sectional study. Retrospective data based on one-off screening for hepatitis B core antibody total (anti-HBc) for all HBsAg negative patients (study population) carried out between May and Oct 2019 was used for analysis. Information was gathered on HBsAg, anti-HBc antibody, surface antibody (anti-HBs) and Hepatitis B virus (HBV) DNA. All anti-HBc antibody positive patients were tested for HBV DNA using quantitative PCR assay. Patients were classified as immune (anti-HBs $>$10 IU/L) and non-immune (anti-HBs $\leq$10 IU/L) based on surface antibody levels. Demographic data were compared using Chi square test for categorical variables and Independent T test/ Mann Whitney U test for continuous variables between the patients with and without HBV core antibody. Baseline characteristics were compared between the immune and non-immune groups using Chi square test and Independent T test/Mann Whitney U test as appropriate.

Results:

A total of 3704 HBsAg negative HD patients (mean age 63.5$\pm$11.3 years, 56.1% male, 57.7% Chinese, 65.4% diabetic and mean vintage of 5.8$\pm$5.4 years) were included in the study after exclusion of 147 patients (3.8%) who had chronic HBV infection from the entire HD cohort of 3851 patients. 895 (24.2%) showed evidence of past HBV infection (anti-HBc positive but HBsAg negative) with only 3 (0.1%) patients having detectable HBV DNA. The HBV core antibody positive patients were predominantly elderly, Chinese, males and with high medical dependency compared to the patients without HBV core antibodies ($p<0.001$). There were no statistically significant differences in diabetic status and dialysis vintage between the patients with and without HBV core antibody. 3202 (86.4%) patients were immune following vaccination (anti-HBs $>$10 IU/L). The non-immune patients (13.5%) were more likely to be diabetic, with high medical dependency and lower vintage compared to immune patients ($p<0.001$). Age, race and gender did not differ significantly between the immune and non-immune patients.

Conclusion:

The prevalence of hepatitis B core antibody positivity was 24.2% in our large racially diverse haemodialysis cohort but the presence of occult HBV was low (0.1%). Elderly Chinese males with high comorbidity and poor functional status were more likely to have evidence of past HBV infection. Occult HBV infection has implications in policy development for the prevention of HBV infection in dialysis centres.

P1457 **COMPARISON OF PEPTIDOMES BETWEEN URINE, PLASMA, AND HEMODIALYSIS FLUID INDICATES SELECTIVITY IN RENAL PEPTIDE PROCESSING**

Tianlin He[1], Julia Raad[1], Joachim Beige[2,3], Harald Mischak[1,4]

[1]Mosaiques Diagnostics GmbH, Hannover, Germany, [2]Martin-Luther-University Halle/Wittenberg, Halle/Wittenberg, Germany, [3]Hospital St. Georg, Department of Nephrology and Kuratorium for Dialysis and Transplantation Renal Unit, Leipzig, Germany and [4]University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom

Background and Aims:

The physiological and related body fluids, urine, plasma and hemodialysis (HD) fluid spent dialysate (a mixture of technical HD fluid and patient's ultrafiltrate) are rich biological sources of information especially in the context of kidney diseases. Of particular relevance are proteins and peptides, as they reflect essentially every biological process. Urine is produced as a result of glomerular plasma filtration and subsequent tubular reabsorption in the kidney. In analogy, HD spent dialysate is a result of ultrafiltration by an artificial kidney (dialysis membrane), but lacking tubular reabsorption and thereby accumulating in huge amounts of $>$ 100 L per session comparable to primary urine. A recent study suggested that tubular reabsorption may be selective for specific proteins, and this process may represent a major difference between "natural" and artificial kidney.

In this study, we aim at gaining insight into the composition of the peptidome/proteome in these body fluids of renal significance in a comprehensive analysis, in order to shed light on the relevant pathophysiological processes that take place in kidney, which may help developing better strategy in advanced-stage chronic kidney disease and detoxification in renal replacement therapies (RRT).

Method:

We collected 15 plasma, 15 urine and 13 HD filtrate (spent dialysate during the first 30min of RRT) from age and sex matched subjects with stage 4 or above chronic kidney disease. Peptide identification and quantification were performed with capillary-electrophoresis coupled mass spectrometry and tandem mass spectrometry (CE-MS). The abundance, overlap and differences of the peptidome/proteome of the three body fluids were evaluated.

Results:

We were able to detect 6281 urinary peptides, 1750 plasma peptides and 1728 peptides from spent dialysate. Of these we could identify 1764, 452 and 374 sequenced peptides, respectively Among them, there are 318 peptides detectable in both urine and spent dialysate, 307 detectable in both plasma and urine and only 191 detectable in both plasma and spent dialysate. Among the most abundant peptides in plasma were Thymosine-ß4 and fragments from hemoglobin, fibrinogen and collagen. In dialysate, the most abundant proteins detected in these patients were ß-2-microglobuline, Thymosine-ß4, and fragments from fibrinogen, while in urine fragments derived from collagen, albumin, and from alpha-1-antitrypsin were of the highest abundance. When investigating proteins/peptides found in at least 2 body fluids, a strong correlation in peptide abundance between urine and spent dialysate (P=4.2e-27, Rho=0.56), and a moderately strong correlation between HD fluid and plasma (P=3.7e-5, Rho=0.29) were detected. However, there is no significant correlation between peptide abundance in urine and plasma (P=0.22, Rho=0.07). Collagen peptides are the most abundant peptides in all three body fluids.

Conclusion:

This dataset will serve as a valid basis to define the protein and peptide contents in blood, urine, and spent dialysate. The data show, as expected, substantial similarity between plasma and spent dialysate, but, surprisingly, very little similarity between urine and plasma. This further supports the hypothesis that tubular reabsorption may be selective for specific proteins and peptides, possibly excluding collagen-derived peptides. A more detailed investigation into the process and relevance of tubular reabsorption appears warranted in the light of the data.

The fact that the samples investigated in this study are derived from advanced stage CKD patients must be taken into account, significant differences exist in comparison to urine produced by healthy kidney.

The identification of molecular differences between urine and dialysate spent may present an opportunity to design future "biologically adapted" removal devices.

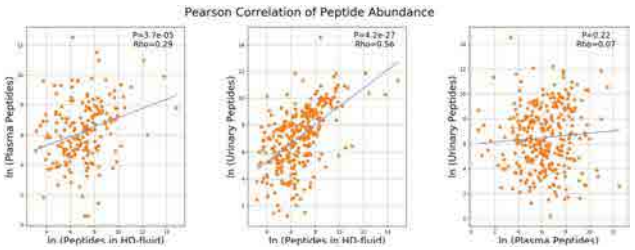


Figure: Correlation of the peptide abundance in HD fluid, plasma and urine

P1458 **CONSERVATIVE MANAGEMENT VERSUS DIALYSIS IN ESKD PATIENTS WITH HIGH COMORBIDITY AND FRAILTY**

João Oliveira[1], Joana Tavares[1], Inês Sala[1], Joana Freitas[1], Josefina Santos Lascasas[1], António Cabrita[1]

[1]*Hospital Geral de Santo António, Medicine - Nephrology, Porto, Portugal*

Background and Aims: ESKD population is increasingly older, frail and with cumulative comorbidities. Conservative management (CM) is a valid approach in selected cases but less well studied than the dialytic or transplant treatment. The objective of our study was to characterize our CM population and compare it with those who induced dialysis.

Method: We present a retrospective study from a tertiary hospital, from 2014-2019. A total of 379 patients presented with dialytic indication at hospital admission and out of these 15.3% (G1, n=58) were managed conservatively. They were characterized using the modified Charlson comorbidity index (mCCI) and Clinical Frailty Scale (CFS). A survival comparison was made between CM population (G1), those who were placed on dialysis (G2, n=321) and a subset of these (G3, n=43) who were older (≥75 years) and with higher level of disability (CFS >4 and mCCI > 4).

Results: CM population was older (G1 vs G2 p <0.01, G1 vs G3 p <0.5), more frail (G1 vs G2 p <0.01, G1 vs G3 p <0.44), and with a higher comorbidity index (G1 vs G2 p <0.01, G1 vs G3 p <0.06). The option for CM was based on the existence of comorbidities associated with less than 6 month survival (n=13, 22.4%), functional detriment (n=33, 56.9%), cognitive status (n=15, 25.9%) or self-choice (n=12, 20.7%); 10.3% (n=6) already had an autologous vascular access implanted. There is a statistically significant (p<0.01) survival benefit among those who begin dialysis even among the subgroup G3. The comparative survival rates between G1 and G3 was 19% (n=11) vs 86% (n=37) at 3 months, and 1.7% (n=1) vs 60.5% (n=26) at 1 year, respectively (p<0.01).

Conclusion:

In our study, dialysis prolonged survival for elderly ESKD patients with significant comorbidity and frailty. The choice between modalities was not an unmodifiable decision as evidenced by the number of patients in the CM group who had a vascular access. Despite these results we still believe that CM is an appropriate treatment option for whom dialytic therapy or transplantation is not expected to bring out benefit. A future focus on quality of life, psychosocial impact, and symptom burden, is needed to establish the true benefits of dialysis in these population.

CHARACTERISTIC		MANAGEMENT					
		CONSERVATIVE (CM)		DIALYSIS			
				Main population		mCCI score >4 Clinical Frailty Scale >4 ≥75 years	
		G1 (n=58)		G2 (n=321)		G3 (n=43)	
Gender (male)	n/%	27	46.6%	181	56.4%	10	23.2%
Age	Mean	82.66 +- 8.72		75.0 +- 5.35		80.4 +- 3	
BMI	Mean	24.57 +- 3.49		24.2 +- 4.08		24.35+-4.09	
eGFR mL/min/m²	Mean	9.77+-3.84		11.89+-4.07		12.07+-14.15	
P albumin g/dL	Mean	3.3 +- 0.48		3.6+-0.5		3.3+-0.47	
Diabetes	n/%	43	74.1%	163	50.8%	34	79%
Cancer	n/%	30	51.7%	58	18%	13	30.2%
CKD etiology							
	Unknown	7	12%	33	10.3%	5	11.6%
	Glomerular	4	6.9%	25	7.8%	1	2.3%
	Diabetic	28	48.3%	165	51.4%	24	55.8%
	Ischemic	10	17.2%	51	15.9%	10	23.2%
	Other	9	15.5%	47	14.6%	3	7%
Vascular access (VA)							
	AVF/AVG	6	10.3%	176	54.8%	19	44%
	CVC	0	-	128	39.9%	23	53.4%
	Tenckhoff	0	-	17	5.3%	1	2.3%
Time from VA implantation to dialysis/CM	Mean	24 +- 16		13.9+-11.3		29.1+-18	
Dialysis (Urgent)	n/%	NA		172	53.6%	33	76.7%
Death (cause)							
	Total	56	96.6%	97	30.2%	24	55.8%
	Cardiac	19	33.9%	27	27.8%	10	41.7%
	Infection	6	10.7%	30	30.9%	4	16.7%
	Cancer	5	8.9%	10	10.3%	2	8.3%
	Other	17	30.4%	14	14.4%	6	25%
	Unknown	9	16.0%	16	16.4%	6	25%
Survival since admission/dialysis induction	Mean	129.59 +- 266.04		384+-272		290.88+-204	
	> 1M	27	46.6%	314	97.8%	42	97.7%
	> 3M	11	19%	296	92.2%	37	86%
	> 6M	7	12%	282	87.9%	33	76.7%
	>1A	1	1.7%	260	81.0%	26	60.5%
Mortality in patients with P albumin < 3 g/dL	N	16		34		21	
	Mean	52.43 +- 39.87		225.1+-5.3		224.29 +- 158.69	
Reason for CM option	Comorbidities < 6 month survival	13	17.8%	NA			
	Functional detriment	33	45.2%				
	Cognitive	15	20.5%				
	Self choice	12	16.4%				
CM decision	Consult	23	39.7%	NA			
	Admission	31	53.4%				
	Other	4	6.9%				

Figure:

P1459 **PREVALENCE AND CONTROL OF HYPERTENSION AMONG PATIENTS ON HEMODIALYSIS USING PREDIALYSIS, POSTDIALYSIS AND HOME BP RECORDINGS.**

Nikolaos Tsikliras[1], Panagiotis Georgianos[1], Vasilios Vaios[1], Varvara Kousouls[2], Aggelina Anagnostara[3], Christos Chatzidimitriou[3], Konstantinos Mavromatidis[4], Vassilios Liakopoulos[1], Pantelis Zebekakis[1], Elias Balaskas[1]

[1]AHEPA Hospital, Aristotle University of Thessaloniki, Hemodialysis Unit, 1st Department of Medicine, Thessaloniki, Greece, [2]Therapeutiki Dialysis Unit, Thessaloniki, Greece, [3]General Hospital of Xanthi, Hemodialysis Unit, Xanthi, Greece and [4]General Hospital of Komotini, Department of Nephrology, Komotini, Greece

Background and Aims: Earlier studies provided considerably variable estimates on the prevalence and control rates of hypertension in hemodialysis because of their heterogeneity in definitions and blood pressure (BP) measurement techniques applied to detect hypertension.

Method: In the present study, 116 clinically stable hemodialysis patients from 3 dialysis centers of Northern Greece underwent home BP monitoring for 1 week with the validated automatic device HEM-705 (Omron, Healthcare). Routine BP recordings taken before and after dialysis over 6 consecutive sessions were also prospectively collected and averaged. Hypertension was defined as: (i) 1-week averaged home BP $\geq$135/85 mmHg; (ii) 2-week averaged predialysis BP $\geq$140/90 mmHg; (iii) 2-week averaged postdialysis BP $\geq$130/80 mmHg. Participants on treatment with $\geq$1 antihypertensives were also classified as hypertensives.

Results: The prevalence of hypertension was 88.8% by home, 86.2% by predialysis and 91.4% by postdialysis BP recordings. In all, 96 participants (82.7%) were being treated with an average of 1.7 antihypertensive medications. Among drug-treated participants, 32.6% were controlled by home, 50.5% by predialysis and 45.3% by postdialysis BP recordings. In multivariate logistic regression analysis, greater use of antihypertensive medications and postdialysis overhydration, assessed with bioimpendence spectroscopy, were both independently associated with higher odds of inadequate home BP control.

Conclusion: This study shows that epidemiology of hypertension in hemodialysis differs considerably between routine dialysis-unit and home BP recordings. Since greater antihypertensive drug use and postdialysis overhydration appeared to be the major determinants of inadequate home BP control, then management of hypertension should be initially relied on strategies targeting to control volume overload.

P1460 **MEDIATORS OF THE IMPACT OF HOURLY NET ULTRAFILTRATION RATE ON MORTALITY IN CRITICALLY ILL PATIENTS RECEIVING CONTINUOUS RENAL REPLACEMENT THERAPY**

Thummaporn Naorungroj[1,2], Ary Serpa Neto[1,3,4], Lara Zwakman-Hessels[1,5], Fumitaka Yanase[1,6], Glenn Eastwood[1], Rinaldo Bellomo[1,6,7,8]

[1]Austin Hospital, Intensive Care, Heidelberg, Australia, [2]Siriraj Hospital, Intensive Care, Bangkok, Thailand, [3]Unidade Morumbi - Hospital Israelita Albert Einstein, Critical Care Medicine, Sao Paulo, Brazil, [4]Academic Medical Centre, Intensive Care, Amsterdam, Netherlands, [5]University of Groningen, Critical Care, Groningen, Netherlands, [6]ANZICS-Research Center, Monash University School and Public Health and Preventive Medicine, Melbourne, Australia, [7]University of Melbourne, Centre for Integrated Critical Care, Parkville, Australia and [8]University of Melbourne, Data Analytics Research and Evaluation (DARE) Centre, Parkville, Australia

Background and Aims: During continuous renal replacement therapy (CRRT), a high net ultrafiltration (NUF) rate is associated with increased mortality. However, it is unknown what might mediate its putative effect on mortality. This study aims to investigate whether the relationship between early (first 48h) NUF and mortality is mediated by fluid balance (FB), hemodynamic instability or low potassium or phosphate blood levels.

Method: We performed a retrospective, observational study in patients treated with CRRT within 14 days of ICU admission who survived >48 hours. The primary outcome was hospital mortality. We applied multiple mediation analysis to identify possible mediators of NUF's putative impact on mortality.

Results: We studied 347 patients [median (interquartile range) age: 64 (53–71) years and Acute Physiology and Chronic Health Evaluation (APACHE) III score: 73 (54–90)]. After adjustment for confounders, compared with a NUF<1.01 ml/kg/h, a NUF rate > 1.75 mL/kg/h was associated with significantly greater mortality (adjusted odds ratio [aOR], 1.15 [95%CI, 1.03 to 1.29]; $p = 0.011$). Adjusted univariable mediation analysis found no suggestion of a causal mediation effect for blood pressure, vasopressor therapy, or potassium levels, but identified a possible effect for FB (average causal mediation effect (ACME), 0.95 [95%CI, 0.90 to 0.99]; $p = 0.062$) and percentage of phosphate measurements with hypophosphatemia (ACME, 0.96 [95%CI, 0.92 to 1.00]; $p = 0.055$). However, on multiple mediator analysis, such variables lost any suggestion of a significant effect. In contrast, NUF rate remained associated with mortality even in their presence (average direct effect, 1.24 [95%CI, 1.11 to 1.40]; $p < 0.001$).

Conclusion: An early NUF greater than 1.75 mL/kg/h was independently associated with increased hospital mortality. Its putative effect was not mediated by FB, low blood pressure, vasopressor use, hypokalemia or hypophosphatemia.

P1461 **FRAILTY IN PREVALENT HEMODIALYSIS PATIENTS. APLICATION OF FRAILTY INDEX BASED ON GERIATRIC INTEGRAL ASSESSMENT (IF-VIG)**

Gloria Anton-Perez[1], Fernando Henriquez[1], Ana Yurena Sánchez[1], Francisco Valga[2], Tania Monzon[2]

[1]CENTRO DE DIALISIS AVERICUM SUR LAS PALMAS, Telde, Spain and [2]CENTRO DE DIALISIS AVERICUM NORTE LAS PALMAS, Las Palmas de Gran Canaria, Spain

Background and Aims: Frailty is defined as a state of greater vulnerability with less compensatory mechanisms to stressors and is related to worse health outcomes, with the estimated prevalence in the general population> 65 years of approximately 10% and is still higher in population with Chronic Renal Disease (CKD) (26-73%). The Frailty Index based on the Geriatric Integral Assessment (IF-VIG) has been described as a simple tool, fast, with discriminative capacity and predictive (with high correlation with mortality) in geriatric population, but its application in Hemodialysis population has not been reported. We study the frailty in prevalent population in Hemodialysis (HD) applying the IF-VIG, its variables associated and its complications.

Method: observational and prospective, non-interventional study, 361 prevalent patients on hemodialysis in Las Palmas, of the centers of AVERICUM and the Hemodialysis Unit at C.H.U.I.M.I. Demographic and clinical data, related to the technique and dose of dialysis, the Malnutrition-Inflammation Scale (MIS) biochemical parameters and anthropometric parameters were collected.

Results: 361 patients, 65% were men, 55% diabetics. Median age: 67 years (57-76), average time in HD o 40 months (20-77). 45% were dialyzed with Central Venous Catheter (CVC) as vascular access (AAVV). The median Charlson Comorbidity Index was 8 (6-9), 242 patients (69% of the population studied) had some degree of malnutrition according to the Malnutrition-Inflammation Scale (MIS), presenting a MIS $\geq$ 5. A total of 239 patients (66% of the population) were fragile (IF-VIG $\geq$ 0.20). The clinical variables predictive of frailty were age, sex, comorbidity, the use of CVC as AAVV in HD, the time in the technique and the dialysis dose measured as the average Kt of the last 12 sessions. Table 1. Exitus and hospitalizations were significantly more frequent in the fragile population.

Conclusion: The prevalence of frailty by applying IF-VIG in HD population is very high (66%), including 54% of patients <65 years. The factors associated with frailty in our population were male sex, age, comorbidity, time in the technique, dose of dialysis measured by Kt and the use of CVC as AAVV in HD. Up to 69% of fragile patients are malnourished according to the MIS scale, presenting an MIS $\geq$5. Exitus and hospitalizations are significantly more frequent in fragile patients. Early identification of fragile patients in HD and the reversible factors associated with this entity would lead to an early multidisciplinary approach, with the aim of reducing the morbidity and mortality of this population.

Table 1. Clinical characteristics and biochemical parameters of non-fragile (IF-VIG<0,2)/ /fragile populations (IF-VIG$\geq$0,2)

Variables	All data(n=361)	IF-VIG< 0,2 (n=122)	IF-VIG$\geq$ 0,2(n=239)	p
SEXO				**0.0498**
H	234 (64.82)	88 (72.13)	146 (59.26)	
M	127 (35.18)	34 (27.87)	93 (38.91)	
AGE	67 (57; 76)	62 (52; 71)	70 (61; 78)	**<0.0001**
I.C. CHARLSON	8(6;9)	6 (4; 8)	8 (7; 10)	**<0.0001**
I.C. CHARLSON WITHOUT AGE	4 (3;6)	4(2; 5)	5 (4; 6)	**<0.0001**
DM				**0.0017**
NO	164 (45.43)	70 (57.38)	94 (39.33)	
YES	197 (54.57)	52 (42.62)	145 (60.67)	
MIS				**<0.0001**
<5	110 (31.25)	55 (45.83)	55 (23.71)	
$\geq$5	242 (68.75)	65 (54.17)	177 (76.29)	
Crp	7.19 (5.51; 8.85)	7.77 (6.03; 9.9)	6.84 (5.38; 8.46)	**0.0022**
Na^{+}	137(135; 139)	138 (136; 139)	136 (134; 138)	**0.0008**
Ca^{++}	8.89 (0.66)	8.79 (0.75)	8.94 (0.61)	**0.0573**
ALBUMINA	3.60 (3.30; 3.90)	3.75 (3.58; 4.00)	3.60 (3.30; 3.80)	**<0.0001**
TRANSFERRINA	184 (161; 210)	194 (172; 222.5)	176 (158.25; 204.25)	**0.0002**
FERRITINA	372 (147.47; 680.33)	314.35 (140.8; 676.35)	391.45 (161.05; 678.8)	**0.0002**
PCR	0.64 (0.28; 2)	0.42 (0.21; 1.06)	0.78 (0.32; 2.51)	**0.0014**
AAVV EN USO				**0.0077**
CVC	161 (44.60)	42 (34.43)	119 (49.79)	
FAV	200 (55.4)	80 (65.57)	120 (50.21)	
Qb	380 (350; 400)	400 (350; 400)	350 (338; 400)	**0.0039**
Kt/V	1.58 (1.41; 1.8)	1.51 (1.4; 1.78)	1.6 (1.43; 1.82)	**0.1902**
Kt (media/12 sesiones)	52.06 (45.43; 59)	55.99 (48.52; 59.88)	51.08 (43.94; 57.62)	**0.0002**

P1462 **IMPACT OF HEART RATE AND BETA-BLOCKER USE ON THE LONG-TERM SURVIVAL OF CHRONIC HEMODIALYSIS PATIENTS**

Takuhiro Moromizato[1], Kunitoshi Iseki[2,3], OCTOPUS Study Group[3]

[1]Okinawa Nanbu Prefectural Medical Center and Children's Medical Center, Renal and Rheumatology, Shimajiri district, Japan, [2]Nakamura Clinic, Clinical Research Center, Urasoe-shi, Japan and [3]Okinawa Dialysis and Transplantation Association, Clinical Research Center, Naha, Japan

Background and Aims:

Increase in resting heart rate might influence mortalities of dialysis patients, and the use of β-blocker might improve their survival probability. However, the influence of heart rate and benefits of β-blocker on their survival are difficult to quantify because of following obstacles: prone to measurement errors; inherent association of heart rate with blood pressures, comorbidities, and medication use; and a necessity of repeated measurements of vital signs and medication use. Therefore, at the design process of our previous randomized control trial on the Olmesartan Clinical Trial in Okinawan patients under OKIDS (OCTOPUS), we included the repeated measures design to quantify the influence of vital sign values on the survival retrospectively. We combined the repeated measurement data and additional the long-term prognosis information of the participants obtained after the OCTOPUS with aim of investigating the influence of time varying covariates: heart rates, blood pressures, and β-blocker use, on the long-term survival of hemodialysis patients.

Method:

We investigated 461 adult OCTOPUS participants who received chronic hemodialysis and antihypertensive medications in Okinawa. The OCTOPUS trial, which was conducted between June 2006 and June 2011, did not detect the survival benefit of angiotensin receptor blocker (ARB)NDT 2013, but the study and the additional follow-up of participants' prognosis provided us with information to investigate influence of predictors on long-term survival in the population. Throughout the OCTOPUS trial, study participants were measured pre-dialysis blood pressures, pre-dialysis resting heart rates, and their medication use for one week at their dialysis centers every six months after their participations. Following the trial, we collected the prognosis information of all participants until July 31st, 2018. Finally, we merged the multiple-measured data during the OCTOPUS with the prognosis data. Mean values of three measurements of blood pressures and heart rates and β-blocker use were introduced to the Cox-regression model as time-varying covariates with essential non-time varying covariates, which include age, gender, and diabetes.

Results:

In this retrospective cohort study, 221 (47.9%) out of 461 participants deceased, and the median follow-up length was 10.21 years. Initial mean resting heart rate and pre-dialysis mean blood pressure were 78(±10) per minute and 159.5(±14) mmHg, respectively. 10% of participants were prescribed β-blocker initially. The resting heart rate of all participants significantly decreased by 1.75 and 2.45 per minutes after two and four years respectively. β-blocker could significantly decrease the mean heart rate by 3.54 and 2.90 per minutes after two and four years. With our Cox-regression with the time varying covariates, increase of heart rate was significantly associated with higher mortality (P=0.002), but the use of β-blocker was not associated with the mortality. (P=0.691) Additionally, we could not detect the interaction of heart rate and β-blocker use on the mortality. (P= 0.796) Although lower blood pressure was significantly associated with higher mortality in our initial Cox-regression analysis, an introduction of interaction term of heart rate and blood pressure remove the significance of influence of blood pressure on the survival.

Conclusion:

In hypertensive chronic hemodialysis patients, higher heart rate is associated with higher mortality. However, use of beta-blocker was not associated with improvement of their mortality.

P1463 EARLY VASCULAR ACCESS CREATION IS NOT ASSOCIATED WITH BETTER OUTCOME IN PATIENTS AFTER CHRONIC DIALYSIS INITIATION

Yukimasa Iwata[1], Hiroki Okushima[1], Taisuke Takatsuka[1], Daisuke Yoshimura[1], Tomohiro Kawamura[1], Yoshiyasu Ueda[1], Tatsuya Shoji[1], Terumasa Hayashi[1]

[1]*Osaka general medical center, nephrology and hypertension, Osaka, Japan*

Background and Aims:

Although initiation of chronic hemodialysis with central venous catheters are associated with higher mortality compared to that with arteriovenous fistula, the association between the timing of vascular access (VA) creation and outcome after dialysis initiation is not fully investigated. Thus, we conducted single center retrospective cohort study on incident hemodialysis patients to investigate the effect of VA types and timing of VA creation on all-cause and cardiovascular mortality after dialysis initiation.

Method:

A total of 1052 patients with accurate clinical data and outcomes was extracted from 1069 patients who started chronic hemodialysis treatment at Osaka General Medical Center between 2006 and 2015. Clinical status at dialysis initiation, all-cause and cardiovascular mortality were compared by three patient groups categorized by VA types and timing of VA creation: temporary catheter (TC) group, dialysis initiation with TC; early VA (EVA) group, dialysis was initiated more than one month after VA creation; late VA (LVA) group, dialysis was initiated within one month after VA creation. Cox proportional hazards analysis was used to examine predictive factors for outcomes.

Results:

Median age was 70 years and 64% of patients were male. Patient number of each group was 285 (27%), 441 (42%), and 326 (31%) for TC, EVA, and LVA groups, respectively. Although there was no significant difference in eGFR at dialysis initiation among three groups ([median] 5.4 vs. 5.4 vs. 5.4 mL/min/1.73m^2, respectively, P=0.881), hemoglobin and albumin were lower in TC group compared to EVA and LVA groups (hemoglobin [median] 8.3 vs. 9.5 vs. 8.9 g/dL, respectively, P<0.001; albumin [median], 3.0 vs. 3.5 vs. 3.2 g/dL, respectively, P<0.001). Kaplan-Meier curves revealed significant difference among three groups for all-cause (P<0.001) and cardiovascular mortality (P<0.001). On multivariate Cox proportional hazards analysis, timing of VA creation was not associated with all-cause and cardiovascular mortality. Although temporary catheter usage at dialysis initiation was significantly associated with all-cause mortality (HR, 1.91; 95%CI, 1.30-2.83; P=0.001), it was not associated with cardiovascular mortality (HR, 1.64; 95%CI, 0.79-3.43; P=0.186).

Conclusion:

Timing of VA creation was not associated with all-cause and cardiovascular mortality, whereas hemodialysis initiation with TC was significantly associated with increased all-cause mortality.

P1463A

MORTALITY AND HOSPITALIZATION PATTERNS IN ELDERLY HEMODIALYSIS PATIENTS. A LARGE SAUDI STUDY

Ayman Moussa[1], Ezzedine Abderrahim[1], Afef Dridi[1], Ibrahim Jubran[1], Saad Alobaili[1], Salwa Alahmadi[1], Wisam Albadr[1]

[1]*Davita Health Care, Saudi Arabia, Clinical Department, Riyadh, Saudi Arabia*

Background and Aims: The aim of the study was to analyze hospitalization and mortality parameters in Saudi elderly patients undergoing hemodialysis for end stage renal disease.

Method: The study population included all patients admitted at Davita-KSA clinics to continue renal replacement by hemodialysis during the period October 2014-December 2018. Two groups were identified according to age at admission to Davita clinics: Group 1 (age>=65 years), Group 2 (age<65 years). Zero time data, including demographic and clinical characteristics were recorded at admission. Also, all deaths and morbid events necessitating hospital admission were regularly recorded during the follow-up period.

Annual mortality and hospitalization rates with the corresponding confident intervals were calculated as appropriate. Survival rates were calculated according to actuarial method logistic regression was used to identify factors influencing hospitalization and mortality.

Results: Elderly patients represented 23.84% of 3508 included patients (G1),). The sex ratio was of 1.07 Vs. 1.21 in control group (NS). ESRD was attributed to diabetes in 52.7% of elderly patients Vs. 36.3% in others (<0.0001). The median duration of HD before joining Davita-clinics was of 6.5 months in G1 Vs. 11.5 months in G2 ($p<0.0001$). There is no significant difference between the 2 groups regarding vascular access type, BMI and hemoglobin rate.

The proportion of patients who were hospitalized was of 30.8% in G1 Vs. 24.6% in G2 ($p<0.0006$) corresponding to an annual rate of 37.33% (CI, 95%: [33.93-40.73]) in G1 Vs. 25.64 (CI, 95%: [24.14-27.15]) in G2. The annual rate of hospital stay was of 4.38 days per patient in G1 (CI, 95%: [4.26-4.49]) Vs. 3.11 in G2 (CI, 95%: [3.06-3.16]). The annual mortality rate was 13.36% in G1 (CI, 95%: [11.32-15.38]) Vs. 5.33% in G2 (CI, 95%: [4.64-6.01]). Survival rates in Group 2 were of 98.6, 95.4, 90.5 and 78.6% at 3, 12, 24 and 48 months respectively Vs. 96.1, 89.3, 78.8 and 55.8% in G1 ($p<0.0001$).

Adjusted hospitalization and mortality risks were of 1.271 (CI, 95%: [1.065-1.516]; $p<0.008$) and 2.257 (CI, 95%: [1.794-2.841]; $p<0.0001$) in elderly patients compared to other patients.

Conclusion: Our study demonstrated that Saudi elderly hemodialysis patients remain a group at high risk for hospitalization and mortality.

P1464

ROUTINELY MEASURED CARDIAC TROPONIN I AND NT-PROBNP AS PREDICTORS OF MORTALITY IN JAPANESE HEMOLIALYSIS PATIENTS: THE DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY

Masahiro Eriguchi[1], Kazuhiko Tsuruya[1], Marcelo Lopes[2], Brian Bieber[2], KP McCullough[2], Roberto Pecoits-Filho[2], Bruce Robinson[2], Ronald Pisoni[2], Eiichiro Kanda[3], Kunitoshi Iseki[4], Hideki Hirakata[5]

[1]Nara Medical University, Department of Nephrology, Kashihara, Japan, [2]Arbor Research Collaborative for Health, Ann Arbor, United States of America, [3]Kawasaki Medical University, Department of Nephrology and Hypertension, Okayama, Japan, [4]Nakamura Clinic, Clinical Research Support Center, Urasoe-shi, Japan and [5]Fukuoka Renal Clinic, Fukuoka, Japan

Background and Aims: Due to the interplay of chronic kidney disease and the heart, it is common for myocardial damage and strain to be present in patients with end stage kidney disease. The cardiac biomarkers Troponin I (cTnI) and the N-terminal fragment of prohormone brain natriuretic peptide (NT-proBNP) are strongly predictive of heart failure in the general population, however the value of their routine measurement for stratification of risk in hemodialysis (HD) patients is unknown. International DOPPS data indicate that these cardiac biomarkers are measured in fewer than 2% of hemodialysis patients in real-world practice. We sought to test the associations of cTNI and NT-proBNP with death in a large HD cohort.

Method: We analyzed data from 1169 prevalent Japanese hemodialysis patients in DOPPS phase 5 (J-DOPPS; 2012-2015) where pre-dialysis levels of cTnI and NT-proBNP at study enrollment by protocol for all participants. We used Cox regression to test the association of the cardiac biomarkers with all-cause mortality, adjusting for potential confounders. We conducted stratified analyses to assess potential effect modification of individual clinical characteristics: age, systolic blood pressure, dialysis vintage, diabetes mellitus, cardiovascular disease, and heart failure (CHF).

Results: Median (interquartile range) cTnI and NT-proBNP levels were 0.018 [0.005, 0.04] ng/mL and 3432 [1580, 8017] pg/mL, respectively. There was a positive direct association between cTNI and NT-proBNP (Spearman correlation coefficient=0.58). We observed 174 deaths during a median [IQR] follow-up time of 2.8 [2.3, 2.9] years. Compared to the reference group of cTNI<0.01 the hazard ratio (HR) of death (95% CI) was 1.23 (0.57, 2.69) for cTNI ≥0.01 to 0.02; HR=1.94 (1.12, 3.37) for cTNI ≥0.02 to 0.04; and HR=3.65 (2.14, 6.23) forcTNI>0.04. Compared to the reference group of NT-proBNP <2000 pg/mL, HR= 1.20 (0.65, 2.23) for NT-proBNP ≥2000 to 4000 pg/mL; HR= 2.06 (1.22, 3.46) for NT-proBNP >4000 to 8000 pg/mL; and 3.23 (1.71, 6.09) for NT-proBNP > 8000pg/mL. For both variables associations with mortality were comparable in patients with and without heart failure (p values for interaction=0.07 and 0.19, for NT-proBNP and cTNI, respectively) and according to other stratification variables (the p values for interaction were >0.15 for all other stratified models).

Conclusion: Routinely measured (not by indication) NT-proBNP and Troponin I are strongly associated with mortality among prevalent Japanese HD patients. Routine evaluation of these cardiac biomarkers in HD patients with or without a previous diagnosis of CHF may help identify patients at risk of death who may have undetected heart failure or cardiac strain due to fluid overload.

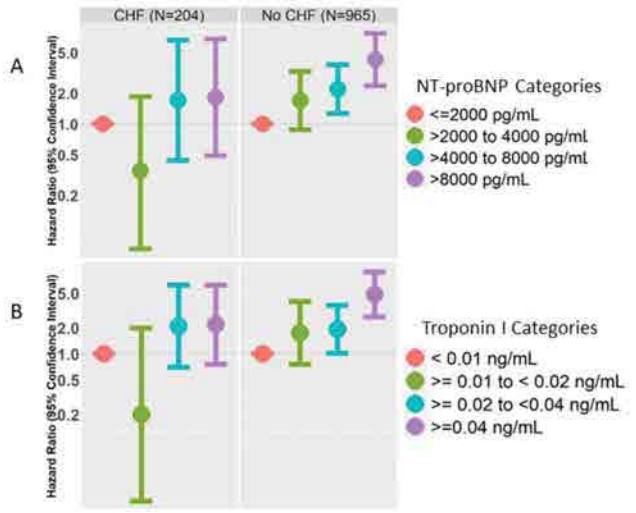


Figure:

P1465 **DEPRESSION AND HEALTH RELATED QUALITY OF LIFE AMONG ELDERLY HAEMODIALYSIS PATIENTS**

Nandakumar Mooppil[1], Seema Aithal[1], Tripti Singh[1], Rajiva Ibakkanavar[1]
[1]NKF Singapore, Medical, Singapore, Singapore

Background and Aims:

The reported prevalence of depression is around 20-30% among dialysis patients according to the literature. Previous studies have shown a strong negative correlation between depression and kidney disease related quality of life (KDQOL) scores in ESRD patients. In this study we examined the relationship between depression and KDQOL scores of a racially diverse cohort of elderly haemodialysis (HD) patients. Additionally we investigated the predictors of depression among this cohort.

Method:

Prevalent HD patients aged 65 years and above who were dialyzing in our institution were included in this cross-sectional study. The Geriatric depression scale (GDS-15) and KDQOL-SF^{TM} version 1.3 were the instruments used to derive depression and KDQOL domain scores respectively. The predictor variable was depression status based on a cut-off of 5 and patients were categorized into 2 groups – depression (Yes)-GDS$\geq$5 and depression (No)–GDS$<$5. The impact of socio-demographic factors and lab parameters was compared using chi square test for categorical variables and Independent T test/Mann Whitney U test for continuous variables. The 3 main KDQOL domains – physical composite summary (PCS) score, mental composite summary (MCS) score and Kidney disease composite summary (KDCS) score were compared using Independent T test among the depression status groups. Multivariate logistic regression was used to determine the predictors of depression among this elderly HD cohort.

Results:

A total of 1034 elderly HD patients (mean age 72.1$\pm$5.6 years, 55.9% male, 65.7% Chinese, 65.8% diabetic and mean vintage of 5.8$\pm$5.6 years) were included in the study. The prevalence of depression was 18.1% among this elderly HD cohort. The patients with depressive symptoms were predominantly non-ambulant, with high medical dependency and increased hospital admissions in the past year compared to the non-depressed group. There were no statistically significant differences in the age, race, gender, diabetic status and dialysis vintage between the groups with and without depression. The group with depression had significantly lower PCS, MCS and KDCS domain scores compared to the group without depression ($p<0.001$). Mobility status was identified as an independent predictor of depression - ambulant patients were 53% (OR-0.47, 95%CI 0.31-0.70, $p<0.001$) less likely to be depressed compared to non-ambulant HD patients ($p<0.001$). Mean scores for KDQOL dimensions like sleep and social support were significantly lower among patients with depression ($p<0.001$).

Conclusion:

Elderly haemodialysis patients with depression had significantly lower mean health related quality of life scores compared to patients without depression. Mobility status was an important predictor of depression among our elderly cohort. Regular screening and management of depression should be part of the routine care of the elderly HD patients so as to improve their quality of life and dialysis outcomes.

Table –KDQOL domain scores according to depression status among elderly HD patients.

Depression status	Number (%)	Physical composite summary score	Mental composite summary score	Kidney disease composite summary score
No (GDS$<$5)	847 (81.9)	38.44 $\pm$ 9.23	51.5 $\pm$ 10.14	73.9 $\pm$ 13.15
Yes (GDS $\geq$5)	187 (18.1)	35.05 $\pm$ 8.22	45.33 $\pm$ 10.78	65.18 $\pm$ 13.18
P value*	-	**<0.001**	**<0.001**	**<0.001**

*$p<0.05$ is significant, based on Independent T test. GDS – Geriatric depression scale

P1466 **SYSTEMATIC LITERATURE REVIEW OF CLINICAL EVIDENCE FOR THE BODY COMPOSITION MONITOR IN DIALYSIS AND CKD**

Agnieszka Raddatz[1], Ulrich Moissl[2], Alistair Ray[3], Christian Eichinger[3], Peter Wabel[2]

[1], Rosbach, Germany, [2]Fresenius Medical Care Germany, GRD, Bad Homburg, Germany and [3]PharmaGenesis Oxford, United Kingdom

Background and Aims: The Body Composition Monitor (BCM) is a bioimpedance spectroscopy device to monitor the hydration status of dialysis and CKD patients. NICE (UK) reported only limited evidence on the clinical effectiveness in its Diagnostic Guidance 29. The aim of this work was to provide a structured review of the available evidence up to September 2018 grouped by the most important clinical outcomes (fluid overload, blood pressure, mortality and cardiovascular events).

Method: MEDLINE, Embase and Cochrane databases were interrogated from 2006 to September 2018. Search and review of identified studies was conducted in compliance with the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Results: Of 4497 articles identified, 843 were included for full-text review; 424 were full publications and were selected for further analysis. Eight randomized controlled trial (RCT) studies and 150 observational studies met the predefined inclusion criteria; of these, observational studies that recruited at least 100 patients and additionally reported important clinical outcomes such as mortality, cardiovascular (CV) events or hospitalization were selected. Two further RCTs were identified by supplementary searches, giving a total of 10 RCTs (total 2.156 patients) and 41 observational studies (total 168.453 patients) included in this review.

The data was grouped by reported outcomes and for each outcome it was analyzed if an effect of BCM-monitored fluid management, or an association between BCM assessment and the respective outcome could be shown. A meta-analysis of the results was not conducted.

Reduction of fluid overload: RCTs have shown that BCM-monitored fluid management and subsequent alteration of dialysis parameters can lead to effective reduction of fluid overload.

Lowering of blood pressure: RCTs have indicated that BCM-monitored fluid management can effectively lower blood pressure.

Impact on mortality / association with mortality: Multiple observational studies have shown a strong association between BCM measurements and mortality. One RCT demonstrated that mortality outcomes can be significantly improved in HD patients with BCM-guided fluid management, while two RCTs reported no significant difference in mortality outcomes.

Impact on Cardio Vascular (CV) related events: Multiple observational studies have indicated that BCM measurements can predict CV events. One RCT indicated that CV events can be reduced by BCM-monitored fluid management, and two further RCTs indicated that using BCM guidance was at least as good as conventional fluid management.

Conclusion: There is a strong body of evidence for various important outcomes covering a large patient basis - additional evidence is needed in well designed randomized controlled trials e.g. to demonstrate the effect of reducing BCM determined dehydration.

	CKD 5 modality	N study	N Patients	Fluid Overload	Blood Pressure	Mortality	CV- related events
RCTs	HD	8	1,808	5	8	4	2
	PD	2	348	2	2	NR	1
	Total	**10**	**2,156**	**7**	**10**	**4**	**3**
Obs.	HD	26	165,792	21	11	23	10
	PD	6	2,691	5	1	5	1
	Total	**32**	**168,453**	**33**	**18**	**28**	**16**

Figure: Studies identified for dialysis patients (Randomized Controlled Trials (RCT), Observational studies (Obs.)), results grouped by the most important clinical outcomes

P1467 **DEMOGRAPHY OF THE DIALYSIS POPULATION IN SWITZERLAND IN 2018**

Rebecca Winzeler[1], Patrice Max Ambühl[1]

[1]*Institute of Nephrology, Waid and Triemly City Hospital, Zurich, Switzerland*

Background and Aims: The national Swiss Dialysis Registry (srrqap) has been established originally in the year 2006. However, participation is substantial only since 2013, when data collection became mandatory by law. The primary aim of the srrqap is to provide quality control and quality improvement for dialysis therapy in Switzerland. In the present analysis, select demographic characteristics of the Swiss dialysis population are given.

Method: All medical establishments in Switzerland (both public and private; N=92) providing chronic treatment by either hemo- and/or peritoneal dialysis, had to provide relevant data for the year 2018. All individuals being on chronic dialytic therapy in the year 2018 were enrolled (N=4646). For patients alive on December 31 2018, data were gathered from this date or closest to this date. For patients who died during 2018 or were being transplanted, data refer to time of event, or to a date closest to the event.

Results: The median age of dialysis patients in 2018 increased almost by one year compared to 2016. More than fifty percent of the patients were older than 71 years, and nearly 1/4 were beyond 80 years. No relevant differences were found between female and male patients regarding mean age (68.6 vs. 68.3 years, respectively). However, women's dialysis vintage is significantly higher than men's (54.4 vs. 45.7 months, respectively) and they are significantly less comorbid than men (4.2 vs. 4.7).

Conclusion: With a coverage of 100% for both centers and patients, the data gathered can be considered highly representative. The incidence of dialysis therapy in Switzerland with 95.9 pmp is clearly lower than in most other countries. In 2018, 3789 prevalent patients (443.7 pmp) were dialyzed in Switzerland. The number of dialysis patients with diabetes increased by almost 1% from 2017, reaching 37.4%.

Table 1: Characteristics (given as mean and median) in dialysis patients

	All (100%)		In Centre (88.9%)		Home (11.0%)	
	Mean	**Median**	**Mean**	**Median**	**Mean**	**Median**
Age, yr	68.4	71.4	69.3	72.0	61.6	65.3
Dialysis vintage, months	48.8	34.0	50.9	36.0	31.6	21.0
Comorbidities, N	2.5	2.0	2.6	2.0	1.8	1.0
Charlson Comorbidity Index	4.5	4.0	4.6	4.0	3.7	3.0
Hypertensive, %	82.1		81.7		84.8	
Sex (male), %	64.9		64.7		66.9	

Table 2: Trend of incident/prevalent count and comorbidities in dialysis patients from 2014-2018

	2014	2015	2016	2017	2018
Total number of patients (cumulative)	4215	4453	4502	4580	4646
Incidence, pmp	91.9	96.6	93.9	91.1	95.9
Prevalence, pmp	423.5	433.5	441.1	435.7	443.7
Comorbidities (mean), N	2.36	2.43	2.52	2.57	2.55
Charlson Comorbidity Index (mean)	4.44	4.42	4.49	4.51	4.49

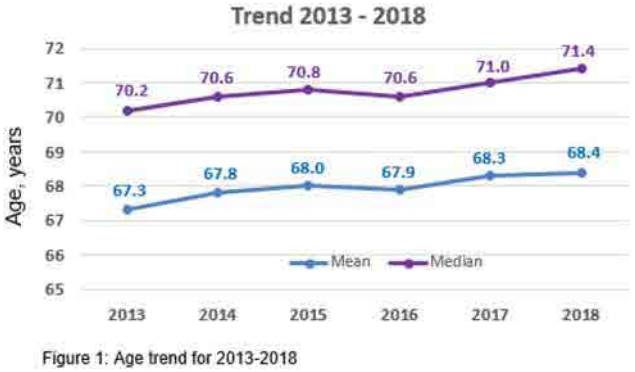


Figure 1: Age trend for 2013-2018

Figure:

P1468 **ASSESSING THE BURDEN OF CHRONIC PAIN IN PATIENTS UNDERGOING HAEMODIALYSIS: A CROSS-SECTIONAL OBSERVATIONAL STUDY**

Samira Bell[1], Emilie Lambourg[1], Greg Guthrie[2], Krithi Murugan[2], Lesley Colvin[1], Jamie P Traynor[3]

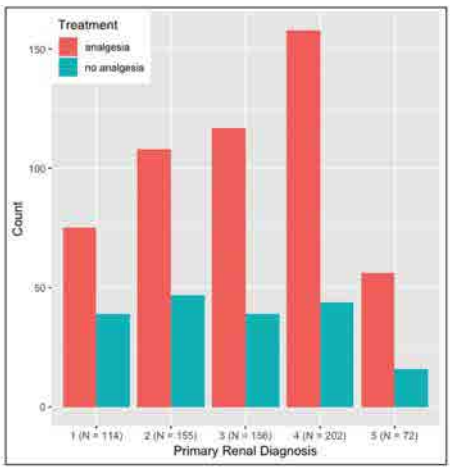
[1]University of Dundee, Division of Population Health and Genomics, Dundee, United Kingdom, [2]Ninewells Hospital, Renal Unit, Dundee, United Kingdom and [3]Queen Elizabeth University Hospital, Glasgow Renal and Transplant Unit, Glasgow, United Kingdom

Background and Aims: Chronic pain is a global health problem estimated to affect between 20- 50% of the population and is associated with increased hospitalisations placing a significant burden on healthcare resources. The burden of chronic pain is thought to be especially high in patients undergoing renal replacement due to underlying co-morbidities such as diabetes, peripheral vascular disease and renal bone disease. There is, however, a lack of data out with the United States quantifying the burden in patients undergoing chronic dialysis. The aim of this study was to establish the burden of chronic pain through examination of prescribing records in patients undergoing chronic dialysis.

Method: We performed a cross sectional observational study in 2 Scottish health boards (together serving 1.9 of Scotland's 5 million population). Data were collated on age, dialysis vintage, primary renal diagnosis and analgesia prescribing specifically examining whether patients were prescribed paracetamol, non-steroidal anti-inflammatory agents, opioids or gabapentinoids. Descriptive statistics were performed.

Results: 721 patients receiving haemodialysis were included in the analysis (141 from the Tayside area and 580 from Greater Glasgow and Clyde). Mean age was 64 years old (SD 14.4) with a median time since commencing renal replacement therapy of 3 years (IQR 1.4-6.4). The primary renal diagnosis was diabetes for 28% of the patients, multisystem diseases for 21.6%, interstitial nephropathies for 21.5%, primary glomerulonephritis for 15.8%, and unknown or related to another disease for 10%. Of these 527 (73%) were prescribed a form of analgesia. 404 patients (56%) were prescribed paracetamol, 14 (1.9%) were prescribed a non-steroidal anti-inflammatory, 96 (35.4%) an opioid, 71 (9.8%) a combination of paracetamol with opioid, 170 (23.6%) a gabapentinoid and 100 (14%) were prescribed both a gabapentinoid and opioid. There was no difference in age between those receiving analgesia and those who were not (63.5 vs 65.2, p=0.13). However patients receiving opioids were significantly younger than those who were not prescribed any opioid (62.2 SD 13.9 vs 65 SD 14.5, p-value = 0.001; Wilcoxon rank sum test). There was no difference in percentage of patients receiving analgesia by primary renal diagnosis: Figure 1 (Chi-square test, p=0.1).

Conclusion: Prescribing rates of analgesia are high in patients undergoing chronic dialysis suggesting a high burden of chronic pain.



Number of patients receiving analgesia (in red) or not (in blue), depending on their primary renal diagnosis. 1=primary glomerulonephritis, 2=interstitial nephropathies, 3=multisystem diseases, 4=diabetic nephropathy, 5=not known or other

Figure:

Number of patients receiving analgesia (in red) or not (in blue), depending on their primary renal diagnosis. 1=primary glomerulonephritis, 2=interstitial nephropathies, 3=multisystem diseases, 4=diabetic nephropathy, 5=not known or other

P1469 **HOW LONG ELDERLY ESRD PATIENTS CAN UNDERGO DIALYSIS TREATMENT?; A NATIONWIDE POPULATION-BASED COHORT STUDY**

Yu Mi Yang[1], Seung Woo Lee[1], Soon Kil Kwon[1,2], Sang Won Nam[1], Hye-Young Kim[1,2], Hyunjeong Cho[1], Sun Moon Kim[1]

[1]Chungbuk National University Hospital, Internal Medicine, Cheongju, Korea, Rep. of South and [2]Chungbuk National University College of Medicine, Nephrology, Cheongju, Korea, Rep. of South

Background and Aims: Elderly population is increasing and the age starting dialysis treatment is also increasing.

It could be an ethical issue that we should do or not do start dialysis treatment in the oldest old people such as 10th decade.

We investigated duration of dialysis therapy via patients age using National Health Insurance calim data to know dialysis survival of patients via their age.

Method: Korean National Health Insurance Database was used and excerpted data from the insurance claim of ICD code of dialysis. We included all new patients starting dialysis more than 3 months between 2004 and 2013 and compared dialysis duration among the age group.

Patients on dialysis before 2003 were excluded, and patients on kidney transplantation were also excluded.

Results: Total 208,202 dialysis patients were included via dialysis insurance calim code from about 50,000,000 South Korean population during the year 2003 to 2015. 126,448 patients were excluded due to dialysis before 2003, < 3 months of dialysis duration, kidney transplatation, and to have missing data.

Among the final 81,754 patients, 73,969 were hemodialysis and 7,785 were peritoneal dialysis. 47,798 were men and 33,956 were wemen.

Observed median dialysis duration of each aged group of 20-40, 41-50, 51-60, 61-70, 71-80, 81-90, and >90 were 5.4 (2.2 - 18.3), 5.0 (1.8 - 17.7), 4.2 (1.5 - 15.1), 3.5 (1.2 - 12.6), 2.7 (0.9 - 10.1), 1.8 (0.5 - 7.1), 1.3 (0.3 - 4.9) years, respectively ($p < 0.0001$).

Comparing with age under 40, dialysis survival hazard ratio of > 40, > 50, > 60, > 70, > 80, and > 90 were 1.493, 2.452, 3.762, 6.113, 9.787, and 15.326, respectively ($p < 0.0001$). Survival probability of the patients by the age was demonstrated in the figure 1.

Lowest socio-econonic status and highest Charson-Comorbidity group showed highest hazard ratio of dialysis mortality, and peritoneal dialysis showed longer dialysis duration (HR 0.704, 95% CI of 0.69 - 0.74, $p < 0.0001$).

Conclusion: We concluded that dialysis durability by the age was rapidly decreased after 70 years old. As the longest patients survival of > 90 years were less than 5 years, we should consider patients' general performance when starting dialysis of oldest old patients.

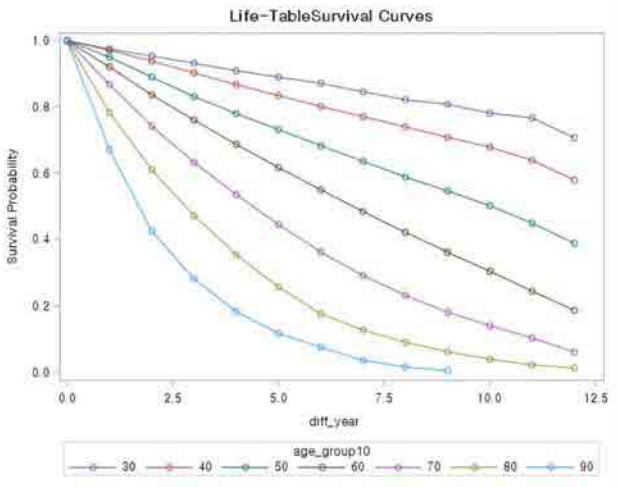


Figure:

P1470 PREGNANCY IN HEMODIALYSIS: EXPERIENCE OF HEMODIALYSIS CENTERS IN SOUTHERN TUNISIA DURING 34 YEARS

Dorsaf Gouja[1], Toumi Selma[2], Zini Olfa[3], Chaker Hanen[2], Dammak Najla[2], Agrebi Ikram[2], Yaich Soumaya[2], Khawla Kammoun[2], Ben hmida Mohamed[2]

[1]CHU HEDI CHAKER SFAX, nephrology, sfax, Tunisia, [2]CHU HEDI CHAKER SFAX, nephrology, Sfax, Tunisia and [3] CHU HEDI CHAKER SFAX, nephrology, Sfax, Tunisia

Background and Aims:

Women with chronic kidney disease are much less likely to become pregnant and pregnany has always been considered as a challenging event both for the mother and the fetus. The challenge is harder in patients undergoing dialysis.

The main objective of our work is reporting our experience of pregnancy's cases in hemodialysis centers in southern Tunisia.

Method:

It was a retrospective study looked at 25 spontaneous pregnancies in 19 patients treated with periodic hemodialysis in different hemodialysis centers in southern Tunisia over a period of 34 years. All pregnancies were spontaneous and are counted even spontaneous or voluntary abortions during the 1st and 2nd trimester of pregnancy

Results:

The maternal age at the onset of pregnancy was, on average, 35.63 years ± 5.62 (between 23 and 44 years). Our study included 19 patients from southern Tunisia, 6 of them belonged to the governorate of Medenine. Hypertension was present in 7 patients (37%). The average duration of hemodialysis before conception is 4.56 years ± 3.55 (1 - 17 years). Seven patients (37%) had residual diuresis of: 1 liter per 24h in 2 cases, 500ml per 24h in other cases and the rest of the patients were anuric. All our patients were anemic before pregnancy with a mean hemoglobin level at 8 ± 1.54 g / dl (5.1 - 10.6 g / dl) with erythropoietin use in 12 (48%), folate in 11 cases (44%), intravenous iron in 11 cases (44%) and transfusion in 6 cases (24%).In our series, the average urea level was 22.19 ± 4.29 mmol / L .The urea level was lower or equal to 20 mmol / L in 8 cases (42%) and greater than 20 mmol / L in 11 cases (58%). Among the 25 pregnancies, 16 (64%) resulted in the birth of a live child: 4 intra-uterine malformations, 4 early abortions and one voluntary termination of pregnancy. There were 2 deaths within 28 days after birth.

Pregnancy was considered a success if it resulted in the birth of a newborn surviving at least 28 days. Thus, the success rate was estimated at 56%. Among the maternal complications, hypertension was the most frequently complication (35% of cases). There were 2 cases of hemorrhage's delivery as obstetrical complication. Among fetal complications, prematurity was frequent and was present in 15 cases (60%): 10 cas (40%) of average prematurity, 4 cases (16%) of great prematurity and 1 case (4%) of extreme immaturity. Hydramnios was found in 3 cases (16%). Intra-uterine growth retardation was found in 13 cases (52%) and 6 cases of death (24%) were described.

Conclusion:

Pregnancy during chronic end stage renal failure is rare but possible. The chance of giving birth to a live child has increased in parallel with advances in hemodialysis techniques and early weight-bearing. Thus, a successful pregnancy in woman on dialysis requires collaboration among nephrologists, dialysis unit staff and obstetricians.

P1471 **FUNNEL PLOTS OF PATIENT-REPORTED OUTCOMES (PROS) TO EVALUATE NEPHROLOGICAL CARE: BASIC PRINCIPLES AND CONSIDERATIONS**

Esmee M. Van der Willik[1], Erik Van Zwet[2], Frans J. Van Ittersum[3], Marc H. Hemmelder[4,5], Friedo W. Dekker[1], Yvette Meuleman[1]

[1]Leiden University Medical Center (LUMC), Department of Clinical Epidemiology, Leiden, Netherlands, [2]Leiden University Medical Center (LUMC), Department of Biomedical Data Sciences, Leiden, Netherlands, [3]Amsterdam UMC, locatie VUmc, Department of Nephrology, Amsterdam, Netherlands, [4]Medical Center Leeuwarden, Department of Internal Medicine, Leeuwarden, Netherlands and [5]Nefrovisie Foundation, Utrecht, Netherlands

Background and Aims: Funnel plots are used to evaluate healthcare quality by comparing hospital performances on certain outcomes. So far, in nephrology, only clinical outcomes like mortality and complications are used for this purpose. However, with the increasing importance of patient-reported outcomes (PROs; e.g. health related quality of life [HRQOL]), PROs should also be taken into account in this quality assessment. Understanding the underlying methods and challenges is needed for optimal use of PROs in this context. Therefore, we aim to provide insight into the use and interpretation of funnel plots by presenting an overview of the basic principles and considerations when applied to PROs, using examples from Dutch routine dialysis care.

Method: Data on PROs (HRQOL and symptom burden), sociodemographic and clinical characteristics of patients receiving dialysis were obtained from the Dutch renal registry and were used to illustrate and explain the different components of a funnel plot, the underlying concepts (e.g. case mix and indirect standardization) and the interpretation of funnel plots. Additionally, some methodological issues are highlighted that should be considered when these methods are applied to PROs.

Results: A funnel plot is a graphical aid that consists of four components: an indicator, reference standard, measure of precision (usually the sample size) and control limits (see Figure). Funnel plots provide insight into hospitals' performances by comparing the observed outcome to the expected outcome. A hospital's expected outcome is calculated using the scores in the reference population (given the hospital's patient population, i.e. case mix) and represents the outcome that would have been observed if the hospital had performed equal to the reference standard. Hospitals may be considered as under- or overperforming when exceeding the upper or lower 95% control limit. Advantages of funnel plots include: clearly visualized precision, detection of volume-effects, discouragement of ranking hospitals and easy interpretation of results. However, without basic knowledge of underlying methods, it is easy to fall into pitfalls, including: overinterpretation of standardized scores, incorrect direct comparisons of hospitals and to assume a hospital to be in-control based on under-powered comparisons. Furthermore, application to PROs is accompanied with additional challenges such as the multidimensional nature of PROs (e.g. HRQOL) which makes adequate case mix correction more difficult, and difficulties with measuring PROs, for instance to achieve high response rates or the dependence on good psychometric properties of the PRO-measures.

Conclusion: PROs partly determine the value of nephrological care and should therefore be considered in healthcare quality assessment. Understanding of the underlying methods using funnel plots is necessary for optimal use and correct interpretation of hospital comparisons on PROs. Some challenges need to be addressed before these methods can be applied to PROs, namely: high and consistent response rates, adequate case mix correction and high-quality PRO measures.

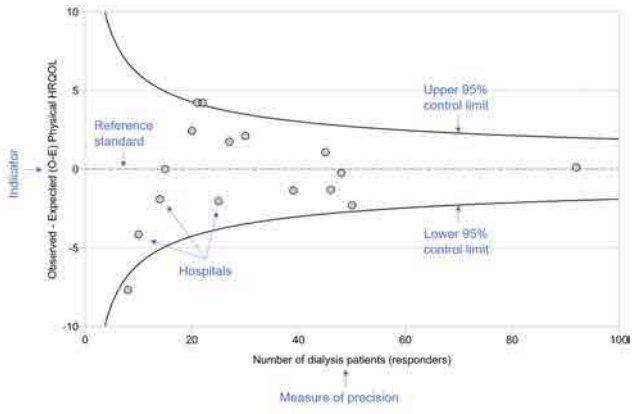


Figure. Example funnel plot for hospital comparison on health-related quality of life (HRQOL) in Dutch dialysis patients.

P1472 RELATIONSHIP OF PHYSICAL PERFORMANCE, MUSCLE STRENGTH AND BODY COMPOSITION WITH QUALITY OF LIFE IN HEMODIALYZED PATIENTS

Maja Nowicka[1], Monika Górska[1], Magdalena Szklarek-Kubicka[2], Zuzanna Nowicka[3], Katarzyna Staniecka[1], Kazanek Adam[4], Malwina Prylińska[4], Tomasz Kostka[5], Ilona Kurnatowska[1]

[1]Medical University of Lodz, Department of Internal Medicine and Transplant Nephrology, Łódź, Poland, [2]Norbert Barlicki Memorial Teaching Hospital No. 1, Dialysis Department, Łódź, Poland, [3]Medical University of Lodz, Department of Biostatistics and Translational Medicine, Łódź, Poland, [4]Medical Center Lodz Baluty, Therapeutic Rehabilitation Outpatient Clinic, Łódź, Poland and [5]Medical University of Lodz, Department of Geriatrics, Łódź, Poland

Background and Aims:

Chronic hemodialysis (HD) is associated with prolonged immobilization, chronic inflammation, and protein-energy wasting, which can decrease muscle mass and impair their function. HD also contributes to excessive fatigue, decreased functional capacity and exercise tolerance, which influence HD patients' everyday lives in multiple areas - personal and professional life as well as everyday activities.

The study aimed to analyze the relationship between HD patients' body composition, muscle mass, strength and physical performance, and their reported quality of life (QoL).

Method:

We enrolled adult, stable patients chronically HD for at least 3 months. Patients' height and weight were measured; their overhydration (calculated as a percentage of dry weight) and body composition (lean tissue mass - LTM, fat tissue mass - FTM) were assessed using an electrical bioimpedance analyzer (BCM Fresenius™). Skeletal muscle mass (SMM) was calculated. The maximal voluntary force of five muscle groups of both lower extremities was assessed with a handheld dynamometer (microFET®2). Physical performance was evaluated with the Short Physical Performance Battery (SPPB), a tool assessing gait speed, chair stand, and balance. All measurements were performed by trained personnel before the same midweek dialysis session.

The Short Form-36 (SF-36), EQ-5D and EQ-VAS questionnaires were utilized in self-assessment of QoL and functional capacity. The SF-36 questionnaire consists of two primary components: physical health (PHC) and mental health (MHC). EQ-5D and EQ-VAS assess patients' health status across five dimensions and their overall health perception.

Coexisting conditions were assessed using the Charlson Comorbidity Index (CCI). Laboratory data (red blood cell and iron metabolism parameters, calcium, phosphate, and PTH) from 3 routine monthly assessments preceding the study were collected from medical records.

Results:

We enrolled 60 HD patients (20F, 40M) with a mean age of 61.9±13.5 years and median time of HD of 34.5 (10-81.8) months.

Mean LTM% was 48.3±13.2%, FTM% 35.6±9.9% and median overhydration was 0.8 (-0.4-2.7) %. Median SPPB score was 9 (6-11) points; 4 patients presented with severe, 12 with moderate and 44 with mild or no functional limitations. The mean score of CCI was 6.1±2.6 points.

The mean SF-36 QoL score was 59.5±17; the score was unrelated to sex (P=.649), age (P=.165) and HD vintage (P=.349). Median values of the PHC and MHC were 54.2 (41.1-69.1) and 67.9 (77.7-17.3), respectively. Both components correlated with each other (R=.67, p<.001). EQ-D5 [median of 1.6 (1.2-2.2) points] and EQ-VAS [median of 60 (50-80) %] scores significantly correlated with SF-36 QoL (R=-.75, P<.001 and R=.50, P<.001, respectively).

SF-36 QoL correlated positively with SMM (R=.36, P=.005), LTM% (R=.39, P=.002) and SPPB scores (R=.28, P=.030), but negatively with FTM% (R=-.36, P=.004). PHC correlated positively with lower extremity muscle strength (R from .29 to .44, every P<.05), SMM (R=.31, P=.017), LTM% (R=.34, P=.008) and SPPB scores (R=.38, P=.003), and inversely with FTM% (R=-.27, P=.030) and CCI scores (R=-.33, P=.009). MHC correlated with positively with SMM (R=.29; P=.024) and LTM% (R=.40, P=.002), but inversely with FTM% (R=.37; P=.003).

No significant correlations between laboratory results and other parameters were found.

Conclusion:

Better physical performance, higher lean tissue percentage, higher muscle mass and strength, as well as lower fat percentage and lesser comorbidity burden are associated with better self-perceived quality of life in HD patients - both physical and mental health.

P1473 **THE EFFECT OF SERUM C-REACTIVE PROTEIN AND FERRITIN LEVELS ON ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN HAEMODIALYSIS PATIENTS**

Dimitrie Siriopol[1], Raluca Popa[1], Vlad Vasiliu[1], Andreea Neamtu[1], Silvia Corina Cusai[1], Mehmet Kanbay[2], Daniela-Caliopi Voiculescu[3], Stefano Stuard[4], Adrian Covic[1]

[1]"Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania, Nephrology Department, Iaşi, Romania, [2]Koc University School of Medicine, Division of Nephrology, Department of Medicine, Istanbul, Turkey, [3]Fresenius Medical Care, Bucuresti, Romania and [4]Fresenius Medical Care, Bad Homburg, Germany

Background and Aims: Ferritin, is commonly used as a surrogate marker of iron storage in haemodialysis (HD) patients. However, besides being an indicator of iron storage, serum ferritin levels are closely influenced by non-iron related factors, such as systemic inflammation.

The aim of this study is to assess the combined effect of serum ferritin and C-reactive protein (CRP) levels on all-cause and cardiovascular (CV) mortality in a large national cohort of HD patients.

Method: This is a retrospective study which included all patients that were on standard HD therapy in 34 Romanian Fresenius dialysis units at January 1st 2014. The main outcomes were all-cause and CV mortality. Patients were censored at December 31st 2016.

Results: Our study included 1255 patients. The mean age of the population at baseline was 59 years. The median values for CRP and ferritin levels were 4.8 (IQR 1.9-11.0) mg/dL and 696.0 (IQR 448.5-996.8) ng/mL, respectively.

Using the tertiles categories for CRP (<2.7, 2.7-8.1, and >8.1 mg/dL) and ferritin (<536.6, 536.6-876.1, and >876.1 ng/mL) our population was categorized into 9 groups of patients: ***Group 1***: CRP<2.7 mg/dL, ferritin<536.6 ng/mL; ***Group 2***: CRP<2.7 mg/dL, ferritin 536.6-876.1ng/mL; ***Group 3***: CRP 2.7-8.1mg/dL, ferritin >876.1 ng/mL; ***Group 4***: CRP 2.7-8.1 mg/dL, ferritin<536.6 ng/mL; ***Group 5***: CRP 2.7-8.1 mg/dL, ferritin 536.6-876.1ng/mL; ***Group 6***: 2.7-8.1 mg/dL, ferritin >876.1 ng/mL; ***Group 7***: CRP>8.1 mg/dL, ferritin<536.6 ng/mL; ***Group 8***: CRP>8.1 mg/dL, ferritin 536.6-876.1ng/mL; ***Group 9***: CRP>8.1 mg/dL, ferritin >876.1 ng/mL;

During the follow-up (mean 1.75, median 1.94 years), 204 patients (16.25%) died with 103 (8.21%) from CV disease.

The central point of our investigation was to assess the combined effect of CRP and ferritin levels on the two outcomes (Table 1). For the all-cause mortality, after adjustment for different demographic, clinical and biological risk factors, only patients with CRP levels in the highest tertile (CRP>8.1 mg/dL), irrespectively of ferritin levels (***Groups 7, 8 and 9***), remained significantly associated with this outcome.

Table 1. Cox survival analysis with baseline variables, by various levels of adjustment

	Number	All-cause mortality*	CV mortality*
Group 1	155	Ref.	Ref.
Group 2	134	1.45 (0.67-3.14)	1.75 (0.63-4.84)
Group 3	147	1.16 (0.55-2.43)	1.00 (0.38-2.63)
Group 4	138	1.81 (0.73-4.45)	**2.08 (1.07-4.05)**
Group 5	153	1.47 (0.74-2.92)	1.39 (0.54-3.56)
Group 6	121	1.93 (0.99-3.78)	1.67 (0.75-3.73)
Group 7	126	**3.24 (1.58-6.66)**	**2.98 (1.52-5.83)**
Group 8	131	**3.19 (1.53-6.64)**	2.19 (0.86-5.61)
Group 9	150	**2.26 (1.15-4.44)**	1.57 (0.59-4.14)

Bold values are statistically significant. All models account for facility clustering effects.

*** Adjusted** for demographics (age, sex, dialysis vintage, BMI and pre-dialysis systolic blood pressure), comorbidities (chronic heart failure, coronary artery disease, cerebrovascular disease, peripheral vascular disease, cancer, diabetes), laboratory data (albumin, equilibrated Kt/V, haemoglobin, calcium, phosphate), catheter use, renal function (anuric or not), smoking status and dialysis modality (HD or haemodiafiltration).

When considering the CV mortality, in the adjusted analysis, only patients from ***Groups 4*** (2nd tertile CRP, 1st tertile ferritin) and ***7*** (3rd tertile CRP, 1st tertile ferritin) remained associated with a higher risk for the outcome as compared with patients from Group 1.

Conclusion: We show that increased levels of CRP are associated with an increased risk for all-cause mortality in the HD population, irrespective of ferritin levels. However, increasing CRP levels are associated with CV mortality only for the lowest tertile of ferritin levels.

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P1474 **IMPACT OF MALNUTRITION ON HEALTH-RELATED QUALITY OF LIFE IN DIALYSIS PATIENTS: A PROSPECTIVE STUDY**

Daniela Viramontes Horner[1], Fiona Willingham[1,2], Zoe Pittman[2], Nicholas Selby[1,2], Maarten Taal[1,2]

[1]University of Nottingham, Centre for Kidney Research and Innovation, Division of Medical Sciences and Graduate Entry Medicine, Derby, United Kingdom and [2]Royal Derby Hospital, Renal Medicine, Derby, United Kingdom

Background and Aims: Health-related quality of life (HRQoL) is severely impaired in dialysis patients compared to the general population. Previous studies have shown that malnutrition, a frequent complication and independent risk factor for mortality in the dialysis population, is associated with poor HRQoL. However, there is no published evidence regarding the impact of malnutrition on change in HRQoL over time. We sought to determine the most important predictors of poor HRQoL as well as the determinants of change in HRQoL over time in dialysis patients, with a particular focus on malnutrition.

Method: We enrolled 119 haemodialysis and 31 peritoneal dialysis patients in a 1-year single-centre prospective observational study. HRQoL was assessed using the physical and mental component scores (PCS and MCS, respectively) from the 36-Item Short Form Health Survey and the health state and visual analogue scores from the European Quality of Life 5-Dimensions (EQ5D) questionnaire. The 7-point scale Subjective Global Assessment (SGA) was performed to evaluate nutritional status. Energy, protein and fat intake, biochemical variables, anthropometric measurements and handgrip strength (HGS) were also measured. All study assessments were performed at baseline, 6 and 12 months.

Results: Mean age was 64±14 years. Malnutrition was present in 37% of the population (as determined by 7-point SGA). Patients with malnutrition and diabetes had significantly lower MCS, PCS and EQ5D scores compared to well-nourished and non-diabetic patients, respectively. At baseline, chronological age, serum albumin, energy and protein intake, and HGS correlated positively with PCS and EQ5D health state score. Multivariable analysis at baseline identified malnutrition as the strongest independent predictor of decreased HRQoL, after adjusting for confounders (Table 1). Patients who stayed or became malnourished during one year showed a significant decrease in MCS, PCS and EQ5D health state score at 12 months compared to baseline. This same group of patients had significantly lower MCS, PCS and EQ5D scores at baseline and 12 months compared to those who stayed or became well-nourished during one year. Prevalent/development of malnutrition was independently and significantly associated with the 1-year decrease in MCS and EQ5D health state score. In addition, a decrease in serum total protein and dietary protein intake (markers of malnutrition) were identified as independent determinants of 1-year decrease in MCS, PCS and EQ5D health state score.

Conclusion: We observed in this prospective observational study that presence of malnutrition was the most important and strongest independent predictor of decreased HRQoL in this dialysis population. Furthermore, prevalence/development of malnutrition and a decrease in markers of nutritional status were independently associated with a decrease in some HRQoL scores over 1 year. These findings strengthen the importance of undertaking screening to identify malnutrition, and providing specialised, individualised nutritional advice to all dialysis patients in order to prevent and/or improve nutritional status. Future studies with larger sample sizes, longer follow-up, and which include evaluation of barriers to effective nutritional interventions are needed to evaluate the impact of nutritional interventions on HRQoL and other long-term outcomes.

Table 1. Multivariable linear regression analysis to identify independent determinants of quality of life at baseline.

Independent variables	*Dependent variable*											
	Mental component score			Physical component score			EQ5D Health state score			EQ5D Visual analogue score		
	B	Beta	p Value	B	Beta	p Value	B	Beta	p Value	B	Beta	p Value
Age (years)	0.374	0.336	<0.0001	0.169	0.148	0.06	0.005	0.242	0.001	0.109	0.065	0.7
Sex (Male vs. Female)	-1.998	-0.063	0.5	-0.514	-0.016	0.9	-0.072	-0.122	0.2	-4.405	-0.093	0.4
Diabetes (No vs. Yes)	-5.148	-0.168	0.02	-7.784	-0.249	0.001	-0.151	-0.264	0.001	-10.22	-0.223	0.008
Previous atrial fibrillation (No vs. Yes)	-0.372	-0.008	0.9	-6.148	-0.135	0.04	-0.091	-0.110	0.1	-4.223	-0.063	0.4
Handgrip strength (kg)	0.137	0.105	0.3	0.246	0.183	0.046	0.007	0.268	0.006	0.047	0.024	0.8
Energy intake (kcal/day)	-0.001	-0.051	0.5	-0.003	-0.118	0.1	-2.968	-0.058	0.5	-0.005	-0.112	0.2
Serum albumin (g/L)	0.209	0.062	0.4	0.064	0.019	0.8	0.000	0.008	0.9	0.014	0.003	1.0
Nutritional status (Well-nourished vs. Malnourished)	-15.21	-0.484	<0.0001	-16.47	-0.512	<0.0001	-0.228	-0.389	<0.0001	-21.30	-0.452	<0.0001
Adjusted R^2		0.380			0.396			0.328			0.193	

Results presented as unstandardized (B) and standardized (Beta) coefficients.

Abbreviations: EQ5D, European Quality of Life 5-Dimensions.

Figure:

P1475

THE THRESHOLD OF BECK DEPRESSION INVENTORY SCORE AS A POTENTIAL PREDICTOR OF ALL-CAUSE MORTALITY IN END-STAGE RENAL DISEASE PATIENTS WITH DIALYSIS IN CHINA

Bo Liu[1], Sha Fu[1], Peifen Liang[1], Jiajia Li[1], Qianqian Han[1], Qiongqiong Yang[1]

[1]*Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Nephrology, Guangzhou, P.R. China*

Background and Aims: Depression is the most frequent psychologic problem among end-stage renal disease (ESRD) patients with dialysis. The Beck Depression Inventory (BDI) is considered to be the standard instrument for assessing symptoms of depression and screening for clinical depression. The level of BDI score associated with mortality in ESRD patients with dialysis remains controversial. High quality evidence is lacking, especially in China. The aim of our study is to evaluate the threshold of BDI score as a potential predictor of all-cause mortality in ESRD patients with dialysis in China.

Method: We conducted a retrospective cohort study involving adults who were treated with dialysis in the department of nephrology of Sun Yat-sen Memorial Hospital in Guangzhou, China between April 2006 to July 2017. Depression symptoms, sleep quality, health-related quality of life were assessed via the BDI- = 2 * ROMAN * MERGEFORMAT II, the Pittsburgh Sleep Quality Index (PSQI) and the 36-item Short Form Health Survey Questionnaire (SF-36) respectively. The primary endpoint of interest was all-cause mortality. Cox proportional hazards regression analysis was performed.

Results: 109 dialysis patients with an mean age of 50.2 years provided complete responses to the BDI-II questionnaire. The median follow-up time for the cohort was 68.6 months until Dec 1, 2019. There were 21 deaths (19.3%). Univariate analyses indicated that age (RR=1.039, 95% CI 1.002, 1.076, ***P*** =0.039), PSQI score (RR=1.170, 95% CI 1.047, 1.306, ***P*** =0.005), pre-existent cardiovascular disease (RR=3.223, 95% CI 1.310, 7.932, ***P*** =0.011), pre-existent diabetes mellitus (DM) (RR=3.321, 95% CI 1.393, 7.919, ***P*** =0.007), and BDI score ≧17 (RR=4.247, 95% CI 1.730, 10.429, ***P*** =0.002) were significantly associated with an increased risk for all-cause mortality, while physical component summary (PCS) of SF-36 (RR=0.971, 95% CI 0.950, 0.992, ***P*** =0.007) and mental component summary (MCS) of SF-36 (RR=0.968, 95% CI 0.948, 0.988, ***P*** =0.002) with a decreased risk for all-cause mortality. In the multivariate Cox regression model, DM (RR=3.658, 95% CI 1.532, 8.733, ***P*** =0.003) and BDI score ≧17 (RR=4.454, 95% CI 1.808,10.974, ***P*** =0.001) were independent predictors of all-cause mortality.

Conclusion: This study revealed that BDI score ≧17 was a predictor of all-cause mortality in ESRD patients with dialysis. Further prospective trials will be required to determine whether the treatment of depression in dialysis patients would alter health-related outcomes, including survival.

P1476 **IRON PARAMETERS PREDICT CARDIOVASCULAR EVENTS IN MAINTENANCE HEMODIALYSIS PATIENTS**

Sayoko Yonemoto[1], Takayuki Hamano[2], Yusuke Sakaguchi[2], Atsushi Wada[2], Ikuto Masakane[2], Kosaku Nitta[2]

[1]Hyogo Prefectural Nishinomiya Hospital, Department of Internal Medicine, Nishinomiya-city, Japan and [2]The Committee of Renal Registry, the Japanese Society for Dialysis Therapy, Bunkyo-ku, Japan

Background and Aims: Previous studies revealed the association between iron deficiency and thromboembolic events, whereas the association between high serum ferritin and poor prognosis of cerebral haemorrhage was reported in the general population. Since few reports have revealed the relationship between iron parameters and cardiovascular events in hemodialysis (HD) patients so far, our purpose was to examine whether iron parameters predict cardiovascular events in HD patients based on the nation-wide database of patients undergoing dialysis in Japan.

Method: We enrolled 126,560 patients aged between 20 and 100 who had been on maintenance HD more than 1 year and three times weekly at the end of 2012. We divided baseline transferrin saturation (TSAT) levels into 3 categories (T1: <20, T2: 20-25, T3: >25%) and serum ferritin levels into quartile (Q1: <31, Q2: 31-73, Q3: 73-158, Q4: >158 ng/mL). The study outcomes were new onset of myocardial infarction (MI), cerebral infarction (CIF), and cerebral haemorrhage (CHM) and death due to these three diseases between 2012 and 2013. We performed multivariate logistic regression for the incident events and also employed Cox proportional hazards analyses for death. Multiple imputation method with 5 data sets was performed for missing values.

Results: During a 1-year follow-up, a total of 2,087 MI (373 deaths), 2,930 CIF (283 deaths), and 1,371 (359 deaths) CHM occurred. After adjustment for demographic and clinical factors, odd ratios (ORs) for MI and CIF were significantly higher among patients with T1 of TSAT than those with T3 (OR; 1.19 (95% confidence interval (CI), 1.07-1.33), 1.16 (95% CI, 1.06-1.27, respectively), and serum ferritin levels were not associated with those outcomes. On the other hand, TSAT was not associated with CHM, however, stepwise increase of OR with the increase of ferritin quartile was observed; patients with Q4 of ferritin had the highest risk for CHM (OR; 1.32 (95% CI, 1.12-1.57) as compared to Q1). In the multivariable Cox regression models, the hazard ratios (HRs) for death due to MI and CIF of the patients with T1 of TSAT were 1.28 (95% CI, 1.00-1.65) and 1.40 (95% CI, 1.06-1.86) as compared to T3, respectively. HR for death due to CHM in patients with Q1-Q4 of ferritin was 1.00 (Reference), 1.59 (95% CI, 1.12-2.25), 1.90 (95% CI, 1.35-2.67), 1.61 (95% CI, 1.13-2.29), respectively (Figure). Furthermore, high dose of erythropoietin stimulating agents was a risk factor of all three cardiovascular events and mortality.

Conclusion: Low TSAT levels predicted MI and CIF and high serum ferritin levels predicted CHM in HD patients. These results suggest that functional iron deficiency could affect thromboembolic events, while increase in storage iron could affect microvascular fragility.

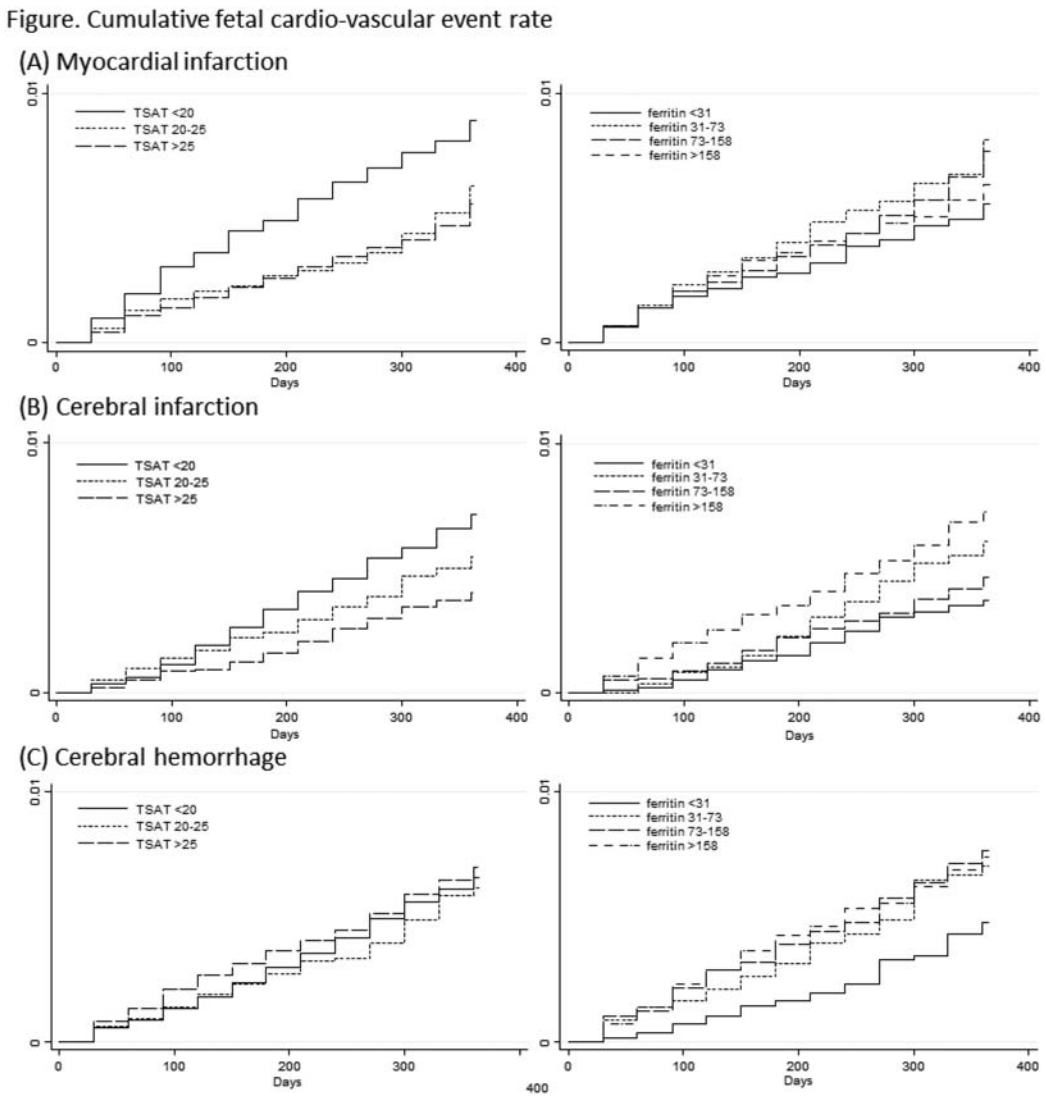


Figure:

P1477 **EFFECT OF INTRADIALYTIC EXERCISE IN A MEXICAN MAINTENANCE HEMODIALYSIS POPULATION.**

Carlos Chavez-Mendoza[1], LUIS IGNACIO MANZO-ARELLANO[1], AIRY SANTILLÁN-CERÓN[1], SAGRARIO CASTILLO-JUÁREZ[1], CÉSAR ULISES RAMÍREZ-SALGADO[1], ADÁN RODRÍGUEZ-GARCÍA[1]

[1]*HOSPITAL CENTRAL MILITAR, NEPHROLOGY, MEXICO CITY, Mexico*

Background and Aims: The use of intradialytic exercise has been associated with improved clearance, oxygen consumption, quality of life, and physical performance. The aim of this study was to describe the association between of intradialytic exercise and some outcomes in a Mexican maintenance hemodialysis (HD) population.

Method: Observational comparative study that included 84 maintenance HD patients from one HD center in Mexico City. The population was grouped according to the intradialytic exercise local record. The aerobic intradialytic exercise protocol includes cycling for 30-45 min during the first 2 hours of the HD according to each patient's ability. A retrospective registry of clinical and biochemical parameters was realized. Also, the hemodynamic parameters of the last six HD sessions for each patient was included. Data analysis was carried out through descriptive and inferential statistics.

Results: Of the total population, 45.2% were men (n= 38) and the mean age was 53.6 ± 17 years. Fifty one percent (n= 43) had diabetes mellitus (DM), which resulted more prevalent in the subgroup of patients without intradialytic exercise (p=0.03) No differences between groups were present in age, history of previous peritoneal dialysis or kidney transplant. The rest of baseline data are shown in Table 1. The subgroup of patients who underwent intradialytic exercise presented higher levels of serum albumin (p=0.03) and lower levels of parathormone (p=0.03). A total of 504 HD sessions were analysed and intradialytic exercise was performed in 64.3% (n=324). Patients in the intradialytic exercise program presented high levels of systolic and diastolic blood pressure (graphic 1). Intradialytic hypotension occurred in 5.2% (n=26) and no differences are shown between groups (p=0.78). No mayor side effects were reported.

Conclusion: The intradialytic exercise could improve nutritional and bone-mineral status markers. The patients in an intradialytic exercise program presented higher levels of blood pressure.

Table 1. Baseline data of the population studied.

	Intradialytic exercise (n=54)	Non intradialytic excercise (n=30)	p-value
Age - years	52.1 ± 16.8	56.2 ± 17.4	0.97
Sex (male) – no. (%)	26 (48.1%)	12 (40%)	0.09
Diabetes mellitus – no. (%)	25 (46.3%)	18 (60%)	**0.03**
HD vintage – months	30.6 ± 22.5	34.9 ± 26	**0.002**
Dry weight – kg	62.6 ± 13.5	61 ± 14.3	0.12
Treatment time – hrs/ session	2.9 ± 0.1	3 ± 0.1	0.33
Interdialytic weight gain – L	2.2 ± 1.1	1.9 ± 1.1	0.96
Ultrafiltration rate – ml/kg/hr	11.9 ± 4.7	10.4 ± 5.1	0.14
Hemoglobin– mg/dL	10.5 ± 1.7	10.2 ± 1.8	0.24
Blood urea nitrogen– mg/dL	57.8 ± 17.7	57.7 ± 19.5	0.08
Serum creatinine – mg/dL	9.7 ± 3.1	9.1 ± 2.9	0.58
Serum sodium – mmoL/L	141.2 ± 4.1	141.8 ± 4.4	0.12
Serum potassium – mmoL/L	5.5 ± 0.6	5.3 ± 0.7	0.33
Serum calcium – mg/dL	8.6 ± 0.9	8.8 ± 0.9	0.69
Serum phosphorus – mg/dL	5.5 ± 1.3	5.6 ± 1.5	0.36
Serum albumine – mg/dL	4.1 ± 0.4	3.9 ± 0.5	**0.03**
Parathormone – pg/mL	758.8 ± 650	990.2 ± 995.1	**0.03**

Figure 1. Blood pressure differences between patients with and without intradialytic exercise program.

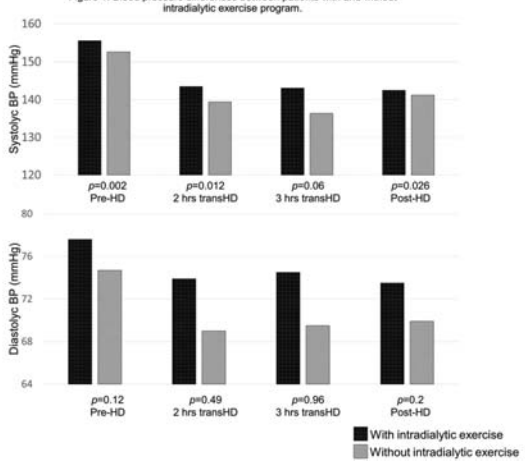


Figure:

P1478 LOWERING PREVALENCE OF ALKALOSIS AND IMPROVING ADHERENCE TO BICARBONATE TARGETS AMONGST HAEMODIALYSIS PATIENTS THROUGH THE USE OF REDUCED DIALYSATE BICARBONATE

Caroline Tulley[1], Richard Hull[2], Martin Ford[1]

[1]King's College Hospital, Renal, United Kingdom and [2]St George's Hospital, Renal, United Kingdom

Background and Aims: There is evidence that metabolic alkalosis in haemodialysis patients is harmful. Bommer *et al* demonstrated association between extremes of bicarbonate and clinical outcomes with significantly increased risk of mortality and hospitalisation with pre-dialysis serum bicarbonate >27mmol/L and <17mmol/L. No overall increased mortality risk was observed with moderate pre-dialysis acidosis (serum bicarbonate 19.1-23.0mmol/L).

2015 Renal Registry Data demonstrated 64.3% of haemodialysis patients overall had bicarbonates within target (18-24mmol/L) compared to 65.7% within our centre. Our reported mean pre-dialysis bicarbonate of 23.7mmol/L was above the mean serum bicarbonate 23.2mmol/L seen nationally. In addition, 33.7% of patients were alkalotic, with bicarbonates >24mmol/L. Given concerns of adverse patient outcomes with extremes of bicarbonate, we aimed to investigate whether reducing our dialysate bicarbonate would culminate in overall attainment of bicarbonate targets.

Method: Mid-week pre-dialysis bicarbonate levels were measured from in centre haemodialysis patients once monthly, from May to August 2017, across 7 dialysis units within our renal service. Following this, in early 2018, we reduced dialysate bicarbonate concentration from 32mmol/L to 31mmol/L. Monthly midweek pre-dialysis bicarbonate levels were then re-measured in March and April 2019.

Results: Initial analysis of 2103 pre-dialysis bicarbonate levels across May to August 2017 demonstrated median monthly bicarbonate levels of 24.0–25.0mmol/L. 40.7–54.2% (n=199-322) were alkalotic with pre-dialysis bicarbonates >24mmol/L across this period. Of note, 15-23% (n=66-120) had bicarbonate levels associated with increased mortality and hospitalisation (i.e. <17mmol/L or >27 mmol/L.

Subsequent analysis of 1070 bicarbonate levels in March and April 2019 demonstrated a reduction in median pre-dialysis bicarbonate to 22.0mmol/L. Similarly, the proportion of alkalotic patients fell to 11.9–15.3% (n=71-91). 5-9% (n=26-46) bicarbonates were <17 or >27mmol/L. In March 2019, 77.9% of patients had serum bicarbonates in target range compared to 65.7% reported in 2015 overall.

Conclusion: Initial findings demonstrated substantial alkalosis amongst our dialysis population. A simple measure of altering dialysate by 1mmol/L achieved reductions in overall alkalaemia, and in turn, reduced the percentage of patients with bicarbonate values theoretically correlating with increased mortality and hospitalization risk.

We have demonstrated that a small change in dialysate bicarbonate increased concordance with bicarbonate targets, without subsequent increased acidaemia. The extent to which adherence with such targets impacts on patient survival and morbidity remains an ongoing debate.

P1479 **HIGHER FREQUENCY OF FRUIT INTAKE IS ASSOCIATED WITH LOWER RISK OF CONSTIPATION IN HEMODIALYSIS PATIENTS - A MULTI-CENTRE STUDY**

Rafaela G. Dos Santos[1], Juliana Malinovski[2], Natália Scatone[3], Jorgiane De Oliveira[4], Andrea Sczip[2], Jyana Moraes[4], FABIANA NERBASS[4]

[1]Centro de Tratamento de Doenças Renais, Jaraguá do Sul, Brazil, [2]Centro de Tratamento de Doenças Renais, Mafra, Brazil, [3]Centro de Tratamento de Doenças Renais, Joinville, Brazil and [4]Fundação Pró-Rim, Research, JOINVILLE, Brazil

Background and Aims: Constipation is a multifactorial gastrointestinal disorder commonly found in hemodialysis (HD) patients. In this multi-centre cross-sectional study, we aimed to evaluate the prevalence and factors associated with constipation, including the frequency of dietary fiber sources intake.

Method: Prevalent HD patients from four dialysis clinics in Southern Brazil were invited to participate (at least 80% of eligible patients from each clinic). Patients were interviewed by the researchers and answered a questionnaire that comprised ROMA III criteria questions to assess constipation status, use of medications and life habits. A food frequency questionnaire (FFQ) with the main dietary fiber sources (fruits, vegetables, legumes, whole grains cereals and seeds) was applied with seven frequency possibilities (from never to more than twice a day). To estimate the weekly frequency of intake, answers were transformed into a score. Every score point corresponded to one time per week (ex.: score 7 = seven times per week). Demographical and laboratory data were obtained from medical records. Univariate analysis was used to compare participants according to constipation status and variables with $P<0.20$ were included in the regression analysis model.

Results: 305 HD patients were included (male: 51%; age: 52.2 $\pm$ 14.7 years old; HD vintage: 46 (19 – 82) months). Ninety-three participants had constipation (30.5%). Median (interquartile) FFQ scores were: fruits: 6 (2-14); vegetables: 6 (3-10); legumes: 3 (1-7); whole-grain: 0 (0-1) and seeds: 0 (0-0). In univariate analysis, participants with constipation were significantly older (55.1 $\pm$ 14.8 versus 51.0 $\pm$ 14.5 years old; P=0.02), had lower literacy (5 (5-11) versus 8 (4-13) years at school; P=0.007), higher prevalence of diabetes (41 versus 23%; P=0.002) and lower total beverage intake (15 (12-20) versus 17 (12-24) ml/kg/day; P=0.04). The logistic regression analysis model also included body mass index; wheelchair need; sedentarism; fruits score and seeds score (all with $P<0.20$ in the univariate analysis).The independent predictors of constipation were diabetes (OR=1.96 (95%IC 1.07-3.6);P=0.03) and fruits intake score (OR=0.95 (95%IC 0.91-0.99);P=0.04)

Conclusion: Almost one-third of participants had constipation, and usual intake of fiber food sources was low. The independent determinants of constipation were diabetes and a lower frequency of fruit intake. Nutritional counselling to increase fiber intake sources can potentially decrease the prevalence of constipation of this population.

P1480 **MOVING TOWARDS OBJECTIVE ASSESSMENT OF FLUID STATUS IN HEMODIALYSIS PATIENTS**

GARYFALIA PERYSINAKI[1], ANDREAS-MICHAHL PASSAM[2], PANAGIOTA PAPADAKI[2], GEORGIOS VLACHOPANOS[2], IRINI NTAOUNTAKI[2]

[1]*RETHYMNON GENERAL HOSPITAL, NEPHROLOGY, RETHYMNON, Greece*

Background and Aims: Correct estimation of the fluid status as represented by the "Dry body weight" (DBW) of hemodialysis (HD) patients is crucial for their cardiovascular health and general well-being. However, DBW assessment through medical history and physical examination by the attending nephrologist may not prove sufficiently accurate. Bioimpedance measurements may offer a more accurate assessment of DBW. Therefore we compared clinical DBW estimation with DBW estimation by bioimpedance. We searched for variables which may correlate with differences between the two methods.

Method: Observational, single center cross sectional study. Fifty HD patients (32 males) consented to participate. Laboratory, clinical and epidemiological data were drawn from the medical records. Bioimpedance measurements were performed by the Body Composition Monitor (Fresenius Medical Care) before a mid- week hemodialysis session and were compared with parallel DBW estimations based on medical history and physical examination. A variable "difference DBW" was derived from the difference between the two parallel estimations of DBW ("difference DBW" = clinical DBW estimation – bioimpedance DBW measurement). Univariate and bivariate correlation analyses were used.

Results: The mean age, years in end stage renal disease (ESRD), Kt/V, serum albumin, body mass index (BMI), lean tissue index (LTI), and adipose tissue mass (ATM) of the participants were 66.8±13.878y, 8±8.132y, 1.48±0.269, 3.8±0.313g/dL, 27.97±4.595, 13.26±3.982, 37.32±13.159Kg respectively. DBW estimated by the nephrologists was significantly lower (72.94 ± 14.637 kg) than DBW estimated by bioimpedance (74.82 ± 15.594 kg), a decrease of 1.882 (95% CI, -2.425 to -1.339kg), $t(49) = -6.963$, $p < 0.001$. Significant negative correlation was found between "difference DBW" and BMI $r(48) = -0.69$, $p < 0.001$. Moderate negative correlation was found between "difference DBW" and LTI $r(48) = -0.42$, $p = 0.002$, and between "difference DBW" and ATM, $r(48) = -0.41$, $p = 0.003$. Moderate positive correlation was found between "difference DBW" and years in ESRD $r(48) = 0.43$, $p = 0.002$. There were no significant correlations between sex, age and "difference DBW".

Conclusion: In our cohort there were significant differences between clinical DBW estimations and corresponding Bioimpedance DBW measurements. This difference was more pronounced in patients with low BMI and ATM, as well as in patients with more years on ESRD. Therefore we consider that these findings should be taken into consideration when determining DBW.

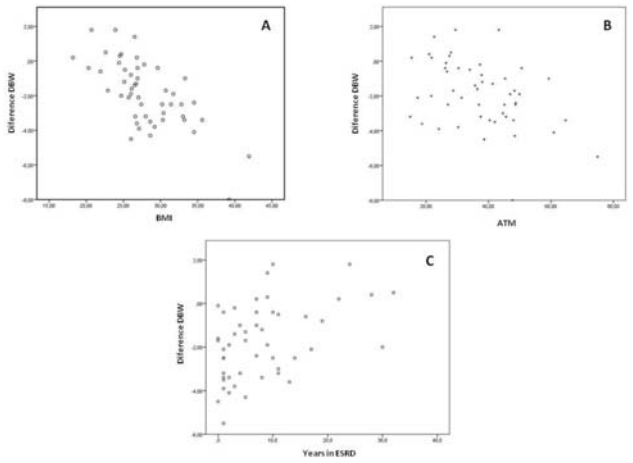


Figure:

Figure SEQ Εικόνα * ARABIC 1: Scatterplots (A) Significant negative correlation between "difference DBW" and BMI $r(48) = -0.69$, $p < 0.001$. (B) Moderate negative correlation between "difference DBW" and ATM, $r(48) = -0.41$, $p = 0.003$. (C) Moderate positive correlation between "difference DBW" and years in ESRD $r(48) = 0.43$, $p = 0.002$. DBW: dry body weight, BMI: body mass index, ATM: adipose tissue mass, ESRD: end stage renal disease

P1481 **STRAIN REPOLARISATION ON ECG, NOT LEFT VENTRICULAR MASS, ASSOCIATES WITH CARDIOVASCULAR OUTCOMES IN A PROSPECTIVE COHORT OF HAEMODIALYSIS PATIENTS**

Sofia Skampardoni[1], Diana Y.Y Chiu[1], Philip A. Kalra[1], Darren Green[1]
[1]*Salford Royal Foundation Trust, Nephrology, Salford, United Kingdom*

Background and Aims:

Cardiovascular disease is common in chronic and end stage kidney disease. Left ventricular hypertrophy (LVH) has been identified as contributor to cardiovascular risk in this population. The aim of the study was to assess whether the combined use of electrocardiography and echocardiography in assessing LVH in a haemodialysis population can provide improved risk stratification.

Method:

Prospective study of 192 prevalent maintenance haemodialysis (HD) patients 12 lead ECGs were performed on a mid week non –dialysis day. Electrocardiographic strain was defined as a down slopping convex ST segment with inverted T waves in leads V5 and / or V6. Transthoracic echocardiographic was performed immediately after ECG .LV mass was indexed to body surface area (LVMIBSA). LVH was determined if LVMI $>116 g/m^2$ for male patients, and $>100 g/m^2$ for female patients. The primary study endpoint was major cardiac events (MACE). A secondary endpoint was all cause mortality.

Results:

192 patients included in the final analysis, 137 (71.4%) male.. The mean ejection fraction (EF) was 60.6± 11.1 % and the mean LVMI (BSA) was 115.0± 36.8 $g/m^{2.}$ During a mean follow up period of 2.4 ± 1.0 years, 50 patients reached a MACE end point and 62 patients died. On univariate Cox regression analysis, the factors associated with MACE were the presence of ECG strain (HR 2.961, CI: 1.254 – 6.990, p= 0.013)) URR (HR 0.968, CI: 0.942 – 0.994, p=0.015) and history of CAD (HR: 2.397 CI: 1.363 - 4.2515, p= 0.002). In multivariate Cox regression analysis adjusting for baseline cardiovascular phenotype and dialysis parameters ECG strain remained significantly associated with MACE.

Conclusion:

The presence of electrocardiographic strain increases the risk for MACE independently of LVH in haemodialysis patients. ECG strain has potential to be a simple bedside prognostic biomarker and even therapeutic target in haemodialysis patients.

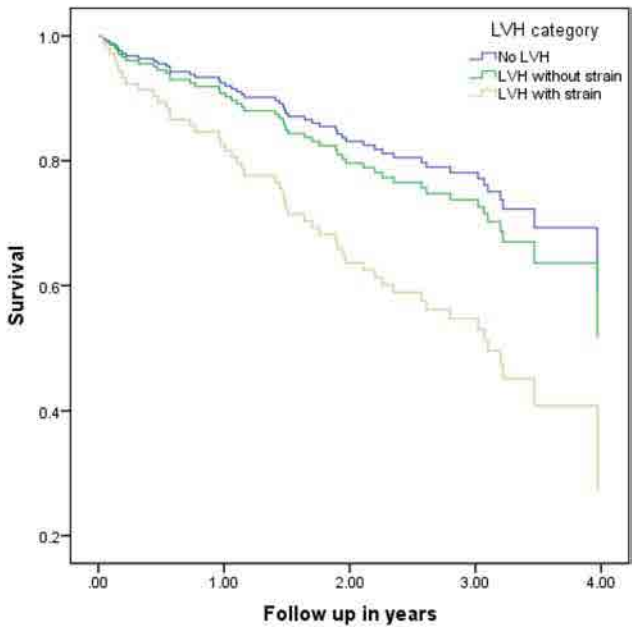


Figure 1. Survival curve for major cardiac events, comparing patients without left ventricular hypertrophy (LVH) against those with LVH but no strain pattern abnormalities on ECG, and those who have LVH with strain.

P1482 **MORTALITY RATE AND RELATED RISK FACTORS IN THE CHINA DIALYSIS OUTCOMES AND PRACTICE PATTERNS**

Xinju Zhao[1], Qingyu Niu[1], Liangying Gan[1], Li Zuo[1,1]

[1]*Peking University People's Hospital, Nephrology, Beijing, P.R. China*

Background and Aims: Mortality risk for maintenance hemodialysis (MHD) patients varies by country and ethnicity. Here, mortality rate and its related risk factors in Chinese HD patients from Dialysis Outcomes and Practice Patterns Study (DOPPS) were studied.

Method: Data from the China DOPPS phase 5 (2012-2015) were used. All included patients were followed to the end of the study. Patients' demographics, primary cause of end stage renal disease (ESRD), comorbidities, abstracted dialysis prescription, laboratory values, date of death, and causes for death were analyzed. All-cause mortality (per 100 patient-years) was calculated. We examined clinical and laboratory differences between died and survived patients. Cox regression was used to explore risk factors of death, accounting for facility clustering and adjusted for case-mix (age, sex, vintage, and comorbid conditions), and laboratory values (albumin, hemoglobin, white blood count, sodium).

Results: There were 1427 MHD patients were enrolled. The mean age at dialysis initiation was 59.4±14.9 years (table 1). The median follow-up time was 1.9 years (IQR 1.1-2.1). There were total 205 deaths. The overall mortality rate was 8.8 per 100 patient-years. Death from cardiovascular disease (CVD) occurred in 50.2% of the patients. Compared with survived patients, patients with mortality were older (58.5 Vs. 70.0 y), more likely with diabetes, with lower pre-dialysis albumin level (Pre-ALB) or hemoglobin level (Pre-HGB), with lower pre or post dialysis diastolic blood pressure (DBP), with some comorbidities and less likely with fistula as their blood access (table 2). Cox regression revealed that risk factors for higher mortality were older age, lower Pre-ALB level, higher pre-dialysis DBP and with CHF, hepatitis, hypertension, and lung disease.

Conclusion: CVD constituted half of the death reasons for Chinese dialysis patients. Our analysis highlighted that there are some modifiable risk factors for patients' survival. Attention should be paid to patients who were older, with lower Pre-ALB level, higher pre-dialysis DBP and with CHF, hepatitis, hypertension, and lung disease.

Table 1. Patient Baseline Characteristics, by Death status

	Survived(n=1222)	Died(n=205)	P-value
Age	58.5 (49.0-69.0)	70.0 (59.0-79.0)	<0.001*
Female	45.2%	43.9%	0.8
BodyMassIndex	21.9±3.7	21.8±4.0	0.8
Dialysis Vintage	2.6 (0.8-5.5)	2.5 (1.0-5.0)	0.4
Catheter and others	13.3%	19.5%	0.066
Fistula	85.7%	80.0%	0.047*
Pre-ALB	3.9±0.5	3.7±0.5	<0.001*
Pre-HGB	10.5±1.9	10.1±2.0	0.006*
UrineOutput	33%	27%	0.1
Pre-Weight	62.0±11.9	61.0±11.5	0.3
Post-Weight	59.7±11.7	58.7±11.2	0.3
IntraDialyticWgtLoss	0.04±0.0	0.04±0.0	0.6
Pre-SBP	147.9±20.3	150.3±20.7	0.2
Pre-DBP	79.7±12.4	77.2±12.6	0.010*
Post-SBP	140.7±22.7	141.8±21.5	0.5
Post-DBP	78.7±12.5	75.6±13.0	0.002*
CHF	21.8%	36.1%	<.0001*
Other CVD	19.5%	29.8%	0.003*
Cerebro-VD	12.7%	24.4%	<.0001*
diabetes mellitus	25.9%	36.1%	0.010*
Fracture	1.9%	5.4%	0.010*
Hypertension	85.9%	80.5%	0.048*
Lung disease	4.0%	10.2%	0.001*
PVD	7.9%	15.1%	0.003*

Table2. Hazard Ratios (HR), for all-cause mortality

Parameter	HR	95% CI-low	95% CI-high	P
age	1.72	1.51	1.97	<.0001
Pre-ALB	0.57	0.43	0.74	<.0001
Pre-DBP	1.02	1.01	1.03	0.004
CHF	1.63	1.21	2.19	0.001
Hepatitis	1.68	1.14	2.46	0.009
Hypertension	0.63	0.44	0.90	0.012
Lung disease	1.69	1.06	2.68	0.026

Abbreviations: ALB, Albumin; HGB, hemoglobin; Pre, pre-dialysis; Post, post-dialysis; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHF, congestive heart failure; other CVD, other cardiovascular disease; Cerebro-VD, cerebrovascular disease; PVD, peripheral vascular disease; CI, confidence interval.

P1483 **INCIDENCE TRENDS IN CHRONIC DIALYSIS: AN IMPORTANT ASPECT, STILL UNDER-REPORTED.**

Elena Mancini[1], Antonio Santoro[1], Gruppo di Lavoro Registro Emilia Romagna[1]
[1]*Ospedale Sant'Orsola - Malpighi, Nephrology, Dialysis and Hypertension, Bologna, Italy*

Background and Aims:

Whereas the progressive increase in the incidence of advanced age patients on chronic dialysis is widely described, the incidence trend concerning younger age patients, a potentially useful datum for the health services programming, has been little investigated.

Method:

The Regional Dialysis Registry of Emilia-Romagna (a region in the north of Italy, near 4,460,000 inhabitants) has been active for 24 years. We analysed the changing incidence in dialysis over time, as a function of 6 different age brackets (excluding the extreme ages, <20 and >90, due to the small numbers involved).

The study considered only hemodialysis patients, not peritoneal dialysis, due to small numbers, and in order to collect data from a more homogeneous population.

For each year from 1994 to 2017, we extracted the percentage incidence on dialysis of each age bracket [(number of cases per bracket/overall number of incident patients)%].

We then carried out a correlation analysis as a function of time.

Results:

The incidence on dialysis turned out to change over time with statistical significance in each one of the age brackets except 70-80. The incidence-time association was positive for the brackets 70-80 and 80-90, and negative for the remaining age brackets (Table 1).

Table1 –Pearson's correlation coefficient and significance

Age brackets→	20-40	40-50	50-60	60-70	70-80	80-90
R	-0.770	-0.481	-0.628	-0.809	0.384	0.906
gdl	22	22	22	22	22	22
p	<0.001	0.02	<0.001	<0.001	0.06	<0.001

A scissor-like trend appeared evident when comparing the most advanced ages with the youngest ones (Figure 1).

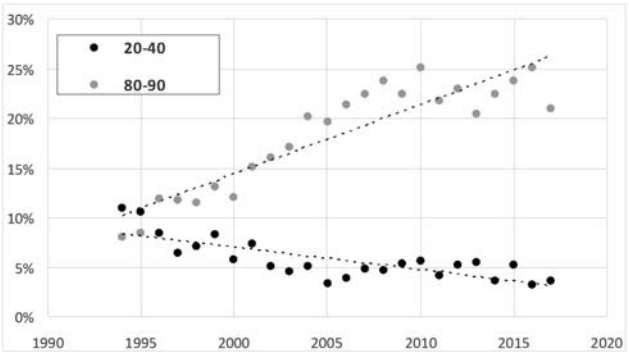


Figure 1 Dialysis incidence trend (%, ordinate) relative to age brackets 20-40 and 80-90 years over 24 years (1994-2017, abscissa) in Emilia Romagna.

Conclusion:

Besides the well-known increase in old patients on chronic dialysis, it should be noted that, on the contrary, younger patients have tended to decrease significantly, at least in our Region. Even bearing in mind the limits of a Registry study, these data may support the value of health programs for the early diagnosis of nephropathy, because prompt pharmacological treatment (at least for glomerular or post-infective, or congenital/hereditary diseases) could reduce the attainment of ESRD and account for the results observed in the lower age-brackets.

P1484

PROGRESSION OF AORTIC ARCH CALCIFICATION IS ASSOCIATED WITH OVERALL AND CARDIOVASCULAR MORTALITY IN HEMODIALYSIS

Hung-Chun Chen[1], Yi-Wen Chiu[1], Jer-Ming Chang[1], Szu-Chia Chen[1]

[1]*Kaohsiung Medical University Hospital, Department of Nephrology, Kaohsiung, Taiwan, R.O.C.*

Background and Aims: Vascular calcification is common and associated with unfavorable outcomes among patients with end-stage renal disease (ESRD). However, little is known whether the progression of vascular calcification outweights the baseline calcification in association with overall and cardiovascular (CV) mortality in hemodialysis (HD) patients.

Method: This study included 140 maintenance HD patients. Vascular calcification was assessed using aortic arch calcification (AoAC) score measured from chest radiographs at the baseline and the second year of follow-up. Progression of vascular calcification (△AoAC) was defined as the difference between the two measurements of AoAC. The association of △AoAC with overall and CV mortality was evaluated using multivariable Cox regression analysis.

Results: During the mean follow-up period of 7.8 years, there were 49 (35%) overall mortality and 27 (19.3%) CV mortality. High brachial-ankle pulse wave velocity was positively correlated with △AoAC, whereas old age and high hemoglobin were negatively correlated with △AoAC. In multivariate adjusted Cox analysis, increased △AoAC (per 1 unit), but not baseline AoAC, was significantly associated with overall mortality (HR, 1.183; 95% CI, 1.056–1.327; $p = 0.004$) and CV mortality (HR, 1.194; 95% CI, 1.019–1.398; $p = 0.028$).

Conclusion: Progression of AoAC outperformed the baseline AoAC in association with increased risk of overall and CV mortality in HD patients. Regular follow-up of chest radiograph and AoAC score assessments are simple and cost-effective to identify the high-risk individuals of unfavorable outcomes in maintenance HD patients.

P1485 **SEVELAMER USE IS ASSOCIATED WITH DECREASED VITAMIN K LEVELS IN HEMODIALYSIS PATIENTS: RESULTS FROM VITAMIN K ITALIAN (VIKI) STUDY.**

Maria Fusaro[1,2], Andrea Aghi[3], Pascale Khairallah[4], Maurizio Gallieni[5], Mario Gennaro Cozzolino[6], Domenico Russo[7], Maria Cristina Mereu[8], Maura Ravera[9], Giovanni Luigi Tripepi[10], Thomas Nickolas[4]

[1]CNR PISA, Institute of Clinical Physiology (IFC), Pisa, Italy, [2]University of Padua, Padua, Italy, [3]Clinica Medica 1, University of Padua, Padua, Italy, [4]Columbia University Medical Center, New York, United States of America, [5]Ospedale San Carlo Borromeo ASST Santi Paolo e Carlo, Milano, Italy, [6]University of Milan, Department of Health Sciences, Milan, Italy, [7]University of Naples Federico II, Napoli, Italy, [8]Asl Sanluri - Ospedale Nostra Signora di Bonaria : Ospedale Nostra Signora di Bonaria Pronto Soccorso, San Gavino Monreale, Italy, [9]St Martino Hospital, Genova, Nephrology and Dialysis Unit , Genova, Italy and [10]Consiglio Nazionale Delle Ricerche, Reggio Calabria, Italy

Background and Aims: Sevelamer (S) is a phosphate binding drug used to treat hyperphosphatemia in patients with CKD. Our aim was to evaluate the hypothesis that the use of (S) could interfere with Vitamin K absorption in hemodialysis (HD) patients of VIKI study.

Method: We tested this hypothesis in VIKI, a cross-sectional study of 387 hemodialysis patients, we established the prevalence of vitamin K deficiency and to assessed the relationship between vitamin K status, vertebral fractures, vascular calcification. We determined serum concentrations of vitamin 25(OH)D; alkaline phosphatase (ALP); vitamers K1, MK4, MK5, MK6, MK7; osteocalcin (BGP) and Matrix Gla Protein (MGP). We highlighted that MK4 deficiency was the strongest predictor of aortic calcification (OR, 2.82; 95% CI, 1.14–7.01) while vitamin K1 deficiency was the strongest predictor of vertebral fractures fractures (OR: 2.94; 95% CI, 1.38–6.26).

Results: 163 of 387 patients (42.1%) were treated with Sevelamer. There were no differences in levels of 25(OH)D, K1, MK5, MK6 and MK7 among patients treated with and without Sevelamer. Remarkably, the prevalence of MK4 deficiency was higher in Sevelamer treated patients (13.5% vs 5.4%, p=0.005). Sevelamer treated patients also had higher median levels of ALK (89 UI/L vs 77.5 UI/L, p=0.001) and total BGP (210 mcg/L vs 152 mcg/L, p=0.002) and lower median levels of total MGP (16.4 nmol/L vs 20.3 nmol/L, p=0.037) (**Table 1** and **Figure 1**). In multivariable logistic regression, the odds ratio of MK4 deficiency (dependent variable) in patients treated with compared to without Sevelamer was ~3-fold higher (OR: 2.64, 95% CI: 1.25-5.58, p=0.011) after adjustment for confounders of Vitamin K levels, including older age, previous myocardial infarction, type of HD, ALP, PTH, MGP, BGP, cholesterol and albumin.

Conclusion: These data support the hypothesis that Sevelamer could interfere with MK4 absorption in HD patients. Longitudinal interventional studies are needed to prove the causal nature of these associations.

Variable	Sevelamer Use N=163, 42,12%	No Sevelamer Use N=224, 57,88%	p-value
Gender, female, n (%)	66 (40.5%)	79 (35.3%)	0.295
Age, years, median	63 (51, 72)	69 (60, 76)	**0.002**
Weight, kg, median	68.5 (59, 80)	69.3 (60.1, 78)	0.504
Height, mean±SD	1.68±0.09	1.67±0.09	0.486
BMI, kg/cm², median	24.2 (21.4, 27.5)	24.7 (22.0, 28.3)	0.260
Alkaline phosphatase, U/L, median	89 (74, 122)	77.5 (61, 105)	**< 0.001**
Total BGP, mcg/L, median	210 (117, 363.2)	152 (83.58, 276)	**0.002**
Decarboxylated BGP, mcg/L, median	11.88 (6.27, 17.00)	10.57 (4.21, 18.75)	0.292
Total MGP, nmol/L, median	16.39 (12.00, 27.63)	20.26 (13.56, 33.29)	**0.037**
Decarboxylated MGP, nmol/L, median	547 (296.9, 920)	584 (265, 944.3)	0.993
MK4, ng/mg, median	0.45 (0.15, 0.67)	0.60 (0.27, 0.67)	**0.010**

Figure 1. MK4 and BGP levels in patients treated with Sevelamer.

P1486 **CHRONIC DIALYSIS IN ELDERLY PATIENTS: FUNCTIONAL PERFORMANCE STATUS AND TREATMENT OUTCOMES - A SINGLE-CENTER STUDY**

Krystsina Kurylovich[1,2], Kirill Komissarov[2,3]

[1]Governmental Research Clinical Hospital №1, Dialysis, Minsk, Belarus, [2]Belarusian Medical Academy of Postgraduate Education, Nephrology, Minsk, Belarus and [3]Minsk Research and Practice Centre of Surgery, Transplantology and Hematology, Nephrology and dialysis, Minsk, Belarus

Background and Aims: The presence of multiple comorbid conditions and different geriatric impairments in elderly patients leads to a certain specificity in the management of this cohort of patients. The aim was to assess changes in functional performance status and treatment outcomes in elderly patients on chronic dialysis.

Method: A single-center longitudinal prospective study was conducted, which included 48 patients aged 65 years and older who underwent dialysis (hemodialysis and continuous ambulatory peritoneal dialysis) for more than 3 months. Participants' functional performance status was measured by the Frailty Scale of Rockwood (FSR) at baseline and after a year of treatment. Functional performance status decline was defined as deterioration by 1 or more positions on the FSR, stable was defined as no difference between baseline and follow-up, and improvement was defined as a gain of 1 or more positions. At baseline, all participants were assessed by the Charlson Comorbidity Index (CCI) and standard lab tests were carried out. All data are presented as median and quartiles (25%; 75%).

Results: The median of age was 69 (67; 74) and 39.6% were women. The main causes of end-stage renal disease were hypertension (33.3%) and diabetes (31.3%). There were 83.3% hemodialysis patients and 31.3% received dialysis up to 1 year.

At baseline 16.7% of patients were frail, 54.2% - pre-frail and 29.1% were fit.

Among frail patients at the 1-year follow-up, 62.5% died, 12.5% had received a kidney transplant (KT), 25% showed a further functional performance status decline.

Among pre-frail patients, almost half (46.2%) experienced functional decline and 15.4% died; the functional status remained unchanged in 30.8% of patients and 3.8% was transplanted; 1 patient (3.8%) had an improvement in functional performance status.

Among fit patients, over half (57.2%) showed stable functional status, a functional decline was observed in 21.4% of patients (all of them became frail), 7.1% died and 14.3% had received a KT.

All patients, who had stable functional performance status after a year of treatment, had target values of kt/v, albumin, and phosphorus at baseline. All deceased patients (20.8%) had CCI $\geq$ 6, 60% of them had high serum phosphorus level. Most functional performance status decline among participants was associated with a loss of mobility, which was most often caused by the progression of chronic heart failure (both independently and after heart attack) or chronic arterial failure (diabetic, due to obliterating atherosclerosis of the lower extremities), including the development of critical limb ischemia, especially in patients on hemodialysis.

The distribution of patients according to the FSR in the initial assessment and re-assessment are presented in the table below.

Conclusion: Functional decline is highly prevalent in elderly patients on chronic dialysis, the risk is higher among frail and pre-frail patients. In most cases, functional performance status decline is associated with a loss of mobility due to the progression of chronic heart or arterial failure. Death probability is higher among frail patients and those with high serum phosphorus level (because of inadequate dialysis due to the initially severe condition of these patients) and high CCI. Achievement in the complex of the target values of kt/v, serum albumin, and phosphorus levels can help to maintain the functional status stable.

Functional performance status	Baseline, N (%)	Follow-up, N (%)	After 1 year follow-up	
			Death, N	Kidney transplantation, N
Fit	14 (29.1)	9 (26.5)	1	2
Pre-frail	26 (54.2)	8 (23.5)	4	1
Frail	8 (16.7)	17 (50.0)	5	1
TOTAL	**48**	**34**	**10**	**4**

P1487 **EFFECT OF PREDIALYSIS FLUID OVERLOAD ON SLEEP QUALITY IN HEMODIALYSIS PATIENTS**

Haitham Ismail[1], Hussein Abdallah[1], Ahmed Emara[1], Mohamed Arafa Ahmed[2]

[1]Ain Shams University, Nephrology department, Cairo, Egypt and [2]El-Sahel teaching hospital, Nephrology department, cairo, Egypt

Background and Aims:

Sleep disorders are common among end stage renal disease (ESRD)patients undergoing hemodialysis (HD). The etiology of sleep disorders in these patients is known to be multifactorial. However, the role of hydration status in sleep disorders in HD patients is not well studied. Therefore, our aim was to study the effect of predialysis fluid overload on sleep quality in HD patients.

Methods:

This cross-sectional study included **100** prevalent HD patients from HD unit of El Sahel teaching hospital. fluid status and fluid compartments [total body water (TBW)], extracellular water (ECW)] and overhydration index (OH) were analyzed by a portable whole-body bio-impedance spectroscopy (Body Composition Monitor 'BCM') before mid-week dialysis session. Overhydration was defined as OH/ECW $\geq$**15%**. HD patients were then classified into 2 groups: Group **1** (non- overhydrated) and Group **2** (Overhydrated) according to OH/ECW. Sleep quality were assessed in all patients by Pittsburgh Sleep Quality Index (PSQI) questionnaire. Patients with Concurrent diagnosis of either obstructive sleep Apnea or psychiatric disorder and patients on any medications which affect the sleep pattern were excluded.

Results:

our study included 100 HD patients (49 male, 51 female - mean age 49.3 $\pm$11). 42 patients (42%) had overhydration (i.e. Group 2). Poor sleep quality (defined as PSQI score $\geq$5) was reported in 57% (n=57) of HD patients included in our study. Poor sleep quality was significantly higher in the HD patients with overhydrated (Group 2). Total PSQI scores were significantly higher in overhydrated patients (Group2) compared to non-overhydrated patients (Group1) (7.92$\pm$3.32 vs 4.83$\pm$2.27, *P*= <0.001). The component scores 1, 2, 3, 4, 6 and 7 of the PSQI showed significant differences between the overhydration and non-overhydration groups with higher values (i.e poor sleep quality) in overhydrated patients (Group2). Moreover, there was significant positive correlation between total PSQI score and overhydration index (OH/ECW %) in all HD patients included in the study (r=0.283, ***P***= 0.004).

Conclusion:

We may conclude from our study that sleep disorders are prevalent in HD patients. Predialysis fluid overload in HD patients may be associated significantly with poor sleep quality.

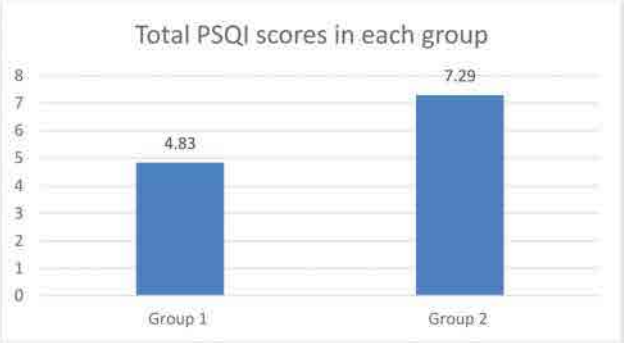


Fig.1: Total PSQI score in each group of overhydration

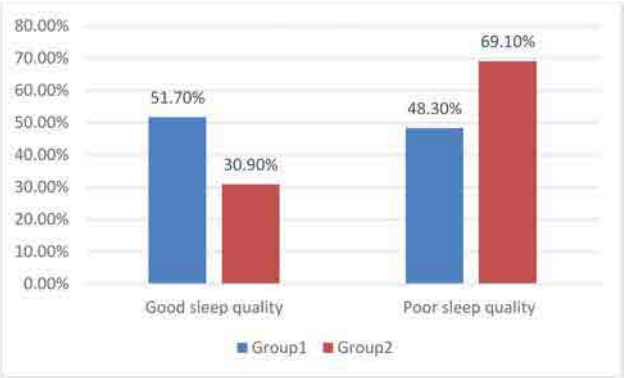


Fig.2: Sleep quality in study population

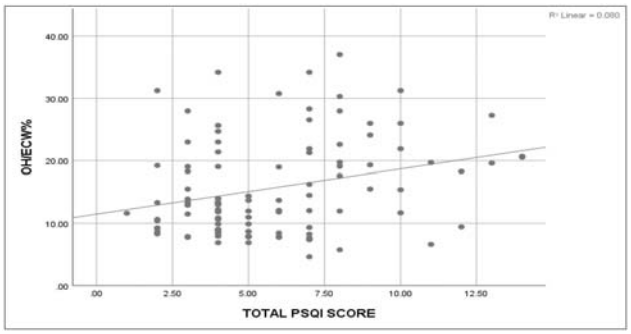


Fig.3: Correlation between total PSQI score and OHI (OH/ECW %) in the whole study population

P1488 RECOVERY OF LOW TRIIODOTHYRONINE CAN IMPROVE MORTALITY IN HEMODIALYSIS PATIENTS

Hong Joo Lee[1]

[1]*Seoul Red Cross Hospital, Nephrology, Seoul, Korea, Rep. of South*

Background and Aims:

Low circulating triiodothyronine (T3) levels are the most frequently encountered thyroid functional test derangement in end-stage renal disease (ESRD) patients on hemodialysis. Low T3 is known as independent predictive value for all-cause mortality and, particularly, for cardiovascular-related death in patients with ESRD on hemodialysis. This study investigated that recovery of low T3 level to normal can lower mortality in ESRD patients on hemodialysis.

Method:

We have constructed the 500 K-cohort of ESRD patients attending the hemodialysis center of 6 tertiary hospitals of South Korea to evaluate the mortality of the ESRD patients since 2016. From this prospective cohort, we invited patients with ESRD from June 2016 to May 2019 The participants were divided into four groups based on the change of the T3 level: normal group showed the normal T3 continuously, low group showed the low T3 continuously, recovery group showed the low T3 change to normal and decrease group showed the normal T3 change to low. We evaluate relationships between change of the T3 level and mortality. Statistical analysis was carried out by using SPSS.

Results:

Of the total 500 patients in K-cohort, 333 patients were enrolled with detailed thyroid hormone profile including T3 level. 167 (50.2 %) patients out of the 333 patients showed low T3 level initially. Normal group include 126 patients(37.8%), low group include 135 patients(40.5%), recovery group include 32 patients(9.6%) and decrease group include 40 patients(12.0%). Patients with the low T3 level were older and more diabetic compare to those with normal T3 level. They had lower K-MMSE score than the others, Low T3 group had lower free T4 level but thyroid stimulating hormone(TSH) showed no significant different comparing normal T3 group. The mortality of normal group was lowest and that of decrease group was highest. The mortality of recovery group recovered to similar with that of the normal group and mortality of decrease group was highest. Lowering of T3 level would affect to mortality than low T3 level continuously.

Conclusion:

Therefore, the change of T3 level is significantly associated with the mortality. Recover lower T3 to normal level can lower the mortality.

P1489 HEPATITIS B AND C IN DIALYSIS UNITS IN ALMATY

Arina Yespotayeva[1,2], Kairat Kabulbayev[3], Abduzhappar Gaipov[4], Zauresh Amreyeva[3], Zhanar Mursalova[2]

[1]Al-Farabi Kazakh National University, Almaty, Kazakhstan, [2]LLP "Diaverum Kazakhstan", Almaty, Kazakhstan, [3]Asfendiyarov Kazakh-National Medical University and [4]Nazarbayev University, School of Medicine

Background and Aims: Patients getting maintenance haemodialysis (HD) are at higher risk for acquiring Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infections than the general population. Strict infection control measures are essential to prevent nosocomial transmission. We aimed to investigate the incidence and prevalence of HBV and HCV infection in the HD population of Almaty dialysis units as well as risk factors for infection.

Method: All adult patients getting maintenance HD (n=700) in Almaty dialysis centres (n=4) were studied between May 2016 and December 2019. Testing for Hepatitis B surface antigen (HBsAg) and anti-HCV antibodies was performed at initiation of dialysis and every 3–6 months thereafter. Serological markers for HBV and HCV were determined with immunoenzymatic assay (ELISA).

Results: Participant median age was 40 years and 58% were male. 110 patients (34.9%) were sero-positive for HBV and/or HCV (anti-HCV positive 31.1%; HBsAg positive 2.6%; both positive 1.2%). Of the sero-positive patients 4.7% were known to be infected before the initiation of HD. The prevalence of HBV±HCV infection varied widely between HD centres from 0% to 75.9%. Sero-positive patients were younger, had longer time on dialysis and more previous blood transfusions. Wide variation in rates of newly acquired infections was observed between dialysis centres. All new HBV cases were referred from centres already treating HBV infected patients. New HCV infections were reported in most centres but the rate of HCV sero-conversion varied widely from 1.5% to 31%. Duration of dialysis, history of previous renal transplant and history of receiving HD in another centre in Almaty were significantly associated with sero-conversion. Major risk factors identified by a standard questionnaire in 302 of 270 patients were the number of blood transfusions individuals had received and duration of dialysis, the latter including patients who received no blood transfusions

Conclusion: HBV and HCV prevalence in our HD patients is still high. These data emphasize the need for stricter adherence to infection control, barrier precaution and preventive behaviors with all patients. In summary, the prevalence of HBV and HCV in our HD patients is still high. These data emphasize the need for stricter adherence to infection control, barrier precaution and preventive behaviors with all patients.

P1490

MONTHLY TREND AND SEASONALITY IN ACUTE AND CHRONIC HEMODIALYSIS; RESULT FROM NATIONWIDE DATABASE OF MEDICAL BILLS OF UNIVERSAL HEALTH CARE INSURANCE SYSTEM IN JAPAN

Ryoya Tsunoda[1], Hirayasu Kai[1], Masahide Kondo[2], Naohiro Mitsutake[3], Kunihiro Yamagata[1]

[1]University of Tsukuba, Department of Nephrology, Faculty of Medicine, Tsukuba, Japan, [2]University of Tsukuba, Department of Medical Economics, Faculty of Medicine, Tsukuba, Japan and [3]Institute for Health Economics and Policy, Minato, Japan

Background and Aims:

Although knowing the accurate number of patients of hemodialysis important, data collection is a hard task. Establishing a simplified and prompt method of data collection for perspective hemodialysis is strongly needed. In Japan, there is a universal health care insurance system that covers almost all population. This study aimed to know a seasonal variation of hemodialysis patients using the big database of medical bills in Japan.

Method:

Japanese Ministry of Health, Labour and Welfare established a big database named National Database (NDB), that consists of medical bills data in Japan. All bills data were sent to the data server from The Examination and Payment Agency, the organization that receives all medical bills from each medical institution and judge validity for payment. Each record of the database consists of bill data of one patient of a month for each medical institution. All data were anonymized before saved in the server and gave virtual patient identification number (VPID) that is unique for each patient. VPID is a hash value calculated by patient's individual data such as name, date of birth, so that the value cannot be duplicate. Calculation of VPID is executed by an irreversible way to make it difficult to decrypt VPID into patient's individual data. This database includes all information about medical care of whole population in Japan except for patients not under the insurance system (patients under public assistance system, victims of the war, or any other specified people under the public medical expense).

Using this database, we investigated monthly number of patients who were recorded to be undergone hemodialysis (HD, includes hemodiafiltration). We searched chronic HD patients who have undergone HD on the month and continued it for 3 months, and acute HD patients who have discontinued HD within 3 months.

Results:

In NDB, the number of chronic HD patients under public insurance system who confirmed to have undergone HD in December 2014 was 284 433. In contrast, the number of HD patients identified from the year-end survey by Japanese Society of Dialysis Therapy in the same year was of 311 193, but this number includes patients not under insurance system. Incidence rate of acute HD in Japan was persisted at 30-39 per million per month. There is a reproducible seasonal variation in number of acute HD patients, that increases in every winter and decreasing in every summer. The significantly highest frequency was observed in February(38.5/million/month) compared with September(30.6/million/month), the lowest month of the year ($p<0.01$).

Conclusion:

We could show the trend in number of HD patients using nationwide bills data. Seasonality in some clinical factors in patients under chronic hemodialysis such as blood pressure, intradialytic body weight gain, morbidity of congestive heart failure, and, mortality, has been reported in many observational studies. Also, there are a few former reports about seasonality in AKI. However, a report about acute RRT is few. From our knowledge, this is the first report that revealed monthly dynamics of HD in a whole nation and rising risk of acute HD in winter. The true mechanism of this seasonality remains unclear. We have to establish a method to collect clinical data such as prevalence of CKD, causative diseases of AKI, kinds of precedent operations, and medications in connection with billing data.

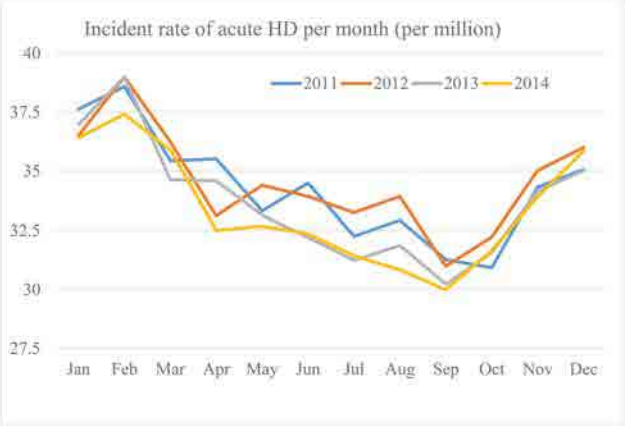


Figure:

P1490A

GAIT SPEED AND HANDGRIP STRENGTH AS PREDICTORS OF ALL-CAUSE MORTALITY AND CARDIOVASCULAR EVENTS IN HEMODIALYSIS PATIENTS

Yu Ho Lee[1], Hyeyun Jeong[1], Dong Ho Yang[1], So-Young Lee[1], Jin Sug Kim[2], Su Woong Jung[2], Hyeon Seok Hwang[2], Ju-Young Moon[2], Kyung Hwan Jeong[2], Dong-Young Lee[3], Gang Jee Ko[4], Hong Joo Lee[5], Yang-Gyun Kim[2]

[1]CHA bundang hospital, Nephrology, Seongnam, Korea, Rep. of South, [2]Kyung Hee University, Nephrology, Seoul, Korea, Rep. of South, [3]Veterans Health Service Medical Center, Nephrology, Seoul, Korea, Rep. of South, [4]Korea University, Nephrology, Seoul, Korea, Rep. of South and [5]Seoul Red Cross Hospital, Nephrology, Seoul, Korea, Rep. of South

Background and Aims: Low physical performance in patients undergoing maintenance hemodialysis is associated with a high mortality rate. We investigated the clinical relevance of gait speed and handgrip strength, the two most commonly used methods to assess physical performance.

Method: We obtained data regarding gait speed and handgrip strength from 277 hemodialysis patients and evaluated their relationship with baseline parameters, mental health, plasma inflammatory markers, and major adverse clinical outcomes. Low physical performance was defined by the recommendations suggested by the Asian Working Group on Sarcopenia.

Results: The prevalence of low gait speed and handgrip strength were 28.2% and 44.8%, respectively. Old age, low serum albumin levels, high comorbidity index, and impaired cognitive functions were associated with low physical performance. Patients with isolated low gait speed exhibited a general trend for worse quality of life than those with isolated low handgrip strength. Gait speed and handgrip strength showed very weak correlations with had different determinant factors (older age, the presence of diabetes, and lower serum albumin for low gait speed, and lower body mass index, and the presence of previous cardiovascular events for low handgrip strength). Patients with low gait speed and handgrip strength had elevated levels of plasma endocan and matrix metalloproteinase-7 and the highest risk of all-cause mortality and cardiovascular events among the groups (adjusted hazard ratio of 2.72, $p = 0.024$).

Conclusion: Gait speed and handgrip strength reflected distinctive aspects of patient characteristics and that their combination improved the prediction of adverse clinical outcomes in hemodialysis patients. Gait speed seems to be a better indicator for poor patient outcomes compared with handgrip strength.

P1491 **INTRADIALYTIC HYPOTENSION AND PROGOSIS IN HEMODIALYSIS PATIENTS**

Yuto Takenaka[1], Satoru Kishi[1], Kyosuke Nishio[2], Kazunobu Masaki[2], Toyohiro Hashiba[1], Satoshi Huruse[1], Naobumi Mise[1], Yoshiyasu Ogura[1]

[1]Mitsui Memorial Hospital, division of internal medicine, Chiyoda City, Japan and [2]shin-koiwa clinic, tokyo, Japan

Background and Aims: The aim of this study was to investigate the prognostic impact of intradialytic hypotension (IDH).

Method: This study comprised 237 hemodialysis patients (158 males, 64±13 years old, dialysis vintage:110±88 months) in a community-based dialysis center. IDH was recorded in 12 consecutive hemodialysis sessions from February to April in 2014. The patients were divided into 2 groups: Group A, patients with IDH, and Group B, those without IDH, and all-cause mortality rates for 4 years were examined. IDH was defined as a rapid symptomatic fall of systolic blood pressure by at least 30 mmHg or that required medical intervention. Logistic regression was used to investigate the association between IDH and mortality.

Results: IDH was observed in 123 patients (52 %). The frequency of IDH was 3.8±3.1 times during 12 hemodialysis sessions in Group A. Mortality rates from all causes of death were significantly higher in Group A than in Group B (40 % and 17 % at 4 years, respectively, $p < 0.05$). Univariate analysis showed that IDH, age, female, dry weight, ultrafiltration rate (UFR), serum albumin level, and serum hemoglobin level were significantly associated with all-cause mortality. In multivariate analysis, IDH, age, UFR, and serum hemoglobin level were independent risk factors for all-cause mortality (Table).

Conclusion: In our population, IDH was associated with a poor prognosis at 4 years.

Table. Risk factors for all-cause mortality

	Univariate			Multivariate		
	OR	95%CI	*P value*	OR	95%CI	*P value*
IDH	3.29	1.80-5.99	<0.01	4.16	1.89-9.16	<0.01
Age (year)	1.08	1.04-1.11	<0.01	1.04	1.00-1.08	0.05
Male	0.42	0.23-0.75	<0.01	1.06	0.46-2.43	0.89
Dialysis Vintage (year)	0.99	1.00-1.01	0.15			
Ischemic Heart Disease	1.53	0.74-3.17	0.25			
History of Stroke	1.46	0.71-3.01	0.30			
Dry Weight (kg)	0.94	0.91-0.97	<0.01	0.96	0.92-1.00	0.08
Ultrafiltrtation Rate (kg/h)	0.08	0.022-0.32	<0.01	0.11	0.012-0.78	0.03
Predialysis Systolic Blood Pressure (mmHg)	1.00	0.98-1.01	0.51			
Albumin (g/dL)	0.13	0.053-0.32	<0.01	0.56	0.18-1.69	0.30
Hemoglobin (g/dL)	0.61	0.42-0.90	0.01	0.62	0.39-0.99	0.04
Phosphate (mg/dL)	0.83	0.66-1.06	0.13			

P1492

HUMAN FACTORS TESTING OF THE QUANTA SC+: DEMONSTRATING EASE OF USE WITH MINIMAL UPFRONT TRAINING IN HEALTH CARE PRACTITIONERS AND PATIENTS

Kathryn Compton[1], Christian Edwards[1], Paul Komenda[1,2,3], Amit Bose[1], John Milad[1]

[1]Quanta Dialysis Technologies, Alcester, United Kingdom, [2]University of Manitoba - Internal Medicine, Internal Medicine, Nephrology, Winnipeg, Canada and [3]Seven Oaks Chronic Disease Innovation Centre, Winnipeg, Canada

Background and Aims: Quanta Dialysis Technologies has developed a compact, powerful personal haemodialysis system intended for home and self-care use designed in collaboration with patients and healthcare practitioners. Human factors testing is necessary to demonstrate ease of use with minimal up-front training.

Method: In compliance with FDA guidance and EU standards, the user interface of the system was evaluated through human factors testing to assess the safe and effective use of SC+. This included a series of user-based tasks whereby representative users independently setup SC+ into a simulated treatment, managed alarms to resolution and external SC+ cleaning/disinfection.

All participants received an introduction to SC+ and completed a competency sign off at the end of training. 17 healthcare professionals (6 renal nurses, 8 dialysis technicians, 1 patient care technician) received up to 4 hours of structured training followed by a 1-day learning decay period. In addition, 10 lay users (8 dialysis patients, 2 caregivers) received between 5.5 and 7.5 hours training followed by a 2-day learning decay period.

Results: Between the two user groups, there were a total of 8,110 opportunities for use errors to occur. Despite minimal training and representative learning decay, only 4 significant use events were observed requiring some user manual enhancements. Other use errors captured were minor or could not be mitigated further due to clinical practices and shared inherent risks across all haemodialysis systems.

Conclusion: The results of the human factors testing demonstrated that healthcare practitioners, patients and caregivers successfully operated SC+ independently with a high level of use safety, despite minimal training and learning decay. The SC+ user interface is optimized for safe and effective use under FDA guidance and EU standards.

P1493

CORRELATION BETWEEN END-DIALYSIS OVER-WEIGHT IN INITIAL STAGE OF HEMODIALYSIS AND PROGNOSIS IN INCIDENT HEMODIALYSIS PATIENTS

Ping Zhang[1], Ying Wang[1], Xi Yao[1], Shaohua Chen[1], Chunping Xu[1], Hulin Lu[1], Jianghua Chen[1]

[1]*the First Affiliated Hospital, College of Medicine, Zhejiang University, kideny disease center, P.R. China*

Background and Aims: The volume factor of maintenance hemodialysis patients is closely related to the prognosis. We hypothesized that the excess weight after dialysis (end-dialysis over-weight, edOW) is an important factor of volume impact survival in hemodialysis (HD) patients. The purpose of this study was to analyze the relationship between edOW and long-term prognosis of patients with maintenance hemodialysis.

Method: This retrospective study observed incident hemodialysis patients who treated in Kidney Disease Center, the First Affiliated Hospital, College of Medicine, Zhejiang University from January 1, 2008 to April 30, 2017, three times a week for at least one year. The end point of follow-up was death, abdominal dialysis, kidney transplantation, transfer or until April 30, 2018. The general data of the patients included age, gender, BMI, primary renal disease, CVD, first hemodialysis access, albumin(Alb), Haemoglobin(Hb), blood pressure, heart rate, ultrafiltration rate(UFR), interdialytic weight gain IDWG, end -dialysis overweight (edOW). Cox multivariate regression was used to analyze the relationship between edow and all-cause mortality and cardiovascular mortality.

Results: Totally 469 patients male, 64% were enrolled, with an average age of 56.9 $\pm$ 17.1 years. During the follow-up period, 102 patients died. The main cause of death was cardiovascular and cerebrovascular events, accounting for 44.7%. The mean value of edow was 0.28 $\pm$ 0.02 kg. Kaplan-Meier(Log-rank test) survival analysis showed that the long-term survival rate of the group with edow $\leq$ 0.28kg was better than that of the group with edow $>$ 0.28kg ($P = 0.042$), and the cardiovascular mortality of the group with edow $>$ 0.28kg was significantly higher than that of the group with edow $\leq$ 0.28kg ($P = 0.001$). Cox multivariate regression analysis showed that edow was an independent risk factor for all-cause death in hemodialysis patients ($P = 0.025$, AhR = 1.541, 95% CI 1.057-2.249), and also an independent risk factor for CVD death in hemodialysis patients ($P = 0.007$, AhR = 1.929, 95% CI 1.198-3.107).

Conclusion: EdOW is an independent risk factor of long-term all-cause and cardiovascular death in hemodialysis patients.

P1494 **THE NEGATIVE EFFECT OF SELENIUM DEFICIENCY ON THYROID HORMONE IMPAIRMENT AND CARDIOVASCULAR DISEASE IN CHRONIC HEMODIALYSIS PATIENTS**

SO MI KIM[1], Jong Tae Cho[2], Yong-Moon Lee[3], Eun Kyoung Lee[4], Ji Hyun Jeon[5], Hwa Young Lee[6]

[1]Dankook University Hospital, Division of Nephrology, Department of Internal Medicine, Cheonan-si, Korea, Rep. of South, [2]Dankook University Hospital, Division of Nep;hrology, Department of Internal Medicine , [3]Dankook University Hospital, Department of Pathology, [4]Dankook University Hospital, Division of Nephrology, Department of Internal Medicine, [5]Dankook University Hospital, Division of Neprhology, Department of Internal Medicine and [6]Jeju national Univeristy Hospital, Division of Nephrology, Department Internal medicine, Jeju national university Hospital, Cheonan-si, Korea, Rep. of South

Background and Aims:

Selenium is an essential trace element. It has been known to protect the cardiovascular disease(CVD) and thyroid disease by protecting the oxidative stress using selenium-dependent glutathione peroxidase. Chronic hemodialysis(HD) patients are more likely to have selenium deficiency compared to healthy subjects. Therefore, we investigated the degree of selenium deficiency in HD patients and try to analyze the effect of selenium deficiency on thyroid hormone impairment and its correlation with CVD.

Method:

A total of 183-chronic HD patients were enrolled. Serum selenium level was assessed before HD using inductively coupled plasma-mass spectrometry. Based on tertile of selenium, the patients were divided into three groups: low-, intermediate-, and high-group. The presence of thyroid hormone impairment and cardiovascular disease were evaluated.

Results:

The value of serum selenium in first and second tertile of subjects was 80.64 and 94.84 g/dL, respectively. Thyroid dysfunction and CVD with respect to serum selenium levels are summarized in Table 1. Although the prevalence of hypothyroidism was not different among the three groups, instances of subclinical hypothyroidism was higher in the lower selenium group than those in the other groups (34% vs. 15% vs. 8%; P=0.005). Moreover, total thyroid dysfunction was significantly higher in the lower selenium group (38% vs. 18% vs. 15%; P=0.005). The prevalence of ischemic heart disease was most prevalent in the lower selenium group among the three groups, (49% vs. 25% vs. 22%; P=0.002). The prevalence of total CVD was highest in the lower selenium groups. (57% vs. 33% vs. 26%; P=0.001). In the analysis of the relationship between thyroid dysfunction and CVD, The prevalence of IHD was highest in the lower selenium group with thyroid dysfunction(p=0.039)

Conclusion:

This study showed that selenium deficiency is associated with thyroid hormone impairment and thyroid disease. And the thyroid hormone impairment showed the synergistic negative effect on CVD in HD with selenium deficiency patients.

Table 1. The thyroid dysfunction and cardiovascular disease, according to selenium deficiency

	Lower-Se (n=61)	Intermediate-Se (n=61)	High-Se (n=61)	P
Hypothyroidism, n(%)	2(3)	2(3)	1(2)	0.814
Subclinical hypothyroidism, n(%)	21(34)	9(15)	8(13)	0.005
Total thyroid dysfunction, n(%)	23(38)	11(18)	9(15)	0.005
Ischemic heart disease, n(%)	30(49)	15(25)	14(22)	0.002
Heart failure, n(%)	13(38)	11(18)	5(8)	0.119
Ejection Fraction, %	58.73±9.62	60.68±10.82	63.62±8.62	0.022
Cardiomyopathy	4(7)	4(7)	2(3)	0.655
Total cardiovascular disease	35(57)	20(33)	16(26)	0.001

P1495 **LOW DIASTOLIC BLOOD PRESURE WITH LOW MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION WOULD DETERIORATE CARDIOVASCULAR MORTALITY IN THE PATIENTS WITH MAINTENANCE HEMODIALYSIS.**

KIYOTSUGU OMAE[1], Ai Horimoto[1], Chieko Higuchi[1], Yumi Hosoda[1], Tomomi Tamura[1], Yoko Nishizawa[1], Tetsuya Ogawa[1]

[1]*Tokyo Women's Medical University Medical Center East, Department of Internal Medicine, Tokyo, Japan*

Background and Aims: In dialysis patients, many literatures have shown the association between predialytic hypotension and poor prognosis. Particularly, decrease in diastolic blood pressure (DBP) will be involved myocardial injury because of reduced coronary blood-flow. Such myocardial damage would also be caused by decreased oxygen-supply capacity. Mean corpuscuar hemoglobin-concentration (MCHC) is a hemoglobin concentration per 1% hematocrit (Ht) and could be considered as an indicator of peripheral oxygen-supply. In several literatures, low MCHC had been associated with increased all-cause mortality in non-dialysis patients with congestive heart-failure. In dialysis patients with low Ht between 32 to 35%, low DBP and low MCHC could additively act on myocardial damage. In this study, we examined the relation between the stratified groups by DBP and MCHC and cardiovascular mortality using Yoshikawa clinic dialysis-database (YCD).

Method: A total of 407 dialysis patients registered in YCD enrolled in this study from April 2006 and on. The cut-off values (COVs) of predialytic DBP and MCHC on cardiovascular death (CVD) were determined from the Receiver Operating Characteristic (ROC) curve. According to these COVs, the whole cohort was divided into 4 groups, group HH (high DBP and high MCHC), group HL (high DBP and low MCHC), group LH (low DBP and high MCHC), and group LL (low DBP and low MCHC). Their survival analysis was estimated by the Kaplan–Meier method, and a log-rank test was used to examine the differences between the survival curves. The prognostic factors for CVD were extracted from background factors, including predialytic DBP, MCHC and above-mentioned grouping, using Cox-regression model.

Results: In 407 patients, mean predialytic DBP and time-averaged MCHC were 73.3 mmHg and 31.5 % respectively. During observation period of 5.1 years 163 patients died, among that 94 were CVD. The COVs of DBP and MCHC were 79 mmHg and 31.16 %, respectively. According to these COVs, 407 patients were divided into 64 of group HH, 65 of group HL, 171 of group LH and 107 patients of group LL. On the survival curve, the group LL had the highest mortality rate, followed by the group HL. The group HH showed the lowest mortality rate. In multivariate analysis, category variables LL and HL were extracted as prognostic factors for CVD. Their Hazard ratio were 1.960 and 3.863, respectively. Age, intradialytic hypotension, DBP, Kt/V, serum sodium, CRP and blood glucose were extracted as the other prognostic factors.

Conclusion: These results suggest that low MCHC level would deteriorate prognosis on dialysis patients with predialytic low-DBP. MCHC level could become a new treatment-target in the low DBP group in the future.

P1496

TRENDS IN THE INCIDENCE AND PREVALENCE OF END-STAGE RENAL DISEASE PATIENTS WITH HEMODIALYSIS IN ENTIRE KOREAN POPULATION: A NATIONWIDE POPULATION-BASED STUDY

Hong Sang Choi[1], Chang Seong Kim[1], Eun hui Bae[1], Seong Kwon Ma[1], Soo Wan Kim[1]

[1]*Chonnam National University Medical School, Department of Internal Medicine, Gwangju, Korea, Rep. of South*

Background and Aims:

Data on the epidemiology and temporal trends of end-stage renal disease (ESRD) with hemodialysis are not well established in the entire Korean population. We aimed to estimate the incidence and prevalence of ESRD with hemodialysis in Korea between 2002 and 2017.

Method:

Using the National Health Insurance Service database, we analyzed entire Korean population from 2002 to 2017. Hemodialysis patients was identified by using rare incurable disease codes (V001) or prescription of medical fee code of hemodialysis (O7020, O7021). We only included patients who have been maintained hemodialysis more than 90 days from the date of dialysis initiation to exclude short-term dialysis due to acute kidney injury or patients who converted to peritoneal dialysis or kidney transplantation.

Results:

During the 16-year follow-up, the number of hemodialysis patients in Korea has steadily increased from 11,251 in 2002 to 67,486 in 2017. The mean age of hemodialysis patients has gradually increased from 55.57±13.31 years in 2002 to 62.13±13.23 years in 2017. Overall, the number of men tended to be somewhat higher than that of women, and the proportion of men increased slightly from 55.56% in 2002 to 58.45% in 2017. The proportion of diabetic patients increased rapidly from 23.84% to 47.84%, and the percentage of hyperlipidemic patients rose from 18.9% to 86.7%, while the percentage of hypertensive patients did not show a significant increase. The number of incident hemodialysis patients increased significantly from 4,406 in 2003 to 12,134 in 2014 and then decreased to 8,090 in 2017. In the incident patients, the increase in the proportion of male patients and the increase in diabetes and hyperlipidemia were observed in similar manner with prevalent patients.

Conclusion:

The incidence and prevalence of hemodialysis in Korea gradually increased from 2002 to 2017. The proportion of men, diabetes and hyperlipidemia among patients with hemodialysis also increased continuously. These findings may contribute as groundwork for epidemiological studies of hemodialysis in Korea.

P1497 INCIDSENCE OF CANCER IN HEMODIALYSIS-TREATED PATIENTS

Ze'ev Katzir[1], Lusia Merkin[2], Ronen Brenner[2]

[1]Assuta Ashdod University Hospital, Nephrology and Hypertension Institute, Ashdod, Israel and [2]E Wolfson Medical Center, Oncology, Holon, Israel

Background and Aims: In recent decades, there has been an increase in the incidence and prevalence of patients with end stage renal disease (ESRD) worldwide. Previous studies have shown an increased incidence of malignancies among ESRD patients, compared to age-matched controls, although it was unclear whether different etiologies of ESRD (diabetes, hypertension, cystic disease) confer different risk ratio.

Our present study intends to re-examine relationships between ESRD, classified according to the etiology of renal disease, cancer incidence and types of malignancies in hemodialysis treated patients.

Method: We conducted a retrospective study, analyzing hemodialysis (HD) treated patients over the age of 18 at the Wolfson Medical Center in Holon, Israel, from 2008-2017. Patients diagnosed with cancer prior to dialysis or with history of transplantation were excluded.

Data on etiology of chronic kidney disease and ESRD, comorbidities and cancer diagnosis was collected from patients' files and verified using the Israeli National Cancer Registry.

A single, multivariate survival analysis was conducted to examine the relationship between the various predictors and the incidence of cancer.

Results: The study included 333 patients, 211 (63.4%) were males, mean age 67.2±13.1 years. The median follow was 4 years (95% CI: 2-6.5). Twenty eight (8.4%), developed primary malignancy during hemodialysis, annual rate: 2.1%, Vs 0.35% age-adjusted annual rate in Israeli general population. The average age of all patients diagnosed with cancer over the study period was higher than that of patients without cancer (72.3±7.7 Vs 66.7±13.4 years. P=0.001).

The most common sites of malignancy were colon (33%), bladder (16.7%), kidney (10%) and prostate (10%). Older age was the only risk factor associated with the onset of malignancy. No statistically significant relationship was found between ESRD etiology, comorbidities and occurrence of malignancy.

Conclusion: Among our cohort of patients on chronic hemodialysis, annual cancer incidence rate is 6 times higher than age matched controls in the Israeli general population. Older age is a risk factor associated with onset of malignancy. We did not found associations between ESRD etiology, comorbidities and cancer incidence.

This study constitutes a platform for a longer period multicenter study.

P1498 ASSOCIATIONS OF HEALTH LITERACY WITH DEPRESSION AND ANXIETY IN DIALYSED PATIENTS IN SLOVAKIA

Ivana Skoumalová[1], Jaroslav Rosenberger[1,2,3], Andrea Madarasova Geckova[1,3]

[1]Faculty of medicine, P.J. Safarik University, Department of Health Psychology and Research Methodology, Kosice, Slovakia, [2]FMC-dialysis services, Kosice, Slovakia and [3]Palacky University, Institute of Social Health, Olomouc, Czech Republic

Background and Aims: Depression and anxiety is common in dialysed patients (Ng et al., 2015; de Brito et al., 2019) and associated with decreased quality of life, worse health outcomes and increased mortality (Schouten et al., 2019, Lopes at al., 2002). Health literacy (HL) as the ability to gain access, understand, and use information to promote and maintain good health (WHO, 1998) may be hampered by emotional problems such as depression and anxiety. The aim of our study is to examine the association of HL with depression and anxiety in dialysed patients in Slovakia.

Method: Cross-sectional study on 542 dialysed patients (mean age = 63.6, males = 60.7%) was conducted in 20 dialysis clinics in Slovakia from January to November 2018. Socio-demographic data, data on 9 domains of HL and data on depression and anxiety were collected by questionnaires. Hierarchical cluster analysis was used to create three clusters of patients (low, moderate, high HL). Depression and anxiety was dichotomized as 0-no/low symptoms and 1-moderate/severe symptoms. Association of HL clusters with depression and anxiety was analysed using logistic regression adjusted for age and gender.

Results: We found that patients in low HL cluster and moderate HL cluster were more likely to have moderate/severe symptoms of depression and anxiety than patients in high HL cluster. Odds ratio (OR) for depression for low HL cluster: 7.60; 95% Confidence Interval (CI): 2.88 – 20.06; $p<0.000$ and for moderate HL cluster: OR: 4.85; 95% CI: 1.87 – 12.56; $p<0.001$. OR for anxiety for low HL cluster: 3.14; 95% CI:1.55 – 6.35; $p<0.001$ and for moderate HL cluster: OR 2.16;95% CI: 1.10 – 4.24; $p<0.05$.

Conclusion: Patients with lower levels of HL suffer from anxiety and depression more than patients with higher levels of HL. These findings point to the need of regular screening of emotional problems such as depression and anxiety and their treatment as they may hamper capacities of dialysed patients for self-management as well as effective treatment of the disease from the perspective of healthcare providers.

P1499 **FGF21 CORRELATES POSITIVELY WITH ARTERIOVENOUS FISTULA OCCLUSION IN HEMODIALYSIS PATIENTS**

Qing Wei[1], Bin Wang[1], Xiao liang Zhang[1], Bicheng Liu[1]
[1]

Background and Aims: Arteriovenous fistula occlusion lead to insufficient dialysis, increases the probability of hemodialysis complications, even life-threatening. Fibroblast growth factor 21 (FGF21) is increased progressively with a decline of renal function and higher plasma FGF-21 level can be used as a meaningful index to evaluate microinflammation, lipid metabolism and predict dialysis-related complications such as cardiovascular diseases in end stage renal disease patients. This study aimed to investigate the relationship and role of FGF21 in arteriovenous fistula occlusion in our hemodialysis patients cohort.

Method: We screened 802 HD patients in Nanjing Zhongda Hospital (n=450) and The First People's Hospital of Changzhou (n=352) according to a strict inclusion criteria and exclusion criteria. We recorded demographic information, blood data before dialysis and serum FGF21 levels and counted the frequency of arteriovenous fistula occlusion in our hemodialysis cohort. We used bivariate correlation analyses to assess the correlation of the frequency of arteriovenous fistula occlusion with serum FGF21 and other clinical parameters. Stepwise multivariate linear regression analyses were employed to evaluate variables independently associated with the frequency of arteriovenous fistula occlusion. $P < 0.05$ was considered to be statistically significant. SPSS Software, version 22.0 was used for all statistical analyses.

Results: In this cross-sectional study, of 802 hemodialysis patients screened, 76 were eligible. The median dialysis vintage was 6.4 years (range 0.5 to 23). Serum FGF21 levels were significantly positive associated with the frequency of arteriovenous fistula occlusion ($r = 0.321$, $P = 0.005$). In addition, the frequency of arteriovenous fistula occlusion was correlated with the level of hemoglobin ($r = -0.277$, $P = 0.015$), the level of albumin ($r = -0.269$, $P = 0.019$) and left ventricular mass ($r = 0.272$, $P = 0.018$). The result showed that serum FGF21 ($\beta = 0.259$, $P = 0.022$) and left ventricular mass ($\beta = 0.223$, $P = 0.048$) were factors independently associated with the frequency of arteriovenous fistula occlusion in hemodialysis patients.

Conclusion: We reported for the first time that serum FGF21 and Left ventricular mass were independently associated with arteriovenous fistula occlusion. These findings provide a novel insight about FGF21 on arteriovenous fistula occlusion in hemodialysis patients and may indicate a new therapeutic target for arteriovenous fistula occlusion.

Table 1. Characteristics and and laboratory data of HD patients.

	All HD patients
Number(n)	136
General data	
Age (years)	55.46 ± 15.18
Gender (male, %)	63.7
Dialysis vintage (years)	6.4 (0.5, 23.0)
Body mass index (kg/cm2)	22.92±3.59
Systolic BP (mmHg)	139.62±23.3
Diastolic BP (mmHg)	78.98±13.57
Blood data	
Hemoglobin (g/L)	102.61±18.73
Albumin (g/L)	37.76±5.88
Total cholesterol (mmol/L)	3.97±1.0
Triglycerides (mmol/L)	1.79±1.16
Calcium (mmol/L)	2.33±0.35
Phosphate (mmol/L)	1.79±0.56
Parathyroid hormone (pg/ml)	354.06±331.08
FGF21 (pg/ml)	372.96±432.32
FGF23 (pg/ml)	14094.51±9586.91
Comorbidity	
Diabetes (%)	26.3
Hypertension (%)	92.5
CVD (%)	31.3
Medicine usage	
Vitamin D (%)	51.2
Calcium supplements (%)	32.5
Cinacalcet (%)	16.3

Table 2. Multivariate linear regression analyses for the establishment of factors independently associated with arteriovenous fistula occlusion.

Variable	β	*P* value
Hemoglobin	-0.172	0.214
albumin	-0.053	0.71
calcium	-0.194	0.087
Phosphate	0.127	0.283
PTH	-0.058	0.628
FGF21	0.259	**0.022**
Left ventricular mass	0.223	**0.048**
Glycerin trilaurate	0.174	0.132
total cholesterol	-0.023	0.839

Figure 1. Correlation of serum FGF21 and LVMI with the frequency of arteriovenous fistula occlusion in HD patients.

P1500 **SEASONAL VARIATIONS AND VARIATIONS DUE TO OTHER CAUSES IN CLINICAL AND LABORATORY PARAMETERS IN HEMODIALYSIS PATIENTS**

KAZUHIKO KAWAHARA[1]

[1]*Kamojimacho Inoo, Yoshinogawa, Japan*

Background and Aims: In hemodialysis patients, seasonal variations and changes in dialysis prescription affect laboratory data, blood pressure, and body weight. We examined whether these fluctuations were due to seasonal variations or other causes. Although there are some reports on seasonal changes in hemodialysis patients, there are few reports on observations over multiple years in the same stable patients.

Method: We studied 65 patients on hemodialysis (36 males and 29 females; average age, 67.7 years; average duration of HD therapy, 13.8 years). The observation period was three years from January 2016 to December 2018; laboratory data and dialysis-related indicators, blood pressure, dry weight, and interdialysis weight gain were examined retrospectively. We excluded cases with dialysis time less than 4 h and patients who were hospitalized during the observation period. Differences in statistical analysis were tested with repeated-measures ANOVA or Friedman test.

Results: Factors that showed an influence on the laboratory parameters in hemodialysis patients more than twice in the same season in the three-year observation period were serum urea nitrogen (UN), serum creatinine (Cr), serum potassium (K), serum inorganic phosphorus (IP), and serum total bilirubin (T-Bil), serum creatine kinase (CPK), serum glycoalbumin (GA), normalized protein catabolic rate (nPCR), % creatinine production rate (% CGR), systolic blood pressure (sBP), diastolic blood pressure (dBP), and inter-dialytic weight gain ($p<0.05$). In contrast, the serum albumin concentration (Alb), serum magnesium (Mg), serum parathyroid hormone-INTACT (iPTH), and standardized dialysis amount of urea (KT/Vurea) exhibited gradual changes during the observation period ($p<0.05$).

Conclusion: There were indeed seasonal variations with UN, Cr, K, IP, T-Bil, CPK, GA, nPCR, %CGR, sBP, dBP, and inter-dialytic weight gain. However, Alb, Mg, iPTH, KT/Vurea changed owing to dialysis prescription and medicines.

Table:

Seasonal variations	Variations due to other causes
1. High in June to September Cr, K, T-Bil, %CGR	1. dialysis prescription Alb, Mg, KT/V2) medicinesiPTH
1. Low in June to September UN, nPCR, sBP, dBP, inter-dialytic weight gain	
1. Others IP (low in October to December)CPK (low in February)GA (high in September to October)	

P1501 KIDNEY FAILURE AND BRAIN FUNCTION DECLINE

Clara Pardinhas[1], Carolina Figueiredo[1], Alice Lança[1], Helena Pinto[1], Helena Sá[1], Luis Escada[1], Rui Alves[1]

[1]*Coimbra University and Hospital Center, Nephrology, Coimbra, Portugal*

Background and Aims: ***Chronic kidney disease (CKD) and cognitive impairment (CI) are two major health problems in an aging population, and both carry out negative prognostic implications. Prevalence in general population appears to be around 22.2% and recent analysis indicates that CI and frailty can be more prevalent in individuals undergoing hemodialysis (HD). Many causes can contribute to this higher prevalence, from vascular calcification to cerebral hypoperfusion, oxidative damage and uremic toxins. Both frailty and CI can lead to an increase morbimortality. Montreal Cognitive Assessment (MoCA) and Mini Mental State Examination (MMSE) are two screening instruments with a good application profile for cognitive evaluation, as well as the Frailty Clinical Scale (FCS). However, there are few studies using these scales on HD patients and demonstrating association between frailty, cognitive impairment and their clinical characteristics.***

The aim of this study is to investigate the prevalence of coexisting cognitive impairment and frailty in our center hemodialysis patients and its association with clinical characteristics and outcomes.

Method: ***Thirty-two patients undergoing hospital hemodialysis program were assessed. The MoCA scale, MMSE*** **and** ***FCS were applied.*** **Data were analyzed using appropriate statistical methods, using SPSS ® version 22.0.** ***The significance level considered was 5%.***

Results: ***Thirty-two patients aged between 30 and 90 years were evaluated, with a mean of 61.63 years (SD ± 18.26), without gender predominance. The prevalence of deficits was 78.1% and 37,5% in MoCA and MMSE, respectively, without differences between gender. The prevalence of frailty (≥3) was 43.8%. Patients with deficit assessed by MoCA and MMSE were on average 15 years and 20 years older, respectively, than patients without deficit (p = 0.002).***

We found a statistically significant association between deficit measured by MMSE and frailty (p <.001), with higher prevalence of frailty (83.3%) in individuals with deficit compared to individuals without deficit, where the prevalence of frailty was 20.0%.

The deficit assessed by MMSE was also associated with time on dialysis (p = .029). No statistically significant associations were detected between MoCA and frailty over time on dialysis or between deficit measured by MoCA and frailty.

Regarding patients' comorbidities, there were no statistically significant differences between deficit assessed by MoCA and MMSE and presence of diabetes mellitus, hypertension and dyslipidemia. Deficits assessed by MoCA, MMSE, and Frailty were not associated with phosphoremia and also there was no association between presence of significative hypotension episodes during HD and these scales. Dialysis efficacy (kt/v) was not statistically associated with MoCA and MMSE deficits. Similarly, no association was found between Kt/v and frailty.

Conclusion: ***In our study, prevalence of CI and frailty in hemodialysis patients was high. Time on dialysis program was related in a statistically significant way with CI and there was higher prevalence of frailty in individuals with deficit measured by MMSE. However, we did not find a correlation between dialysis efficacy, comorbidities and vascular risk factors and cognitive deficit or frailty score. The epidemiology and natural history of cognitive impairment and its association with frailty are important to understand among patients on HD for early intervention and management.***

P1502 **IS AGE JUST A NUMBER? - HEMODIALYSIS IN OCTOGENARIAN PATIENTS IN A PORTUGUESE CENTRAL HOSPITAL**

Daniela Alferes[1], Marinha Silva[2], Joana Couto[3], Ana Ventura[1], Clemente Sousa[4], Paulo Teles[5], Sónia Sousa[1], Maria Clara Santos[1], João Carlos Fernandes[1]

[1]Centro Hospitalar Vila Nova de Gaia/Espinho, Nephrology Department, Vila Nova de Gaia, Portugal, [2]Hospital Santa Maria Maior, Internal Medicine Department, Barcelos, Portugal, [3]Unidade Local de Saúde do Alto Minho, Internal Medicine Department, Viana do Castelo, Portugal, [4]Escola Superior de Enfermagem do Porto, Porto, Portugal and [5]Universidade do Porto, Faculdade de Economia da Universidade do Porto, Porto, Portugal

Background and Aims: The option of a non-dialytic or conservative approach to elderly patients with End-Stage Renal Disease (ESRD) as an alternative to dialysis has a great interest in clinical practice. Among elderly patients with ESRD, the octogenarian ones raise the most difficult decisions with respect to indication and dialysis therapy management, furthermore the evidence about the clinical outcomes is lacking in this group of patient. The main objectives of this study were the analysis the comorbidities and clinical condition of pre-ESRD octogenarians who initiated dialysis and the estimation of the effect of such treatment on this patient group's comorbid status.

Method: The authors performed a retrospective and statistical analysis on patients with aged $\geq$ 80 years who initiated hemodialysis treatment in a Portuguese Central Hospital between 2007 and 2017. A total of 88 patients were included in the study.

Results: The mean age of the group was 84$\pm$2.8 years; 61.4% were men. Nearly all the patients (97.7%) had one or more comorbid conditions of which the most common were hypertension (86.4%), heart disease (58%) and diabetes (43.2%). In 60.2% of the patients the functional activity was normal (Karnofsky score $\geq$80). Hemodialysis was initiated in an emergency situation in 58% of the patients and the majority (59.1%) had an arteriovenous fistula as vascular access. In the 2 years previous to dialysis therapy, most patients (54.5%) had at least one hospitalization (min=1; max=4). During the two years of follow-up, the number of hospital admissions decreased (p=0.034) and only 39.8% of the patients required hospital admission (min=1; max=3) (table 1), with shorter average hospital stay (p=0.013) (table 2). The main causes of hospitalization in the pre-dialysis period were renal related-diseases, in contrast the admissions were due to non-access related infections and vascular access complications after dialysis had initiated. Most patients died (67%) at the end of follow-up mainly due to non-vascular access infections or sepsis (32.2%). The significant causes of death found by Cox regression were chronic kidney disease secondary to systemic disease, Karnofsky score and hospital stay in the 2-year-dialysis period (table 3).

Conclusion: Advanced age in itself should not be used as an excluding factor of dialysis treatment. Comorbidity and performance status are the factors that should exert the greatest influence on such decision. In this sample, the majority of patients had few comorbidities, a good functional activity and they initiated dialysis by an autologous vascular access which may have contributed to the good outcomeS. This study found a decrease in the number of hospitalizations in the dialysis period which can be explained by regular clinical monitoring in every dialysis treatment, preventing or even treating intercurrent illnesses and avoiding hospital admissions.

Table 1 – Number of hospital admissions

Hospital admissions	Previous 2 years		After 2 years	
	n	%	n	%
0	40	45.5	53	60.2
≥ 1	48	54.5	35	39.8
Total	88	100.0	88	100.0

Minimum; Maximum	1; 4	1; 3
Mean	1.6	1.1
Quartiles (Q1; Med; Q3)	1; 1; 2	1; 1; 1
Std. deviation (c.v.)	0.87 (55%)	0.36 (31.1%)

Table 2 – Hospital stay (days)

	Previous 2 years	After 2 years
Minimum; Maximum	2; 82	1; 45
Mean	17.1	12.7
Quartiles (Q1; Med; Q3)	9; 13; 22	5; 10; 16
Std. deviation (c.v.)	13.9 (81.5%)	10.4 (82.2%)

Table 3 – Regression results

Variable	Estimate	p	Hazard ratio	90% CI Lower	90% CI Upper
ESRD secondary to systemic disease	2.560	< 0.001	12.941	4.105	40.800
Karnofsky 50-70	2.510	0.014	12.307	2.291	66.098
Karnofsky ≥ 80	2.465	0.011	11.760	2.365	58.473
Hospital stay after 2 years	0.025	0.088	1.025	1.001	1.049

Figure:

P1503

A MULTICENTER STUDY OF THE CLINICAL, LABORATORY CHARACTERISTICS AND POTENTIAL PROGNOSTIC FACTORS IN PATIENTS WITH AA AMYLOIDOSIS ON HEMODIALYSIS

Ece Bilgic[1], İhsan Ergün[2], Tevfik Ecder[3], Gökhan Nergizoğlu[4], Kenan Keven[4]

[1]Ankara University School of Medicine, Department of Internal Medicine, Ankara, Turkey, [2]Ufuk University Faculty of Medicine, Department of Nephrology, Ankara, Turkey, [3]Istanbul Bilim University Faculty of Medicine, Department of Nephrology, İstanbul, Turkey and [4]Ankara University School of Medicine, Department of Nephrology, Ankara, Turkey

Background and Aims: While, AL amyloidosis is more common in western countries, the most common type of amyloidosis is AA amyloidosis in eastern Mediterranean region including Turkey. Although worse prognosis has been attributed to the AL amyloidosis, AA amyloidosis can also be related to higher mortality under renal replacement therapies. However, there are no sufficient data regarding etiology, clinical presentation and prognostic factors of AA amyloidosis. The objective of our study is to evaluate the clinical, laboratory characteristics and possible predictive factors related to mortality in patients with AA amyloidosis undergoing hemodialysis (HD).

Method: This multicenter, cross-sectional study was a retrospective analysis of 2100 patients on HD and carried out in 14 selected hemodialysis centers throughout Turkey. Thirty-two patients with biopsy proven AA amyloidosis and thirty-two control patients without AA amyloidosis undergoing HD were included between October 2018 and October 2019. There was no significant difference between the groups in terms of the age and dialysis vintage. Causes of AA amyloidosis, treatment (colchicine and/or anti-interleukin 1 (IL) treatment; canakinumab or anakinra) and number of Familial Mediterranean Fever (FMF) attacks in the last year in case of FMF, systolic and diastolic blood pressures, biochemical values such as mean CRP, hemoglobin, serum albumin, phosphorus, calcium, PTH, ferritin, transferrin saturation, total cholesterol levels and EPO dose, erythropoietin resistance index (ERI), interdialytic fluid intake, body mass indexes, heparin dosage, UF volume and Kt/V data in the last year were collected by retrospective review of medical records.

Results: Prevalence of AA amyloidosis was found 1.87% in HD centers. In amyloidosis and control groups, 56% and 53% were male, mean age was 54±11 and 53±11 years, mean dialysis vintage was 104±94 and 107±95 months, respectively. FMF was the most common cause of AA amyloidosis (59.5%). All FMF patients received colchicine and the mean colchicine dose was 0,70 ±0,30 mg/day. 26,3 % of FMF patients were unresponsive to colchicine and anti-IL-1 treatment was used in these patients. In AA amyloid and control groups, ERI were 7,88±3,78 and 5,41±3,06 IU/kg/week/g/dl, respectively, (p=0.008). Additionally, higher CRP values (18,78±18,74 and 10,61±10,47 mg/L, p=0.037), lower phosphorus (4,68±0,73 mg/dL vs 5,25±1,04, p=0.014), total cholesterol (135±42 vs 174±39 mg/dL, p<0.01) and serum albumin (3,67±0,49 mg/dL, 4,03±0,22, p<0.01) were observed in patients with AA amyloidosis compared to the control group.

Conclusion: In this study, we found that long term prognostic factors including higher inflammation, malnutritional parameters and higher ERI were more frequent in AA amyloidosis patients under hemodialysis treatment.

	Amyloidosis group (n=32)	Non-amyloidosis group (n=32)	p
Dialysis vintage (months)	104,47±94,68	107,91±95,22	0,885
Age (years)	54,16±11,87	53,47±11,56	0,815
BMI (kg/m2)	23,10±3,99	24,65±3,81	0,118
Hemoglobin (g/dL)	10,94±1,24	11,41±0,80	0,078
CRP (mg/L)	18,78±18,74	10,61±10,47	**0,037**
Serum albumin (mg/dL)	3,67±0,49	4,03±0,22	**<0.01**
Serum calcium (mg/dL)	8,81±0,57	8,90±0,60	0,535
Serum phosporus (mg/dL)	4,68±0,73	5,25±1,04	**0,014**
Total cholesterol (mg/dL)	135,66±42,14	174,11±39,64	**<0.01**
Parathormon (pg/mL)	364,22±330,15	418,22±279,60	0,483
Heparin dosage (IU/session)	2709,26±866,66	3257,45±1212,27	**0,05**
ERI (IU/kg/week/g/dl)	7,88±3,78	5,41±3,06	**0,008**

Figure: Demographic, clinical and laboratory characteristics of patients

P1504 RELATIONSHIP OF LOW BODY MASS INDEX AND SURVIVAL IN HEMODIALYSIS PATIENTS

Ha Yeon Kim[1], Jeong Ho Lee[2]

[1]Gwangju Veterans Hospital, Department of Internal medicine, Gwangju, Korea, Rep. of South and [2]Gwangju Veterans Hospital,, Department of Internal medicine, Gwangju, Korea, Rep. of South

Background and Aims:

Malnutrition is common in patients with hemodialysis and major risk factor of mortality. The Korean Society of Nephrology (KSN) collected data of end-stage renal disease registry since 1985. We evaluated whether body mass index (BMI) can affect mortality in patient with hemodialysis.

Method:

From 2004 to 2015, a total of 32,163 patients starting hemodialysis were included. The patients were divide four groups according quartiles of BMI measurement.

Results:

At baseline, mean age was 59.0 ± 14.3 years old, and 60.0% were men. The 5-year mortality of hemodialysis patients was 16.9 % (N=5,435) and ratio of unknown state was 24.9 % (N=7,996). The mean of BMI in each quartiles were 18.2 ± 1.2, 20.8 ± 0.5 22.8 ± 0.6, 26.4 ± 2.6 kg/m^2 respectively. The mean of BMI between survivor and non-survivor were different (22.3 ± 3.3 vs. 21.5 ± 3.2 kg/m^2). Cox-proportional regression multivariate analysis revealed that the 5-year all-cause mortality was associated with age (HR 1.04, CI 1.03-1.05), diabetes (HR 1.34, CI 1.07-1.7) coronary heart disease or heart failure (HR 1.3, CI 0.9-1.7), 2nd BMI quartile (HR 0.7, CI 0.5-0.9), 3rd BMI quartile (HR 0.6, CI 0.46-0.88), 4th BMI quartile (HR 0.59, CI 0.43-0.82), hypoalbuminemia (HR 2.9, CI 2.3-3.7) and anemia (HR 1.6, CI 1.2-2.0) .

Conclusion:

Higher quartiles of BMI was significantly associated with better survival rate in hemodialysis patients in Korea. Traditional risk factors of malnutrition, such as hypoalbuminemia, anemia were also independent risk factor for mortality. This result suggests that hemodialysis patients needed to nutritional support.

P1505 **COMORBIDITY AND AGE OF DIALYSIS PATIENTS OUTPERFORMS FRAILTY BURDEN AS A PREDICTOR FOR MORTALITY**

Mimoza Milenkova[1], Adrijana Spasovska Vasilova[1], Aleksandra Canevska[1], Vladimir Pushevski[1], GJULSEN SELIM[1], Aleksandar Sikole[1], Irena Rambabova Bushljetikj[1], Lada Trajcheska[1], Goce Spasovski[1]

[1], *University Clinic of Nephrology, Skopje,*

Background and Aims: The life expectancy in dialysis patients depends on patients' age and comorbidities. Frailty in elderly patients is a state of impaired homeostasis with loss of physiologic reserve and a consequent impaired responses to dialysis burden. In this study we assessed the impact of age, comorbidities and frailty on dialysis patients' survival.

Method: The study enrolled 162 prevalent patients on chronic hemodialysis with mean dialysis vintage of 100 months, 55% were women and 21 % had diabetes. Patients were divided into three groups by the Khan Comorbidity index score, highest score was considered worse. Frailty was assessed by presence of 3 or more symptoms (unintentional weight loss, feeling exhausted, weak grip strength, slow walking speed and low physical activity) and expressed as absolute number. Estimates of five years life expectancy were assessed by Kaplan Meier survival log-rank test and Cox regression hazard model.

Results: There were 26 (16%) with lowest score, 85 (52%) with medium score and worst highest score in 51 (31%). During the 5 years of follow up 69(43%) patients died of all-cause mortality. There were no deaths in the group with lowest score and mortality rates in the intermediate and worse score group increased by double (0; 30%; 69%, respectively). Significantly higher mean life expectancy was found in lower Khan Score groups: 60mo; 48.40 $\pm$ 18.51; 32.44 $\pm$ 22.06, log-rank: $p < 0.012$. Patients that scored worse had four folds higher risk for death HR 4.2 (95% CI: 2.72 – 6.36), p=0.0001. In the multivariate model Khan Score was a more powerful predictor of mortality than frailty in elderly, with HR 3.2 (95% CI: 2.88 – 5.41), p=0.0001.

Conclusion: Comorbidities and age outperforms frailty burden as a predictor of mortality in dialysis patients.

P1506

IMPROVEMENTS IN MICROVASCULAR AND MACROVASCULAR DIABETES-RELATED COMPLICATIONS IN DIALYSIS PATIENTS

Kofod Dea[1], Thomas Peter Almdal[2], Vibeke Rømming Sørensen[1], Bo Feldt-Rasmussen[1], Mads Hornum[1]

[1]Copenhagen University Hospital, Department of Nephrology, Copenhagen, Denmark and [2]Copenhagen University Hospital, Department of Endocrinology, Copenhagen, Denmark

Background and Aims: Newer data suggests that there has been a substantial reduction in the incidence of diabetic complications over the past 30 years. However, little is known about whether this reduction also applies to patients with diabetes and end stage renal disease. The present study examined the current prevalence and the changes in microvascular and macrovascular diabetes-related complications in dialysis patients.

Method: The study was carried out as a cross-sectional study of all 119 diabetic patients in chronic dialysis at our department during June 2019. Data on diabetes-related complications was obtained from the patients' electronic medical records and compared with a historic control group of all 38 diabetic dialysis patients examined in 2004.

Results: Currently, 12.3% had foot ulcer, while 40.3% had a history of foot ulcer. Lower extremity amputations were seen in 19.3%, with 7.6 % being amputated above-knee level. Development of Charcot foot was seen in 3.4%, and 64.1% had diabetic retinopathy (27.2% with proliferations), 27.2% had maculopathy, and 18.4% had a visual acuity lower than 0.3. A total of 31.1% had atrial fibrillation or flutter, 14.3% had angina pectoris and 20.2% had a history of myocardial infarction. A history of stroke or transient ischemic attack was observed in 21.8% and 6.7%, respectively. Compared with data from the 2004 cohort, we found a significant reduction in the prevalence of current foot ulcers (p=0.013), proliferative retinopathy (p=0.007) and visual acuity lower than 0.3 (p=0.028).

Conclusion: The findings of this study indicate that there has been a reduction in current foot ulcers and eye complications over the past 15 years among diabetic dialysis patients, whereas the prevalence of amputations, cardiovascular and cerebrovascular complications remains high.

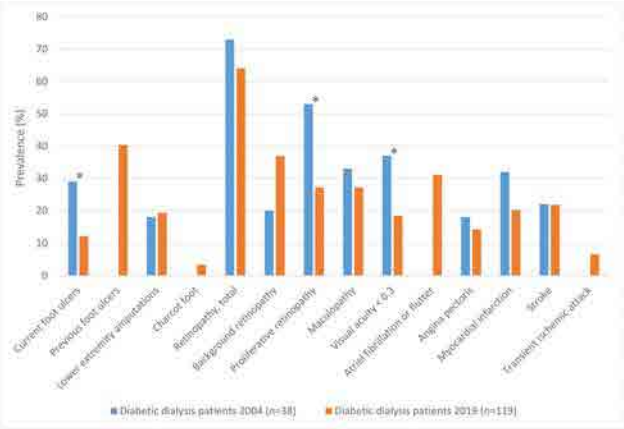


Fig. 1. Histogram of the prevalence of diabetes-related complications in diabetic dialysis patients in 2004 and 2019. * for significant difference in prevalence at $p<0.05$ (Chi-square).

P1507 **COMPETING RISKS MODELING IN PERITONEAL DIALYSIS: THE URGE FOR A CHANGE IN SURVIVAL ANALYSIS METHODOLOGY**

Anabela Malho Guedes[1,2], Roberto Calças[1], Ana Domingos[1], Teresa Jerónimo[1], Pedro Neves[1], Rosário Martins[2], Sara Dias[2]

[1]Centro Hospitalar Universitario Algarve, Portugal and [2]Universidade Nova de Lisboa, Portugal

Background and Aims: Survival analysis is a cornerstone in medical research. For this purpose Kaplan-Meier is the most widely used statistical test, but the presence of competing risks violates the fundamental assumption that the censoring mechanism is independent of survival time. This leads to overestimation of the cumulative probability of cause-specific failure. Cumulative incidence estimate and competing risks analysis are preferred. The purpose of this study was to compare different survival analysis methods: Kaplan-Meier and cumulative incidence function estimates in a cohort of Peritoneal Dialysis (PD) patients.

Method: The survival of 115 incident patients on PD in a university hospital was evaluated after establishing 2 cohorts: patients starting renal replacement therapy with PD (PD first; n=85) and patients switching to PD on the first 6 months of dialysis (PD transfer; n=30). Kaplan-Meier, cumulative incidence function, cause-specific and subdistribution hazards were performed. The event of interest was death and the competing risk events were transfer to hemodialysis and renal transplantation.

Results: Besides higher residual renal function (RRF) and kt/V in the PD first group, there were no other significant differences between groups. There were 22 deaths. PD first group had a better survival with both Kaplan-Meier (log-rank test, p=0.013) and cumulative incidence function (p=0.021) approaches. The Cox regression model showed, as protecting variables, higher albumin (HR=0.174; CI95% 0.054-0.562), higher RRF (HR=0.785; CI95% 0.666-0.925) and PD first (HR=0.350; CI95% 0.132-0.927). Higher Charlson Index predicted worse outcome (HR=1.459; CI95% 1.159-1.835). PD as first dialysis therapy was associated with 65.0 % lower risk of death comparing with PD transfer. The subdistribution multivariable model found higher Charlson Index (HR=1.389; CI95% 1.118-1.725) and lower RRF (HR=0.798; CI95% 0.680-0.936) were statistically associated with death, but not PD transfer or albumin. This result differs from the obtained using the cause-specific hazard model. Analyzing the competing events, patients submitted to renal transplantation had a lower Charlson Index.

Conclusion: The probability of death was overestimated by the Kaplan-Meier method. The bias of Kaplan-Meier is especially great when the hazard of the competing risks is large. This study consisted on a statistical critical analysis of a real medical example, broader clinical conclusions related with "PD first initiative" should be cautious in this context.

It is primordial to recognize the presence of competing risks in studies with multiple outcomes, as in Peritoneal Dialysis studies, to estimate cumulative incidence and yield more accurate results. This study shows how different conclusions are attained with different statistical methodology and its relevance in clinical context.

P1508 **COGNITIVE IMPAIRMENT A RISK FACTOR FOR NON ADHERENCE TO MEDICAL MANAGEMENT AMONG PATIENTS ON MAINTENANCE HEMODIALYSIS.**

Larisa Shehaj[1], Merita Rroji (Molla)[1]

[1]*University Hospital Center ' Mother Tereza", Tirana, Department of Nephrology, Tirana, Albania*

Background and Aims: Patients with chronic kidney disease (CKD) are at substantially higher risk for developing cognitive impairment (CI) compared with the general population. Subtle changes can impact engagement with healthcare, comprehension, decision-making, and medication adherence. The Montreal Cognitive Assessment (MoCA) test was reported to represent a suitable cognitive screening tool for hemodialysis patients. Our study aimed to assess the prevalence of CI in CKD patients undergoing hemodialysis, socio-demographic and patient-related variables affecting CI and relationship with medical adherence.

Method: Out of 65 patients in the HD unit, 58 patients (mean age 59.16±10.61 years old and meantime in therapy 6.93±5.03 years) accepted to participate in the study. The Montreal Cognitive Assessment (MoCA) scale was administered to patients. Patients with a MoCA global score 24/30 were considered cognitively impaired. Descriptive analysis was done for the socio-demographic and clinical variables.

Results: The mean total MoCA score for all the patients were 22.77679±3.8. Thirty seven patient 63.7% were evaluated with CI where 67.5 % with Mild CI (MCI) and 32.5% with severe CI (SCI) under 20 points). MoCA subscale analysis revealed that the mean score for visuospatial/executive domain and attention were the lowest with 5.38±1.3 /8max and 2.82±1.67/6 max and scores for orientation were the highest 5.94±0.59/6 max. MCI was related to vintage to dialysis ($p < .00001$) and education years ($p<0.05$) but not with age ($p>0.05$) and gender ($p>0.05$) where severe CI was related to age and comorbidity ($p<0.05$ and $P<0.01$, respectively. We found a strong association between low scores and medical adherence ($p<0.001$).

Conclusion: In hemodialysis, we have a relatively high prevalence of CI and screening for impairment should be considered in all adults with ESRD. Older age, vintage on dialysis, and comorbidity were associated with lower scores. The visuospatial/executive domain and attention were mostly affected. The association between low scores and medical adherence show a high risk for this group of patients.

P1509 **SEVERITY OF PRURITUS IN HEMODIALYSIS PATIENTS: RELATIONSHIP TO UREMIC TOXINS AND DIALYSIS MODALITY**

Suguru Yamamoto[1], Takahiro Tanaka[2], Kentaro Omori[3], Isei Ei[4], Nobutaka Kitamura[2], Ichiei Narita[1]

[1]Niigata University Graduate School of Medical and Dental Sciences, Division of Clinical Nephrology and Rheumatology, Niigata, Japan, [2]Niigata University Medical and Dental Hospital, Clinical and Translational Research Center, Niigata, Japan, [3]Omori Clinic, Niigata, Japan and [4]Santo-Second Clinic, Niigata, Japan

Background and Aims:

Pruritus is a complication that can impair the quality of life of patients with chronic kidney disease (CKD). A previous report has suggested that the severity of pruritus is correlated with high serum concentrations of β_2-microglobulin, calcium, and phosphorus, however recent developments in hemodialysis (HD), especially use of high-flux membrane and online hemodiafiltration (OLHDF), may improve the severity of pruritus. Protein-bound uremic toxins (PBUTs), such as indoxyl sulfate and p-cresyl sulfate, are known to be factors associated with atherosclerosis and impaired bone metabolism in CKD and may also be associated with pruritus, especially in those undergoing dialysis treatments. The aim of our study was to assess the severity of pruritus using a new tool, the 5D-itch scale (5D), as well as its relation to circulating PBUTs and dialysis modality in patients with end-stage kidney disease.

Method:

This was a prospective cohort multicenter study, wherein we analyzed the baseline data. The 5D score (5–25 points) was measured in maintenance dialysis patients. The serum concentrations of indoxyl sulfate, p-cresyl sulfate, phenyl sulfate and hippuric acid were measured with mass spectrometry before a dialysis session. The correlations of the 5D scores with serum PBUTs, dialysis modality (HD or OLHDF) and the other background factors were assessed with Spearman correlation coefficients and the generalized linear model.

Results:

This study included 135 dialysis patients (98 HD and 37 OLHDF). The mean 5D score was 6.84 ($\pm$SD 3.14). The mean serum concentrations of indoxyl sulfate, p-cresyl sulfate, indole acetic acid, phenyl sulfate, and hippuric acid were 2.99 $\pm$ 1.40, 2.05 $\pm$ 1.54, 0.11 $\pm$ 0.08, 0.94 $\pm$ 0.71, and 4.52 $\pm$ 3.17 mg/dL, respectively. There was a significant correlation between the 5D score and dialysis modality (correlation coefficient = 0.24, $p < 0.01$). Dialysis method was associated with the 5D score by the generalized linear model, and OLHDF was associated with a lower 5D score. There were no significant associations between the 5D score and serum concentrations of the various PBUTs (e.g., for indoxyl sulfate, the correlation coefficient was 0.11, $p = 0.20$)

Conclusion:

Pruritus, as assessed by the 5D score, was associated with dialysis modality, but not with the serum concentration of PBUTs. Further studies will be needed to understand the mechanism of the effect of OLHDF on pruritus as well as the role of uremic toxins in the itchy skin in CKD patients.

P1510 **INCIDENCE AND OUTCOME HEMODIALYSIS PATIENCE WITH HEPARIN INDUCED THROMBOCYTOPENIA - FOUR YEAR EXPERIENCE ZVEZDARA UNIVERSITY MEDICAL CENTER**

Ana Bulatovic[1], Vesna Maslarevic Radovic[1], Katarina Markovic[2], Petar Djuric[1], Jelena Tosic Dragovic[1,3], Aleksandar Jankovic[1,3], Marina Paunovic[4], Tatjana Damjanovic[1], Zdenka Majster[1], Verica Stankovic Popovic[1], Radomir Naumovic[1,3], Nada Dimkovic[5]

[1]Zvezdara University Medical Center, Nephrology and Dialysis, Beograd, Serbia, [2]Zvezdara University Medical Center, Hematology, Belgrade, Serbia, [3]University School of Medicine, Serbia, [4]Zvezdara University Medical Center, Laboratory and diagnostic, Belgrade, Serbia and [5]Serbian Medical Assosiation, Medical Academy, Serbia

Background and Aims: Heparin-induced thrombocytopenia (HIT) is a potentially fatal adverse reaction after administration of unfractionated or fractionated heparin, which underlies the generation of antibodies to the heparin complex and platelet factor 4 (PF4). It occurs in 5% of patients treated with unfractionated heparin and 0.5 - 1.5% fractionated heparin. The aim of the study is to determine the incidence and outcome of hemodialysis patients with HIT over 4 years period.

Method: Our retrospective study analyzed patients who were tested for evidence of positive anti-heparin antibody in the period from 2015 to 2019 in Zvezdara University Medical Center. The diagnosis was confirmed by the 4T clinical scoring system, a positive antiheparin-PF4 ELISA test and a positive platelet aggregation test with heparin.

Results: During observation period, total of 54 tests were performed on HIT suspected patients, out of which 21 patients were positive. Out of them, 14 patients were on HD, and other 7 (geriatric, surgery and cardiology departments) received therapy due to peripheral thrombosis, AIM or arrhythmia. All patients treated at nephrology, started hemodialysis (HD) with unfractionated heparin, while others were treated with LMWH. 4T scoring showed that 64% of patients had a moderate risk of developing HIT, while high risk was assessed in 36% of patients. Thrombotic complications in the form of deep venous thrombosis had 50% of patients, pulmonary thromboembolism had 11% of patients. The greatest decrease in Tr was most commonly observed between 10th and 14th day (61% of patients) and 39% from 4th to 10th day from start of heparin administration. In addition to heparin withdrawal and treatment with alternative non-heparin anticoagulation (fondaparinoux), 5 patients needed plasma treatment. 11 patients on HD were transferred to peritoneal dialysis (PD), and 2 patients recovered renal function. Overall mortality was 52%, while in nephrology patients was below 30%.

Conclusion: HIT should be considered in patients at risk. It is necessary to abolish heparin treatment and use alternative method (PD) or alternative anticoagulation. Hemodialysis patients have better prognosis than other comparable patients.

P1511

MODELO PREDICTIVO DE SUPERVIVENCIA DE INTELIGENCIA ARTIFICIAL (BOSQUE ALEATORIO) EN HEMODIALISIS. DATOS DEL REGISTRO ANDALUSINA DE ENFERMEDADES RENALES. SICATA

Manuel Benítez Sánchez[1], Guillermo Martín[2], Luis Gil Sacaluga[3], Maria Jose Garcia Cortes[4], Sergio García Marcos[5], Magalena Palomares Bayo[6], Ana Morales[7], Raquel Ojeda[8], Carolina Lancho Novillo[9]

[1] JUAN RAMON JIMENEZ UNIVERSITY HOSPITAL, NEPHROLOGY, HUELVA, Spain, [2]Hospital Universitario Carlos Haya, Nephrology, Malaga, Spain, [3]Virgen del Rocio Hospital, Nephrology, Sevilla, Spain, [4]Hospital Regional Jaen, Nephrology, Jaen, Spain, [5]Del Poniente Hospital. Almeria, Nephrology, Almeria, Spain, [6]Virgen de las Nieves Hospital, Nephrology, Granada, Spain, [7]Hospital Clinico San Cecilio, Nephrolgy, Granada, Spain, [8]Reina Sofia Hospital, Nephrology, Cordoba, Spain and [9]Regional Hospital Cadiz, Nephrology, Cadiz, Spain

Background and Aims: Random Forest (RF) is an analytical technique of Artificial Intelligence (AI) that consists of an assembly of trees built by bootstrapping (resampling with replacement). In each node a subset of predictor variables is selected and for them the best cut point is determined. Each division of the tree is based on a random sample of the predictors. The trees are as long as possible. In the construction of each RF tree a part of the observations is not used (37% approx.). It is called an out-of-bag (OOB) sample and is used to obtain an honest estimate of the predictive capacity of the model. So it does not require validation. In each analysis, a few hundred Regression or classification trees are carried out, depending on whether the response variable is numerical or qualitative respectively. The result is an average of the repeated predictions of the model (Bagging). RF allows to calculate the importance of the predictor variables, which can be used later to be included in a multivariate regression model.

Method: We analyzed 14750 records between 2011 and 2014 contained in Information System of the Autonomous Transplant Coordination of Andalusia (SICATA) a system that includes clinical-epidemiological variables, about anemia, bone bone metabolism, adequacy of dialysis and vascular access. 1911 patients presented the event of interest (exitus). Three predictive and explanatory models of survival are developed: 1-RF. 2-.Multivariate Logistic Regression. 3- Multivariate Logistic Regression that includes the important variables of the previous RF model. We compare them in terms of accuracy (AUC of the ROC curve).

Results: AUC of the ROC curve of the multivariate model without prior RF was: 0.75 AUC of the ROC curve of the multivariate model with previous RF was: 0.81. AUC of the ROC curve of the Random Forest model: 0.98

Conclusion: The Random Forest model has a 98% discrimination in the mortality of patients on Hemodialysis, far superior to the classic multivariate analyzes. The Multivariate Logistic Regression performed with the important RF variables improves the AUC of the previous model 0.81 vs. 0.75.

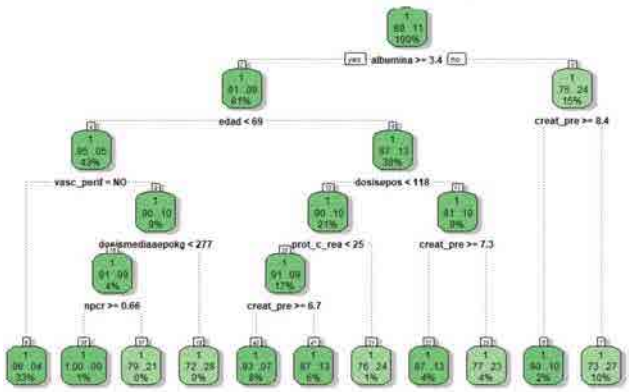


Figure: Decision Tree Live / Death

P1512 **THE RELATIONSHIP AMONG ANXIETY, DEPRESSION AND FRAILTY IN MAINTENANCE HEMODIALYSIS PATIENT**

Lirong Yao[1], Lianghong Yin[1], Fanna Liu[1]

[1]*The First Affiliated Hospital of Jinan University, Nephrology, Guangzhou, P.R. China*

Background and Aims: The population undergoing maintenance hemodialysis (MHD) is increasing dramatically worldwide, particularly in China. MHD patients have a high prevalence of frailty, which can cause increased vulnerability to adverse health outcomes, such as psychological disorders and reduced health-related quality of life. Both psychological disorders and frailty are prevalent and burdensome in MHD patient. However, the relationships between these entities are unclear. The aim of this study was to investigate the prevalence and associations between frailty and psychological disorders in Southern Chinese MHD patients.

Method: A multicenter, cross-sectional and observational investigation was conducted at 4 hemodialysis centers. Frailty was evaluated with the Tilburg Frailty Indicator (TFI) and it was used as the self-reported questionnaire. Anxiety symptoms was assessed by the Self-Rating Anxiety Scale (SAS), depressive symptoms was assessed by the Self-Rating Depressive Scale(SDS). The sociodemographic and clinical characteristics of the patients who complete the scales were collected. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software version 20.0 for Windows.

Results: Of the 623 patients visiting each institution, 300 were enrolled in this study. The mean age was 61.95±13.64 years, with mean duration of HD 30.7 (43.39±2.36) months.116 patients (38.7%) were female and 133 (44.3%) had diabetic kidney disease. In total, there were 225 patients (75%) were evaluated as frailty (Fig 2). The prevalence of frailty increased steadily with age and was more prevalent in the diabetes mellitus patients.

A multivariate logistic regression analysis revealed that the factors independently associated with frailty were the following: age (odds ratio [OR] =1.053, 95% confidence interval [CI] 1.026∼1.08), Charlson comorbidity index (CCI) (OR = 1.705, 95% CI 1.378∼2.109, P<0.001), diabetes mellitus (DM) (OR =2.107, 95% CI 1.035∼4.288), SAS (OR = 1.157, 95% CI 1.062∼1.26), SDS(OR = 1.094, 95% CI 1.028∼1.165).

The number of subjects with frailty increased steadily with age. Among the elderly subjects, the population ≥ 75 years old had the highest prevalence of frailty (Fig 1). Furthermore, 50% of ≤45 years old patients were frailty, even though frailty is a geriatric syndrome. There was no relationship between the duration of HD and frailty status.

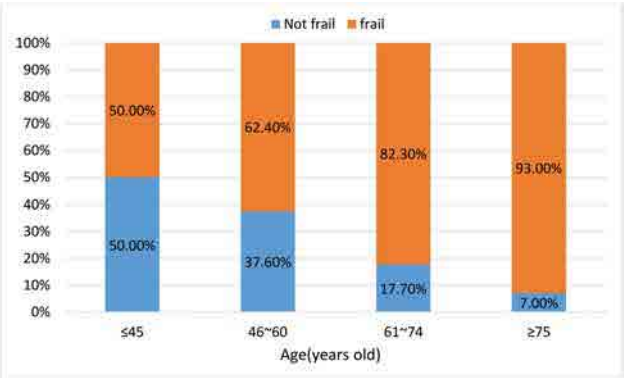


Fig 1 The ratio of the frailty phenotypes according to the age

Anxiety and depression symptoms by SAS and SDS were identified in 52.6% and 72.0% of MHD patients. MHD patients with both anxiety and depression generally had higher frailty score. The coexisting frailty and psychological disorder were present in 45.0% patients (Fig 2). There was an additive effect of psychological disorder and frailty on nutritional status. For the groups with frail and psychological conditions and no frail and no psychological conditions, both serum albumin (36.27±3.66, 37.76±3.51 g/L, respectively, p=0.02) and creatinine (842.94±282.97, 1028.84±332.64, respectively, p< 0.0001) decreased; overall SAS score was 55.36±3.87, 42.59±3.69, respectively (p< 0.0001), and SDS score was 65.05±6.50,58.50±9.03, respectively (p< 0.0001).

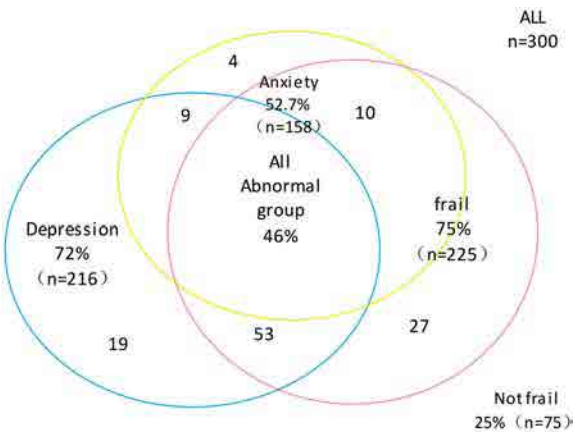


Fig 5.The condition of frail, depression and anxiety

Conclusion: This study demonstrated that anxiety and depressive symptoms are associated with prevalent frailty in Southern Chinese MHD patients. Older age, diabetes mellitus, CCI and lower serum albumin were associated with frailty among patients on MHD. anxiety and depressive symptoms are independent risk factors of frailty. In addition, age and diabetes are also independent risk factors for frail. And physical frailty should receive more attention in mental health care planning for Chinese MHD patients.

P1513

EDEMA SCORE OF CHRONIC KIDNEY DISEASE (CKD) 5D PATIENTS SHOW DIFFERENT CORRELATION WITH NON-CKD PATIENTS AND ARE STRONGLY INFLUENCED BY THE SERUM ALBUMIN VALUE ; PROPENSITY SCORE MATCHING ANALYSIS.

Takuya Murakami[1], Osamu Saito[1], Takako Saito[2], Koushi Ueno[2], Tetsu Akimoto[1], Daisuke Nagata[1]

[1]Jichi Medical University, Nephrology, Shimotsuke, Japan and [2]Ikou-kai Kawashima internal medicine clinic, Nephrology, Chikusei, Japan

Background and Aims:

Previously studies reported bioelectrical impedance analysis (BIA) method is useful for body fluid evaluation, especially for evaluation of edema in CKD patients. However, it is still unelucidated what factor affects edema score in CKD patients. In this study, we investigated the factors that determine edema score of CKD 5D patients and reported new findings on the differences from non-CKD patients by using propensity score matching analysis.

Method:

We measured the edema score of 117 CKD 5D patients and 303 non-CKD patients using the BIA method and analyzed the relationship with clinical laboratory factors. The edema score was expressed as the ratio of the total body weight (TBW) to the extracellular water (ECW) and was measured with InBody 20® (InBody Japan). All patients with CKD 5D were undergoing hemodialysis and the data were measured immediately after dialysis treatment.

Results:

There were differences between CKD 5D patients and non-CKD patients in age, sex, and BMI. Since these factors were estimated to affect edema scores, we performed propensity score matching with age and sex, BMI in CKD 5D patients and non-CKD patients.

After performing propensity score matching, the differences of age, sex, and BMI between the two groups disappeared. The number of patients became 70 in both groups.

By analyzing the model, the edema score of CKD 5D patients indicated significantly higher than that of non-CKD patients (CKD 5D; 0.400 ± 0.012 v. s. non-CKD; 0.389 ± 0.008, $P < 0.001$).

Edema score and factor which indicated significant difference by single regression analysis were examined using stepwise multiple regression analysis. As a result, we clarified that muscle mass is the most influential factor ($p < 0.0001$), and age is the next ($p = 0.025$) on edema score in non-CKD patients, however, in CKD 5D patients, serum albumin level is the most influential factor, and no significant influence was found in muscle mass and age ($p = 0.0006$).

Conclusion:

For CKD 5D patients, the edema score is defined by serum albumin, and serum albumin value has much greater influence than age. It is known that low level of serum albumin is associated with poor prognosis in CKD 5D patients. From these results, it was suggested that edema score could be a better prognostic factor than ageing for CKD 5D patients.

P1514

PERIPHERIAL VASCULAR DISEASE IN DIABETIC PATIENTS ON HEMODIALYSIS - RISK OF HOSPITALIZATION AND MORTALITY IN A LARGE EUROPEAN COHORT

Szymon Brzosko[1,2], Maciej Drozdz[3], Joao Frazao[4,5,6], Werner Kleophas[7,8], Partha Das[3], Fatima Silva[4], Stefan H. Jacobson[9]

[1]DaVita Poland, Wroclaw, Poland, [2]Medical University of Bialystok, 1st Department of Nephrology and Transplantation, Bialystok, Poland, [3]DaVita International, London, United Kingdom, [4]DaVita Portugal, Lisbon, Portugal, [5]São João Hospital Center, Department of Nephrology, Porto, Portugal, [6]University of Porto, School of Medicine, Porto, Portugal, [7]DaVita Germany, Düsseldorf, Germany, [8]Heinrich-Heine University, Clinic for Nephrology, Düsseldorf, and [9]Department of Clinical Sciences Karolinska Institutet, Division of Nephrology, Danderyd University Hospital, Stockholm, Sweden

Background and Aims:

Patients with diabetes mellitus on hemodialysis (HD) are at increased risk of development and progression of vascular calcification, atherosclerosis and peripheral vascular disease (PVD). Presence of PVD constitute a major risk factor for the development of cardiovascular events, such as myocardial infarction, stroke, hospitalization or cardiovascular death. The presence of PVD is also associated with a reduced quality of life and disability. A significant proportion of patients with PVD are asymptomatic with no or few classical symptoms and early detection to prevent progressive disease is therefore very important. Both the ACC/AHA and KDIGO guidelines recommend screening of individuals who are at risk.

Method:

We analyzed the frequency of foot complications following implementation of a standardized foot examination in 345 prevalent diabetic hemodialysis patients in 12 DaVita centers; 8 in Poland (n=177 patients) and 4 in Portugal (n=168 patients). The protocol includes: history of ulcers, amputation and examination of the pedal pulses (a dorsalis pedis and a tibialis posterior). Foot complications were classified according to Wagner (grade 0-5). PVD was classified by clinical pulse measurement (normal vs weak or missing). We analyzed associations between foot complications and peripheral pulses with risk of hospitalization and mortality using Cox proportional hazard models.

Results:

The mean age in all diabetic HD patients (58% men) was 70.4 (14 SD) yrs. Charlson comorbidity index (CCI) was 8.8 (2.4), Kt/V 1.8 (0.4), s-albumin 39 (4) g/L, Hb 11.1 (1.3) g/dL. A normal pulse in both a dorsalis pedis and both a tibialis posterior was found in 18% and 10% of patients. All other patients had weak or absent pulses. The Wagner classification score was 0 in 79% of patients, 1-3 in 16 % patients and 4-5 in 5 %. All-cause mortality was 31% during the 2 year follow up and 71% of patients had at least one hospital stay In patients hospitalized during follow up, a dors ped was normal/abnormal in 12% and 88% respectively ($p<0.05$); a tib post was normal/abnormal in 8% and 92%, respectively ($p<0.05$). There were no associations between Wagner score 0-5 and hospitalization or mortality. In unadjusted Cox models presence of weak or absent pulses in a dorsalis pedis was significantly associated with all-cause mortality RR 2.1 (CI 1.1-4.3; $p<0.05$). In adjusted analyses including age, sex, Hb, albumin, Kt/V, vascular access, phosphorus, PTH and CCI, only albumin was associated with mortality (RR 0.89, CI 0.84-0.94; $p<0.001$) and risk of hospitalization (RR 0.92, CI 0.89-0.96; $p<0.001$).

Conclusion:

Diabetic patients on HD have a high prevalence of PVD that warrant close clinical attention. Documentation of peripheral foot pulses for early detection of PVD is simple and suitable to identify patients at high risk of future complications and mortality. This standardized protocol could be the basis of a program to improve overall health outcomes in this vulnerable group of patients.

Table 1. Survival and mortality during follow up

	Age (years)	CCI	Kt/V	Alb (g/L)	Hb (g/dL)	A Dors ped normal	A Tib post normal	Hospitalization (episodes)	Hosp (days)
Survived	70	8.5	1.8	40	11.2	22%	13%	1.8	14
Died	72	8.9	1.8	38	11.0	10%	5%	2.4	23
*p**	0.002	0.004	NS	0.001	NS	0.014	0.047	0.001	0.001

Table 2. Characterization of patients with normal pulses in both feet vs at least one abnormal pulse.

A Dors ped	Age (years)	CCI	Kt/V	Alb (g/L)	Hb (g/dL)	Survived (%)	Hospitalization Yes (%)	Hospitalization (episodes)	Hosp (days)
Normal	68	8.3	2.0	40	10.8	83%	46	1.1	9.3
Abnormal	71	8.8	1.7	38	11.1	65%	77	2.2	21.7
*p**	0.081	NS	0.001	0.001	NS	0.014	0.001	0.001	0.019

*t-test and Chi-2 analysis

P1515 IMPACT OF POLYPHARMACY ON ALL-CAUSE MORTALITY, ALL-CAUSE HOSPITALIZATION AND CARDIOVASCULAR EVENTS IN INITIAL JAPANESE HEMODIALYSIS PATIENTS

Tatsunori Toida[1,2], Reiko Toida[3], Shou Ebihara[2], Shigehiro Uezono[3], Hiroyuki Komatsu[4], Yuji Sato[5], Shouichi Fujimoto[1]

[1]University of Miyazaki, Department of Hemovascular Medicine and Artificial Organs, Faculty of Medicine, Miyazaki city, Japan, [2]Miyazaki Prefectural Nobeoka Hospital, Department of Internal Medicine, Nobeoka city, Japan, [3]Chiyoda Hospital, Hyuga city, Japan, [4]University of Miyazaki, Center for Medical Education and Career Development, Faculty of Medicine, Miyazaki city, Japan and [5]University of Miyazaki Hospital, Dialysis division, Miyazaki, Japan

Background and Aims: Polypharmacy (PP) is common in end-stage chronic renal disease patients, largely because of the existence of multiple comorbid conditions. PP has the potential for harm and benefits, and the association between PP and mortality and morbidity in hemodialysis patients currently remains unclear. We examined the association of PP and the risk of clinical outcomes, such as all-cause mortality, all-cause hospitalization and cardiovascular events, in initial hemodialysis patients at admission and discharge.

Method: Study design: Cohort study.

Setting: Participants: One hundred and fifty-two initial hemodialysis patients (female vs. male, 88 vs. 64; mean age, 70.3 years) were enrolled between February 2015 and March 2018 at the Nobeoka Prefectural Hospital and Chiyoda Hospital.

Predictor: Patients were divided into 2 groups according to PP (6 or more drug prescriptions, or less) during admission and discharge for the initiation of hemodialysis.

Outcomes: All-cause mortality, all-cause hospitalization and cardiovascular events (hospitalization due to stroke, ischemic heart disease or peripheral artery disease) during the mean 2.8-year follow-up.

Measurements: Hazard ratios (HRs) were estimated using Cox's model for the relationships between PP and the clinical outcomes, and adjusted for potential confounders, including age, sex, body mass index, systolic and diastolic blood pressure, Charlson comorbidity risk index, hemoglobin, serum levels of albumin, albumin-corrected Ca, phosphate, parathyroid hormone, C-reactive protein and NT-proBNP; and use of erythropoietin stimulating agents. The group with 5 or less drug prescriptions was set as reference.

Results: Among the patients in this cohort study, the number of prescribed drugs per patient averaged 7.4 at admission and 6.9 at discharge for initial hemodialysis. One hundred (65.8%) and 94 patients (61.8%) had PP at admission and discharge, respectively. During follow-up, 20 patients died, 71 patients were hospitalized and 25 patients had cardiovascular events. PP at admission is significantly associated with cardiovascular events (HR 8.50, 95%CI 1.45-49.68). Furthermore, PP at discharge is significantly associated with all-cause hospitalization and cardiovascular events (HR 1.95, 95%CI 1.01-3.70; HR 53.16, 95%CI 2.70-104.62, respectively). However, PP is not significantly associated with all-cause mortality at admission or discharge.

Conclusion: Among Japanese patients starting hemodialysis, PP may be associated with clinical outcomes. However, it remains unclear whether PP is the direct cause of the outcomes or is simply a marker for increased risk of outcomes.

P1516 DEMONSTRATION OF FLUID REMOVAL ACCURACY USING THE SC+ HAEMODIALYSIS SYSTEM

Clive Buckberry[1], Paul Komenda[1,2,3], Keith Heyes[1], Eric Westenbrink[1], Mark Wallace[1], John Milad[1]

[1]Quanta Dialysis Technologies, Alcester, United Kingdom, [2]University of Manitoba - Internal Medicine, Winnipeg, Canada and [3]Seven Oaks Chronic Disease Innovation Centre, Winnipeg, Canada

Background and Aims:

Fluid management is an integral component for managing patients to correct abnormalities in plasma composition and maintain fluid balance. Consequently, accurate fluid removal during treatment is a critical design element of haemodialysis machines. The SC+ haemodialysis system developed by Quanta Dialysis Technologies, is a small, simple-to-use dialysis system designed to improve patient access to self-care and home haemodialysis. This paper describes the design, evaluation and performance of the flow balance and ultrafiltration module of SC+ to deliver specified fluid removal in accordance with the international technical standards for haemodialysis defined in IEC 60601-2-16 using a number of unique proprietary technologies.

Method:

SC+ uses volumetric flow balancing chambers which are contained within a single use disposable cartridge. During normal operation of SC+, dialysis fluid flows through the cartridge in discrete packets. This is achieved by the application of pneumatic pressure and vacuum to manipulate a flexible PVC membrane that, in turn, opens and closes a sequential series of valves and pump cavities that constitute the flow balance chambers.

Proof of system performance was undertaken using a range of dialysers and venous pressures, with and without ultrafiltration, to quantify the net fluid removal error, in order to simulate a range of patient conditions in typical clinical practice.

Results:

In total, the tests comprised 22 separate runs on multiple machines, with 88 individual 30-minute measurement samples, taken over a range of environmental conditions, dialyser types (with differing KuF), dialysate flowrates, and venous pressures.

Across all results, there was a mean error of 7.4g/hour rate error, (max allowed is 100g/hr) of positive flow from the blood to the dialysate side with a standard deviation of 19.88g/hr. The maximum permissible rate stated in IEC 60601-2-16 is +/-100g/hr.

In specific detail, without ultrafiltration the flow balance error was measured as 2.2g/hr with a deviation of 19.0g/hr, and with ultrafiltration the mean error was 12.8g/hr with a standard deviation of 19.5g/hr.

Conclusion:

It has been demonstrated that flow balance error and fluid removal attainable with the SC+ haemodialysis system lies well within the acceptable standards permitted for haemodialysis machines. This essential performance parameter as defined within IEC 60601-2-16 has been demonstrated across a range of clinically relevant parameters at dialysate flow rates of up to 500ml/min

P1517 **SURVIVAL ON DIALYSIS: SWITZERLAND IN COMPARISON WITH OTHER COUNTRIES - A FOLLOW UP**

Rebecca Winzeler[1], Patrice Max Ambühl[1]

[1]*Institute of Nephrology, Waid and Triemli City Hospital, Zurich, Switzerland*

Background and Aims: Survival in dialysis patients is substantially reduced compared to the general population. The aim of the present analysis was to compare the survival of Swiss dialysis patients with other countries with an additional year of follow up and a higher number of patients.

Method: Incident dialysis patients (hemo- or peritoneal dialysis; N=4525) from the Swiss dialysis registry were followed up from 2014 on until December 31, 2018 (mean follow up days=684). Deaths occurring during this time (N=976) were recorded and survival was examined using the Kaplan Meier method, censored for transplantation.

Results: Characteristics of the dialysis population stratified according to survival status are provided in Table 1.

Dialysis patients in Switzerland have an approximately 8% higher survival in the first and second year after start of dialysis compared to other European countries (Annual ERA-EDTA Report 2016). In the oldest age group, it amounts to up to 13 and 14%, in the first and in the second year, respectively. The proportion in survival rates between genders is similar in Switzerland, as well as in Europe. Dialysis patients aged younger than 45 years have a worse survival in Switzerland compared to other European countries.

Conclusion: The markedly better survival in dialysis patients in Switzerland compared to other European countries could be confirmed with an additional year of follow up and more patients. Also, causes of death vary widely among European countries. With an additional year of follow up, data to analyze 5-year survival probability will be available for comparison with the ERA-EDTA report. In addition, we will be able to verify whether dialysis patients under 45 years in Switzerland have an increased mortality or whether this is due to the small number of patients in these two age groups.

Table 1: Characteristics (given as mean±SD or percentage) in incident dialysis patients according to their survival status

	Non-Survivors, n=976	Survivors, n=3550	p-value
Age, years	73.7 ± 12.5	64.8 ± 16.3	0.000
Male gender, %	67.1	66.0	0.526
Body mass index, kg/m^2	24.6 ± 5.9	26.2 ± 5.6	0.430
Dialysis vintage, days	578 ± 402	713 ± 496	0.000
Dialysis duration per week (h)	11.2 ± 1.5	11.5 ± 1.4	0.000
Kt/V	1.50 ± 0.41	1.60 ± 0.45	0.024
Hemoglobin, g/dL	10.6 ± 1.8	11.1 ± 1.4	0.000
Ferritin, ng/mL	554.6 ± 622.1	452.5 ± 375.6	0.000
Calcium, mmol/L	2.21 ± 0.22	2.21 ± 0.22	0.316
Phosphate, mmol/L	1.54 ± 0.50	1.63 ± 0.47	0.021
PTH, ng/L	305.5 ± 349.8	367.1 ± 309.5	0.251
Iron substitution, %	74.2	74.0	0.909
EPO substitution, %	82.9	81.9	0.496
Comorbidities, n	3.6 ± 2.1	2.2 ± 1.9	0.000
CCI*	6.0 ± 2.7	4.1 ± 2.1	0.000

*Charlson Comorbidity Index

Table 2: One-, two-, 3- and 4-year survival probability (%) of incident dialysis patients, unadjusted, stratified by age, gender and cause of renal failure

	1 year srrqap	ERA-EDTA	2 year srrqap	ERA-EDTA	3 year srrqap	4 year srrqap
0-19 yrs (N=51)	88.4	97.6	88.4	94.2	88.4	88.4
20-44 yrs (N=396)	97.3	96.7	90.5	93.4	89.0	89.0
45-64 yrs (N=1252)	93.4	90.6	87.3	83.4	82.5	78.6
65-74 yrs (N=1231)	90.7	83.2	79.5	71.6	69.8	60.0
75$^+$ yrs (N=1595)	87.3	74.0	72.9	58.1	60.7	47.8
Men (N=2998)	90.7	83.4	79.6	71.7	70.6	61.1
Women (N=1527)	90.8	83.6	80.6	72.6	70.7	59.6
Diabetes (N=913)	90.3	85.2	78.9	72.8	72.0	56.2
Renal vascular disease (N=1015)	91.1	82.4	77.6	69.3	68.1	56.5
Glomerulonephritis (N=690)	94.1	91.2	90.1	84.3	81.4	77.9
Other causes (N=1905)	89.4	81.7	78.2	70.7	67.5	59.8
All (N=4525)	90.7	83.5	79.9	72.1	70.6	60.6

Continued

Continued

	1 year srrqap	ERA-EDTA	2 year srrqap	ERA-EDTA	3 year srrqap	4 year srrqap
0-19 yrs (N=51)	88.4	97.6	88.4	94.2	88.4	88.4
20-44 yrs (N=396)	97.3	96.7	90.5	93.4	89.0	89.0
45-64 yrs (N=1252)	93.4	90.6	87.3	83.4	82.5	78.6
65-74 yrs (N=1231)	90.7	83.2	79.5	71.6	69.8	60.0
75$^+$ yrs (N=1595)	87.3	74.0	72.9	58.1	60.7	47.8
Men (N=2998)	90.7	83.4	79.6	71.7	70.6	61.1
Women (N=1527)	90.8	83.6	80.6	72.6	70.7	59.6
Diabetes (N=913)	90.3	85.2	78.9	72.8	72.0	56.2
Renal vascular disease (N=1015)	91.1	82.4	77.6	69.3	68.1	56.5
Glomerulonephritis (N=690)	94.1	91.2	90.1	84.3	81.4	77.9
Other causes (N=1905)	89.4	81.7	78.2	70.7	67.5	59.8
All (N=4525)	90.7	83.5	79.9	72.1	70.6	60.6

P1518 5 YEAR ALL-CAUSE MORTALITY ACCORDING TO PRIMARY RENAL DISEASE IN HEMODIALYSIS PATIENTS

Ha Yeon Kim[1], Jeong Ho Lee[2]

[1]Gwangju Veterans Hospital, Department of Internal medicine, Gwangju, Korea, Rep. of South and [2]Gwangju Veterans Hospital, Department of Internal medicine, Gwangju, Korea, Rep. of South

Background and Aims:

The Korean Society of Nephrology (KSN) collected data of end-stage renal disease registry since 1985 and internet registry program was available since 2001. We explored the hypothesis that the 5-year mortality of hemodialysis patients was different depending on primary renal disease.

Method:

From 2004 to 2015, in total, 32,163 patients starting hemodialysis were determined. The cause of primary renal disease were divided to diabetic nephropathy (49.9%, n=16,038), hypertensive nephrosclerosis (18.5%, n=5,958), histologically confirmed glomerulonephritis 3.3% (n=1,067), cystic kidney disease (2.0%, n=656) and the miscellaneous (26.3%, n=8,444). The miscellaneous included renal tuberculosis, interstitial nephritis, lupus nephritis, kidney tumor.

Results:

The 5-year mortality of hemodialysis patients was 16.9 % (N=5,435) and ratio of unknown state was 24.9 % (N=7,996). The mortality of diabetic nephropathy, hypertensive nephrosclerosis, histologically confirmed glomerulonephritis, cystic kidney disease and the miscellaneous were 27.1% (n=3,323), 17.0% (n=768), 8.4% (n=62), 13.9% (n=67), and 19.7% (n=5,435), respectively. Kaplan-Meier survival analysis showed that diabetic nephropathy was worst survival rate following hypertensive sclerosis, cystic kidney disease and the miscellaneous, while histologically confirmed glomerulonephritis showed highest survival rate (log-rank $p < 0.001$). After adjusting for confounders, cox-proportional regression analysis revealed that 5-year mortality was associated with diabetic nephropathy compared hypertensive nephrosclerosis (HR, 1.62 CI, 1.17-2.24) while histologically confirmed glomerulonephritis was not significant.

Conclusion:

The overall mortality was associated with primary renal disease in hemodialysis paitents. This result suggests that hemodialysis patients with diabetic nephropathy require further medical attention.

P1519 A TWICE-WEEKLY HEMODIALYSIS : A SINGLE CENTER STUDY

Sirine Bchir[1], Malek Mojaat[1], Mariem Ben salem[1], Boukadida Amine[1], Insaf Handous[1], Haouala Faouzi[1], Ltaief Ahmed[1], Mouna Hammouda[1], Sabra Aloui[1], Skhiri Habib[1]

[1]*Monastir University Hospital, Nephrology departement, Faculty of medecine of monastir, Tunisia*

Background and Aims: Conventional hemodialysis consists of a thrice-weekly in-center Hemodialysis with a mean duration of 4 hours per session. The concept of incremental dialysis has allowed a better adjustment of its prescription guided by clinical and biological parameters. Thereby a twice-weekly regimen may maintain a good quality of life, a good survival rate and adequate dialysis in comparison to a thrice-weekly hemodialysis. The aim of our study was to investigate the profile of patients undergoing a twice-weekly regimen in our center.

Method: It is a monocenter transversal-descriptive study gathering patients on a twice-weekly regimen in the center of hemodialysis of Fattouma Bourguiba University Hospital in Monastir Tunisia.

Results: We identified 32 patients with a sex ratio of 2.2 (22 men and 10 women) with a mean age of 48,96 +/- 13,74 years. Regarding the intitial nephropathy, a chronic glomerulopathy was seen in 16 patients, a chronic tubulo-interstitial nephritis In 5 patients, and kidney polykystosis among 3 patients and in 8 patients the initial nephropathy remained undetermined. The indications for a twice-weekly HD regimen were: defavourable socio-economic conditions in 9 patients, a medical reason in 17 patients and a rejection of thrice-weekly regimen in 6 patients. The mean diuresis was 850 +/- 560 cc/24h and only one patient with anuria. The mean interdialytic weight gain was 2, 64 +/- 0, 83 Kg. Normal blood pressure and volemia were reported in 27 patients (84, 37 %). The mean number of anti-hypertensive drugs used was 1,5 per patient. The mean percentage of Urea reduction was 68, 8 % and a mean Kt/V of 1.26. The average of both kalemia and calcemia was respectively 5.27 mmol/l and 1, 94 mmol/l and the mean dosage of phosphoremia was 1, 63 mmol/l. The average of PTH and Hemoglobine was respectively 403 pg/ml and 9, 97 g/dl.

Conclusion: According to these results, a twice-weekly hemodialysis should be guided by the residual kidney function, clinical status (volemia), cardiovascular symptoms and comorbidities, biological parameters (Hemoglobine, potassium, phosphore) and the nutritional state. By meeting the above criteria, many studies have shown that a twice-weekly regimen or incremental dialysis help preserve the residual kidney function with a good quality of life.

P1520 **PULMONARY HYPERTENSION AS NEW RISK FACTOR FOR MORTALITY IN HEMODIALYSIS**

ROBERTO RAMIREZ MARMOLEJO[1,2], LUIS MIGUEL MUÑOZ ZAPATA[3], Laura Garcia Blanco[3]

[1]Santiago De Cali University, MEDICINE, CALI VALLE, Colombia, [2]DAVITA Sur, NEPHROLOGY, Cali, Colombia and [3]Santiago De Cali University, MEDICINE, CALI, Colombia

Background and Aims: The prevalence of pulmonary hypertension HTP in patients receiving dialysis therapy is not completely clear, it is an independent risk factor for cardiovascular mortality, which indicates the serious need to sensitize the clinic with this comorbidity and maintain an active search for it.

Objective: Raise awareness about the prevalence of HTP in a hemodialysis population and identify the associated risk factors.

Method: Descriptive, retrospective study, in which echocardiograms of the patient (peritoneal dialysis PD and hemodialysis HD) in renal facility were reviewed, at least 12 months in therapy, Nice 2013 classification were used for the diagnosis of HTP, multivariate analysis (echocardiograHTPic, demograHTPic, clinical and biochemical variables) was performed and the statistical significance of P <0.05 with the X2 method was searched for the associated risk factors.

Results: 24 male patients (45%), 75% with systemic hypertension, 34% with diabetes mellitus T2, on average 5 years on dialysis (+/- 2.7), age of 64 years (+/- 13.6) and 3 very elderly patients (> 85y); 35 patients (66%) on hd and 18 (34%) on PD. 51% had fistula ArterioVenosa (FAV). 100% of patients in hd with KtVe> 1.25 and 73% in pd with KtV> 1.7.

Regarding the HTP, 27 positive patients were found (51%), the significant (p <0.05), were: hd 54% vs 44% PD, having a 76% central catheter with HTP vs 33% with fav, and patients with severe vs mild Hiperparatiroidism

The severity of HTP, in hd vs pd was more severe, PSP average of pressures in the positive 43mmHg vs 34.3mmHg respectively (p <0.033)

Conclusion: HTP is a comorbidity that impoverishes the cardiovascular prognosis and its management must be specific, especially due to the preference of calcium antagonists over the use of renin angiotensin system blockers. The prevalence of PHT in the hemodialysis population is very high, which makes the clinician an active search and effective treatment, especially in patients with catheters. Hyperparathyroidism plays a role within the remodeling mechanisms of the pulmonary arterial endothelium, aggravating this situation and increasing mortality

Table #1**DemograHTPic characteristics of studied patients**

Item	Percentage
Female	55 %
Diabetes	34 %
Hypertension	75 %
Payed Health System	51 %
Average time on dialysis	5 +/- 2.7 years
Peritoneal Dialysis	34 %
Hemodialysis	66 %

Table #2**Significant variables of the analysis in patients found with HTP**

Item	Percentage	Significance P<0.05
Age > 85 yrs	3	p<0.05
Hemodialysis	54	<0.023
Dialysis Catheter	76	<0.001
severe vs mild Hyperparathyroidism		< 0.012
Severe Pulmonary Hypertension in Hemodialysis vs Peritoneal	3 vs 0	<0.033

P1521 LRG-1 LEVEL PREDICTS 5-YEAR MORTALITY IN ESRD

Feng-Jung Yang[1,2]

[1]National Taiwan University Hospital Yulin Branch, Internal Medicine, Taiwan, R.O.C. and [2]National Taiwan University, Graduate Institute of Clinical Medicine, College of Medicine, Taipei, Taiwan, R.O.C.

Background and Aims:

Plasma Leucine-Rich alph-2-Glycoprotein 1(LRG1) is an new biomarker for inflammatory and angiogenetic diseases. whether levels of plasma LRG1 correlate with the co-morbidities of End stage renal disease (ESRD) patients is unknown.

Method:

Plasma LRG-1 and high-sensitivity C-reactive protein were analyzed by ELISA in samples from 169 hemodialysis patients from the Immunity in ESRD study (iESRD study). Baseline co-morbidities were recorded through chart review of medical history.

Results: High level of LRG 1 showed high mortality in the ESRD. In multivariate-adjusted logistic regression models, higher LRG1 was significantly associated with 5 year mortality after adjusting for gender, hemoglobin, diabetes, hypertension, and level of C-reactive protein.

Conclusion: LRG1 is a possible poor prognosis marker in ESRD. Higher LRG-1 showed high prevalent CAD and PAOD in our study before. The role of LRG1 and the associated cardiovascular diseases should be analyzed the mechanism in this patient population.

P1522

THE RELATIONSHIP BETWEEN AORTIC STENOSIS AND NORTALITY RATE: A PROSPECTIVE COHORT STUDY IN JAPANESE HEMODIALYSIS PATIENTS

Yuji Sasakawa[1], Daijo Inaguma[1]

[1]*Fujita Health University, nephrology, Toyoake-shi, Aichi-ken, Japan*

Background and Aims: Aortic stenosis (AS) in Japanese hemodialysis (HD) patients is sometimes pointed out by periodic transthoracic echocardiography. In general population, heart failure symptoms become severer with progress of AS. In HD patients, there is a possibility that AS cause blood pressure decline and congestive heart failure which are one of the reasons for censoring HD. There were no large-scale prospective observational studies relating to cardiovascular (CV) events and mortality in HD patients with AS, therefore we investigated whether AS was associated with incidence of CV events and mortality in HD patients.

Method: This study was a prospective cohort analysis which 4 facilities in Japan participated. The subjects who were over 20 years and underwent maintenance HD for at least 12 months were enrolled at timing of receiving transthoracic echocardiography. Patients were classified into following 2 group (AS group: mean pressure gradient (PG) $\geq$ 20 mmHg or aortic valve area (AVA) $\leq$ 1.0 cm^2 or maximum blood velocity (Vmax) $\geq$ 2.0 m/s, no AS group: others). Four hundred sixty-four patients were followed up for 2 years. The primary outcome was defined as all-cause mortality. The secondary outcomes were incidences of CV events, stroke and hospitalization due to peripheral artery disease (PAD). Baseline was set at the time of transthoracic echocardiography examination. We compared the mortality and incidences of events between the 2 groups by a multivariate Cox proportional hazard model. In addition, we extracted risk factors relevant to AS by a multivariate logistic regression model.

Results: There were 79 patients (17.0 %) in the AS group among 464 patients. Older age and longer dialysis vintage were significantly associated with comorbidity of AS (multivariate-adjusted odds ratio [OR], 1.06; 95% confidence interval [CI], 1.03-1.10; $p < 0.001$, OR, 1.05; 95% CI, 1.01-1.08; $p = 0.01$, respectively). Meanwhile, gender, diabetes mellitus and serum phosphate were not associated with comorbidity of AS. During follow up period (median, 2.3 years), 31 patients (6.7 %) died. There was no significant difference in all-cause mortality between the 2 groups (multivariate-adjusted hazard ratio [HR] for no AS group, 0.68; 95% CI, 0.24 – 1.91; $p = 0.46$). Furthermore, there were no significant associations between comorbidity of AS and the 3 secondary outcomes (HR, 0.25; 95% CI, 0.03 – 2.00; HR, 1.33; 95% CI, 0.34 – 5.21; HR, 1.50; 95%CI, 0.36 – 6.29, respectively). There were also no significant associations between comorbidity of severe AS defined as Vmax $\geq$ 2.0 m/s to $\geq$ 3.0 m/s and all the outcomes including all-cause mortality. On the other hand, tumor bearing was a risk factor for all-cause mortality (HR, 1.65; 95% CI, 1.04 - 2.61), and hypoalbuminemia was a risk factor for mortality from infection (HR, 0.13; 95% CI, 0.02-0.90).

Conclusion: This research showed that there were also no significant associations between comorbidity of AS and outcomes such as all-cause mortality, incidence of CV events, stroke, and PAD during the follow-up period of 2 years. The death caused by infection and malignant tumor accounted for more than 50 % of total all-cause death. It indicates that physical condition and tumor-bearing affect the mortality stronger than AS in a short term. We continue annual follow up and evaluate the impact of AS itself and vascular calcification causing AS after a long term like 5 years.

P1523

TREATMENT OF ADVANCED NON-SMALL CELL LUNG CANCER IN DIALYSIS PATIENTS; FINDINGS FROM OSAKA CANCER REGISTRY DATA

NANAMI KIDA[1,2,3], Yoshiharu Tsubakihara[4], Toshitaka Morishima[1], Ryo Sato[1], Isao Miyashiro[1]

[1]Osaka International Cancer Institute, Cancer Control Center, Osaka, Japan, [2] Osaka University Graduate School of Medicine and Health Science, Health Economics and Management, Suita, Japan, [3]Osaka College of High Technology, Clinical Engineering, Osaka, Japan and [4] Graduate School of Health Care Sciences, Jikei Institute, Safety Management in Health Care Sciences, Osaka, Japan

Background and Aims: Recent advances in dialysis technic for end-stage renal disease have resulted in a longer survival. Consequently, they have an increased risk of suffering from various neoplastic diseases. The survival outcome and treatment rate in non-small cell lung cancer(NSCLC) patients on dialysis has not been well evaluated. In patients with unresectable stage disease, chemotherapy may best be started soon after the diagnosis of unresectable NSCLC has been made. The aim of this study was to investigate the practice pattern and survival rate in advanced NSCLC patients on dialysis.

Method: This retrospective study used population-based cancer registry data from Osaka Prefecture, Japan and administrative claims data produced under the Diagnosis Procedure Combination reimbursement system. We performed record linkage between these datasets to obtain patient-level information on dialysis, cancer diagnoses, treatment, and vital statuses. Patients who were diagnosed with advanced NSCLC between 2010 and 2015 and were at the age of 80 years or younger. We calculated the performance proportions of chemotherapy (including molecular-targeted drugs) in dialysis patients and non-dialysis chemotherapy. In addition, we computed one-year survival rate of patients in dialysis patients who underwent chemotherapy and who did not undergo.

Results: We identified 42 dialysis patients with a median age of 71 years and 18,425 non-dialysis patients with a median age of 70 years who were diagnosed with advanced NSCLC. Dialysis patients (n=11, 26.2 %) were less likely to receive chemotherapy when compared with non-dialysis patients (n=12247, 66.3%). Among dialysis patients, there was no significant difference in 1-year survival rate between the receipt (40.0%) and the non-receipt (29.6%) of chemotherapy (Log-rank test, p=0.41).

Conclusion: Dialysis patients might receive suboptimal treatment for advanced NSCLC. Further studies are needed to assess whether chemotherapy improves survival outcomes in dialysis patients with advanced NSCLC.

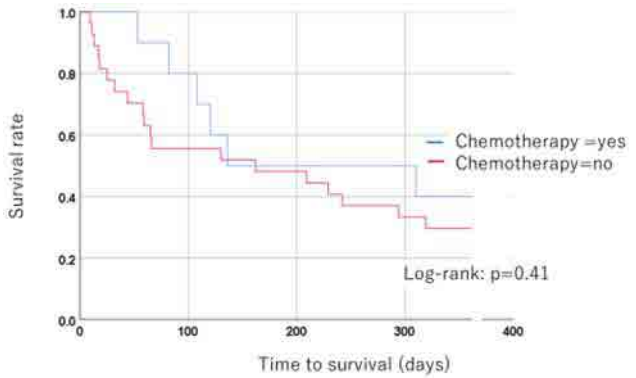


Fig1 Kaplan-Meier survival curves in dialysis patients who underwent or did not undergo chemotherapy for lung cancer.

Figure:

P1524 **ABSOLUTE BLOOD VOLUME AND VASCULAR REFILLING IN HAEMODIALYSIS PATIENTS**

Marta Álvarez Nadal[1], Elizabeth Viera Ramírez[1], Irene Martin[1], Gloria Ruíz-Roso López[1], María Delgado Yagüe[1], Milagros Fernandez Lucas[1]

[1]*Hospital Ramón y Cajal, Nephrology, Madrid, Spain*

Background and Aims: The imbalance between UF and refilling rate is considered a major cause for intradialytic hypotension. Recent studies report a feasable and noninvasive method to estimate vascular refilling by determining absolute blood volume. It was the aim of this study to analyze absolute blood volume in a group of haemodialysis patients and to examine vascular refilling volume.

Method: Thirty stable chronic HD patients were studied (36,7% female, 63,3% male), aged 71,07 ± 13,31 years. Dialysis duration and UF requirements were based on physician prescription. Vascular refilling was calculated as: $V_{REF} = V_{UF} - \Delta V$, where ΔV is the difference between absolute blood volume at the beginning and the end of dialysis. Relative blood volume monitor (BVM) was used. *Hemodial Int. 2016;20(3):484–91.*

Results: Absolute blood volume at the beginning of the dialysis was 6,27 ± 2,78 L (92,44 ± 32,66 ml/kg) and at the end 5,83 ± 2,77 L (85,94 ± 30,44 ml/kg). Ultrafiltration (UF) volume was 2,64 ± 0,82 L (11,14 ± 4,02 ml/kg/h). Vascular refilling was calculated as 2,24 ± 0,74 L, with a refilling fraction of 85,33 ± 11,07%. We found a strong correlation between refilling volume and UF volume (r^2 0,861) (Figure 1), and a mild correlation between refilling volume and predialysis volume overload (r^2 0,529).

Conclusion: Measurement of absolute blood volume is easy and noninvasive, and it allows us to study refilling volume. We found a strong correlation between UF volume and refilling volume.

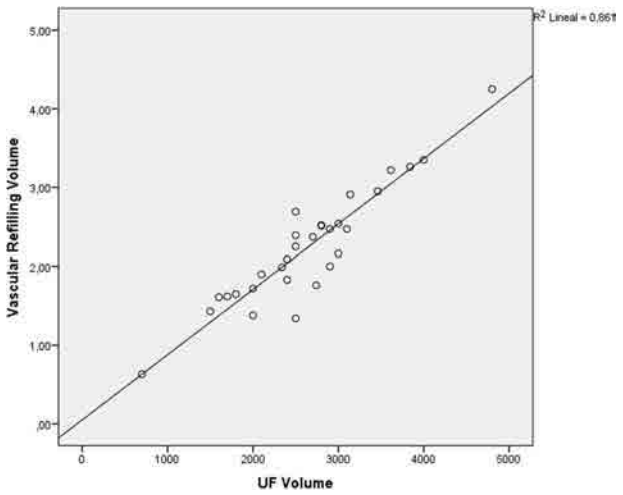


Figure 1:

P1525

90 DAY MORTALITY DATA OF PATIENTS INITIATING MAINTENANCE HEMODIALYSIS AT A TERTIARY CARE FACILITY IN PAKISTAN

Sonia Asif[1], Mohammad Saleem[1], Ahad Qayyum[1]

[1]*Bahria Town International Hospital, Renal Unit, Lahore, Pakistan*

Background and Aims: Mortality of end stage renal disease patients is 10 to 30 times higher than that of the general population. Timing of death related to dialysis vintage remains unclear. Mortality risk among hemodialysis patients may be highest soon after initiation of hemodialysis, the reason for which remains elusive. Additionally mortality on initiating hemodialysis is related to arteriovenous vascular access.

Poor planning for dialysis initiation may contribute to hemodialysis catheter use and the associated high rate of infections. This study was carried out to determine the 90-day mortality in patients starting maintenance hemodialysis at a tertiary care facility in Pakistan.

Method: This is a cross sectional study which included all consecutive patients who initiated maintenance hemodialysis at Bahria Town Hospital Lahore. A total of 485 participants were included and the collected data was entered into the SPSS software and their mortality rate was calculated within 90 days after initiation of maintenance hemodialysis. Additionally 90-day mortality based on type of vascular access at initiation was also noted.

Results: The mean age of the participants included in the study was 44 with 50% of the patients were male. The 90-day mortality of patients initiating maintenance hemodialysis at our centre was found to be 37%. 90% of the patients initiating maintenance hemodialysis started through a double lumen temporary dialysis catheter. Amongst these patients the mortality rate was 39%. 10% of the patients initiating maintenance hemodialysis started through an arteriovenous fistula. Amongst these the mortality rate was 19%.

Conclusion: Our study showed that the mortality rate is high in patients undergoing hemodialysis with in first 90 days. Early planning for permanent vascular access may result in a reduction of mortality.

P1526 HOW TO DEAL WITH PREGNANCY IN DIALYSIS? A CENTER EXPERIENCE ABOUT 7 CASES

Ramia BENHAMOU[1], Meriem Chettati[1], Wafaa Fadili[1], Inass Laouad[1]

[1]*Mohammed VI University Hospital Center of Marrakesh, Cadi Ayyad University, Nephrology, Marrakesh, Morocco*

Background and Aims: Outcomes of pregnancy in patients with end-stage renal disease (ESRD) have long been considered to be extremely poor, and the literature concerning pregnancy while on dialysis is rather meagre. We reported our center experience about pregnancy management in patients on hemodialysis: how to deal with hypertension, ultrafiltration rate, dose dialysis in order to improve maternal and fetal outcome.

Method: We reported pregnancy outcomes of 7 pregnancies in the Tensift Region Pregnancy registry between March 2015 and March. 2019 The primary outcome was the live birth rate and secondary outcomes included gestational age and birth weight.

Results: We reported 7 pregnant women cases on hemodialysis. Mean age of our patients was 29,5 ±6,57 years. It was the first pregnancy for 3 patients (42,9%). In about half of patients dialysis was initiated during their pregnancy. The mean duration of pregnancy was 35±1,2 weeks and mean fetal weight was 1,950 ±0,353 kg. All patients were dialyzed over 20 hours per week. The mean urea value was 0,46 ±0,04g/L. Two patients needed anti hypertensive drugs (33,3%) mainly nicardipine. The live birth rate of our cohort (71,4%), all vaginal delivery, was significantly higher than the rate in the American cohort (61.4%). In your series we reported one fetal death at 28 SA explained by tocolysis failure for preterm labor. At 9 months all children had good cognitive and psychomotor involvement.

Conclusion: We conclude that pregnancy may be safe and feasible in women with ESRD receiving intensive hemodialysis. A multidisciplinary medical care with obstetricians is highly recommended. Despite a trend of increasing live birth rate over recent decades, pregnancies on dialysis high risk, with increased rates of adverse of adverse pregnancy outcomes including pregnancy loss.

P1527 **SURVIVAL COMPARISON:HEMODIALYSIS VS PERITONEAL DIALYSIS: TEN YEARS OBSERVATIONAL STUDY.**

Vincenzo Terlizzi[1], Bernardo Lucca[2], Chiara Manenti[2], Paola Gaggia[2], Roberto Zubani[1,2], Alessandra Pola[2], Valerio Vizzardi[2], Massimo Sandrini[2], Ezio Movilli[2], Francesco Scolari[1,2]

[1]Università degli Studi di Brescia - Facoltà di Medicina e Chirurgia - and [2]U.O. Nefrologia - ASST Spedali Civili di Brescia

Background and Aims: Survival comparison between peritoneal dialysis (PD) and hemodialysis (HD) is still controversial. While some retrospective studies have shown better survival in PD, particularly in the first year, others have not identified this difference. The only RCT published so far showed a 3-year mortality rate similar between two groups. However, the number of patients was too small to provide sufficient statistical power to identify any survival differences between the two dialysis techniques. Aim of this study was to compare HD and PD in term of survival rate and factors possibly involved in a ten-years observational study.

Method: We retrospectively evaluated all the incident patients that started a dialytic treatment, either HD or PD, due to uremia from 01-01-2008 to 31-12-2018 at the U.O. Nephrology ASST Spedali Civili of Brescia. Exclusion criteria were: duration of dialysis treatment less than 3 months, and previous dialytic treatment or kidney transplantation. For each patient anthropometric, clinical-anamnestic data and comorbidities at dialysis start were recorded.

Results: One thousand and six patients were identified. 130 patients were excluded due to dialysis treatment less than 3 months. A total 876 patients were analyzed. 77% of patients started dialysis on HD while 23% chose PD. Age was significantly higher in HD patients (69±15 vs 65±16 years; p<0.05). No differences were found in the incidence of: ischemic heart disease (HD 24%, PD 25%, p=0.90), diabetes (32% vs 32%, p=0.83), cancer (20% vs 17%, p=0.37), cardiac arrhythmia (20% vs 25%, p=0.08) and peripheral vascular disease (25% vs 25%, p=0.89). An increased incidence of COPD (HD 17% vs PD 8%, p<0.05) and hypertension (73% vs 87%, p<0.05) was present in PD patients. During follow-up, 17% of patients treated with PD shifted to HD due to catheter malfunction, recurrent infections, insufficient dialytic adequacy or ultrafiltration failure. Kidney transplants were performed more frequently in PD patients (HD 12%; PD 24%, p<0.05). At an intention to treat analysis of the data, univariate analysis showed better survival in PD patients (p<0.05, Figure 1). This difference was not confirmed at multivariate analysis (Figure 2), where age, cardiac arrhythmia, cirrhosis, diabetes and peripheral vascular disease were independently associated with an increased risk of mortality. No independent influence on mortality of the dialysis treatment modality was found.

Conclusion: This ten years observational study shows that HD and PD are similar in term of patient survival. Age and comorbidities seem to play the most important role in patient survival.

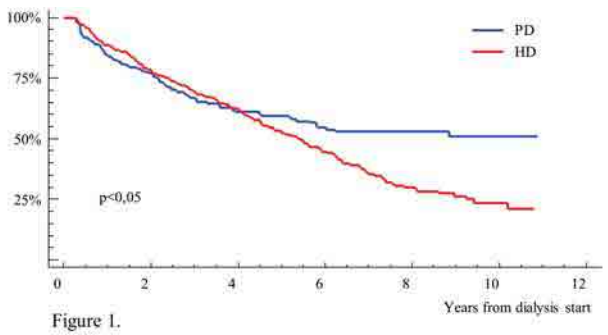


Figure 1.

	HR	Upper limit	Lower limit	p
Age	***1,05***	*1,05*	*1,05*	*<0.05*
Cardiac arrhythmia	***1,49***	*1,27*	*1,75*	*<0.05*
Cirrhosis	***1,61***	*1,31*	*1,97*	*<0.05*
Diabetes mellitus	***1,41***	*1,23*	*1,62*	*<0.05*
Peripheral vasculopathy	***1,33***	*1,14*	*1,54*	*<0.05*

Figure 2.

	HR	Upper limit	Lower limit	p
Age	***1,05***	*1,05*	*1,05*	*<0.05*
Cardiac arrhythmia	***1,49***	*1,27*	*1,75*	*<0.05*
Cirrhosis	***1,61***	*1,31*	*1,97*	*<0.05*
Diabetes mellitus	***1,41***	*1,23*	*1,62*	*<0.05*
Peripheral vasculopathy	***1,33***	*1,14*	*1,54*	*<0.05*

Figure 2.

Figure:

P1528 EPIDEMIOLOGICAL SURVEY OF A POPULATION UNDERGOING URGENT HEMODIALYSIS

Eya Felah[1], Barbouch Samia[2], Hajji Mariem[2], Shedha Ben amor[2], Soumaya Chargui[2], Raja Trabelsi[2], Cyrine Karoui[3], Hafedh Hedri[2], Rym Goucha[2], Mondher Ounissi[2], Fethi Ben Hmida[2], Taieb Ben abdallah[2]

[1]Charles Nicolle Hospital. Tunis, Tunisia., Department of Nephrology and Laboratory of kidney pathology LR00SP01, Tunis, Tunisia, [2]Charles Nicolle Hospital. Tunis, Tunisia., Departement of nephrology and Laboratory of kidney pathology LR00SP01, Tunis, Tunisia and [3] Mahmoud Matri Hospital, Nephrology and dialysis departement, Tunis, Tunisia

Background and Aims: Urgent hemodialysis is a very common situation in nephrology and is burdened with high morbidity and mortality. The aim of this work is to study the epidemiological, etiological, clinico-biological and indications of dialysis emergencies, the parameters of the session and the potential complications.

Method: This is a descriptive study conducted over a period of 12 months (January – December 2017), including all patients who have been admitted to the nephrology department for urgent management in hemodialysis.

Results: Our study collected a total of 318 patients (sex ratio =1.52), the mean age 60.54 ± [18-95 years]. Patients came mainly from the emergency department (69.8%). 40.9 % of the patients were diabetic and 66,4 % hypertensive, 15.1% had coronary artery disease. Among patients, 80.9% had chronic renal insufficiency, of which 29.6% were end-stage (28% hemodialysis and 1.6% peritoneal dialysis). Urgent hemodialysis was undertaken for threatening hyperkalemia in 58.2% of cases, a poorly tolerated uremic syndrome in 50.8% acute pulmonary edema (APO) in 36.5% of cases, and anuria greater than 12h were the indication in 44.4% of cases and a severe metabolic acidosis in 11.3% of cases.

The average duration of the session was 3 hours. Ultrafiltration was necessary in 63.7% of the cases. The blood access was a femoral catheter in 80.6% of the cases. Blood transfusion was indicated in 13.8% of cases. Main complications were dominated by symptomatic arterial hypotension in 12.9% requiring stopping the session in half of cases hypoglycemia in 6.9%, neurological disorder in 6.6% chest pain in 3.5 %. After a year of follow up care, overall mortality was 40% in this population. On multivariate analysis, age (p=0.006) and neurological state according to the glasgow score (p=0.01) were retained as independent factors of mortality in this population.

Conclusion: A greater prevalence of urgent hemodialysis is observed in our country testifying to the accessibility of this method of extrarenal replacement. Hyperkalemia, uremic syndrom and PAO are the main indications for urgent hemodialysis. Early diagnosis, prompt and relevant management of these patients will determine their prognoses in the short and medium term.

P1529 MORTALITY PREDICTORS IN INCIDENT HEMODIALYSIS PATIENTS - HAVE HEY CHANGED IN TEN YEARS?

Cátia Raquel Figueiredo[1], Rachele Escoli[2], Hernâni Gonçalves[2], Karina Lopes[2], Flora Sofia[2], Ana Vila Lobos[2]

[1]Hospital Rainha Santa Isabel - Torres Novas (Centro Hospitalar Médio Tejo, EPE), Nephrology, Torres Novas, Portugal and [2]Hospital Rainha Santa Isabel - Torres Novas (Centro Hospitalar Médio Tejo, EPE), Nephrology, Torres Novas, Portugal

Background and Aims: In the last years there has been an increase in elderly patients with multiple comorbidities inducing hemodialysis (HD). Since dialysis treatment itself may be associated with a further deterioration in functional status, nephrologists are increasingly careful in selecting these patients for HD. Concerned with this reality we tried to understood if early mortality predictors (in the first 6 months) in incident HD patients have changed in almost 10 years, in the same hospital HD unit.

Method: This is a retrospective observational study of incident HD patients between 01 January 2017 and 30 June 2019. We evaluated similar clinical, analytical and demographic data to those used to predict mortality in the same HD unit from 1 January 2010 to 30 September 2014. Logistic regression analysis was used to evaluate 6 month mortality predictors. Statistical analysis was performed using SPSS version 25 for Windows.

Results: The average age of 163 incident HD patients were 70.63±3.9 years (similar to the previous population: n= 235; 70.7 ± 14.9 years) and 57.1% were male. During this study we observed 26 (16%) deaths, 12 of which (46.15%) occurred in the first 6 months of hemodialysis. Pneumonia and cachexia were the major causes of mortality, unlike the previous population, in which majority of deaths were attributed to cardiovascular events. Between January 2010 to 30 September 2014 the strongest predictors of early mortality were dementia [adjusted odds ratio (OR) 15.94 (CI: 4.09–62.10)], central venous catheter use [(OR) 12.29; (CI: 3.54-42.65)], cancer [(OR) 4.64 (CI: 1.48-14.54)] and heart failure [(OR) 3.57 (CI: 1.08-11.75)]. Differently, in this study, the institutionalization and the presence of metastases were the predictors that showed a higher risk of death [p=0.005; adjusted odds ratio [(OR) 10.4 (CI: 2.017–49.9) and p=0.01; (OR): 14.9 (CI: 1.89-42), respectively]. Longer hospitalizations at the time of HD induction [(p=0.044; (OR):1.103; CI: 1.003-1.213)] and albumin values <2.5 mg/dL [(p=0.03; (OR): 3.8 (CI: 1.14-13)] were also strong mortality predictors. which were not previously observed.

Conclusion: Nowadays, nephrologists are less liberal in initiating dialysis to elderly patients with dementia and cardiovascular comorbidities. However, the population is getting older and our recent mortality predictors may reflect the aging of chronic kidney disease patients, who have multiple comorbidities as cachexia, requiring institutionalization and longer hospitalizations. It is increasingly important to evaluate patients prior to dialysis initiation, so our goal is to create an adjusted mortality score in our HD unit to help make the decision about inducing or not HD in our patients.

P1530 **QUALITY OF LIFE AND MORTALITY IN PATIENTS UNDERGOING HEMODIALYSIS**

Gun Woo Kang[1], Seoung Gyu Kim[1], In Hee Lee[1], Ki Sung Ahn[1]
[1]*Catholic University of Daegu School of Medicine, Internal Medicine, Daegu, Korea, Rep. of South*

Background and Aims: The mortality of patients with end-stage renal disease (ESRD) undergoing hemodialysis (HD) is higher than the general population. And it is well known that quality of life (QOL) falls immediately after receiving HD. However, studies on the relationship between reduced QOL and mortality in HD patients were very rare. This study aims to observe the correlation between impaired QOL and mortality in HD patients and to identify risk factors that affect mortality.

Method: The study included 160 patients with ESRD undergoing HD during over 3 months. The QOL was evaluated using WHO Quality of Life-BREF (WHOQOL-BREF). The WHOQOL-BREF instrument comprises 26 items, which measure the following four domains: physical health (domain 1), psychological health (domain 2), social relationships (domain 3), and environment (domain 4). Univariate analysis was used to determine the relationship between comorbidities, sex, age, laboratory findings, and QOL and mortality in HD patients. Multivariate analysis was performed by cox proportional hazard regression. Expected survival at 5 and 10 years was determined by two-sample t-tests.

Results: The mean age was 58.1 years old. 95 patients (59.7%) received HD due to diabetes mellitus. 42 patients (26.4%) had been diagnosed with coronary heart disease. In univariate analysis, age, coronary heart disease, malignancy, comorbidities, and blood calcium level were positively correlated with mortality. In particular, the domain 1 and 2 of WHOQOL-BREF were negatively associated with mortality. The mean scores of domain 1 and 2 was 18.2±5.2 and 15.9±4.5 for survivors and 15.5±5.7 and 13.7±4.9 for deaths. Multivariate analysis identified the age, comorbidity, serum calcium, and domain 1 of WHOQOL-BREF were independent risk factors for mortality (Table 1). Additionally, predicting 5- and 10- year survival, mortality was correlation with older age, higher Charlson Comorbidity Index, lower serum calcium, and lower domain 1 of WHOQOL-BREF (Table 2).

Conclusion: The impaired QOL of patients with ESRD undergoing HD was closely related to mortality. In particular, low QOL in physical health domain significantly increased mortality. Therefore, in order to improve the survival of HD patients, we should be considered about QOL as well as medical problems

Table 1. Multivariate analysis for death using cox proportional hazard regression with forward conditional method as variable selection.

Variable		HR	95% CI	p-value
age	<60	1	-	-
	≥60	2.664	1.172 to 6.054	0.019*
Charlson Comorbidity Index	<4	1	-	-
	≥4	2.366	1.155 to 4.850	0.019*
Calcium	≥8.7	1	-	-
	<8.7	3.566	1.554 to 8.185	0.003*
WHOQOL-BREF domain 1	≥19	1	-	-
	<19	2.696	1.112 to 6.535	0.028*

Table 2. Result of survival rate for 5 and 10 year

Variable		Survival Rate, % (95% CI)		p-value§
		5 year	10 year	
age	<60	0.904(0.858, 0.950)	0.788(0.725, 0.851)	<0.001*
	≥60	0.785(0.721, 0.849)	0.425(0.348, 0.502)	
Charlson Comorbidity Index	<4	0.901(0.855, 0.947)	0.764(0.698, 0.830)	0.019*
	≥4	0.747(0.680, 0.814)	0.375(0.300, 0.450)	
Calcium	≥8.7	0.912(0.868, 0.956)	0.776(0.711, 0.841)	0.001*
	<8.7	0.796(0.734, 0.858)	0.360(0.286, 0.434)	
WHOQOL-BREF domain 1	≥19	0.922(0.880, 0.964)	0.844(0.788, 0.900)	0.022*
	<19	0.792(0.729, 0.855)	0.482(0.405, 0.559)	

P1531 DIURETIC USE IN HEMODIALYSIS PATIENTS: BENEFIC ASSOCIATION WITH RESIDUAL RENAL FUNCTION AND ALL-CAUSE MORTALITY

Maria do Sameiro Faria[1,2], Maria João Valente[1], Susana Rocha[3], Susana Coimbra[1,4], Cristina Catarino[1], Petronila Rocha-Pereira[1,5], Elsa Bronze-da-Rocha[1], José Gerardo Oliveira[6,7], José Madureira[8], João Carlos Fernandes[9], Vasco M.P. Miranda[10], Luís Belo[1], Alice Santos-Silva[1]

[1]UCIBIO, REQUIMTE, Laboratory of Biochemistry, Department of Biological Sciences, Porto, Portugal, [2]Hemodialysis Clinic of Felgueiras, Felgueiras, Portugal, [3]LAQV, REQUIMTE, Laboratory of Applied Chemistry, Department of Chemical Sciences, Porto, Portugal, [4]CESPU, Institute of Research and Advanced Training in Health Sciences and Technologies (IINFACTS), Gandra PRD, Portugal, [5]Health Science Research Centre, University of Beira Interior, Covilhã, Portugal, [6]Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal, [7]Hemodialysis Clinic of Porto, Porto, Portugal, [8]NefroServe, Hemodialysis Clinic of Barcelos, Barcelos, Portugal, [9]NefroServe, Hemodialysis Clinic of Viana do Castelo, Viana do Castelo, Portugal and [10]Hemodialysis Clinic of Gondomar, Gondomar, Portugal

Background and Aims: In patients with end-stage renal disease (ESRD) on hemodialysis, the preservation of residual kidney function may result in a diversity of benefits in terms of survival and quality of life. The control of fluid and electrolyte homeostasis may play an important role in this setting. Elevated predialysis serum potassium is a common electrolyte disturbance that may worsen patient's outcomes. Our aim was to study the impact of furosemide therapy in predialysis serum potassium levels, indicators of estimated residual renal function, and inflammatory markers, in ESRD patients under hemodialysis; moreover, we aimed to study the impact of furosemide-associated changes on mortality rate.

Method: A cross-sectional study was carried out on 289 adult patients on chronic dialysis therapy (hemodiafiltration and high flux hemodialysis). Patients were divided in 2 groups: the diuretic group (DG, n=116; 120.0 (IQR: 80-160) mg/daily median furosemide dose) and the non-diuretic group (NDG, n = 173), in which patients did not use furosemide. A large set of data was analyzed, encompassing hematological data, serum electrolyte parameters, inflammatory markers, dialysis adequacy, and biomarkers of residual kidney function. A 2-year follow up study was also performed by registering events of death (all-cause mortality).

Results: The DG patients, compared with NDG patients, presented: significantly lower predialysis serum potassium; more favorable blood biomarkers of kidney function - lower β-trace protein, cystatin C, creatinine and urea; greater residual glomerular filtration rate derived from equations with cystatin C, creatinine and creatinine–cystatin C; lower inflammation (significantly lower levels of high-sensitivity C-reactive protein); intradialytic ultrafiltration volume (L) was similar for the two groups. Mortality was significantly lower for DG patients, compared with NDG (13.6% versus 24.7%; P=0.029).

Conclusion: In ESRD patients under chronic dialysis, we found a significant association between current diuretic therapy and lower predialysis serum potassium levels, more favorable biomarkers of kidney function and a decreased inflammatory response that seem to contribute to a higher survival rate.

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P1532

PARATHYROID HORMONE SERUM LEVELS AND MORTALITY AMONG HEMODIALYSIS PATIENTS IN THE GULF COOPERATION COUNCIL COUNTRIES: RESULTS FROM THE DOPPS (2012-2018)

Issa Al Salmi[1], Brian Bieber[2], Mona AlRukhaimi[3], Ali AlSahow[4], Faissal Shaheen[5], Saeed M. G. Al-Ghamdi[6], Jamal Al Wakeel[6], Fadwa Al Ali[7], Ali Al Arriadi[8], Fayez Hejaili[9], Yacoub Al Maimani[1], Essam Fouly[10], Bruce Robinson[2], Ronald Pisoni[2]

[1]Royal Hospital, Muscat, Oman, [2]Arbor Research Collaborative for Health, Ann Arbor, United States of America, [3]Dubai Medical College, Dubai, United Arab Emirates, [4]Jahra Hospital, Al Jahra, Kuwait, [5]Dr. Soliman Fakeeh Hospital, Jeddah, Saudi Arabia, [6]King Abdulaziz University, Jeddah, Saudi Arabia, [7]Hamad General Hospital, Doha, Qatar, [8]Salmaniya Medical Complex, Manama, Bahrain, [9]King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia and [10]Amgen UAE, Dubai, United Arab Emirates

Background and Aims: The prospective Dialysis Outcomes and Practice Patterns Study (DOPPS) has collected data since 2012 in all six Gulf cooperation council (GCC) countries (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates). Here, we report the relationship of PTH with mortality in this largest GCC hemodialysis patient cohort studied to date.

Method: Data were from randomly-selected national samples of hemodialysis facilities in GCC DOPPS phases 5 and 6 (2012-2018). PTH descriptive findings and case-mix adjusted PTH/mortality Cox regression analyses were based on 1825 and 1422 randomly-selected hemodialysis patients, respectively.

Results: Mean patient age was 55 years (median dialysis vintage = 2.1 years). Median PTH ranged from 259 pg/mL (UAE) to 437 pg/mL (Kuwait), with 22% having PTH <150 pg/mL, 24% (PTH 150-300), 34% (PTH 301-700), and 20% (PTH >700) pg/mL. Patients with PTH >700 pg/mL were younger, on dialysis longer, less likely to be diabetic, have urine>200 mL/day, prescribed 3.5 mEq/L dialysate calcium, had higher mean serum creatinine and phosphorus levels, lower white blood cell counts, and more likely to be prescribed cinacalcet, phosphate binders, or IV vitamin D. A "U-shaped" PTH/mortality relationship was observed with >2-fold and 1.5 fold higher adjusted HR of death at PTH>700 pg/mL and <300 pg/mL, respectively, compared to PTH 301-450 pg/mL.

Conclusion: Secondary hyperparathyroidism is highly prevalent among GCC hemodialysis patients, with a strong U-shaped PTH/mortality relationship seen at PTH <300 and >450 pg/mL. Future studies are encouraged for further understanding this PTH/mortality pattern in relationship to unique aspects of the GCC hemodialysis population.

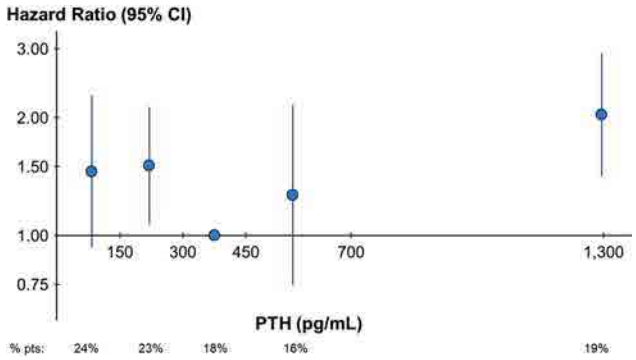


Figure: PTH categories and mortality, GCC DOPPS (2012-2018)

Footnote: N=1,422 patients and n=222 deaths; adjusted for age, sex, vintage, body mass index, comorbidities (diabetes, coronary artery disease, cerebrovascular disease, congestive heart failure, other cardiovascular disease), serum creatinine, and single pool Kt/V; stratified by GCC region; placement of estimates along the x-axis determined by mean PTH in each group (< 150, 150-300, 301-450, 451-700, > 700). Categories chosen to yield approximate similar sample sizes across categories. The PTH of 301-450 pg/mL category served as the reference group.

P1533 **SURVIVAL ANALYSIS OH HAEMODIALYSIS PATIENTS: IMPACTO OF UREMIC TOXINS**

Mari Sargsyan[1], Juan Robles[2], Sheila Cabello Pelegrin[1], Juana Maria Ferrer Balaguer[3], Juan Rey Valeriano[1], Sonia Cleofe Jimenez Mendoza[1], Cristina Egea Sancho[1], Tania Villagrasa Villagrasa[1], MIGUEL URIOL[1], Gonzalo Gomez Marques[1], Bernardino Barcelo Martin[2], Joan Manuel Gasco Company[1]

[1]Hospital Universitario Son Espases, Nephrology, Palma de Mallorca, Spain, [2]Hospital Universitario Son Espases, Clinical Analysis, Palma de Mallorca, Spain and [3]Hospital Universitario Son Espases, Inmunology, Palma de Mallorca, Spain

Background and Aims: HEMO study showed that β_2M level over time was predictive of all-cause mortality in haemodialysis patients (HD). Later studies suggested that protein-bound uremic toxins are associated with mortality in HD patients but with recent contrasting results.

Aim of study was to analyse β_2M and indoxyl sulfate (IS) as predictor factors of mortality.

Method: 5 years follow-up of 60 prevalent HD patients of our hospital. Demographic data was described. Baseline midweek pre-dialysis serum β_2M was determined by nephelometry and total IS levels by high performance liquid chromatograph connected to a UV detector. We considered high serum β_2M group as if was equal or higher than 27,5 mg/L. As to IS, patients were divided into quartiles (1q <9,7 mg/L, 2-3q ≥9.7-26.5mg/L, 4q>26.5 mg/L).

Survival curves were assessed using the Kaplan–Meier analysis at 1,2,3 and 5 years in univariate analysis for albumin (≥38 g/L or lower), β2M, and total IS groups, and evaluated by the proportional hazards Cox's model. *P* -values <0.05 were considered statistically significant.

Results: 60 prevalent patients with mean vintage of 46,8 months (range 3-299 months). Mean age was 60±20 years. Males were more prevalent (53,3% vs 46,6%). 35% had diabetes. 51,6% underwent conventional hemodialysis (HD), 48,3% post-dilution haemodiafiltration, with mean convective volume of 23,8±2,8L. Mean eKt/V was 1,67±0,4, mean nPCR was 1±0,27g/kg/day. Only 8,3% of patients had urine volume>500cc/24hours. Mean β_2M level was 35,6±1,9mg/L (X±SE) and mean total IS level was 18,9±1,6mg/L.

The overall mortality at 5 years was 57%. Albuminemia lower than 38g/L was associated with mortality at 2, 3, and 5-years in univariate analysis (Cox's F test p=0.03, figure 1). We found no difference in survival rate between patients with high or low serum β_2M levels at 3- or 5-years analysis (Cox's F test p=0.27). At 2 years analysis, patients in the lower β_2M group had better survival (Cox's F test p=0.04, Figure 1). There was no statistically significant association between albumin, β_2M, IS level and all-cause mortality on Cox regression multivariate analysis. We observe no statistically significant association between IS levels and all-cause mortality neither on univariate, nor on multivariate analysis.

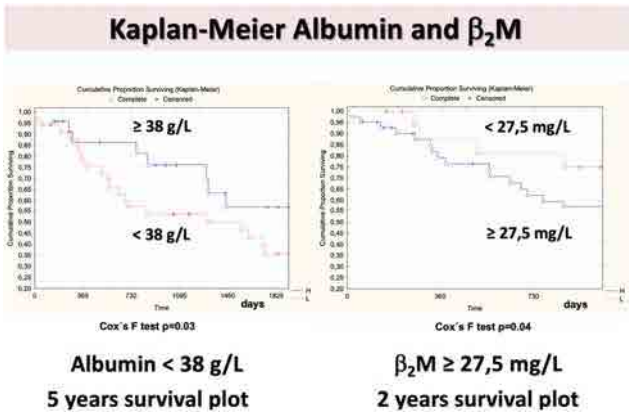


Figure 1: Conclusion: β_2M < 27,5 mg/l was associated with better survival at 2 years univariate analysis. IS had no statistically significant association with all-cause mortality in our cohort.

P1534 EFFECT OF HIGH-FLUX DIALYZER MEMBRANE SURFACE AREA ON SURVIVAL IN CHRONIC HEMODIALYSIS PATIENTS

Kazuya Takasawa[1], Chikako Takaeda[2], Yuta Yamamura[2], Tomoaki Hunamoto[2], Norishi Ueda[3]

[1]Public Tsurugi Hospital, Department of Nephrology, Hakusan, Japan, [2]Public Central Hospital of Matto Ishikawa, Renal Division, Hakusan, Japan and [3]Public Central Hospital of Matto Ishikawa, Department of Pediatrics, Hakusan, Japan

Background and Aims: High-flux dialyzer membrane material has been shown to improve mortality in hemodialysis (HD) patients. However, little is known about the impact of surface area of dialyzer membrane on prognosis in HD patients. A retrospective analysis was undertaken to investigate whether the difference in high-flux dialyzer membrane area affects survival rate.

Method: We observed 119 patients (43 females, mean age; 68 years, and HD duration; mean 84.4 months) maintained on HD for up to 5 years and 7 months. All patients were divided into two groups according to the surface area of dialyzer membranes; S group, 39 patients treated with the dialyzer membrane area of $<1.5m^2$ (mean 1.0 ± 0.1 m^2) and L group, 80 patients treated with that of $\geq1.5m^2$ (mean 2.0 ± 0.2 m^2). We analysed survival rate by Kaplan-Meier method.

Results: The patients were treated with four types of high-flux dialyzer membranes. S group included 21 patients with cellulose triacetate (CTA), 17 patients with polysulfone (PS) and 1 patient with polymethylmethacrylate. L group included 2 patients with CTA, 71 patients with PS and 7 patients with polyethersulfone (PES). Thirty-two patients, including 12 patients in S group and 20 patients in L group, had diabetes mellitus (DM). Survival rate was compared between the two groups, patients treated with CTA, PS and PES, and those with and without DM by Kaplan-Meier method. Type of dialyzer membranes used did not affect survival rate at the final observation (65.2% in CTA, 75% in PES and 50% in PS, p=0.26). The surface area of dialyzer membrane did not have a significant impact on mortality; survival rate at 3-year for S group, 71% vs L group, 77%, at 5-year for S group, 51% vs L group, 59%, and at the final observation for S group, 48%, vs L group, 58% (p=0.352). Among 32 diabetic patients, survival rate at the final observation did not differ between the two groups (S group, 33%, vs L groups, 45%, p=0.477). Among 87 non-diabetic patients (S groups; 27 patients), survival rate did not differ between the two groups at the final observation (S group, 56%, vs L group, 63%, p=0.575).

Conclusion: We conclude that difference in high-flux dialyzer membrane area is unlikely to affect survival rate in HD patients.

P1535 ANXIETY AND DEPRESSIVE DISORDERS IN HEMODIALYSIS PATIENTS

Emna Chaabouni[1], Hela Jbali[1], Mami Ikram[1], Chermiti Mohamed[2], El Kateb Hanene[3], Rais Lamia[1], Zouaghi Karim[1]

[1]La Rabta, Nephrology, tunis, Tunisia, [2]kef Hospital, Nephrology el Kef, kef, Tunisia and [3]Mannouba, hemodialysis, Mannouba, Tunisia

Background and Aims:

Dialysis impacts the patients' quality of life drastically, increasing the risk of mortality. Depression and anxiety are commonly reported among dialysis patients.

But little is known about their prevalence.

The aim of this study is to examine the prevalence of anxiety and depression and associated factors among patients receiving hemodialysis

Method:

A cross-sectional study was carried out among 94 hemodialysis patients treated at four hemodialysis center in a mediterranean country during a period of two months . The patients were interviewed while undergoing their dialysis session using the Hospital Anxiety and Depression Scale (HAD). The score of HAD was correlated with demographic and clinical variables.

Results:

Based on Hospital Anxiety and Depression Scale, 49 patients (52%) had symptoms of depression, 41 patients (43%) had mild symptoms of anxiety, whereas moderate or severe symptoms of anxiety were present in 30 patients (32%).

In univariate analysis, HAD score for symptoms of depression correlated significantly with age (p=0,012) and past medical history of hypertension (p=0,024). Anxiety correlated significantly with female gender (p=0,039), smoking (p=0,017) and coffee addiction (p=0,024).

Conclusion:

These results underline the important prevalence of anxiety and depression in hemodialysis patients .

Strategic options are necessary to improve the diagnosis of anxiety and depressive disorders, potentially enhancing quality of life and medical outcome in hemodialysis patients.

P1536 **EVOLUTION OF A COHORT OF PATIENTS UNDERGOING HOME ONLINE HEMODIAFILTRATION DURING A THREE YEAR FOLLOW UP PERIOD**

Ana Garcia-Prieto[1], Almudena Vega[1], Soraya Abad Esttebanez[1], Diego Barbieri[1], ANDRÉS FELIPE DELGADO[1], Marian Goicoechea[1]

[1]*HOSPITAL GENERAL UNIVERSITARIO GREGORIO MARAÑON, NEPHROLOGY, MADRID, Spain*

Background and Aims: Online haemodiafiltration (OL- HDF) is the gold standard therapy in hemodialysis, as it has shown to reduce all-cause mortality in hemodialysis patients. Frequent hemodialysis has also shown to improve survival and quality of life. Home hemodialysis facilitates frequent therapy, and it is possible to perform OL-HDF at home, althought there is lack of evidence on its use. We report the evolution of a cohort of patients undergoing home OL-HDF during a 3 year follow up period.

Method: We designed a prospective, descriptive study to determine the evolution of prevalent and incident patients in home OL-HDF since 2016. Demographic and clinical variables were collected, including those related to hemodialysis technic and its potential complications.

Results: Three patients with a mean age of 47 years underwent home OL-HDF during follow up. All patients were males and caregiver was the couple in all cases. Two patients had an arteriovenous fistula (AVF) and one had a catheter. After a mean training period of 2.5 months at hospital, they started home OL- HDF with the assitance of a nephrologist, a nurse and a technician in the first session at home. We used the "5008-home"®FMC monitor and the AquaC®FMC for water treatment. Water cultures allways fulfilled the criteria for ultrapurity. Dialysis scheme was 2 hour sessions daily, 6 days a week.

During a mean follow up of 15 months, one patient received a kidney transplant. None needed hospitalization. One patient attended the emergency room once for fluid overload and needed ultrafiltration. The patient with catheter needed a catheter replacement due to hole infection. No vascular access problems were recorded in patients with AVF. Regarding dialysis efficacy, mean week KtV was over 2.1 in all cases and mean convective volumen achieved was 94 l/week.

Conclusion: In our experience, home OL-HDF is a safe and effective technic.

P1537 **HEMODIALYSIS EMERENGIES IN A NEPHROLOGY DEPARTEMENT : ABOUT 117 CASES**

Chifaa Triqui[1]
[1]Hospital Charles Nicolle, nephrology department, Tunis, Tunisia

Background and Aims:

Hemodialysis (HD) emergencies in nephrology are very common. Prompt diagnosis and management are needed as it can be life-threatening. We aim to determine epidemiological, clinical, biological aspects as well as the etiological profile of our population.

Method:

We conducted a cross-sectional study during 3 months (February, March and April 2019) collecting patients who underwent at least one session of HD at our nephrology department. Were included patients aged over 18 years old. Were excluded chronic dialysis patients presenting for their usual session. Data collection was conducted from HD registers. We collected the following parameters: age, gender, comorbidities, initial nephropathy, clinical data(blood pressure, pulmonary auscultation, diuresis, oxygen saturation),the current treatment and biological data(creatinin, kalemia, hemoglobin, and gasometry).

Data were entered and analyzed using SPSS software. Chi-squared test with a level of significance of 0.05 was used for the qualitative variables.

Results:

A total of 117 patients were included, mean aged 60.71 years old (range:28-90) with a sex ratio M/F at 1.3. Our population consists in 42 chronic HD patients(37.9%), 34 Patients with moderate to severe renal failure(RF) (29.9%) and 41 patients with acute kidney injury (AKI) (35%). Initial nephropathy causes were vascular in (40%), glomerular in(25%) and undetermined in(35%) of cases. Our patients had hypertension, diabetes, dyslipidemia in respectively (58%),(45%) and (7.6%). Twenty two chronic HD patients were anuric (48.8%). Seventy-nine patients were admitted from the emergency department(68%), 21 patients from the surgical and urology departments(18.4%),8 patients from the intensive care unit (7.6%) and 4 patients from other departments(4.2%). HD indications were acute pulmonary edema in (41.8%), metabolic acidosis in (41.8%), hyperkalemia in (37.6%), Uremic signs in (22.2%). Inadequate hyperkalaemic treatment was noted in(22.7%)of cases. Conventional HD was performed with mean session duration of 3 hours.

Ultrafiltration was required in 46 cases (36.8%) with an average of 1860ml(range:500-4000).

Perdialytic complications were observed in(12.5%)of cases. Hypotension was the most common complication which leads to the interruption of the session in(5.9%)of cases. Disequilibrium syndrome was observed in 2 patients. Arrhythmia and acute cardiac failure were noted in 2 patients. Death occurred in 1 case caused by arrhythmia.

Advanced age, anuria and underlying RF were independent risk factors of emergency dialysis with respectively (p=0.02, p=0.01 and p=0.05).

Conclusion:

Dialysis emergencies remain frequent in our country. Acute Pulmonary edema and metabolic acidosis were the main indications followed by hyperkalemia and anuria. Poor and delayed chronic renal failure management could explain the frequent use of emergency HD. The analysis of the causes and dialysis modalities in emergency situations, contributes to adopt a preventive strategy in order to identify high-risk patients and to optimize treatment protocols.

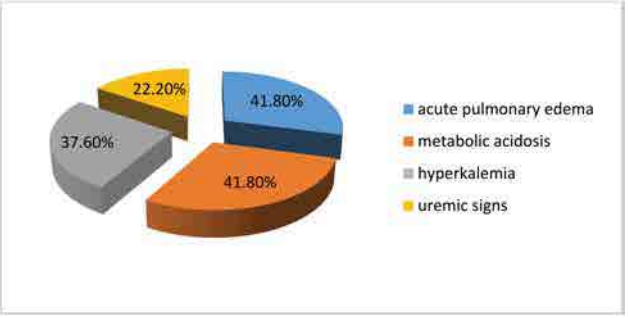


Figure 1: HD indications

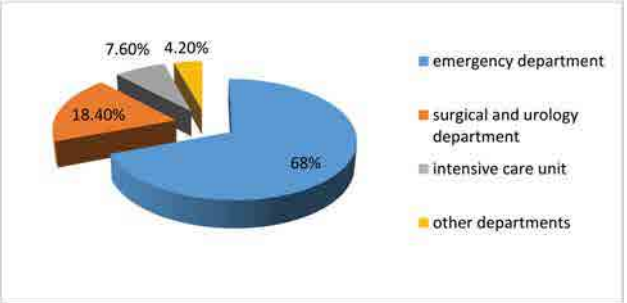


Figure 2 : Departments of patients admitted for HD

P1538 **AN EXPERIENCE OF FORCED SHUTDOWN OF HEMODIALYSIS UNIT IN SOUTHERN INDIA DUE TO FLOODS.**

Mohammed Shoeb Ahmed Khan[1], Ummer Saidali[1], Bipi Prasannan[1], Vinod Kumar K[1], Vishnu Urs[1], V. Narayanan Unni[1]

[1]*Aster Medcity, Nephrology, Kochi, India*

Background and Aims: The southern state of India, Kerala was hit by the worst flood in the last century on 16.08.18, due to unprecedented monsoon rains. The Indian government had declared it a Level 3 Calamity. According to the Kerala government, over 483 people died, about a million people were evacuated. This paper describes the experience of the Hemodialysis (HD) unit at Aster Medcity, which was forcibly closed due to floods. The Nephrology department does over 1100 dialysis treatments per month and about 60 kidney transplants per year.

Aim: To study unexpected shutdown of hemodialysis unit and its effect on maintenance hemodialysis patients.

Method: This is a descriptive study of forced closure of HD unit due to floods. The sequence of events till shut down after the decision of closure has been retrospectively studied by reviewing the minutes of meetings with chief of medical services and memory recall of the Nephrology team involved in the process. Role of HD nurses during the period of flood was also studied. HD patients were interviewed and impact of floods on them was recorded, including, ability to find an alternate HD unit, any missed HD sessions, access to medicines and admissions in hospital. The characteristics of HD patients was recorded. After reopening of our HD unit, 30days assessment was done for clinical consequences including, hospitalization, infections, vascular access problems and seroconversion.

Results: The services of HD unit were suspended from midnight 17.08.18 to 27.08.18. The HD unit is at the ground floor of the hospital. The HD unit has 13 HD machines, which were used for 77 maintenance HD patients (Males: 55; Females: 22). The mean age was 61 ±14 years and the median dialysis vintage was 2 years. Vascular access was a catheter (tunnelled and non-tunnelled) in 19 patients, arterio-venous fistula in 57 patients and arterio-venous graft in 1 patient. Patients known to have Diabetes were 77.7%, Hypertension 91%, Coronary artery disease were 26 in number and chronic liver disease were 5. Hospital authorities decided to evacuate the hospital 24 hours before the floods hit the hospital premises. The Nephrology team comprised of 4 consultants, 6 residents, 33 dialysis nurses and technicians and a social worker. The HD unit was closed after draining the reverse osmosis (RO) plant at 10pm on 16.08.18. The lead consultant contacted potentially safe HD units in other parts of the state; willingness for accepting HD patients and the surge capacity of each HD unit was recorded. The HD patients were informed over telephone the centers they can approach and HD summary (includes diagnosis and HD details) was sent to them via e-mail. All HD patients were reminded to comply with diet restrictions and inform the shelter camp regarding the same. Accordingly, 77 HD patients were accommodated in 25 HD units. 12 dialysis nurses provided their services voluntarily at other HD units unaffected by floods. 15 HD patients were displaced from their homes due to floods. 19 HD patients missed one HD session; 5 HD patients missed two HD sessions; 1 patient missed three HD sessions. Our HD unit reopened on 27.08.18 after complete disinfection of the RO plant and servicing of HD machines by the manufacturer. All patients returned to our HD unit. In the first 30 days after floods, 3 patients were admitted to intensive care unit with fluid overload, 3 patients were admitted with respiratory tract infection, 2 patients had an AV fistula dysfunction, 3 patients developed catheter related blood stream infection. There was no seroconversion. There was no mortality in HD patients during and one month after flood.

Conclusion: The timely decision to suspend dialysis services played a crucial role in preparing for HD unit closure, arranging alternate HD places for patients and providing treatment summaries. However, the increase in adverse clinical consequences heralds the drop in the quality of healthcare services during natural disasters.

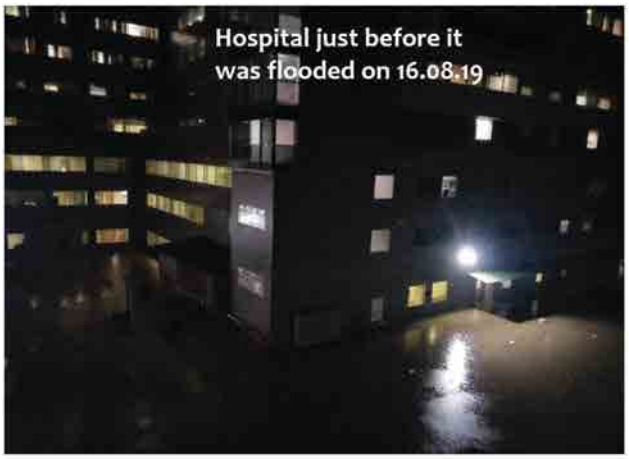




Figure:

P1539

THE INFLUENCE OF DIFFERENT HEMODIALYSIS FREQUENCY ON MHD PATIENTS WAS ANALYZED BASED ON THE DATA OF THREE CONSECUTIVE YEARS

Hua Liu[1], Quan He[2], Limin Wei[3], Kehui Shi[3], Meng Wang[3], Jinhong Xue[3], Lei Chen[3], Lingshuang Sun[3], Meng Wei[3], Hongli Jiang[3]

[1]the first affiliated hospital of Xi'an Jiaotong University, the blood purification, Xi'an, P.R. China, [2]the first affiliated hospital of Xi'an Jiaotong University, the blood purification, Xi'an, and [3]the first affiliated hospital of Xi'an Jiaotong University, the blood purification, Xi'an, P.R. China

Background and Aims: By analyzing the follow-up data of patients on maintenance hemodialysis (MHD) in the department of blood purification of the first affiliated hospital of Xi'an Jiaotong university from 2016 to 2018, the effects of different dialysis frequency on patients were compared and the continuous improvement of clinical quality was promoted.

Method: The general data of MHD patients in our center from 2016 to 2018 and annual laboratory monitoring indicators [including hemoglobin (HGB), calcium (Ca), phosphorus (P), parathyroid hormone (iPTH), serum albumin (ALB)] and their control rates were analyzed, and the differences in the above indicators of patients with hemodialysis frequency (2-times weekly, 5-times in two weeks and 3-times weekly) were compared.

Results: The proportion of patients older than 60 years old and the proportion of autologous arteriovenous fistula (AVF) increased year by year, while the use of the cuffed-tunneled catheter (TCCs) decreased. All indicators except iPTH have increased their control rates. Among the different dialysis frequencies: the average value of HGB and Ca was the highest at 3 times/week, and the control rate of P was not much different among the three groups. ALB was significantly lower in patients with 2 times/week than in other frequency groups ($P<0.05$). The average age of 3 times / week patients was significantly lower than 2 times / week and 5 times / 2 weeks ($P<0.05$).

Conclusion: In northwest China, the hemodialysis frequency to twice per week for most. The results of this study suggest that compared with the higher frequency, the major differences in the control rates are in albumin hemoglobin and serum calcium.

Table 1 the year-end control rates of HGB, Ca, P, iPTH and ALB, and the standard of every indicators

	hemoglobin (g/L)	Blood calcium (mmol/L)	Blood phosphorus (mmol/L)	Parathormone (pg/ml)	Albumin (g/L)
2016 year-end control rates	51.8%	43.6%	37.8%	60.7%	80.8%
2017 year-end control rates	60.3%	43.5%	40.9%	61.4%	87.4%
2018 year-end control rates	64.7%	46.1%	41.2%	59.1%	87.6%
P	0.001	0.693	0.608	0.003	0.016
X^2	13.702	0.733	0.996	11.960	8.272
2016 national registration report	57.1%	53.4%	36.2%	55.3%	82.6%
P	0.036	0.000	0.510	0.043	0.404
X^2	4.383	13.564	0.435	4.112	0.696
2017 national registration report	60.5%	59%	39.2%	58.4%	86.3%
P	0.962	0.000	0.449	0.000	0.001
X^2	0.002	41.197	0.456	14.739	10.133
The standard of every indicators	HGB≥100 g/L	2.1-2.5mmol/L	1.13-1.78mmol/L	2 to 9 times normal	≥35g/L

Table 2 the control rates of indicators of different dialysis frequencies

		hemoglobin	blood calcium	blood phosphorus	parathormone	albumin
2016 year-end	2 time per week	48.15%	32.12%	36.03%	64.49%	85.40%
	5 times/2 weeks	53.00%	32.50%	34.12%	60.00%	87.95%
	3 times per week	71.79%	58.11%	34.21%	58.18%	97.18%
	P	0.002	0.000	0.994	0.631	0.050
	X^2	12.596	15.509	0.115	0.920	6.010
2017 year-end	2 time per week	56.29%	36.53%	43.11%	62.18%	84.38%
	5 times/2 weeks	64.96%	44.78%	40.74%	59.38%	88.62%
	3 times per week	68.85%	57.97%	34.78%	57.58%	92.06%
	P	0.092	0.005	0.471	0.719	0.175
	X^2	4.772	10.492	1.505	0.659	0.491
2018 year-end	2 time per week	56.21%	22.35%	44.38%	64.50%	82.14%
	5 times/2 weeks	72.79%	45.58%	42.18%	60.56%	90.71%
	3 times per week	71.57%	54.17%	37.08%	50.53%	91.11%
	P	0.005	0.000	0.493	0.093	0.047
	X^2	10.556	28.935	1.413	4.761	6.117

Table 3 Comparison of the mean values of indicators of different dialysis frequencies

Hemodialysis Frenquency (%)	In 2016			In 2017			In 2018		
	2 times per week (47.4%)	5 times/ 2 weeks (29.6%)	3 times per week (23%)	2 times per week (44.8%)	5 times/ 2 weeks (36.7%)	3 times per week (18.5%)	2 times per week (40.9%)	5 times/ 2 weeks (35.7%)	2 times per week (23.4%)
Haemoglobin(g/L)	99.89±1.51	100.4±1.98	110.9±4.68*,Δ	101.9±1.49	106.2±1.65	107.5±2.61	101.2±1.39	108.4±1.61*	112.0±2.21*
Blood calcium(mmol/L)	1.97±0.02	2.02±0.02*	2.12±0.03*,Δ	2.027±0.02	2.070±0.02	2.097±0.03	2.039±0.02	2.105±0.02*	2.147±0.03*
Blood phosphorus(mmol/L)	1.97±0.06	1.91±0.06	1.91±0.07	1.667±0.04	1.765±0.05	1.637±0.07	1.746 ±0.05	1.806±0.04	1.837±0.07
Parathormone(pg/mL)	511.5±35.35	459±37.94	459.8±51.2	415.1±28.81	516.4±44.08*	477.7±52.86	370.9±25.16	458.5±36.39*	366.9±39.20
Albumin(g/L)	39.37±0.45	39.56±0.67	42.03±0.56*,Δ	39.94±0.45	45.33±0.81*	42.07±0.68*	38.78±0.35	40.43±0.34*	40.50±0.58*
Age(years)	52.62±1.31	51.13±1.63	43.28±1.70*,Δ	53.89±1.18	51.08±1.31	43.3±1.53*,Δ	56.86±1.17	51.99±1.23*	43.88±1.53*,Δ

*compared with average value of 2 times per week group, $P<0.05$;

Δcompared with average value of 5 times / 2 weeks group, $P<0.05$

Table 3 Comparison of the mean values of indicators of different dialysis frequencies

Hemodialysis Frenquency (%)	In 2016			In 2017			In 2018		
	2 times per week (47.4%)	5 times/ 2 weeks (29.6%)	3 times per week (23%)	2 times per week (44.8%)	5 times/ 2 weeks (36.7%)	3 times per week (18.5%%)	2 times per week (40.9%)	5 times/ 2 weeks (35.7%)	2 times pe week (23.4%)
Haemoglobin (g/L)	99.89±1.51	100.4±1.98	110.9±4.68*Δ	101.9±1.49	106.2±1.65	107.5±2.61	101.2±1.39	108.4±1.61*	112.0±2.21
Blood calcium (mmol/L)	1.97±0.02	2.02±0.02*	2.12±0.03*Δ	2.027±0.02	2.070±0.02	2.097±0.03	2.039±0.02	2.105±0.02*	2.147±0.03
Blood phosphorus (mmol/L)	1.97±0.06	1.91±0.06	1.91±0.07	1.667±0.04	1.765±0.05	1.637±0.07	1.746 ±0.05	1.806±0.04	1.837±0.0
Parathormone (pg/mL)	511.5±35.35	459±37.94	459.8±51.2	415.1±28.81	516.4±44.08*	477.7±52.86	370.9±25.16	458.5±36.39*	366.9±39.2
Albumin (g/L)	39.37±0.45	39.56±0.67	42.03±0.56*Δ	39.94±0.45	45.33±0.81*	42.07±0.68*	38.78±0.35	40.43±0.34*	40.50±0.58
Age (years)	52.62±1.31	51.13±1.63	43.28±1.70*Δ	53.89±1.18	51.08±1.31	43.3±1.53*Δ	56.86±1.17	51.99±1.23*	43.88±1.53

***compared with average value of 2 times per week group, $P<0.05$; Δcompared with average value of 5 times / 2 weeks group, $P<0.05$**

Figure:

P1540 **EFFECT OF ONLINE HEMODIAFILTRATION ON ANEMIA AND NUTRITIONAL STATUS ON MAINTENANCE HEMODIALYSIS PATIENTS**

Hyeyun Jeong[1], Yu Ho Lee[2], So-Young Lee[2], Dong Ho Yang[2]

[1]CHA Bundang Medical Center, CHA University, Division of Nephrology, Korea, Rep. of South and [2]CHA Bundang Medical Center, CHA University, Division of Nephrology

Background and Aims: The global prevalence and incidence of maintenance dialysis are increasing. Among the modalities of RRT, maintenance hemodialysis (HD) has been a major method worldwide for patients with end-stage renal disease (ESRD). The recent introduction of online-hemodiafiltration (OL-HDF) may offer major advantages in clearing molecules of various sizes, reducing HD-associated amyloidosis and chronic inflammation. Because this modality has been officially approved for ESRD patients, the number of patients worldwide undergoing OL-HDF therapy have consistently increased. However, evidence of clinical effects of OL-HDF is scarce. In this study, we investigated changes in laboratory values over more than 12 months after switching to OL-HDF.

Method: The present study included data from a K-cohort (CRIS no. KCT0003281) of prospectively enrolled adult patients with ESRD undergoing hemodialysis in 6 tertiary hospitals in South Korea. A total of 435 patients was recruited, and 339 patients were on HD at the beginning of the study period. Among the 339 patients, 182 were followed up for more than 24 months. During the follow-up period, 135 patients remained on HD and 47 switched to HDF. However, 3 of the 47 who switched to HDF later returned to HD. We compared clinical parameters in 44 patients who switched to OL-HDF and 135 patients who remained on HD (Figure 1). We used a paired t-test to compare baseline and 24-month follow-up results.

Results: The mean age of the study subjects was 61.2 $\pm$ 12.2 years, and 62.6% were male. The duration of dialysis was 2.9 $\pm$ 4.4 months. In the group that was switched from HD to OL-HDF, the levels of Hgb and serum albumin increased significantly (10.46 $\pm$ 1.03 vs. 11.08 $\pm$ 0.82, $P = 0.001$, and 3.73 $\pm$ 0.29 vs. 3.87 $\pm$ 0.30, $P = 0.001$, respectively). Although the normalized protein catabolic rate (nPCR) decreased from baseline after 24 months, the change was not significant (1.07 $\pm$ 0.25 vs. 1.03 $\pm$ 0.21, $P = 0.433$). Calcium and calcium-phosphorus products also increased significantly after OL-HDF therapy (8.32 $\pm$ 0.75 vs. 8.75 $\pm$ 0.80, $P < 0.001$ and 41.89 $\pm$ 12.62 vs. 50.80 $\pm$ 20.79, $P = 0.013$, respectively).

To determine possible confounding effects of clinical factors, we conducted a linear regression analysis with multiple adjustments for changes in various laboratory values after HDF conversion. Conversion to HDF resulted in elevation of serum calcium and albumin levels, both of which were significant even after adjustment for baseline demographics, inflammation, and dialysis duration.

Conclusion: In conclusion, long-term OL-HDF treatment over 12 months or longer was associated with no detrimental effects on anemia or nutritional status. To investigate the effects of OL-HDF therapy, evaluating more parameters over a longer follow-up period with a larger number of patients is needed.

Figure 1.

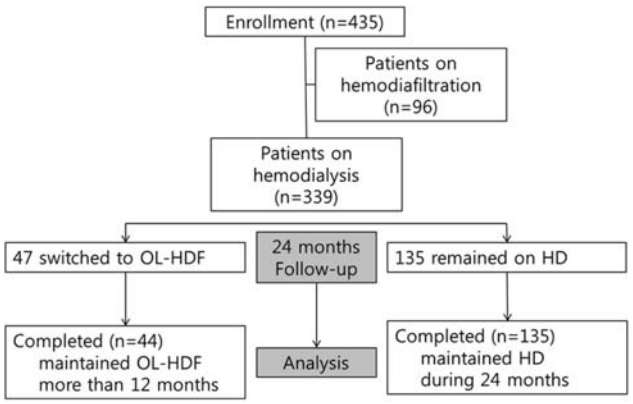


Figure:

P1541 HEMODIALYSIS IN END-STAGE RENAL DISEASE PATIENTS OVER 75 YEARS OLD

Tasnim Mesbahi[1], Barbouch Samia[1], Fattoum Safa[1], Najjar Mariem[1], Jebali Hela[2], Smaoui Wided[2], Rais Lamia[2], Ben Hamida Fethi[3], Zouaghi Mohamed Karim[2], Ben Abdallah Taieb[1]

[1]Charles Nicolle Hospital, Department of Nephrology, Tunis, Tunisia, [2]Hospital Rabta, Department of Nephrology, Tunis, Tunisia and [3]Charles Nicolle Hospital, Laboratory of kidney pathology LR00SP01, Tunis, Tunisia

Background and Aims: Over the last decade, the age of dialysis patients has been increasing steadily worldwide. The benefits of dialysis in older people with end stage renal disease (ESRD) are not clear. We will try to evaluate whether dialysis in older has survival advantage compared to younger people.

Method: It is a prospective descriptive and analytic study including 229 patients who initiated chronic hemodialysis during the period between January and June 2017. Patients were classified into two groups by age at dialysis initiation. Patients above 75 years of age were considered old (old group OG). Patients aged less then 75 years old were considered young (young group YG). Primary outcome was old patient's survival during the first 3 and 12 months from the dialysis initiation.

Results: Among a total of 229 new patients who began dialysis treatment, 41 (17,9%) ESRD were above 75 years of age.The sex ratio was 0,95 and 1,54 in respectively in OG and YG ($p = 0{,}167$). Diabetes was present in 56% of the elderly and in 59% of the younger group ($p = 0{,}72$) and was more frequently the cause of ESRD in the two groups. The average of modified Charlson Comorbidity Index was $6{,}7 \pm 2{,}3$ and $3{,}9 \pm 2{,}6$ respectively in OG and YG($p = 10^{-3}$). Younger patients had been referred earlier to nephrologists than the older ones. In fact, glomerular filtration rate at the beginning of the follow up was $18{,}7 \pm 8{,}9$ ml/min/1,73 in OG and $25{,}4 \pm 16{,}2$ in YG ($p = 0{,}004$). There was no statically significant difference between the two groups in the frequency of the use of temporary catheters at dialysis initiation ($p = 0{,}778$) and the urgent or planned initiation of dialysis ($p = 0{,}298$). Younger patients required hospitalization to organize dialysis initiation more than older patients (51,6% VS 26,8%; $p = 0{,}005$). Compared with the group of younger patients, Cox model showed an incremental increase in mortality associated with older patients' group during the first year of HD ($p = 0{,}036$). However, there was no difference between OG and YG in the mortality rate during the first 3 months of HD ($p = 0{,}102$).

Conclusion: We may conclude that life expectancy of patients who began dialysis above 75 years is significantly shorter than younger patients in the first year of HD. In the other hand, the difference between the 2 groups wasn't significant regarding the conditions of dialysis initiation.

P1542 DIALYSIS MODALITY AND OUTCOMES IN GERIATRIC END STAGE RENAL DISEASE (ESRD) PATIENTS. AN ASIAN SINGLE CENTER EXPERIENCE.

Jeevita Supayah[1], Hin Seng Wong[1], Fei Yee Lee[2], Suryati Yakob[1]

[1]Selayang Hospital, Nephrology, Batu Caves, Malaysia and [2]Selayang Hospital, Clinical Research Centre, Batu Caves, Malaysia

Background and Aims:

The prevalence of CKD increases with age and more elderly patients are on maintenance dialysis as advanced age is no longer an impediment. The selection of dialysis modality can be difficult for the simultaneous benefit and burden of individual modality on top of the complexity of co-morbidity and quality of life.

To study the survival outcomes based on dialysis modality in geriatric ESRD patients

Method:

The cohort of geriatric patients (aged > 65 years) with ESRD who were referred to our pre-dialysis clinic from 1st January 2016 to 31st December 2018 and started on maintenance dialysis were identified via the hospital information system. Demographics, co-morbidities, dialysis modalities and clinical outcome in terms of survival were obtained from the hospital electronic medical record. Glomerular filtration rates (eGFR) were calculated using the CKD-EPI formula in mls/min/1.73m2. The statistical analysis was done using SPSS version 23.

Results:

A total of 145 geriatric ESRD patients were initiated on chronic dialysis. The cohort was predominated by male with 77 patients (53.1%). The mean age was 72.5±5.2 years. Majority had multiple comorbidities with 95% having hypertension, 82.8% with diabetes, 65.5% and 32.8% having dyslipidemia and ischemic heart disease, respectively. The mean eGFR at point of referral and dialysis initiation were 12.5±4.9 mls/min/1.73m2 and 6.57±2.33 mls/min/1.73m2 respectively. Mean duration to initiate dialysis from first review was 6.7±5.8 months.

Majority opted for hemodialysis (HD) with 106 patients (73.1%). 74% patients in the HD cohort initiated dialysis via a catheter and remainder with an arteriovenous fistula (AVF). 39 patients (27.1%) opted for peritoneal dialysis (PD) and all were initiated via tenckhoff catheter. Mean eGFR at dialysis initiation were 6.44±2.47 (HD) and 6.9±1.9(PD) respectively.

At 6 months, all PD patients survived and 18.2% of HD patients died with statistically significance difference at p=0.003. No survival predictors were identified.

Conclusion:

PD modality has advantage in survival outcome in geriatric ESRD patients.

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DIALYSIS. HEALTH SERVICES RESEARCH

P1543 FACTORS ASSOCIATED WITH CHANGE IN FUNCTIONAL STATUS IN HEMODIALYSIS PATIENTS

Keigo Imamura[1], Yuta Suzuki[1], Shohei Yamamoto[1], Manae Harada[2], Haruka Ito[1], Sachi Yamabe[1], Shun Yoshikoshi[1], Kentaro Kamiya[1], Atsusi Yosida[2], Atsuhiko Matsunaga[1]

[1]Kitasato Univercity, Graduate School of Medical Sciences, Kanagawa, Japan and [2]Hemodialysis Center, Sagami Circulatory Organ Clinic, Kanagawa, Japan

Background and Aims: Hemodialysis (HD) patients have poor functional capacity. Expert clinical practice guidelines strongly recommend an assessment of functional status (FS) and treatment strategies in chronic kidney disease patients. A previous study demonstrated a high level of disability in daily activities in most HD patients, and a dose-response association was seen between poor FS at baseline and adverse clinical outcomes in HD patients. Moreover, a recent study reported that patients with a decline in FS over a 1-year period are at an elevated risk of mortality. Therefore, identifying factors that predict a decline in FS is important for developing treatment strategies. The purpose of this study was to investigate the factors that predict this decline in HD patients.

Method: A total of 146 outpatients (mean age of 66.1 ± 11.0 years; 48% were female) undergoing maintenance HD thrice a week at an HD center were included. FS was assessed based on the ability to perform activities of daily living (ADLs) and instrumental ADLs (IADLs) as self-reported on the Katz Index of Independence and the Lawton-Brody IADL scale, respectively The Katz Index of Independence examines five tasks of ADLs, and the Lawton-Brody IADL scale examines eight tasks of IADLs. Both have been validated in the general population. We then calculated the FS score by combining the scores of the Katz Index of Independence and Lawton-Brody IADL scale in accordance with the algorithm developed in a previous study, and the assessments were conducted at baseline and after 1 year. We classified patients into two groups based on having or not having at least a 1-point decline in the FS score. Background factors such as age, sex, body mass index, comorbidities score, hemodialysis time, primary kidney disease, hemoglobin level, and geriatric nutritional risk index were collected at baseline. In addition, for physical function, the usual gait speed and handgrip strength and for body composition, the skeletal muscle mass by bioelectrical impedance analysis were analyzed at baseline. To investigate factors predicting a decline in FS 1 year later, logistic regression analysis was used.

Results: Over the study period, 29.5% of the patients showed a decline in the FS score. Patients who showed a decline were older (71.2 years vs. 64.0 years), had weaker handgrip strength (22.9 kg vs. 24.8 kg), and exhibited slower usual gait speed (1.06 m/s vs. 1.22 m/s) than those who did not show decline at baseline. To predict a decline in FS 1 year later, age (odds ratio: 1.07, 95% confidence interval [CI]:1.02-1.13, p=0.003) and usual gait speed (odds ratio: 0.17, 95% CI: 0.03-0.96, p=0.04) were determined as significant factors.

Conclusion: Gait speed was a predictor of a decline in FS after 1 year. These findings underscore the significance of gait speed assessment in addition to monitoring the patient's FS. Moreover, intervention in maintaining gait speed may be essential in preventing the FS from deteriorating over time.

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P1544 SHARED DECISION MAKING FOR TREATMENT OPTIONS FOR ELDERLY PATIENTS ON DIALYSIS

Akihisa Kato[1], Yosuke Saka[1], Tomohiko Naruse[1]

[1]*Kasugai Municipal Hospital, Nephrology, Japan*

Background and Aims: The numbers of elderly patients on dialysis are increasing rapidly around the world. The quality of life (QOL) should be emphasized rather than survival for such patients. Shared decision making (SDM) regarding dialysis treatment options is one way to increase patient satisfaction with treatment, which should result in a better QOL. Thus, we investigated whether SDM affects the lives of elderly patients after dialysis initiation.

Method: We retrospectively collected clinical information about patients aged ≥ 80 years who started dialysis at our hospital between January 2013 and December 2017. The experience of SDM was defined as whether patients participated in a multidisciplinary approach to decision making about dialysis treatment options. Mortality rates, length of hospital stay and place of death during 2 years after dialysis initiation were determined.

Results: Among 124 patients, 40 participated in SDM. Functional activity, dementia, and daily assistance did not differ between patients with and without SDM. Participants in SDM were more likely to select PD (SDM vs. non-SDM: 50.0% vs. 3.6%; $p < 0.001$). Mortality rates did not differ between patients with and without SDM, but the rate of hospitalization for > 240 days was higher among patients without SDM (with vs. without SDM: 0.0 vs. 15.5%; $p = 0.009$). Among 70 deceased patients within two years, 59 died in hospital. Patients without SDM died in hospital more frequently (with vs. without SDM: 66.7% vs. 91.8%; $p = 0.006$).

Conclusion: Shared decision making reduced long-term hospitalization and death in hospital, indicating that more desirable home care therapy should be available for elderly patients on dialysis.

P1544A

ASSOCIATION BETWEEN PHYSICAL FRAILTY AND INSOMNIA SYMPTOMS AMONG PATIENTS ON HEMODIALYSIS

Shun Yoshikoshi[1], Shohei Yamamoto[1], Yusuke Matsunaga[1], Manae Harada[2], Takaaki Watanabe[1], Yuta Suzuki[1,2], Yusuke Isobe[1], Keigo Imamura[1], Haruka Ito[1], Sachi Yamabe[1], Atsushi Yoshida[2], Kentaro Kamiya[3], Atsuhiko Matsunaga[1]

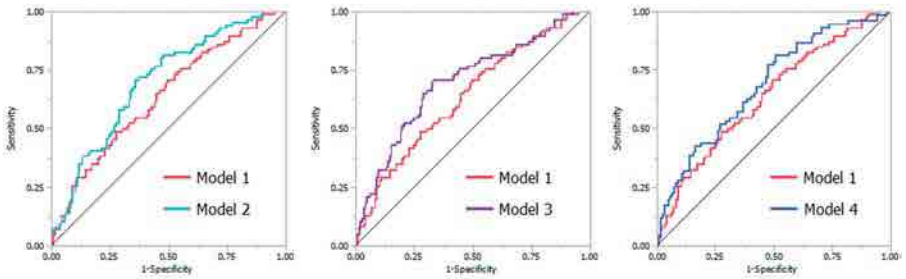
[1]Kitasato University Graduate School of Medical Sciences, Department of Rehabilitation science, Sagamihara, Japan, [2]Sagami Circulatory Organ Clinic, Sagamihara, Japan and [3]Kitasato University, Department of Hygiene, Sagamihara, Japan

Background and Aims: Community-dwelling older adults with physical frailty have been suffering from symptoms of insomnia, which have been associated with higher risk of falling and cardiovascular events. Therefore, insomnia symptoms should be assessed for disease management. Most of patients undergoing hemodialysis (HD) have both physical frailty and insomnia symptoms. However, only a few studies reported the association between physical frailty and insomnia symptoms in patients undergoing HD. Therefore, this study aimed to investigate whether insomnia symptoms were one of the useful factors to discriminate physical frailty in patients undergoing HD.

Method: This study included 231 outpatients undergoing HD three times a week. Physical frailty was measured using the frailty screening index, consisting five components (shrinking, physical function, physical activity, forgetfulness, and exhaustion). Insomnia symptoms were measured using the Athens Insomnia Scale (AIS), a self-administered questionnaire consisting of eight questions, each scored from 0 to 3. Age, sex, body mass index (BMI), HD vintage, comorbidity score, dialysis shift, depressive symptoms, use of sleep medications, usual gait speed, and physical activity (steps/non-HD day) were also investigated. Patients were classified as frailty (the frailty screening index score ≥ 3) and non-frailty (< 3). The analysis of covariance (ANCOVA) was used to compare the AIS scores between frailty and non-frailty. To examine whether the AIS score had the discriminative ability of the frailty complementary to clinical characteristics comparable to the usual gait speed and physical activity, receiver operating characteristic (ROC) curves were constructed, and the area under the curve (AUC) was compared using four models: clinical characteristics (age, sex, BMI, and comorbidity score) only (Model 1), Model 1 plus AIS score (Model 2), Model 1 plus usual gait speed (Model 3), and Model 1 plus physical activity (Model 4).

Results: The median age was 68 (interquartile range: 59–75) years, 59% were men and 37% had frailty. In ANCOVA, the AIS score in the group of frailty was significantly higher than those of non-frailty even after adjusting age, sex, BMI, HD vintage, comorbidity score, dialysis shift, depressive symptoms, and use of sleep medications ($p = 0.004$). Through the ROC analysis, Model 2 [AUC: 0.70, 95% confidence intervals (CI): 0.63–0.76], Model 3 (AUC: 0.70, 95%CI: 0.63–0.77), and Model 4 (AUC: 0.69, 95%CI: 0.61–0.76) showed significantly better discriminative ability as compared to Model 1 (AUC: 0.64, 95%CI: 0.56–0.71, all $P < 0.05$) (Figure). Moreover, AUCs were significantly increased by adding the AIS score to Model 3 (from 0.70 [95%CI: 0.63–0.77] to 0.74 [95%CI: 0.67–0.80], $p < 0.05$). In addition, AUCs were increased by adding the AIS score to Model 4 (from 0.69 [95%CI: 0.61–0.76] to 0.73 [95%CI: 0.65–0.80], $p = 0.07$) with a trend toward statistical significance.

Conclusion: This study examined the association between physical frailty and insomnia symptoms in patients undergoing HD. The AIS score had the discriminative ability of the frailty complementary to clinical characteristics comparable to the usual gait speed and physical activity. Future studies should investigate the causal relationship between physical frailty and insomnia symptoms in patients undergoing HD in detail.



		AUC	95% CI	p value
Model 1	patients characteristics*	0.64	0.56-0.71	ref
Model 2	Model 1+AIS score	0.70	0.63-0.76	0.043
Model 3	Model 1+usual gait speed	0.70	0.63-0.77	0.034
Model 4	Model 1+physical activity	0.69	0.61-0.76	0.035

AUC, the area under the curves; 95% CI, 95% confidence intervals; AIS score, Athens Insomnia Scale score.

*Adjusted for age, sex, body mass index, comorbidity score.

Figure: Receiver operating characteristic curves for 4 models: comparing the discriminative ability of the frailty.

P1545

LOW SOCIOECONAMIC STATUS INCREASES MORTALITY RISK IN KOREAN MAINTENANCE HEMODIALYSIS PATIENTS: A LONGITUDINAL COHORT STUDY USING HEMODIALYSIS QUALITY ASSESSMENT DATA

Young-Ki Lee[1], Hayne Cho Park[1], Ajin Cho[1], Do Hyoung Kim[1], Juhee Kim[1], Jong-Woo Yoon[1], Young Eun Kwon[2], Dong-Ryeol Ryu[3]

[1]Hallym University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of South, [2]Myongji Hospital Hanyang University College of Medicine, Internal Medicine, Goyang, Korea, Rep. of South and [3]College of Medicine, Ewha Womans University, Internal Medicine, Seoul, Korea, Rep. of South

Background and Aims: The number of hemodialysis (HD) patients and their medical expenses are growing rapidly in Korea due to entry into aging society and accompanying diseases such as diabetes and hypertension. Whether low socioeconomic status (SES) affect poorer HD survival is controversial with most reports come from the USA. Therefore, this study was performed to evaluate the effect of SES upon mortality in Korean maintenance HD patients using periodic HD quality assessment data.

Method: The HD quality assessment has been performed periodically by Health Insurance review and Assessment Service (HIRA) since 2001. We used 4th and 5th HD quality assessment data from the year of 2013 and 2015 respectively for collecting demographic and clinical data. The 4th survey was a sample survey while the 5th survey was a complete enumeration survey. We also collected data on patient comorbidity using the diagnosis codes from the health insurance claims database. The mortality data was collected until Dec 2017. As a proxy indicator reflecting SES, we classified subjects as a Medical Aid (MA) recipients ("low" SES) or a National Health Insurance (NHI) beneficiary ("middle/high" SES). We analyzed mortality risk based on SES using Cox proportional hazard model.

Results: A total of 21,786 HD patients from 4th survey and 35,454 HD patients from 5th survey were included in the analysis. The ratio between NHI beneficiary and MA recipient was 76.7% versus 23.3%. Mean age of the subjects was 59.0 years old in 4th survey and 60.3 years old in 5th survey. The MA recipients were younger and showed higher proportion of male, shorter duration of HD, lower body mass index (BMI), higher systolic and diastolic blood pressures before HD compared to the NHI beneficiary. The NHI beneficiary demonstrated higher proportion of diabetes, hypertension, cerebrovascular accidents, and dementia compared to the MA recipients. Two groups did not differ in dialysis efficiency presented as single pool Kt/V. A total of 7,173 deaths occurred in 2013 participants, while 7,306 deaths occurred in 2015 participants. After adjusting for age, gender, Charlson's comorbidity index, BMI, presence of atrial fibrillation, serum albumin, and serum creatinine, MA recipients showed significantly higher mortality risk compared to the NHI beneficiary (hazard ratio 1.162; 95% confidence interval 1.092-1.237, $p<0.001$ in 4th survey and hazard ratio 1.078; 95% confidence interval 1.013-1.146, $p=0.017$ in 5th survey).

Conclusion: Low SES independently increased mortality risk in Korean maintenance hemodialysis patients.

P1546 UK ANNUAL THERAPY COST OF DIALYSIS WITH THE QUANTA SC+ PERSONAL HAEMODIALYSIS SYSTEM

Thomas Ferguson[1,2], Paul Komenda[1,2,3], Gerard Harper[3], John Milad[3]

[1]University of Manitoba - Internal Medicine, Winnipeg, Canada, [2]Seven Oaks Chronic Disease Innovation Centre, Winnipeg, Canada and [3]Quanta Dialysis Technologies, Alcester, United Kingdom

Background and Aims:

The number of patients receiving dialysis is increasing in the United Kingdom, costing the National Health Service (NHS) over 500 million GBP annually. New personal haemodialysis systems are being developed, such as the Quanta SC+, that are smaller and simpler to use by patients while providing the clearances of conventional systems. Increasing uptake of lower intensity assistance and full self-care dialysis may provide economic benefits to the public health payer. In addition, promotion of every other day dialysis (3.5x weekly) may improve costs to the health system by helping to close the "post-weekend effect" with increased emergency department use and hospitalisations following the long interdialytic gap. As such, we aimed to describe the annual therapy costs of using SC+ in the UK for 3x weekly and 3.5x weekly dialysis regimens, both for self-care haemodialysis provided in-centre and at home in comparison to dialysis provided with conventional machines from the perspective of the health care system.

Method:

Cost minimisation approach. Costs for human resources, equipment, and consumables were sourced from the dialysis machine developer (Quanta Dialysis Technologies). Other costs, such as facility expenses, dialysis-related drugs, avoided emergency department and hospitalisation events, and utilities were taken from a review of the literature. Costs are provided in 2018 GBP.

Results:

Therapy provided as self-care in-centre or full self-care at home were found to have similar costs (£33,721 in-centre versus £33,836 at home for the 3x weekly regimen). Costs increased to £37,238 for self-care in-centre and £35,557 at home for the 3.5x weekly regimen. A comparator cost of £39,416 was established for dialysis provided with conventional machines in-hospital 3x weekly. For each dialysis patient, the health care system is anticipated to save £3,666 in costs associated with excess hospital stays and £2,176 in costs associated with excess emergency department visits.

Conclusion:

In the UK, SC+ offers cost savings when used both for self-care in-centre and full self-care at home in comparison to dialysis provided in the clinic using conventional machines.

P1547

THE EFFECT OF INTERNET-BASED CLOSED-LOOP MANAGEMENT ON QUALITY OF LIFE IN PATIENTS ON PERITONEAL DIALYSIS, A SELF-CONTROL STUDY

Fang Cao[1]

[1]*Fujian provincial hospital, Nephrology, Fuzhou, P.R. China*

Background and Aims: With the continuous advancement of information technology, mobile Internet has entered every family and shown its unique advantages. The development of hospital's information construction on the management of chronic disease, the continuous improvement of hospital APP and Wechat public number functions have provided intelligent services for patients throughout the process. Along with this process, the way of hospital patient follow-up has gradually expanded and improved, and the automation and intellectualization of follow-up work has become a reality. However, The establishment of peritoneal dialysis health management professional team and the implementation of closed-loop health management model, which is based on the Internet closed-loop management model has no clear impact on the self-management ability, quality of life and treatment effect of peritoneal dialysis patients. To explore the effectiveness of Internet based in-hospital and out of hospital closed loop management on the quality of life of patients with peritoneal dialysis, it is necessary to establish a set of closed loop management system for chronic diseases patients with promotion and practical significance.

Method: From July 2017 to July 2018, 214 patients with continuous peritoneal dialysis were followed up regularly in the Department of Nephrology of our hospital, and voluntarily participated in this study. The mean follow-up time was 12.6 $\pm$ 1.5 months. The differences of blood electrolytes, quality control indexes, self-management ability, quality of life of renal disease and hospital satisfaction were observed before and after closed-loop management.

Results: Ability of self-management behavior ($p < 0.001$), quality of life ($p < 0.001$), satisfaction ($p < 0.001$), the incidence of infection ($p < 0.05$), serum albumin ($p < 0.05$), hemoglobin ($p < 0.05$)were improved after participating in the closed-loop management.

Conclusion: The closed-loop management system based on Internet closed-loop management model is effective for the quality of life and treatment effect of peritoneal dialysis patients, which integrates the core functions of follow-up records, intelligent early warning, doctor-patient communication and health education. Through this closed-loop management, medical staff can digitally collect, store, transmit and process the information of in-hospital and out-of-hospital conditions through follow-up analysis, health guidance and remote assistance to achieve the purpose of patient health management. This study shows that this closed-loop management system can effectively manage the health of peritoneal dialysis patients, and provides a replicable model for the management of chronic diseases. Therefore, a comprehensive closed-loop management system based on mobile Internet and information technology, with clinical care as the leading factor and peritoneal dialysis patients as the terminal is a feasible and acceptable follow-up management method for peritoneal dialysis patients and hospitals.

P1548 **THE VALUE OF BEING A NETWORK: CLINICAL GOVERNANCE AND DIALYSIS CLINIC PERFORMANCE MANAGEMENT IS ASSOCIATED WITH IMPROVED PATIENTS SURVIVAL**

Luca Neri[1], Jasmine Ion Titapiccolo[1], Francesco Bellocchio[1], Otto Arkossy[1], Mario Garbelli[1], Stefano Stuard[1]

[1]*Fresenius Medical Care, Bad Homburg, Germany*

Introduction. In order to help facilitate the uptake of best clinical practices, improve outcomes, enhance efficiency and reduce costs, few healthcare organizations have introduced Continuous Quality Improvement (CQI) programs. Since September 2014, dialysis centers belonging to the EMEA Fresenius Medical Care (FME) network have introduced a CQI policy called Medical Peer Review (MPR) based on key performance indicators (KPI) related to patient's clinical status. We exploit the quasi-experimental setting generated by the introduction of FMC CQI policy, to evaluate the association between improvement in intermediate outcomes (key performance indicators) and prolonged survival among dialysis patients registered in the EMEA FME network.

Methods. We conducted a historical cohort study. We included adult patients on chronic dialysis with less than 90 days between renal replacement therapy (RRT) initiation date and first treatment date in FME clinics. We compared KPI target achievement (P-BSC score) and 2-year mortality for patients enrolled prior to MPR-CQI policy onset (Cohort A) and a cohort of patients enrolled after MPR-CQI policy onset (Cohort B). Structural Equation model was adopted to estimate the association of MPR-CQI policy on patients' survival through changes in intermediate outcomes (P-BSC score).

Results. The Cohort A and Cohort B consisted of 2397 and 1873 patients, respectively. We observed no difference across groups concerning the distribution of age (63.1 vs 62.8 years), gender (59% vs 60% males) and body mass index (27.6 vs 26.4 kg/m^2); Cohort A showed lower Charlson's comorbidity index (3.3±1.5 vs 3.8±1.9, p<0.01) and higher dialysis vintage (32.9±27.0 vs 21.3±22.2 days, p-value<0.01) compared to Cohort B. P-BSC scores over the 6-month ascertainment period was 5.25±1.47 in the pre CQI-MPR policy cohort, while it was significantly higher (6.67±1.63) in the post CQI-MPR policy cohort. Mediation analysis demonstrated a strong indirect effect of CQI-MPR implementation on mortality trough improvement of P-BSC rating score occurring in the post-implementation era (OR=0.70, p<0.001)

Conclusion. We showed that, after discounting for potential unmodifiable confounding factors and potential unmeasured selection/chronological bias, improvement of intermediate outcomes and performance indicators occurred after MPR-CQI policy implementation, was associated to a strong improvement in survival.

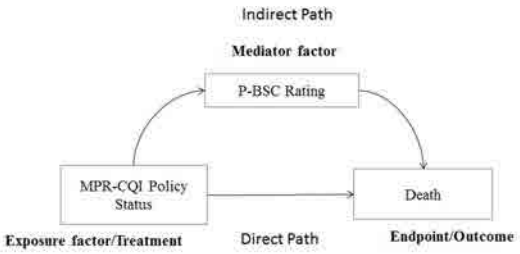


Table 4. Results from mediation analysis (n=4270).

	Odds Ratio Estimate	Confidence Interval Limits		p-value
Total Effect	0.85	0.70	0.99	0.04
Direct Effect	1.21	0.98	1.43	0.07
Indirect Effect	0.70	0.65	0.76	<.001

Figure:

P1549

TREATMENT BURDEN AND ITS IMPACT ON QUALITY OF LIFE AMONG CHRONIC KIDNEY DISEASE PATIENTS WITH DIABETES MELLITUS IN QATAR

Fadwa Al-Ali[1], Rania Ibrahim[1], Mincy Mathew[1], Nadir Kheir[2], Ahmed Awaisu[3], Mohamed Izham[2], Asmaa Almansouri[4], Abdullah Hamad[1]

[1]Hamad Medical Corporation, Doha, Qatar, [2]Qatar University, Pharmacy Department, Qatar, [3]Qatar University, Pharmacy, Qatar and [4]Hamad Medical Corporation, Qatar

Background and Aims: Diabetes mellitus (DM) is the leading cause of chronic kidney disease (CKD) and on of its top comorbidities. Its management places significant burden on patients and results in impairment of their health-related quality of life (HR-QOL). Little is known about diabetes mellitus treatment-related burden in patients with CKD. This study aimed to investigate the impact of diabetes mellitus on treatment-related burden and HR-QOL among CKD patients in Qatar.

Method: This was a mixed-method, sequential explanatory study conducted at Fahad Bin Jassim Kidney Center in Qatar on hemodialysis and pre-dialysis (GFR<20 but not on dialysis yet) patients. Treatment-related burden and HR-QOL were assessed quantitatively using the Treatment Burden Questionnaire (TBQ) and the Kidney Disease Quality of Life (KDQOL^{TM}) questionnaire, respectively. To gain a deeper insight, qualitative one-to-one semi-structured interviews were conducted among the CKD patients. Quantitative data were analyzed descriptively and inferentially using SPSS version 24. Thematic content analysis was performed for the qualitative data.

Results: Two hundred-eighty CKD patients (hemodialysis = 223 and pre-dialysis (GFR <20) = 57) were included. 157 has DM and 66 were non-DM (in hemodialysis) while 32 patients had DM vs 25 non-DM (in pre-dialysis). In general, 35% of patients reported moderate to high burden. Hemodialysis patients experienced significantly higher treatment burden compared to pre-dialysis patients with median (IQR) of 45 (36) versus 25 (33), respectively ($p<0.001$). DM patients expressed significantly higher TBQ score compared to non-DM (47(40) vs. 36(27) $p<0.001$). Retinopathy was associated with worsened treatment burden (TBQ 46.5(29) vs. 40(38) $p=0.019$). Medication burden and lifestyle change burden were the highest perceived treatment-related burden, followed by administrative, social, and financial burden. The presence of antidiabetic medications correlated with worse TBQ score (0.207 $p<0.001$). There was a strong, negative correlation between TBQ score and KDQOL-36^{TM} score [rs (251) = -0.616, $p <0.001$]. Presence of DM was associated with worse KDQOL (2110(1055) vs. 2685(1170) $p<0.001$). Thematic content analysis identified religion and faith in God as well as quality of the care provided as factors that reduce perceived treatment burden and improve patients' HR-QOL. Conversely, medication burden, lifestyle changes, challenges with international travelling, financial burden, and empathy were factors that worsen perceived treatment-related burden and HR-RQOL.

Conclusion: This study suggests that diabetes mellitus and its treatment negatively impacts treatment-related burden and quality of life in CKD patients. This result should be considered in management strategies when designing healthcare interventions directed to CKD patients with diabetes mellitus.

P1550 **ACCESS TO KIDNEY TRANSPLANTATION IN A NON-PROFIT FACILITY IN GERMANY**

Stephan Kemmner[1], Wolfgang Arns[2,3], Gero Von Gersdorff[3,4], Rolf Dieter Bach[3], Michael Fischereder[3,5]

[1]University hospital Munich, Ludwig-Maximilians-University (LMU), Transplant Center, Munich, Germany, [2]Cologne Merheim Medical Center, Department of Nephrology and Transplantation, Cologne, Germany, [3]Kuratorium für Dialyse und Nierentransplantation e.v., Neu-Isenburg, Germany, [4]University of Cologne, Faculty of Medicine and University Hospital Cologne, Department II of Internal Medicine and Center for Molecular Medicine Cologne, cologne, Germany and [5] Medizinische Klinik und Poliklinik IV, Klinikum der Ludwig-Maximilians Universität (LMU),, Renal Division, Munich, Germany

Background and Aims: Recent studies demonstrate that US patients undergoing chronic dialysis treatment for end stage renal disease (ESRD) at for-profit facilities had a lower access to kidney transplantation than patients at non-profit facilities. However, even at non-profit facilities only around 20% of patients were placed on the kidney transplantation waiting list. At first glance, this number appears rather low, as kidney transplantation is the only way to curatively treat ESRD.

We want to compare these figures with a recently performed survey in Germany.

Method: We analyzed the status of transplant evaluation in the largest non-profit facility in Germany, the Kuratorium für Dialyse und Nierentransplantation e.V. (kfh, www.kfh.de). In total, the transplant status was assessed in 16,705 patients.

Results: Out of these only 19.4% of patients (n=3241) are on the kidney transplant waiting list, comparable to recently performed US studies. The reason why patients are not waitlisted are multifaceted as seen in attached figure. Due to severe comorbidities about 50% are considered too sick to benefit from transplantation, in turn representing the complex and high multi-morbidity of patients with ESRD. On the other hand, approximately 10% of dialysis patients actively decline listing for renal transplantation at least at some point.

Conclusion: We conclude that further research is needed to identify and break the mechanisms behind the low likelihood for access to kidney transplantation waiting list.

	Patients with documented transplant status for kidney transplantation (KTx) in a German non-profit dialysis facility:	**n=16,705**
	Of these. . ..	n (%)
No obvious contraindication against access to KTx	on the deceased KTx waiting list	3,241 (19)
	• on the active waiting list	1,848 (11)
	• currently not transplantable	1,393 (8)
	under evaluation to be placed on the waiting list	3,418 (21)
	listing for transplantation declined by patient	1,623 (10)
Access to KTx not possible	access to transplantation not possible due to comorbidities (medical reasons)	8,051 (48)
	removed from waiting list due to medical reasons	372 (2)

Figure:

Distribution of patients with surveyed transplant status in the largest non-profit dialysis facility (kfh, www.kfh.de) in Germany

P1551 FAMILY SUPPORT IS CRUCIAL FOR DIALYSIS PATIENTS TREATMENT ADHERENCE AND QUALITY OF LIFE

Lada Trajcheska[1], Irena Rambabova Bushljetikj[2], Gjulsen Selim[3], Aleksandar Sikole[4], Goce Spasovski[2], Adrijana Spasovska Vasilova[5], Mimoza Milenkova[2], Aleksandra Canevska[6], Igor Nikolov[2]

[1]University Clinic of nephrology, Dialysis, Skopje, Republic Of North Macedonia, [2]University clinic of nephrology Skopje, Transplantation, Skopje, Republic Of North Macedonia, [3]University clinic of nephrology Skopje, ICU, Skopje, Republic Of North Macedonia, [4]University clinic of nephrology Skopje, Dialysis, Skopje, Republic Of North Macedonia, [5]University clinic of nephrology Skopje, transplantation, Skopje, Republic Of North Macedonia and [6]University clinic of nephrology, Clinical nephrology, Skopje, Republic Of North Macedonia

Background and Aims: Non-compliant dialysis patients are at increased risk of mortality. Compliance depends on patient demographics, educational level and income. Family support and marital status might also influence the patients compliance, as well as the quality of life. Missed/shortened dialysis sessions, adherence to prescribed medications, excessive phosphate serum values and interdialytic weigh gain, smoking and adherence to medical investigations provide indicators of non-compliance. Aim: To assess the impact of family support on different compliance indicators in the dialysis patients.

Method: In this observational study 134 dialysis patients were scored for different indicators of compliance from 0-2 and summary scores of compliance were assessed. Clinical and laboratory data were obtained from the previous two years. Patients with mean IDWGs >4.5% of body weight (BW) and/or phosphorous level above 1.6 mmol/L were scored with 1, patients with IDWG/BW more than 5.7% and/or 2.0 for mean phosphorous level were scored with 2. Summary scores of non-compliance were also assessed. Patients were scored for quality of life with SF-36 questionnaire. Patients non-adherence was analysed for predictors in multivariate analysis.

Results: Estimated rates of noncompliance varied: Medical investigations 63%, phosphorous 33, IDWG 22, therapy 14%, HD treatment 9%. When the complete dietary fluid, medications and treatment regimen were studied noncompliance rate was 73%, and when adherence to medical investigations was added the rate rose up to 87%. Patients with family support above median level ($\geq$25) were significantly more often men (0.049), with diabetes (p=0.014), lower socioeconomic status (0.001) and married (0.003). The quality of life scores were significantly worse in the low family supported patients (56.73$\pm$26.15 vs 39.23$\pm$24.05, p=0.0001). They also scored worse in overall non-compliance scores 2.04$\pm$1.71 vs 2.97$\pm$2.06, p= 0.007). In the multivariate analysis the non-compliance was predicted most powerfully in patients with younger age, low social status and lower family support (β=-0.202, p=0.023, β=0.220, p=0.036, β=-0.175, p=0.019, respectively).

Conclusion: Family support is crucial for dialysis patients adherence to treatment and Quality of life. Efforts should be done to recognize the patients real needs and adequately help those confronting dialysis burden and improve their quality of life.

P1552 **CAN WE GET ADEQUATE DIALYSIS WITH LIQUID AT 300 ML/MIN ?**

Guillermina Barril[1,1], Pedro Sobrino[1], Martin Giorgi[1], Almudena Nuñez[1], Begoña Santos[1], Natalia Pascual[2], Pilar Sanz[2], Francisco Cano[2], Angel Nogueira[1], Jose Antonio Sanchez Tomero[1]

[1]Hospital Universitario de la Princesa, Nephrology, Madrid, Spain and [2]Hospital Universitario de la Princesa, biochemical laboratory

Background and Aims: The portable HD monitors achieve a good adaptation with HD dialysate at 200ml / min using the concept of saturation of the HD dialysate. We decrease from 800ml / min to 500ml / min with good adaptation some years ago.

To assess the effectiveness of HD in both HD-standard and HDF-online with dialysate flow at 300ml / min by establishing approximate mathematical model of clearance.

Methods: We conducted an HD session with dialysate flow at a speed of 300ml / min, half week session to 52 patients in our unit. We value vascular access, session time, liters of blood-purified and total infusion in HDF online. We review HD monitor and dialyzer.

We perform pre and postHD blood determinations: Urea, B2microglobulin, P and uric acid, assessing urea reduction rate (PRU), b2microglobulin reduction rate (PR2microg) with both dialysate flows at 300ml / min and 500ml / min. We also have evaluated the differences between the two methods.

In the HD dialysate flow we determine at 300ml / min at 5, 10, 30, 45 and 60min (total dialysate collection in the first hour with sample of the mixture) urea, B2microg, Uric acid and P and at 2, 3 and 4 hours establishing a mathematical model with an approximation curve in both HD and online HDF.

Results: Five patients in standard HD (4h), 35 HDF online (4h) (x Liters infused 24.87 ± 2.79 l) and 12 short-daily HD (2h30min). 18 catheter and 34 FAV. Xliters purified blood = HD daily 54.41 ± 5.63l, HD standard 87.38 ± 6.01 and HDFonline 82.02 ± 16.13l.

The xPRU = 76.17 ± 10.49%, PRB2microg = 73.82 ± 13.49, Kt / V = 1.52 ± 0.28. By scheme at 300ml / min of HD fluid flow: HDFonline xPRU = 81.54 ± 5.25, Standard HD = 78.01 ± 3.03, Daily HD = 60.19 ± 6.71; xPRb2microg HDFonline = 76.70 ± 14.76%, Standard HD 65.44 ± 11.81, Daily HD = 69.16 ± 6.49.

Comparing the xPRU at 300ml / min of liquid vs 500ml / min we didnt found significant differences, nor in the x preHD of urea and B2microglobulin.

With the dialysate samples we obtain a polynomial model of order 7 allowing cuantitative adjustment of the curve.R2 0.9, observing in the first 2 hours the greater removing.

Conclusions: 1. The results are sufficient to consider the result of the removing in each scheme adequate. 2. The decrease in costs would be important (40% of water + energy saving and longer duration elements water treatment. 3. Further study are necessary.

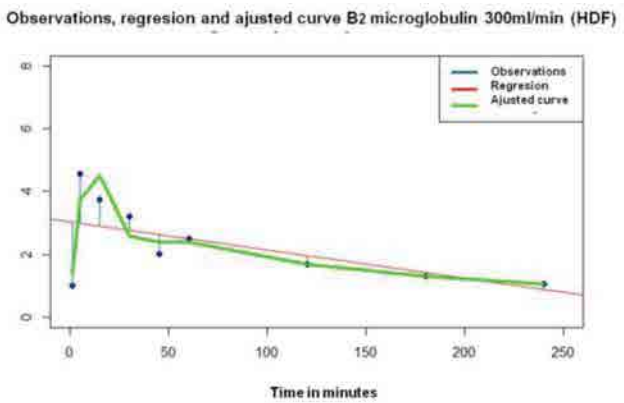


Figure: Proposed mathematical model

P1553 QUESTIONNARIE-BASED SURVEY ON PRACTICE PATTERNS OF INPATIENTS WITH HEMODIALYSIS AT ALL 42 NATIONAL HOSPITALS IN JAPAN

Takeshi Nakata[1], Yuji Kamijo[2], Tsuneo Konta[3]

[1]Oita University, Department of Endocrinology, Metabolism, Rheumatology and Nephrology, , [2]Shinshu University School of Medicine and [3]Yamagata University Graduate School of Medical Science, Japan

Background and Aims:

General physicians reportedly play an essential role in improving inpatient care. Hemodialysis (HD) management physicians are expected to become "hospitalists" for managing HD inpatients. However, the actual clinical practice patterns of HD inpatients management are not well known.

Method:

To clarify the actual clinical practice patterns of inpatients with HD, we conducted a questionnaire-based survey among HD management physicians who worked at the HD centers of 42 national university hospitals in Japan. These universities are members of the "Council of Blood Purification Division in Japanese National University Hospitals." This survey investigated the affiliations of each HD management physician and their clinical management of inpatients under the care of other departments, via online correspondence or letters. We asked questions about (1) the department managing the HD center; (2) physicians' experience (by 5 years); (3)working style (full time or part-time); (4) management policy of each facility; (5) how to communicate with other department doctors; (6) how often are laboratory data checked; (7) how often are chest X-ray data checked; (8) how often do they advise doctors from other departments regarding fluid, medication, and nutrition; (9)what do they think about the importance of physicians' involvement in HD management; and (10)do they find it difficult to manage HD inpatients under the care of other departments. We analyzed whether these aspects were influenced by physicians' experience or department or working style via statistical analysis. We used the linear regression model, Fisher's exact probability test, or Chi-square test as appropriate. The ethics committee of Oita University approved this survey.

Results:

Thirty-seven of 42 facilities(90%) and 173 of 249 HD management physicians (69%) answered this survey. Furthermore, 31 HD centers (84%) were managed by the physicians from a single department (Nephrology = 24, Urology = 6, Emergency = 1), whereas 6 HD centers (16%) were managed by the physicians from two departments (Nephrology and Urology = 5, Nephrology and Emergency = 1). Besides, 87% of HD management physicians were aware of the importance of medical intervention by HD specialists on HD inpatient management. However, only approximately 10% of HD management physicians regularly performed blood examination and chest X-ray for managing the HD inpatients under the care of other departments, whereas 70% of physicians only performed the tests when necessary. Even in the same hospital, the management policy differed among individual physicians. Only 28% of facilities had a shared management policy among physicians. The physicians with little experience faced more difficulty in managing HD inpatients than experienced physicians (with five years of experience; $|r| = 0.75$, $p < 0.05$). The main reason for this difficulty was poor communication with attending physicians, lack of management rules, and short duration of hospital stay.

Conclusion:

The clinical practice patterns of HD inpatient management who were under the care of other departments were different for each HD management physician. The physician's clinical experiences might affect the outcomes of HD management. In addition, good communication and established HD management rules between departments appear to be important.

P1554 **TYPES OF INCIDENTS MANAGED AT TWO DIFFERENT MEDICAL LEVELS IN A LARGE MULTINATIONAL RENAL SERVICES PROVIDER NETWORK**

Belén Marrón[1], Israel Silva[2], Carlos Lucas[3], Marietta Torok[4], Charlotta Wollheim[5], Filiz Akdeniz[2], Suzanne Pearce[2], Ulf Westesson[6], Fernando Macário[7]

[1]Diaverum Renal Services, Corporate Home Therapies & Patient Safety. Medical Office., Mälmo, Sweden, [2]Diaverum Renal Services, Corporate Nursing Director. Medical Office, Mälmo, Sweden, [3]Diaverum Renal Services, Corporate Medical Protocols & Standarization. Medical Office, Mälmo, Sweden, [4]Diaverum Renal Services, Corporate Medical Integrations Director. Medical Office, Mälmo, Sweden, [5]Diaverum Renal Services, Corporate Data Management Director, Mälmo, Sweden, [6]Diaverum Renal Services, Corporate Data Protection Director. Medical Office, Mälmo, Sweden and [7]Diaverum Renal Services, VP Medical Office, Mälmo, Sweden

Background and Aims:

Patient safety programs need a well-structured organization to facilitate proactive and fair reporting, prompt evaluation analysis and timely feedback followed by measure implementation and auditing.

To analyze all types of incidents in our network from Jan.1st to Sept. 30th, 2019 by two different levels (Corporate and Country) of medical management alert.

Method:

Our institution has tracked all incidents under a structured process program for the last 10 years, according to 4 incident types (Patient related, Staff-visitors, Products and Equipment) and 54 subcodes. Incidents are considered as serious when they may be life-threatening or result in death, impaired body function/structure and/or are deemed serious based on appropriate medical judgment. Communication to Health Authorities applies in accordance with local country regulations. "Serious incidents" are immediately notified to the Corporate Office and to each Country Medical lead, whilst different codes may generate alerts into Corporate or Country.

Results:

A total of 68.399 incidents (2.7 incident/patient/year) were reported during Q1-Q3 2019. Total incidents/1000 treatments were 17.1 (12.1 were patients related incidents). Causes for alerts at corporate level (n=65) were: cardiorespiratory arrest (28%); unexpected death (15%); seroconversion (9%); hemolysis (8%), severe hypotension (6%) and air embolism (3%). Reported incidents at country level (n=655) were almost half ascribed to equipment [water supply, power failure and flooding (41%)], medication errors (36%), venous needle dislodgment (19%) and Injuries (3%).

Conclusion:

Despite continuous efforts to get better results, there is room for improvement on better staff compliance with our standard operating procedures especially regarding medications and venous needle dislodgment risk assessment.

P1554A

EFFECT OF HAEMODILUTION ON THYROID FUNCTION BEFORE AND AFTER HAEMODIALYSIS IN PATIENT WITH END-STAGE RENAL DISEASE

Toru Sanai[1], Ken Okamura[2], Yuji Ikeda[3], Motoaki Miyazono[3], Tomorow Onoue[1], Toma Fukumitsu[1], Kazumasa Shimamatsu[4], Takanari Kitazono[2]

[1]Fukumitsu Clinic, Int. Med., Fukuoka, Japan, [2]Kyushu Univ., Int. Med., Fukuoka, Japan, [3]Saga Univ., Int. Med., Saga, Japan and [4]Shimamatsu Naika Inc., Int. Med., Chikushinoshi, Japan

Background and Aims: To study the factors involved in the low thyroid hormones in end - stage renal disease (ESRD), we compared thyroid function before and after hemodialysis (HD).

Method: The serum free thyroxine (fT_4), free triiodothyronine (fT_3), and thyroid - simulating hormone (TSH), thyroxine binding globulin (TBG) and thyroglobulin (Tg) levels were measured before and after HD in 12 patients with chronic glomerulonephritis (CGN, age; 48.7 $\pm$ 11.8 [mean $\pm$ SD]) and 11 patients with diabetic nephropathy (DN, age; 57.6 $\pm$ 6.5), comparing with controls (n = 13, age; 40.9 $\pm$ 11.3).

Results: The serum fT_4, fT_3 and TBG levels were low before HD but increased almost in parallel with the increase in hematocrit and albumin levels after HD in both ESRD groups. The serum TSH level was high before HD but decreased after HD and Tg level remained almost unchanged. In DN, serum fT_4 levels was almost the same, but fT_3 levels was lower with slightly higher TSH level, compared with CGN.

Conclusion: Significantly lower fT_4, fT_3 and TBG levels in ESRD before HD seemed to be due to hemodilution and almost corrected after HD. The TSH level was promptly normalized with elevated fT_4, and Tg levels remained unchanged probably due to the balance between corrected hemodilution and rapid response to decreased TSH stimulation. It may better to evaluate thyroid function after HD in ESRD. Accelerated senile changes were suggested in DN.

P1555 **REVERSIBLE AKI AND HEART INVOLVEMENT RESULTING FROM AMANITA PROXIMA POISONING TREATED WITH HAEMODIALYSIS: A SINGLE-CENTER CASE SERIES**

Giuseppe Leonardi[1], Brigida Di Renzo[1], Patrizia Covella[1], Alessandra Spinelli[1], Antonio Flores[1], Alessio Montanaro[1], Annarita De Giorgi[1], Cosima Balestra[1], Amalia Mariotti[1], Palmira Schiavone[1], Massimo Marangio[1], Giuseppe Coppolino[2], Luigi Vernaglione[1]

[1]Perrino Hospital Brindisi - ASL BR, Nephrology and Dialysis Unit, Brindisi, Italy and [2]University 'Magna Graecia" of Catanzaro, Nephrology and Dialysis Unit, Catanzaro, Italy

Background and Aims: Worldwide, amatoxin-containing mushrooms account for >95% of mushroom poisoning-related death. Recently, *Amanita* species not containing amatoxin, such as *Amanita Proxima*, have been implicated in poisonings resulting in acute kidney injury. Allenic norleucine has been isolated from these fungi and accounts for their nephrotoxicity. AKI is characterized by interstitial nephritis on renal biopsy and resolves over weeks. Here we report several case of AKI associated with cardiac involvement. We aimed to describe improvement of cardiac output and resolution of AKI after replacement dialysis treatment.

Method: From January 2013 to January 2020, eight consecutive patients with AKI from Amanita Proxima poisoning were enrolled in a large Italian community hospital. We collected clinical data including hepatic, cardiac and renal function parameters. In all the cases studied, in addition to renal failure, there were a worsening of cardiac function.

Results: We identified 8 patients suffering from Amanita Proxima intoxication, with a mean age of 57.8±24.5 years (62.5% were female). All patients presented preliminary gastrointestinal symptoms occurred within 24 hours from the mushroom intake and suddenly developed kidney injury and underwent replacement dialysis treatment using standard bicarbonate dialysis. At baseline, patients' mean eGFR was 7±2.3 mL/min/1.73㎡, with a mean BUN of 124±41 mg/dl, AST 52,6±42,5 IU/L, ALT 115,5±105,7 IU/L,. Cardiac involvement was also found in all cases, evidenced by ECG alteration (62,5%), an increase in myocardial necrosis enzymes (87,5%) and a reduction in the ejection fraction (50%) of about 15 percent. In 25% of cases, typical chest pain was also found. Mean troponin was 3,82±7,31 ng/ml, myoglobin 243,55±275,18 ng/ml CPK 187,6±42 IU/L and CK-MB of 13,72±14,96 IU/L. Kidney failure and cardiac impairment was successfully resolved in 87.5% of poisonings. At the end of treatment all renal and cardiac parameters significantly decreased ($P<0.001$): mean eGFR was 57±24 mL/min/1.73㎡, mean BUN was 69±12.7 mg/dl, AST 23,57±9,77 IU/l, ALT 25±10,64 IU/L. Mean troponin was 0,04±0,03 ng/ml, myoglobin 111,8±93,39 ng/ml, CPK 68,33± IU/L and CK-MB 0,66± 0,61 IU/L.

Only one patient died for intoxication-related complication. The mean number of dialysis treatments to achieve the resolution of renal failure was eight.

Conclusions: The cases reported suggest that Amanita proxima have a potential severe cardiac toxicity that request a precise cardiac evaluation. Early identification of intoxication and rapid start of dialysis therapy are crucial for the resolution of heart damage.

P1556 HEALTH CARE STAFF ACCEPTANCE OF ULTRAFILTRATION RATE RECOMMENDATIONS MADE BY A NOVEL FEEDBACK CONTROLLER.

Leticia Tapia[1], Lemuel Rivera-Fuentes[1], Sabrina Rogg[2], Stephan Thijssen[1], Peter Kotanko[1]

[1]Renal Research Institute, New York City, United States of America and [2]Fresenius Medical Care Deutschland GmbH, Global Research and Development, Bad Humburg, Germany

Background and Aims:

Preciado et al. have identified half-hourly relative blood volume (RBV) targets during hemodialysis (HD) that are associated with significantly improved patient survival. Attainment of these RBV targets would require frequent adjustments to the ultrafiltration rate (UFR) by the dialysis nurse, which is logistically not feasible. We developed a novel proportional-integral controller that takes RBV data from the commercially available CLiC® device as an input and provides UFR suggestions to guide the RBV curve into the desired targets. In this study, we investigated the degree to which the dialysis nurses accepted the UFR recommendations made by this novel feedback controller.

Method:

We conducted a single-arm, prospective, interventional pilot study in subjects on chronic HD at three Avantus Renal Therapy Dialysis Centers in New York City. Subjects were treated with Fresenius 2008T HD machines. RBV was measured with the CLiC® device. CLiC® and HD machine data were fed into a research laptop running the UFR Feedback Controller software. The UFR recommendations (generated every 10 minutes) were evaluated by dialysis nurses who then either implemented or rejected them as they deemed clinically appropriate.

Results:

Fifteen subjects (58.9 ± 15.3 years, 33% white, 53% black, dialysis vintage 4.1 ± 2.4 years, baseline interdialytic weight gain 2.6 ± 0.8 L, treatment time 222 ± 28 min) were studied. Fifty-six study visits (48 complete, 8 partial) from 14 subjects had analyzable data. Out of 1,038 UFR recommendations made by the Controller, 926 (89.2%) were accepted by the dialysis nurses, while 112 (10.8%) were overridden. In 48% of all 48 complete treatments, the Controller ran without a single override by the nurses. Of the other half of the treatments, about a quarter only saw one override per treatment (only half of which were due to low blood pressure or clinical symptoms). Only 1 of 59 study visits was incomplete due to a staff intervention for medical reasons that disengaged the Controller. For the 25 complete study treatments (from 11 subjects) that had at least one Controller suggestion overridden by the nurses, we analyzed the direction and magnitude of disagreement between the Controller-suggested and the implemented UFR (Fig. 1). Out of a total of 109 overridden Controller suggestions, 20 implemented UFRs were greater than the respective Controller-suggested UFRs (i.e., not indicated for medical reasons). Another 70 implemented UFRs were less than 100 mL/h (on average 49.7 mL/h) lower than the Controller-suggested UFRs (i.e., very mild disagreements). Together, these two categories make up 83% of all "disagreements" between healthcare staff and the Controller, leaving only 19 more pronounced disagreements. Of note, of the 109 UFR overrides, 65 (59.6%) were due to staff preference in the absence of low blood pressure or clinical symptoms; 41 were due to low blood pressure, 2 due to hypotension with clinical symptoms, and 1 due to clinical symptoms without low blood pressure.

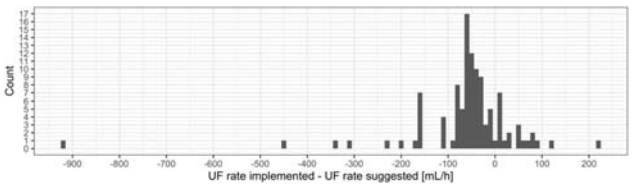


Figure 1. Distribution of the differences between UF rates suggested by the feedback controller and those implemented by the healthcare team for the 25 study treatments (11 subjects) where the staff chose to override the Controller.

Conclusion:

The proportion of UFR recommendations generated by this UFR Feedback Controller that were accepted by the nurses was very high (≈90%). Importantly, of the relatively few cases where nurses chose to override the Controller's recommendation, the majority (≈60%) were due to "staff preference" in the absence of low blood pressure or clinical symptoms. The high rate of "staff preference" overrides is likely owed to the fact that, for this study, the nurses exclusively attended to only one patient (the study subject) at a time for the entire HD session.

P1557 **EFFECTIVENESS OF INTERVENTION FOR SAFETY CONFIRMATION OF HEMODIALYSIS PREPARATION PROCESS**

Yasunori Higashitsuji[1], Itoko Tobita[1], Takashi Kano[1], Kumiko Shima[1], Masako Sasaki[1], Masako Ogawa[1]

[1]*Graduate School of Health Care Sciences, Jikei Institute, Osaka, Japan*

Background and Aims: It has been determined that more than half of the medical errors related to haemodialysis treatment are due to the preparation process at the initial stage of treatment, and that the errors are mainly caused by insufficient confirmation behaviour of healthcare professionals. Pointing confirmation and double check have been proven effective as safety treatments, but no specific strategy has been established to verify these insufficient confirmation behaviours. This study clarified the actual behaviour of healthcare professionals engaged in haemodialysis during the preparation process at the initial stage of treatment and defined the confirmation behaviour necessary to start safe haemodialysis based on the results. Moreover, the aim was to assess the effectiveness of an intervention program for enhancing adherence to confirmation practice.

Method: A first study was conducted to investigate the actual state of behaviour, and a second study to verify the effectiveness of an intervention program. In the first study, we monitored and analysed the actual behaviours of 23 clinical engineering technicians and 14 registered nurses at a dialysis centre during the preparation process (218 steps) at the initial stage of treatment, and calculated their adherence rates. In the second study, the final confirmation process at the initial stage of treatment was determined (13 steps), and an intervention program aimed at adherence was devised. To verify its effectiveness, 18 clinical engineering technicians and 8 registered nurses were randomly divided into an experimental group (E) and a control group (C). The intervention program for Group E comprised baseline without intervention, intervention 1 (verbal explanation of confirmatory behaviour), intervention 2 (adding graphic feedback), intervention 3 (adding video feedback), and follow-up without intervention. That of Group C comprised only baseline and intervention 1. The adherence rate to the final confirmation process in both groups was calculated.

Results: In the first study, the adherence rate to the preparation process at the initial stage of treatment was 67.2%, and the adherence rate in the confirmation process immediately after the start of dialysis was 21.0%, which was remarkably low. In the second study, the adherence rate to the final confirmation process in Group E was 17.1% at baseline, 45.5% after intervention 1, 65.5% after intervention 2, 90.4% after intervention 3, and 93.9% at follow-up. In contrast, the adherence rate in Group C was 8.6% at baseline and 50.4% after intervention 1.

Conclusion: The adherence rate to the preparation process at the initial stage of treatment was less than 70%. Furthermore, the intervention program using graphic feedback and video feedback increased the adherence rate to the final confirmation process. Intervention programs aimed at the behaviour modification of healthcare professionals involved in haemodialysis have increased the adherence rate to confirmation actions in the final confirmation step of haemodialysis, and it has become clear that verbal teaching and visualized feedback are effective.

P1558 THE "HOME JAIL HEMODIALYSIS" PROJECT IN MILAN, ITALY: AN UNIQUE EXPERIENCE ABLE TO SAVE MONEY AND IMPROVE SECURITY

Laura Cosmai[1], Matteo Stocco[2], Cesare Lari[2], Andrea Galassi[1], Andrea Stucchi[1], Ulisse Zoni[1], Michela Ippolito[1], Michela Frittoli[1], Mario Cozzolino[3]

[1]ASST Santi Paolo e Carlo, San Paolo Hospital, Nephrology and Dialysis, Milan, Italy, [2]ASST Santi Paolo e Carlo, San Paolo Hospital, Milan, Italy and [3]university of Milan, Department of Health Sciences, Milan, Italy

Background and Aims: Chronic kidney disease (CKD), and especially end-stage renal disease (ESRD) are relevant worldwide public health problems, since they are linked to poor quality of life, serious adverse health outcomes (including cardiovascular diseases, infections, duration of hospitalization and, more importantly, overall mortality), as well as increased healthcare costs. Moreover, renal replacement therapy with either dialysis (both hemodialysis and peritoneal dialysis) or kidney transplantation represents the economic burden of ESRD, which continues to grow substantially. Future projections are for an increasing prevalence of ESRD globally. Worldwide, more than 2.5 million people were treated for ESRD in 2015, and this number is projected to more than double, thus reaching the astonishing number of 5 million by 2030.

Method: In our San Paolo Hospital, in Milan, a Division of Penitentiary Medicine has been established, allowing us to serve, with wide medical and surgical support, all the four prisons present in the Milan area, since several years. During the last decade, we were required to comprehensively manage renal patients as well. In particular, we followed also a number of ESRD patients on replacement treatment with hemodialysis thrice weekly. The Dialysis Unit received prisoner patients and treated them under the security control of several penitentiary policemen. Among them, we had also two high-surveillance prisoners who needed as many as six higly armed policemen each for security. The presence of these agents caused a relevant discomfort to both the other patients, as well the whole medical and nursing staff. After a long period of organization, we started an innovative project called 'Home Jail Hemodialysis'. Since July 2018 until now, hemodialysis sessions for these two high-surveillance prisoners (on separate days) have been performed within one prison, with the need of just one policeman to control them. Nurses had to be provenly skilled for a comprehensive care for hemodialysis patients and were also specifically trained for the management of patients subjected to high-surveillance detention, as particular behavioral and relational precautions are obviously essential. After a run-in period, in which management protocols/procedures were shared with those of our hospital, all the activities started taking place only within the prison's Health building. The care setting includes single security rooms, with a nurse present throughout the treatment period; once monthly, a Nephrologist re-evaluates the patients, updates the treatment, and shares with the nursing coordinator all eventual issues.

Results: The feasibility and safety of this approach, aimed at integrating the penitentiary structure with the hospital with a decentralized assistance, was tested using two indicators of performance: the number of adverse events reported in 12 months (about 310 dialyses), and costs. In 12 months of observation, there were no serious adverse events. Furthermore, in just one year approximately 1,000,000 € were saved (considering that the cost of traveling to the hospital and of high-level surveillance for detained patients is close to € 500,000 per year).

Conclusion: The 'Home Jail Hemodialysis' thus appears an easy way to save money and improve security.

P1559 PERFORMANCE EVALUATION OF REAL-TIME MULTI-BED MONITORING SYSTEM FOR BLOOD LEAKAGE IN DIALYSIS

HsiangWei Hu[1], Chih-Hao Liu[2], HsuanMing Lin[3], Chou-ching Lin[4], KuanYu Chen[5], YuChih Lin[6]

[1]National Cheng Kung University, Biomedical Engineering PhD student, Tainan, Taiwan, R.O.C., [2]AcuSense BioMedical Technology Corp, Data scientist, Tainan, Taiwan, R.O.C., [3]An Nan Hospital, China Medical University, Nephrologist division, Internal medicine, Tainan, Taiwan, R.O.C., [4]National Cheng Kung University, Biomedical Engineering professor, Tainan, Taiwan, R.O.C., [5]AcuSense BioMedical Technology Corp, CEO, Tainan, Taiwan, R.O.C. and [6]AcuSense BioMedical Technology Corp, Project manager, Tainan, Taiwan, R.O.C.

Background and Aims: In HD treatment, venous needle dislodgement (VND) is a major concern in healthcare systems worldwide. Although VND is not an extremely common occurrence, it could be life-threatening or even cause death. The report of the Taiwan Patient Safety Reporting System listed the dislodgement of needles, catheters, and similar devices as third among thirteen common incident types that threaten patient safety. Hospitals are jointly liable for the blood leakage and have to provide emergency treatment such as emergency hemostasis, blood transfusion, Erythropoietin (EPO) injection and hospitalization. To a worse extent, hospitals, physicians and paramedics have to face criminal charges and the claims raised by the patients' families.

This study employed digital technology to develop a real-time multi-bed monitoring system to detect fluid leakage and control the state of multi-bed blood leakage simultaneously, allowing paramedics to respond to and solve issues swiftly. The research evaluated the IoT system for the leakage detector system with multi-bed monitoring interface by clinical trials.

Method: Our research used the Acusense IoT platform, which is a multi-bed monitoring system that includes leakage detection device, IoT gateway, and cloud analysis system to monitor multiple HD patients in real-time. Any single IoT gateway can be utilized to pair with eight blood leakage detection devices and collects data with multi-point Bluetooth 4.2, and the information gathered by IoT gateway will be uploaded to database via WiFi.

The selecting criteria for participants, who has low risk of blood leakage and the participants who did not have blood leakage within two months, were all excluded from our analysis. Before a clinical trial, 20 nurses were trained to use the leakage detection system for two times. And then we have set this platform on different areas for 1 month.

For the results of blood leakage detection system in the clinical settings, we calculated accuracy, recall, precision, and averaged F score, which are the most common metrics for evaluating the performance of binary classification.

Results: In this study, a total of 50 subjects with an average age and standard deviation (SD) of 62.2 and 9.1 were recruited from the Tainan Municipal An-Nan Hospital (TMANH) in Taiwan. After deploying Acusense IoT platform in clinical workflow, there were a total of 682 dialysis sessions and 15 events of venous needle dislodgement or bleeding occurred of which 13 were detected by the device. The performance metrics reach 99.7% accuracy, 100% recall, 99.7% precision, and 99.9% Averaged F-measure. There are no adverse reactions to patients. It indicates that the proposed blood leakage detection system showed favorable performance, and was proven to be capable of accurately detecting blood leakage.

Conclusion: The blood leakage detector combined with information system realizes the multi-bed monitoring system and provides support for real-time clinical decision support system. When venous needle dislodgement happens, the monitoring system will timely warn nurse to increase the relationship between doctors and patients. It may result in the prevention of VND, and decreased hospitalization to reduce the side effects of hemodialysis.

Table 1 Confusion matrix

		True Condition	
		Condition Positive	Condition Negative
Predicted condition	Predicted condition positive	667	2
	Predicted condition negative	0	13

Table 2 performance metrics

Accuracy = (TP + TN) /(TP + TN + FP + FN)	99.7%
Recall = TP / (TP+FN)	100%
Precision = TP / (TP+FP)	99.7%
Averaged F-measure = 2 * TP /(2 * TP + FN + FP)	99.9%

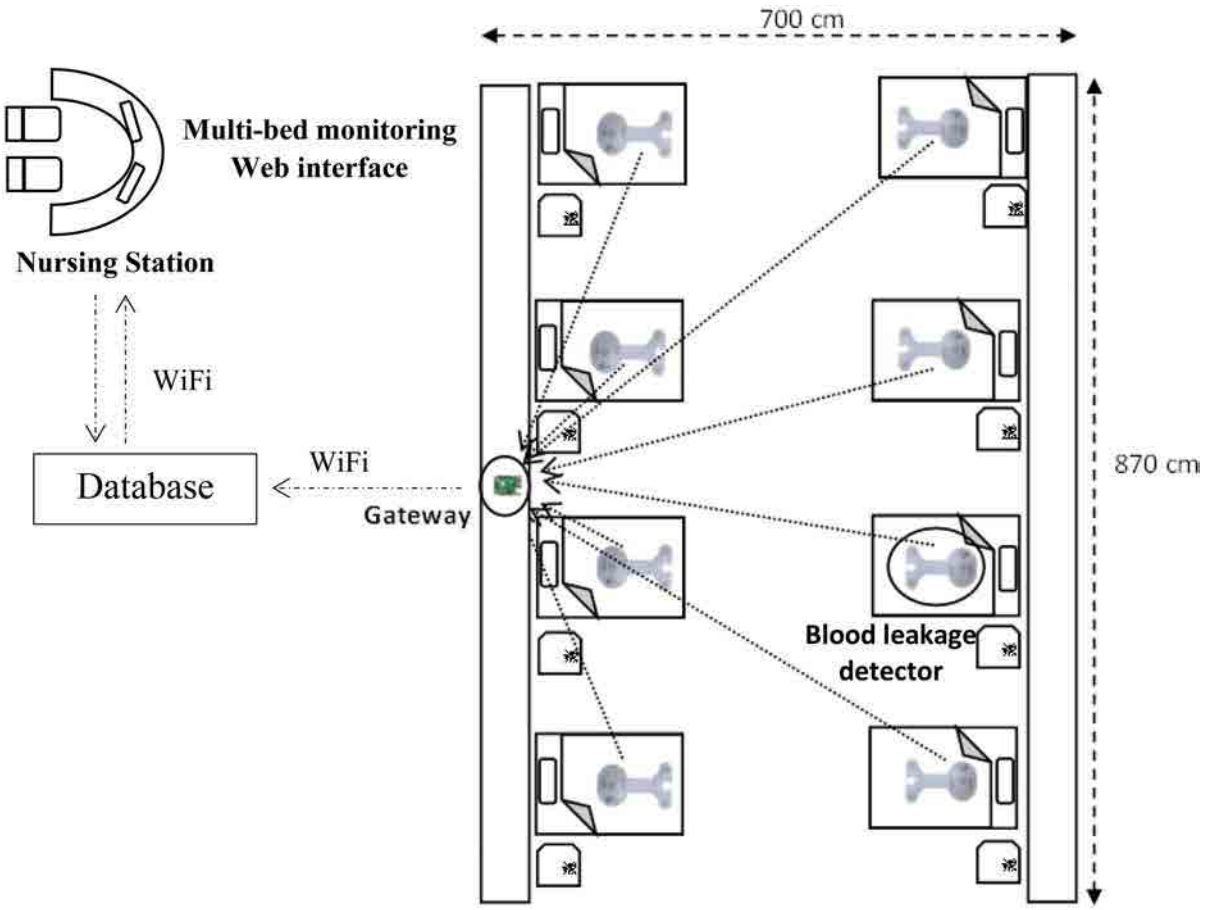


Figure 1. Clinical field configuration **The direction of arrow indicates the direction of information flow.**

P1560 **ANXIETY AND DEPRESSION AMONG HEMODIALYSIS PATIENTS**

Helaoui Fadwa[1,1]

[1]*Hospital Charles Nicolle, nephrology, Tunis, Tunisia*

Background and Aims: Procedure of haemodialysis (HD) treatment is associated with an impaired quality of life in chronic kidney disease patients. It is due to changes in family, social and professional relationships. These changes can also lead to mental health problems. The purpose of our study is to determine the prevalence of depressive and anxiety disorders in hemodialysis patients.

Method: Fifty chronic hemodialysis patients were enrolled in our cross-sectional study during four months (September -October- November- December 2019). The HADS (Hospital Anxiety and Depression Scale) survey was used to assess depressive and anxiolytic disorder in our hemodialysis population. Were excluded patients aged less than 18 yearsold as well as kidney transplant patients and psychiatric patients.

Results: The mean age of our patients was 49.5 range (24-79).The sex ratio was 1.27. The prevalence of anxiety syndrome was 40% with a female predominance of 54.5% versus 54,5%. Depressive syndrome was noted in 48% of our patients with a male predominance of 58.3% versus 41,7%.

48% of our HD patients have shown depression in various degrees. It was about mild depression of 20,8% of pts, moderate depression of 41,6% of pts and severe depression of 37,5% of pts. Somatic symptoms of depression in our population were respectively noted in 52,8% of loss of energy, 57,5% fatigue, 63,4% sleep disturbances, and 38,5% changes in appetite. The most common psychological symptoms were: pessimism (79,1%), loss of interest in appearance (41,6%), psychomotor retardation (75%).

On the other hand, 37, 5% of patients felt cheerful and 16,6% still enjoy doing some activities. For patients with anxiety syndrom, we noted: concentration disturbance (45,4%), palpitations (50%), abdominal pain (59,09%) and headache (81,8%).

With regard to psychological symptoms, the most emphasized were: sudden feelings of panic (54,5%), worrying thoughts (72,7%),77,2% are feeling restless and 59,09% are feeling wound up.

On the other hand, 68,1% feel relaxed especially after the hemodialysis session. It seems that gender, marital status and HD duration did not influence significantly in occurrence of depression with respectively (p=0,08, p=0.1 and p= 0.08). Older patients were significantly more depressed in compared to younger patients (p= 0.003). Unemployed patients were significantly more depressed in relation to employed patients(p=0.01). Finally, as the educational level of patients increased, level of depression significantly decreased (p=0,04).

Conclusion: Depression is the most frequent psychological complication of hemodialysis (HD) patients. Our results showed a high prevalence of depressive symptoms among the study group. The exact prevalence of depression in dialysis patients is unclear because of different criteria utilized for diagnosis of depression. A close collaboration between nephrologists and psychiatrists is needed to ensure a better quality of life in HD patients.



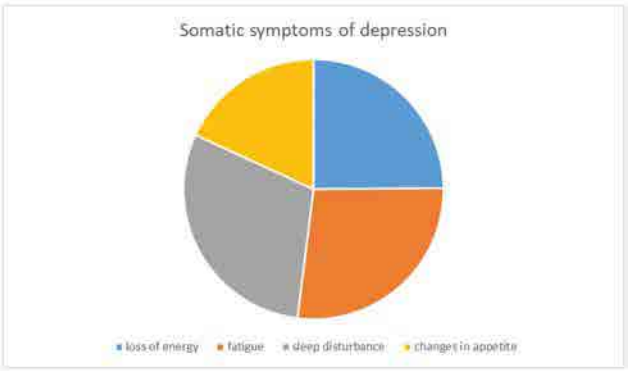


Figure:

P1561

PREVALENCE OF DEPRESSION IN PATIENTS ON MAINTENANCE HAEMODIALYSIS AND FEASIBILITY OF GROUP BASED COGNITIVE BEHAVIOURAL THERAPY - A SINGLE CENTRE EXPERIENCE

Ishthiaque Ahmed[1], Ganesh Srinivas[1], Diwakar Goutham[2], Annapandian V. M[3]

[1]*Mazumdar Shaw Medical Center, Department of Nephrology, Bangalore, India,*
[2]*Mazumdar Shaw Medical Center, Department of Psychiatry, Bangalore, India and*
[3]*Narayana Hrudayalaya Foundations, Department of Pharmacology, Bangalore, India*

Background and Aims:

The reported prevalence of depression in dialysis population ranges from 20-45%, which varies across regions. Limited data are available on association with co-morbidities, clinical symptoms and quality of life, especially from India. Present study was aimed to explore the prevalence of depression in patients on maintenance haemodialysis, quality of life and feasibility of group based cognitive behavioural therapy (CBT) in this set of patients.

Method:

This is a single centre prospective study conducted at a tertiary care referral hospital, Bangalore, India, over the period of 22 months (Dec-2017 to Apr-2019). Patients aged >18 years and on maintenance haemodialysis for >6 months were included in the study. Any patients with known psychiatric illness or substance abuse were excluded. Beck depression inventory (BDI) score and quality of life by kidney disease quality of life short form-36 (KDQOL-SF) were used for diagnosis of depression. Group based CBT is offered to patients with mild to moderate depression.

Results:

A total of 100 (85 males) patients were studied, the mean±SD age was 54.0±12.9 years (range, 23-76). Forty-six (46%) patients had depression (mean BDI score 35.04±10.8), out of whom, 8 (17.4%) had mild depression, 6 (13.1%) had moderate depression, 14 (30.4%) had severe depression and 18 (39.1%) people had extreme levels of depression. Females, unemployed and retired persons, low socioeconomic status and frequent dialysis related complications are more prone for depression.

Age, dialysis vintage, duration from diagnosis to dialysis, associated co-morbid conditions, frequency of emergency dialysis requirement, hospitalization rates did not significantly differ in both groups. Low serum phosphate levels and high Kt/V values had association with depression, while haemoglobin, serum albumin and serum calcium levels did not have association with depression. We were unable to complete the group based CBT due to medical and social reasons.

Conclusion:

Depression is common in haemodialysis patients, patients with depression had poor medication compliance and lower quality of life. Group based CBT is not feasible due to high attrition rates.

P1562

IMPLEMENTATION FOR INTEGRATED PROGRAM OF HEMODIALYSIS VASCULAR ACCESS PUNCTURE TRAINING AND AN ALARM SYSTEM MAY REDUCE THE INCIDENT OF VENOUS NEEDLE DISLODGMENT AND BLEEDING

Chi-Yang Hsin[1], HsuanMing Lin[2], KuanYu Chen[3], YuChih Lin[3], HsiangWei Hu[4]

[1]An Nan Hospital, China Medical University, Tainan, Taiwan, Internal medicine, Tainan city, Taiwan, R.O.C., [2]An Nan Hospital, China Medical University, Tainan, Taiwan, Nephrologist division, Internal medicine, Tainan City, Taiwan, R.O.C., [3]AcuSense BioMedical Technology Corp., Tainan City, Taiwan, R.O.C. and [4]National Cheng Kung University, Department of Biomedical Engineering, National, Tainan city, Taiwan, R.O.C.

Background and Aims: A puncture of vascular access is commonly used in clinical treatment, such as hemodialysis or central venous catheters. At this time, leakage or infection associated with Venous needle dislodgement(VND) is a high risk of fatality, especially for patients with restlessness, impaired cognition, isolation, or home dialysis. In general dialysis procedures, medical personnel relies on patient reports and caregivers to manually inspect the site of dialysis puncture and detect the occurrence of needle removal and blood transfusion. There are some devices for detecting the presence of needle dislodgement in the market. Still, there are no large-scale reports for the integrated program for nursing training and device implantation. This study aims to conduct a program for an integrated training course and the VND device and hopes to reduce the incidence of needle removal and blood leakage.

Method: This study was divided into two phases, the control phase, and the study period. In the first phase, the abnormal events of ou venous needle dislodgement and blood leakage was recorded in the hemodialysis unit room during the first three months. Before the study period, we introduced an integrated program, including the standard process of fistula puncture, care during hemodialysis, an inspection of the venous puncture site, and an alarm system. In the study period, we also conducted the standard program and collected the data of the events of venous dislodgement or bleeding.

Results: The control phase was conducted during the three months from July 2019 to September 2019, and the study period was performed in November 2019. A total of 62 patients completed the study. During the control period, there were a total of 2087 dialysis treatments, of which 30 patients had venous needle dislodgement or bleeding. There were a total of 70 events of venous needle dislodgement or bleeding occurred, and the incidence rate was 3.3 events per 100 sessions. After the conduction of the integrated program and implantation of the alarm system in November 2019, there were a total of 682 dialysis sessions, and 15 events of venous needle dislodgement or bleeding occurred. The incidence rate was 2.2 events per 100 courses.

Conclusion: This study introduced venous needle dislodgement or bleeding alarm system in the hemodialysis unit. Compared with the traditional method, after the integrated care program, including fistula puncture, care, inspection, introduction, and use of the alarm system, venous needle dislodgement or bleeding dropped from 3.3 to 2.2 per 100 sessions. Therefore, through standardized training and program, it may be related to the decrease in the incidence of venous needle dislodgement or bleeding. This training mode can be worth promoting to more dialysis units to improve the quality of patient care. More follow-up studies are needed to provide multiple evidence.

P1563

THE ANALYSIS OF RISK FACTORS FOR THE PATIENTS EXPERIENCED VENOUS NEEDLE DISLODGEMENT OR BLEEDING DURING DIALYSIS

Hsiu Wen Wu[1], HsuanMing Lin[2], KuanYu Chen[3], YuChih Lin[3], HsiangWei Hu[4]

[1]I-Shou University, Executive Master Program Department of Healthcare Administration, Kaohsiung City, Taiwan, R.O.C., [2]An Nan Hospital, China Medical University, Tainan, Taiwan, Nephrologist division, Internal medicine, Tainan City, Taiwan, R.O.C., [3]AcuSense BioMedical Technology Corp., Tainan City, Taiwan, R.O.C. and [4]National Cheng Kung University, Department of Biomedical Engineering, National, Tainan city, Taiwan, R.O.C.

Background and Aims:

A puncture of vascular access is commonly used in clinical treatment, such as hemodialysis or central venous catheters. At this time, leakage or infection associated with Venous needle dislodgement(VND) is a high risk of fatality, especially for patients with restlessness, impaired cognition, isolation, or home dialysis. At present, a few studies believe that many risk factors are associated with venous needle dislodgment and bleeding, including difficult needle fixation, restlessness, unconsciousness, or abnormal movement. However, only a few studies are focusing on patient disease, medication, and other risk assessments. Therefore, this study aims to explore the risk factors of patients with venous needle dislodgment and bleeding and hope to establish the risk classification.

Method:

This study was a prospective study conducted in the hemodialysis room of Tainan Regional Hospital. Before starting to collect the venous needle dislodgment and bleeding data, we performed a training program for medical and nursing staff, including venous puncture, fixation, puncture site assessment, and management. During the three months from July 2019 to 2019/9, we collected clinical data were collected, including patient sex, gender, diseases, records of dialysis access blockage, anticoagulant dose, and a high-risk assessment record (eight risk factors). Finally, we analyzed the data and compared the data between the two groups of patients who experienced needle dislodgement and bleeding. We applied statistical software STATA, chi_square, z-test. $P<0.05$ was defined as significant.

Results:

Seventy patients were included in this study, with an average age of 63.23 ($\pm$ 1.2 years) and 45 males (64.28%). In 2019 / 7-9, there were a total of 32 patients with 72 venous needle dislodgment and bleeding. The patients with the condition as below were considered high-risk patients. In terms of gender, whether it is a high risk, diabetes, high blood pressure, whether to use sleeping pills, diabetic hypotension, whether to use warfarin or to use anticoagulant doses are all not statistically significant. The proportion of patients with vascular-access and undergoing percutaneous transluminal angioplasty was 35.2% (11) in high-risk patients and 10.3% (4) in low-risk patients, $p<0.01$.

Conclusion:

Before data collection in this study, a standardized training program was performed for medical care and vascular access monitoring. However, there were no new risk factors were found. This research model can provide a new direction for further research.

Table 1 Association bewteen Venous Needle dislodgement and bleeding and other risk factors.

	Control(38 patients)	VND(32 patients)	P-Value
Male	27 (71.1%)	18 (56.3%)	0.19 [b]
Age	63.23±0.16	62.65±0.17	0.02[a] *
Q1	5	4	
Q2	0	1	
Q3	3	0	
Q4	0	0	
Q5	1	0	
Q6	0	1	
Q7	16	10	
Q8	2	1	
High Risk	19	12	0.29 [b]
PTA	9	6	0.61 [b]
DM	23	23	0.31 [b]
HTN	23	24	0.19 [b]
BZD exposure	6	8	0.33 [b]
Intradialytic hypotension	12	5	0.12 [b]
Wafarin	8	7	0.57 [b]
Anti-coagulation dose[c]	1013.19	1247.5	0.17 [a]

[a] Z-test

[b]chi-square test

[c]Innohep Equalibrition dose

*significant

Table 2 Risk assessment

No	Risks	Positive
1	Frequent intradialytic muscle cramping	9
2	Conscious disturbance or confused	1
3	Difficult vascular access puncture or required to re-do needle pucture	3
4	Venous needle dislodgment in recent three months	0
5	Difficult to fix needle	1
6	Allergy to tape for fixation of needle	1
7	The towel or quilt usually covered the injection site	26
8	Frequently pause of hemodialysis to go to rest-room	3
	Any of above	31

P1564 SLEEP QUALITY ASSESSMENT ON HÉMODIALYSIS

Cheikh Maha[1], Chargui Soumaya[1], Ben hmida Fathi[1], Ben abdallah Taieb[1]

[1], *Tunis, Tunisia*

Background and Aims: sleep disorders are a major public health problem, affecting the majority of patients with end-stage chronic kidney disease.

The purpose of this work is to assess the quality of sleep and identify the associated factors.

Method: This is a single-center cross-sectional study of 57 patients on conventional hemodialysis. Clinical screening was conducted using the Epworth Sleepiness Scale.

Results: The average age of the patients was 53.43 years (between 25 and 82 years), with a sex ratio of 1.08. The socio-economic level was considered bad in 70% of the cases. The main co-morbidities are hypertension in 50.8% of cases and diabetes in 24.5% of cases. The average seniority on hemodialysis was 7.47 years. 53% of patients had sleep disorders and they were insomnia in 39% of cases, daytime sleepiness in 59% of cases of which it was excessive (Epworth score> 15) in 15% of cases, a syndrome restless legs in 3% of cases and obstructive sleep apnea with snoring in 13% of cases.

Conclusion: The prevalence of sleep disorders is higher in hemodialysis patients than in the general population, and they are associated with a non-negligible cardiovascular risk, hence the importance of early detection and adequate management, thereby improving the quality of life of these patients.

Nephrology Dialysis Transplantation 35 (Supplement 3): iii1885–iii1919, 2020

DIALYSIS. PROTEIN ENERGY WASTING, INFLAMMATION AND OXIDATIVE STRESS

P1565

THE COMBINATION OF MALNUTRITION-INFLAMMATION AND LIMITATIONS IN FUNCTIONAL STATUS IS ASSOCIATED WITH A HIGH RISK OF MORTALITY IN HEMODIALYSIS PATIENTS: RESULTS FROM THE DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY.

Eiichiro Kanda[1], Marcelo Lopes[2], Angelo Karaboyas[2], Brian Bieber[2], Kazuhiko Tsuruya[3], Hideki Hirakata[4], Kunitoshi Iseki[5], Stefan Jacobson[6], Indranil Dasgupta[7], Bruce Robinson[2]

[1] Kawasaki Medical School, Medical Science, Okayama, Japan, [2]Arbor Research Collaborative for Health, DOPPS, Ann Arbor, United States of America, [3]Nara Medical University, Department of Nephrology,, Nara, Japan, [4]Fukuoka Renal Clinic, Nephrology, Fukuoka, Japan, [5]Yuuaikai Tomishiro Central Hospital, Division of Nephrology, Tomigusuku, Okinawa, Japan, [6]Karolinska Institutet, Danderyd University Hospital, Department of Clinical Sciences, Stockholm, Sweden and [7] University of Warwick, Heartlands Hospital Birmingham and Warwick Medical School, Conventry, United Kingdom

Background and Aims: The malnutrition-inflammation-complex (MIC) is a risk factor for mortality and lower quality of life in haemodialysis (HD) patients. The identification of MIC and its risk factors, which include the limited ability to perform functional status (FS), is key to improve the patient experience on HD. Our study investigates the association of MIC and FS combinations with mortality in HD patients.

Method: We analysed data from a cohort of 5465 HD patients from Australia, France, Germany, Italy, Japan, New Zealand, Spain, Sweden, and United Kingdom, enrolled in the Dialysis Outcomes and Practice Patterns Study phases 4 (2009-2011) and 5 (2012-2015). MIC syndrome was defined as low serum albumin (<3.8 g/dL) and high serum C-reactive protein (>3mg/L in Japan; >10 mg/L elsewhere). Poor functional status was defined as the sum of scores from the self-reported limitations in the Katz Index of Independence in Activities of Daily Living (score ranges from 0 to 5) and the Lawton-Brody Instrumental Activities of Daily Living Scale (score ranges from 0 to 8) less than 11. We investigated the association between combinations of MIC (+/-) and FS (low/high) with death, using Cox proportional hazards models adjusted for possible confounders including patient demographics, comorbidity history, catheter use, serum creatinine, phosphorus levels, WBC count, haemoglobin level, and time on dialysis therapy.

Results: The prevalence of different combinations were: MIC-/High FS 57%, MIC-/Low FS 24%, MIC+/High FS 9%, and MIC+/Low FS 10%. Patients with MIC-/high FS were younger, better nourished, and had lower prevalence of comorbidities. Compared to this reference group, the adjusted hazard ratios [HR (95% CI)] for all-cause mortality were 1.56 (1.24-1.98) for MIC-/ low FS, 1.75 (1.32-2.32) for MIC+/ high FS, and 2.97 (2.31-3.82) for MIC+/ low FS groups. The adjusted HRs for infection-related mortality were 1.57 (0.91, 2.71) for MIC-/low FS, 1.67 (0.84, 3.31) for MIC+/High FS, and 5.45 (3.15, 9.45) for MIC+/low FS groups.

Conclusion: The combination of MIC and low FS is a strong predictor of mortality, and infectious mortality in particular, in HD patients. Identification of patients with MIC and FS status may plausibly help to direct interventions to improve patients' experiences and lessen adverse clinical outcomes in the HD setting.

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P1566 **SKELETAL MUSCLE MASS BY COMPUTED TOMOGRAPHY AT THE LEVEL OF THE THIRD LUMBAR VERTEBRA AND MORTALITY IN END-STAGE KIDNEY DISEASE**

Alice Sabatino[1,2], Giuseppe Regolisti[1,2], Marco Delsante[1,2], Tommaso Di motta[1,2], Alice Parmigiani[2], Francesco Peyronel[1,2], Umberto Maggiore[1,2], Enrico Fiaccadori[1,2,2]

[1]Parma University Medical School, Nephrology Unit, Department of Medicine and Surgery, Italy and [2]University of Parma, Postgraduate School in Nephrology, Parma, Italy

Background and Aims: Protein-Energy Wasting (PEW) is highly prevalent in patients with end-stage kidney disease on chronic hemodialysis (ESKD-HD). In such clinical setting PEW is associated to poor outcomes. The assessment of nutritional status is essential for the identification of patients at risk for the development of PEW. In the contest of nutritional evaluation, increasing attention is currently paid to the assessment of muscle mass, which represent the major protein asset in the body. Currently available bedside tools used for the assessment of nutritional status are not accurate enough for the assessment o skeletal muscle mass. In this clinical setting, the use of "gold standard" imaging methods (such as CT sca, DEXA or MRI) could allow a more accurate assessment of body composition. The aim of our study was to assess the correlation between skeletal muscle mass on the level of the third lumbar vertebra (L3) assessed by CT scan with mortality in ESKD-HD.

Method: In a retrospective observational study, 1260 ESKD-HD patients undergoing chronic hemodialysis treatment were identified between 2008 and 2015 in the Dialysis Centers of the National Health Service in the province of Parma. Among these patients, those with at least one available abdomen CT scan after the patient had already been on dialysis for at least 6 months were enrolled. The CT images obtained at the level corresponding to the L3 were analyzed using a dedicated software, in order to extrapolate the data related to the quantity of skeletal muscle tissue.

Results: We enrolled 183 ESKD-HD patients, aged 68.8 (± 15.1) yrs, 64% (117/183) males, median hemodialysis vintage 43.9 (range 6 – 208) months. The cohort was characterized by a high comorbidity burden, with a median Charlson Comorbidity Index of 9 (range 2-17). Baseline skeletal muscle mass at L3 was 118.5 cm^2 (± 30.6). Median follow-up was 65.6 (range 6.6 – 132.5) months. During follow-up, 67% (122/183) of patients died.

Patients were divided based on quartiles of muscle mass. Patients in the first quartile had 83% mortality, while mortality of patients in the fourth quartile was 52% (OR = 4.16 95% CI = 1.59 – 10.87; P = 0.003). Kaplan-Meier analysis identified significantly lower survival in patients in the first quartile of muscle mass compared to those in the fourth quartile (P = 0.03 at the Mantel-Cox Log-rank test) (Figure 1).

Conclusion: Low muscle mass by CT scan appears to be associated with an increased risk of mortality in ESKD on chronic hemodialysis.

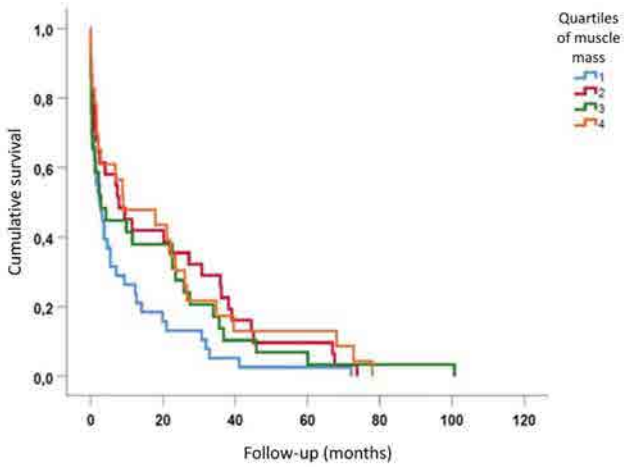


Figure 1. Cumulative survival of ESKD patients on hemodialysis divided by quartiles of muscle mass.

P1567 **THE ANNUAL VARIATION OF CRA/ALBUMIN RATIO IS AN ACCURATE PROGNOSTIC FACTOR IN DIALYSIS PATIENTS**

Kaoru Yasuda[1], Hiroshi Takahashi[2], Kunio Morozumi[3], Shoichi Maruyama[4]

[1]Masuko memorial hospital, Nephrology, Nagoya, Japan, [2]Fujita Health University, Nephrology, Japan, [3]Masuko Memorial Hospital, Nephrology, Japan and [4]Nagoya University, Nephrology, Japan

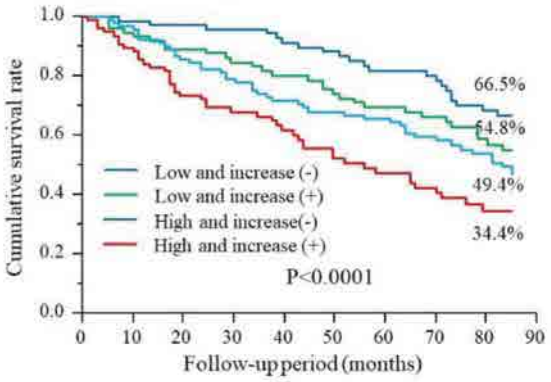
Background and Aims: Protein energy wasting (PEW) is a distinctive malnutrition status in hemodialysis(HD) patients, and it is closely related to poor prognosis. We previously reported that CRP/Alb ratio is useful marker for assessment of malnutrition status in HD patients. However, the value of CRP/Alb ratio calculated by CRP and serum albumin level is considered to be varied over time, and correlation between the amount of change and the prognosis is uncertain. The purpose of this study is to investigate the effect of the changing in CRP/Alb ratio within a certain period of time on prognosis of dialysis patient.

Method: 320 patients who were received stable dialysis therapy were enrolled in the study. It was analyzed that the relation between the changing in CRP/Alb ratio within one year and the prognosis. Furthermore, patients were divided by the values of CRP/Alb (>0.35) and ΔCRP/Alb ratio (>0.05) as a threshold (4 groups of 2×2), and analyzed for the prognostic value.

Results: During the observation period (median 71 months), 138 patients were died (43.1%). Baseline CRP/albumin ratio, both of continuous value and cut-off value of 0.34 as median, was identified as an independent predictor for 7-year mortality. The CRP / Alb ratio at one year increased from 0.40 (0.46-1.7) to 0.47 (0.22-1.48) ($p = 0.0040$). The 7-year survival rate was 44.7% in the group with increased ΔCRP / Alb ratio and 57.0% in the group with non-increased ($p = 0.020$). The adjusted hazard ratio was 1.45 (95% CI 1.02-2.06, $p = 0.037$, increase group vs non-increase group). On combined setting of each predictors, mortality risk was clearly stratified, and patients with high and increased CRP/albumin ratio had 2.84-fold (95%CI 1.65-5.03) higher risk of mortality compared to patients with low and no-increased CRP/albumin ratio

Conclusion: The increasing rate of CRP/Alb ratio were strong predictors of mortality as well as the baseline CRP/Alb ratio levels, and both of them additively improved the predictability for mortality in chronic HD patients.

Fig. 3 Kalan-Meier survival in groups according to baseline and 1-year increased CRP/albumin ratio



Figure

P1568 EFFECTS OF VOLUME STATUS ON BODY COMPOSITION IN INCIDENT PERITONEAL DIALYSIS PATIENTS

Seok Hui Kang[1], Jong Won Park[1], Kyu Hynag Cho[1], Jun Young Do[1]

[1]*Yeungnam University Medical Center, Internal Medicine, Daegu, Korea, Rep. of South*

Background and Aims: Volume control is the most important issue in peritoneal dialysis (PD). Inadequate fluid removal or high water intake leads to overhydration, which result in malnutrition. Sarcopenia (SP) as a result of malnutrition is more prevalent in PD than in the general population, and is associated with high mortality and low quality of life in PD patients. The aim of the present study was to evaluate the effects of volume status on body composition in incident PD patients.

Method: This retrospective study was performed at a tertiary medical center from January 2001 to March 2015. All incident PD patients who survived $\geq$1 year after PD initiation were considered eligible. 366 incident PD patients were finally included and divided into 3 tertiles according to the time-averaged-edema index (TA-EI). Edema index was calculated by dividing extracellular water values by total body water values. The mean of the EI values at 1 month and 1 year was defined as TA-EI. The body composition parameters measured using bioimpedance analysis included the EI, fat mass index (FMI, kg/m^2), and appendicular muscle mass index (AMMI, kg/m^2). dFMI and dAMMI were defined as delta values for each variable. The cutoff value for sarcopenia (SP) was defined as previously reported (The cutoff value for SP was defined as AMMI $\leq$ 7.0 kg/m^2 in men and $\leq$ 5.7 kg/m^2 in women). Patients with AMMI below the cutoff values were defined as having SP.

Results: The number of participants in the low, middle, and high tertiles was 126, 100, and 140, respectively. The TA-EI in the low, middle, and high tertiles was 0.384 $\pm$ 0.006, 0.398 $\pm$ 0.003, and 0.413 $\pm$ 0.009, respectively ($P < 0.001$). A high volume status was associated with high solute clearance, peritoneal albumin loss, and glucose absorption through the peritoneal membrane, which led to high dialysate glucose. In addition, volume status was inversely associated with increases in AMMI, but was not associated with changes in FMI. SP as a categorical variable was positively associated with a high volume status. On subgroup analyses, TA-EI had the greatest negative correlation coefficients for dAMMI.

Conclusion: Overhydration in PD patients was associated with decrease in muscle mass indices and the development of SP.

P1569 ADIPONECTIN IS ASSOCIATED WITH DECLINE IS SKELETAL MUSCLE MASS AND BONE MINERAL CONTENT IN PATIENTS ON HEMODIALYSIS

Hiroshi Ogawa[1], Toshimitsu Koga[1], Daisuke Fuwa[1], Hirofumi Tamaki[1], Takayuki Nanbu[1], Yuko Kojima[1], Yoshihiro Ota[1], Azumi Sato[2], Akihiro Kindaichi[3], Keiko Hiraga[4]

[1]Shinseikai Dai-ichi Hospital, The Department of Internal Medicine, Nagoya, Japan, [2]The Bio-Dynamics Research Institution, the Shinseikai Foundation, Nagoya, Japan, [3]Shinseikai Dai-ichi Hospital, The Department of Clinical Engineering, Nagoya, Japan and [4]Shinseikai Dai-ichi Hospital, The Department of Clinical Nutrition, Nagoya, Japan

Background and Aims: Patients on hemodialysis are prone to undernutrition, malnutrition-inflammation-atherosclerosis (MIA) syndrome, and protein-energy wasting (PEW). One of the major adipocytokines adiponectin (ADPN) is involved in anti-arteriosclerotic and anti-inflammatory processes. However, ADPN is implicated in muscle weakness and loss of muscle mass in the elderly in addition to sarcopenia.

At the 2019 ERA-EDTA Congress, we announced that total plasma ADPN levels in patients on hemodialysis (HD) showed a significant inverse correlation with BMI, body fat in percentage, mass and estimated skeletal muscle mass, and ADPN may be involved in sarcopenia in patients on HD. Herein, we investigated the association of ADPN level with sarcopenia in patients on HD using a method different from the one used in our previous study. We examined the relationship between total plasma ADPN level and the rate of change in estimated skeletal muscle mass, bone mineral content, and body fat mass over 5 years after the plasma ADPN measurement. Furthermore, we analyzed whether an elevated ADPN level was predictive of a subsequent decline in these parameters.

Method: Total plasma ADPN levels were measured using ELISA (Bio Vendor-Laboratorni Medicina a.s., Czech Republic) in 42 male patients on HD (age: 51.1 ± 9.0 years, dialysis vintage: 144.8 ± 99.2 months, BMI: 21.8 ± 3.2, dry BW: 62.0 ± 10.9 kg, dialysis time: 15.6 ± 3.1 hours/week). The estimates of skeletal muscle mass, bone mineral content, and body fat mass were made using multi-frequency bioelectrical impedance analysis (MFBIA) within the same year when total plasma ADPN level were first measured in 2011 as well as in 2016. We then calculated the rates of change in the estimated skeletal muscle mass, bone mineral content, and body fat mass over the 5 years and correlated these parameters with the total plasma ADPN measurements.

Results:

1. The total plasma ADPN level (mean ± SD) of the 42 patients on HD in 2011 was 12.45 ± 6.86 μg/ml.
2. The estimated bone mineral content in 2011 was 2.62 ± 0.34 kg, whereas in 2016 it was 2.57 ± 0.34 kg. The observed small decrease in bone mineral content was not statistically significant. However, a significant inverse correlation was observed between the total plasma ADPN level in 2011 and the rates of change in estimated bone mineral content over the following 5 years ($R = -0.333$; $P = 0.031$).
3. The estimated skeletal muscle mass of patients on HD (mean ± SD) was 21.14 ± 3.41 kg in 2011 and 20.43 ± 3.66 kg in 2016. This decrease in estimated skeletal muscle mass was not statistically significant. However, a significant inverse correlation was observed between total ADPN level in 2011 and the rate of change in the estimated skeletal muscle mass over the following 5 years ($R = -0.352$; $P = 0.022$).
4. The body fat mass (mean ± SD) of patients on HD was 18.51 ± 7.77 kg in 2011 and 16.39 ± 8.82 kg in 2016. Thus, body fat mass decreased over the examined 5-year period; however, this change was not statistically significant. In this case, no significant correlation was observed between total plasma ADPN level in 2011 and the rate of change in body fat mass over the following 5 years ($R = -0.013$; $P = 0.93$).

Conclusion: Total plasma ADPN levels inversely correlate with larger rates of decrease in estimated skeletal muscle mass and bone mineral content in patients on HD. This suggests that ADPN may play a role in the decline in skeletal muscle mass and bone mineral content over time in patients on HD.

P1570 **INTERLEUKIN-6 (RS1800795) AND PENTRAXIN 3 (RS2305619) GENETIC POLYMORPHISMS AND THEIR RELATION WITH INFLAMMATION AND ALL-CAUSE MORTALITY IN ESRD PATIENTS ON DIALYSIS**

Susana Rocha[1], Maria João Valente[2], Susana Coimbra[2,3], Cristina Catarino[2], Petronila Rocha-Pereira[2,4], Maria do Sameiro Faria[2,5], José Gerardo Oliveira[6,7], José Madureira[8], João Carlos Fernandes[9], Vasco M.P. Miranda[10], Luís Belo[2], Alice Santos-Silva[2], Elsa Bronze-da-Rocha[2]

[1]LAQV, REQUIMTE, Laboratory of Applied Chemistry, Department of Chemical Sciences, Porto, Portugal, [2]UCIBIO, REQUIMTE, Laboratory of Biochemistry, Department of Biological Sciences, Porto, Portugal, [3]CESPU, Institute of Research and Advanced Training in Health Sciences and Technologies (IINFACTS), Gandra PRD, Portugal, [4]Health Science Research Centre, University of Beira Interior, Covilhã, Portugal, [5]Hemodialysis Clinic of Felgueiras, Felgueiras, Portugal, [6]Hemodialysis Clinic of Porto, Porto, Portugal, [7]Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal, [8]NefroServe, Hemodialysis Clinic of Barcelos, Barcelos, Portugal, [9]NefroServe, Hemodialysis Clinic of Viana do Castelo, Viana do Castelo, Portugal and [10]Hemodialysis Clinic of Gondomar, Gondomar, Portugal

Background and Aims: Chronic inflammation plays an important role in progression and outcome of chronic kidney disease (CKD) patients. The interleukin-6 (IL-6) polymorphism, rs1800795, is a single nucleotide polymorphism (SNP) in the promoter region (-174G/C) that regulates gene transcription and affects the levels of this cytokine. Genetic variants in the promotor region have been associated with a poor outcome in several pathologies, namely in coronary artery disease. Pentraxin 3 (PTX3) is an inflammatory protein, produced locally by different cell types (e.g. mononuclear phagocytes, dendritic cells, fibroblasts and endothelial cells). PTX3 polymorphism, rs2305619, is a SNP (+281A>G) in the intron 1 of PTX3 gene. PTX3 polymorphisms have been described as risk factor for development of coronary artery disease and for an impairment of kidney function. Our aim was to determine the allelic frequencies of IL6 and PTX3 in end-stage renal disease (ESRD) patients and controls, as well as their relationship with the inflammatory response.

Method: We studied 289 ESRD patients on hemodialysis (high-flux hemodialysis or hemodiafiltration) and 22 healthy individuals, matched for gender, body mass index, and, as far as possible, for age. Real-Time PCR TaqMan SNP genotyping assays were used to assess allelic frequencies of IL6 (rs1800795) and PTX3 (rs2305619). We evaluated the circulating levels of PTX3, growth differentiation factor (GDF)-15, high-sensitivity C-reactive protein (hsCRP), IL-6, tumor necrosis factor-alpha (TNF-α), soluble TNF receptor 2 (sTNFR2), hepcidin and transferrin, using commercially available kits. Deaths occurring along 1-year follow-up period were recorded and mortality rates were evaluated for homozygous and heterozygous alleles.

Results: Compared to controls, all inflammatory biomarkers were significantly higher in ESRD patients. Allelic frequencies in ESRD patients and controls were similar for both SNPs, IL-6 -174G/C and PTX3 +281A>G, considering the homozygous and the heterozygous alleles. For the IL-6 -174G/C, the CC patients, compared to GG and heterozygous patients, showed significantly higher GDF-15 and CRP concentrations and significantly lower values of transferrin; moreover, we found that CC patients presented a trend towards higher mortality rate (21%, 10% and 7% for CC, GG and GC, respectively; P=0.072). For PTX3 +281A>G polymorphism, the AA patients, compared to GG and heterozygous patients, presented higher hsCRP; no significant differences were found in mortality rate between different allele carrier groups (P=0.703).

Conclusion: Although no differences were found in the allelic frequencies between controls and ERSD patients, the CC patients for IL6 polymorphism (rs1800795) and AA patients for PTX3 polymorphism (rs2305619), showed an enhanced inflammatory response; the association of the IL6 polymorphism with a higher mortality needs further studies.

P1571 **WEEKLY VERSUS MONTHLY ORAL CHOLECALCIFEROL ON OXIDATIVE STRESS AND INFLAMMATORY MARKERS IN HEMODIALYSIS PATIENTS: A PROSPECTIVE RANDOMIZED TRIAL.**

Mona Alshahawey[1], Lamia ElWakeel[1], Tamer El Said[2], Nagwa Sabri[1]

[1]Faculty of Pharmacy - Ain Shams University, Clinical Pharmacy and [2]Faculty of Medicine - Ain Shams University

Background and Aims: Vitamin D deficiency is now considered a global problem in general population, but it seemed to be more prominent in chronic kidney disease (CKD) patients, especially those on regular hemodialysis. Being a key regulator in mineral metabolism, there's also emerging evidences linking vitamin D deficiency with inflammation and oxidative stress, which are both recognized as constant threats to cardiovascular outcomes in hemodialysis patients. However, data is still limited regarding an exact treatment protocols or regimens for vitamin D supplementation in such category.

Method: A prospective, randomized trial was carried out to evaluate the effect of weekly versus, monthly oral cholecalciferol, on vitamin D (25(OH)D) levels, oxidative stress markers, inflammatory markers and secondary hyperparathyroidism in hemodialysis patients. Fifty eligible hemodialysis patients were randomly assigned to either Group A (Oral 50.000IU Cholecalciferol, once weekly) or Group B (Oral 200.000IU Cholecalciferol, once monthly), for 3 months. Serum levels of (25(OH)D), serum malondialdehyde (MDA), serum superoxide dismutase (SOD), serum high sensitive (hsCRP), calcium, phosphorus, and parathormone (PTH) levels, were all assessed at baseline and at the end of the study.

Results: Cholecalciferol significantly increased serum levels of 25(OH)D in both groups, with a higher significant increase ($p = 0.003$) in Group A vs. Group B. Only Group A had a significant decrease in both serum MDA and serum hsCRP levels ($p < 0.001$), while it had a significant higher increase ($p = 0.011$) in serum SOD when compared to Group B. Regarding PTH levels, a significant higher change from baseline (-30 pg/mL vs. -3 pg/mL) was noticed in Group A vs. Group B. However, neither calcium nor phosphorus levels had a significant difference in both groups. No side effects were reported from both study groups.

Conclusion: Weekly (50.000 IU) oral cholecalciferol seems to be an effective safe option to replenish vitamin D levels in hemodialysis patients, with an ameliorating effect on oxidative stress, inflammation and PTH levels.

P1572 **EFFECTIVENESS OF COENZYME Q10-MICELLE COMPARED WITH COENZYME Q10 ON TACROLIMUS-INDUCED RENAL INJURY**

Sheng Cui[1], Kang Luo[1], Yi Quan[1], Sun Woo Lim[1], Chul-Woo Yang[1]

[1]*The Catholic University Of Korea, Seoul St. Mary's Hospital, Seoul, Korea, Rep. of South*

Background and Aims: We and others have recently demonstrated that Coenzyme Q10 (CoQ10) has protective effects against diabetes mellitus and various types of renal injury. This study investigated whether CoQ10-micelle treatment would affords superior renoprotection compared with CoQ10 in the governing tacrolimus (Tacrolimus)-induced renal injury in the rats.

Method: Male adult Sprague-dawley Rats were treated daily with Tacrolimus (1.5mg/kg/day, subcutaneous), CoQ10 (20mg/kg/day, oral), and CoQ10-micelle (20 mg/kg/day, oral) for 4 weeks. The effects of CoQ10 orCoQ10-micelle on Tac-induced renal injury were assessed in terms of renal function, histopathology, oxidative stress and apoptotic cell death.

Results: After 4 weeks of Tacrolimus treatment to rats caused renal dysfunction, typical pathologic lesions, and oxidative stress marker. The serum creatinine was reduced by Tac co-treatment with CoQ10 or CoQ10-micelle groups compared with the Tac and VH group (0.31 ± 0.03 in the VH group vs. 0.43 ± 0.041 in the Tac group vs.0.37 ± 0.031 in the Tac+CoQ10 group 0.30 ± 0.02123 in the Tac+CoQ10-micellegroup; $1P<0.05$ vs. VH. $2P<0.05$ vs. TAC. . $3P<0.05$ vs. TAC+C.) The administration of CoQ10-micelle improved renal immunoreactivity, which was accompanied by reductions in oxidative stress and apoptosis. Assessment of the mitochondrial ultrastructure by electron microscopy revealed that tacrolimus co-treatment with CoQ10-micelle increased the size and number of mitochondria more than co-treatment with CoQ10, compared with that induced by TAC treatment alone.

Conclusion: These findings suggest that both CoQ10 and CoQ10-micelle effectively attenuates Tac-induced renal injury, and CoQ10-micelle provides more benefits than that of CoQ10.

P1573 EFFECT OF INFLAMMATION ON MUSCLE-BONE INTERACTIONS IN HEMODIALYSIS PATIENTS

Jerzy Królikowski[1], Bogumila Górczewska-Królikowska[1], Michal Nowicki[1]

[1]*Medical University of Lodz,, Central University Hospital, Dept. Nephrology, Hypertension and Kidney Transplantation, Lodz, Poland*

Background and Aims:

Chronic hemodialysis patients show decreased muscle mass, low physical activity and chronic weakness. Hemodialysis treatments results in increased risk of inflammation, which impairs physical activity. The calcium-phosphate and bone metabolism, as well as muscle mass, are regulated by a range of factors like FGF-23 and its co-factor Klotho protein, myostatin, follistatin and sclerostin. Complex interactions between these cytokines and inflammation have been described.

The aim of the study was to assess the influence of inflammation on plasma concentrations of factors that regulate muscle and bone-mineral metabolism

Method:

55 hemodialysis patients were divided into study group (32 patients) and the reference group (23 patients). The former were the patients who had inflammation confirmed by plasma CRP >50 mg /L. Blood was collected before and after hemodialysis during the inflammation, and before hemodialysis after the resolution of inflammation

Results:

Mean CRP in study group was 105.9±73.9 mg/l. The mean period between blood sampling during inflammation and resolution of inflammation was 15±7.9 days. Statistically significant increase of plasma cFGF-23 concentration was observed after hemodialysis. Its median concentration increased from 1992.8 RU/ml; IQR = [1350; 4320 RU/ml] before hemodialysis to 2421.3 RU/ml IQR = [1351; 7348 RU/ml] after HD ($p = 0.001$). Significant increase of sclerostin was observed after hemodialysis. Serum sclerostin increased from 1346.2 pg/ml IQR = [1034; 2243 pg/ml] before HD to 1583.8 pg/ml IQR = [1198; 2559 pg/ml] after HD ($p = 0.002$). Follistatin concentration increased from 2669 pg/ml IQR = [2129; 5702 pg/ml] before HD to 4220.5 pg/ml IQR = [2583; 6727 pg/ml] ($p = 0.009$). Hemodialysis had no significant effect on plasma Klotho protein, iFGF-23, FGF-21, and myostatin. After the resolution of inflammation there was statistically significant decrease in FGF-21 from 3591.4 pg/ml. IQR = [1174.3; 6,537.3 pg/ml] to 2454 pg/ml IQR = [1221.1; 3448.4 pg/ml] $p = 0.006$). There were significant changes of the concentration of Klotho protein, cFGF-23, iFGF-23, sclerostin, myostatin, follistatin after the resolution of inflammation vs. baseline.

Conclusion:

Hemodialysis modulates the concentration of factors involved in regulation of calcium-phosphate metabolism, bone turnover and muscle growth and strength. The resolution of inflammation in hemodialysis patients leads to the decrease of plasma FGF-21 concentration.

P1574 **EFFECTS OF BRAZILIAN GREEN PROPOLIS EXTRACT (EPP-AF) ON INFLAMMATION IN HEMODIALYSIS PATIENTS.**

Marcelo Silveira[1,2,3], Flavio Teles[4], Erica Melo[5], Valeria Borges[6], Filipe Miranda[5,7], Fábio Dutra[5,7], Andresa Berretta[8], Rodrigo Cezar[5], Jéssica Silva[6], Hayna Santos[6], Paulo Benigno[1,2], Rogério Passos[1,2,7]

[1]D'Or Institute for Research and Education, Rio de Janeiro, Brazil, [2]Hospital São Rafael, Nephrology, Salvador, Brazil, [3]Laboratorio de Investigacao Medica 12 (LIM12), Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil., Medical Clinic, São Paulo, Brazil, [4]State University Of Health Sciences Of Alagoas, Maceió, Brazil, [5]Hospital São Rafael, Salvador, Brazil, [6]Oswaldo Cruz Foundation, Salvador, Brazil, [7]Hospital Português, Salvador, Brazil and [8]Faculdade de Ciências Farmacêuticas de Ribeirão Preto - USP, Ribeirão Preto, Brazil

Background and Aims: End-stage chronic kidney disease is associated with the condition of chronic inflammation, impacting increased cardiovascular mortality in this specific population. Patients on hemodialysis are known to be predisposed to several factors that predispose to inflammation: dialysis membranes, central venous catheters, oxidative stress, fluid overload, sodium overload, uraemic toxins. Propolis, a natural resin produced by bees from plant materials, has anti-inflammatory, immunomodulatory, and anti-oxidant properties. The aim of this study was to evaluate the impact of Brazilian green propolis extract on inflammation in hemodialysis patients. Here we present preliminary results of the trial NCT04072341.

Method: We performed a prospective trial, open-label 9-week crossover study examining the effect of Brazilian green propolis (250mg/day, in capsules) on inflammation in hemodialysis patients. We included patients over 18 years, under intermittent hemodialysis (thrice per week), on hemodialysis for at least 1 month and until now 37 patients were included. We excluded pregnant women, cancer carried and patients who developed infection or underwent any surgical procedure during the study period. Each period was 4 weeks in duration with a 1-week washout period in between. The primary end point was change in serum level of high-sensitivity c-reactive protein (HsCRP). Secondary end point evaluated the safety of propolis use in hemodialysis patients.

Results: Their mean age was 58.6 ± 15.2 years (mean ± SD), and 22 (59.4%) were men. The proportion of patients with hypertension was 14 (37.8%) and diabetes was 9 (24.3%). The number of patients using arteriovenous fistula were 26 (70.2%). The HsCRP presented (mean ± SE) 5.31 ± 1.02 mg/L at baseline, 4.26 ± 0.76 mg/L after propolis period and 4.56 ± 1.32 mg/L in control period, p = 0.0042. Safety parameters were analyzed such as amylase, aspartate aminotransferase (AST) and creatine phosphokinase (CPK); there was no difference between them before and after the use of propolis. None of the participants reported any adverse effects or allergic reactions during the treatment.

Conclusion: Patients on hemodialysis have an increased inflammatory state. For the best of our knowledge it was the first clinical trial who demonstrated the safety of propolis in hemodialysis patients. Brazilian green propolis demonstrated a tendency to reduce inflammation in these patients.

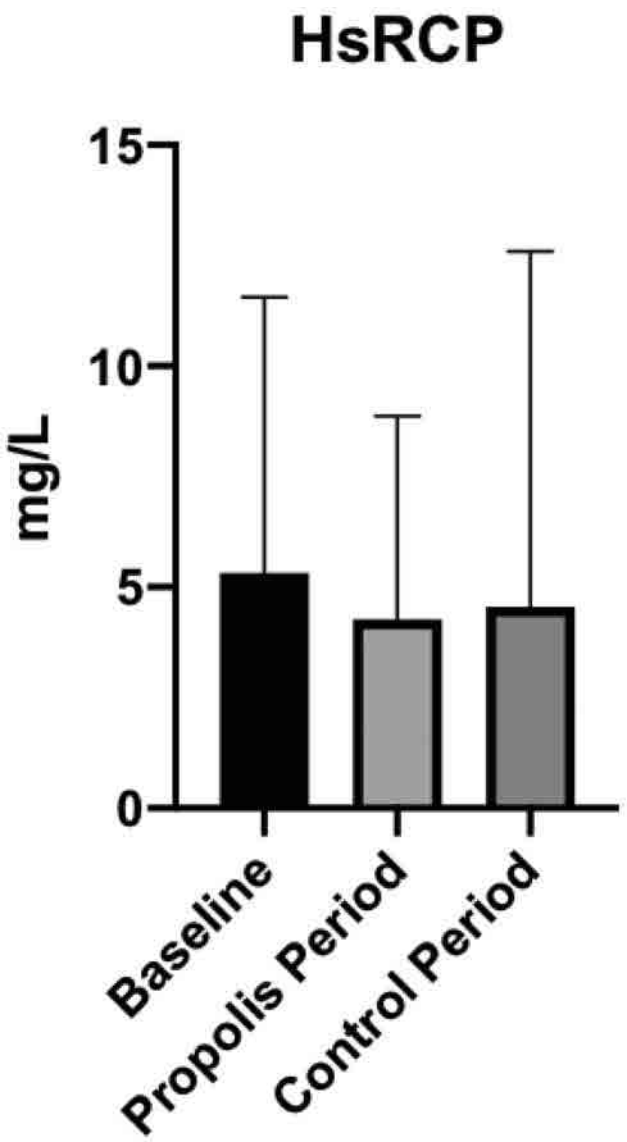


Figure: HsCRP level at different study periods. Each patient is his own control, the analysis demonstrated statistical significance by evaluating their individual values. p = 0.0042.

P1575 **STUDY ON THE CLINICAL CHARACTERISTICS OF PROTEIN-ENERGY WASTING AND PERSISTENCY RATE OF EXERCISE TRAINING IN PATIENTS ON HEMODIALYSIS**

Takayasu Taira[1]

[1]*Yokohama, Nephrology, Yokohama, Japan*

Background and Aims: Frailty is common among elderly patients on hemodialysis (HD), and is associated with protein-energy wasting (PEW), sarcopenia and dynapenia. Frailty and PEW are associated with impaired physical performance, poor quality of life (QOL), disability and reduced survival. Prevention and treatment of these conditions often requires a multifaceted approach. In this study, we examine the effect of PEW and the persistency rate of exercise training among elderly patients on HD.

Method: Study (1): The HD program included 722 patients (515 males, 207 females), who underwent 4-h HD sessions, were assigned to 2 groups (PEW group and non-PEW group). We collected the biochemical data and investigated dry weight (DW: kg), duration of HD (months), body mass index (BMI), % creatinine generation rate (%CGR), and normalized protein catabolic rate (nPCR). Study (2): This was retrospective, multi-center study and included 53 patients on HD (25 males, 28 females; mean age: 72.5±9.1 years, BMI; 22.5±3.5 kg/m^2). The HD patients were non-randomly assigned to an exercise training group during HD (E group) or to an exercise training group at home (H group). The E group used medicine balls during the first 2 h of the HD sessions. The H group strengthened the quadriceps and the gastrocnemius muscles by half-squatting by raising the heel or single-leg standing, respectively. We collected the main biochemical data after 6 months of exercise training and measured the left and right knee extension strength using a hand-held dynamometer. We investigated the persistency rate of exercise training and its factors.

Results: Study (1): The mean age of the patients was 67.0±13.1 years; the mean HD duration was 83.2±83.6 months. PEW and non-PEW groups consisted of 162 HD patients (22.4%; 112 males, 50 females, HD duration 76.5±91.5 months) and 560 HD patients (77.6%; 403 males, 157 females, HD duration 85.1±78.4 months), respectively. The mean age of the PEW group was significantly higher than that of the non-PEW group (71.0±12.5 vs 66.0±13.1 years; P<0.01). The mean DW (54.6±13.8 vs 60.4±13.4 kg, P<0.01), mean serum albumin (3.3±0.3 vs 3.5±0.4 g/dL, P<0.01), mean BMI (20.4±4.3 vs 22.5±3.9 kg/m^2, P<0.01), mean %CGR (72.0±24.0 vs 96.7±22.5 %, P<0.01), and mean nPCR (0.75±0.16 vs 0.91±0.14 g/kg/day, P<0.01) of the PEW group were significantly lower than those of the non-PEW group. By multiple logistic regression analysis, the partial regression coefficient of age was 0.28, and the odds ratio was 1.029. Study (2): After 3 months, the persistency rate of exercise training was 77.4% (41 HD patients). After 6 months, the persistency rate of exercise training was 50.3% (27 HD patients). The factors of dropout of exercise training were loss of motivation (42.9%), leg pain (21.4%), physical deconditioning (14.3%), change in blood pressure (7.1%), hospitalization (7.1%), and admission to a nursing facility (7.1%). In the H group, the muscle strength of the knee extensors significantly increased from 25.7±7.1 kgf (baseline) to 28.6±7.7 kgf (after 3 months of exercise training; p=0.023).

Conclusion: (1) The PEW group showed significantly lower %CGR than the non-PEW group. (2) An adapted low-intensity exercise program improved the muscle strength of patients with HD patients. The persistency rate of exercise training after 6 months was 50.3%, and the main reasons for dropout of exercise training were loss of motivation and leg pain.

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THE EFFECT OF CHANGING DIETARY PHOSPHORUS-PROTEIN RATIO ON NUTRITIONAL STATUS OF HEMODIALYSIS PATIENTS

Song Wang[1], Xinkui Tian[1], Xinhong Lu[1], Hanmin Liu[2], YUE WANG[1]

[1]Peking University Third Hospital, Nephrology, Beijing, P.R. China and [2]Joint Laboratory of Medical Food, Chinese Academy of Sciences Tianjin Institute of Industrial Biotechnology, Tianjin, P.R. China

Background and Aims: To investigate the effect of changing dietary phosphorus-protein ratio on the nutritional status of maintenance hemodialysis patients.

Method: Hemodialysis patients who had average serum phosphorus $\geq$1.78 mmol/L for three consecutive months were enrolled in this self-controlled trial. Patients received low phosphorus diet instruction for 4 weeks as baseline, followed by changed the diet of staple foods with the same amount of low protein rice for 10 weeks. The difference of protein intake between the low protein rice and staple foods was replaced by low phosphorus whey. Then the patients reverted to staple food for 8 weeks. Serum phosphorus, albumin and nutritional status before and after dietary changes were observed and analyzed.

Results: 29 patients completed the study. At baseline dietary phosphorus-protein ratio was (15.85$\pm$3.29) mg/g, and serum phosphorus was (2.05$\pm$0.32) mmol/L. After switch to low protein rice and low phosphorus whey for 10 weeks, dietary phosphorus-protein ratio decreased to (12.18$\pm$2.45) mg/g ($p<0.001$). Simultaneously serum phosphorus decreased to (1.87$\pm$0.44) mmol/L ($p=0.048$). Nutritional status evaluation showed the patients' serum albumin increased significantly compared with baseline (42.29$\pm$3.51 vs. 39.84$\pm$3.23 g/L, $p<0.001$), as well as dry body weight (65.09$\pm$15.30 vs. 64.71 $\pm$ 15.07 kg, $p=0.030$), upper arm muscle circumference (22.57$\pm$2.83 vs 22.00$\pm$3.03 cm, $p=0.013$), and the grip strength (27.89$\pm$7.82 vs. 26.54$\pm$7.90 kg, $p=0.032$). Subjective global assessment (SGA) and serum lipid level did not change significantly after the food change.

Conclusion: For hemodialysis patients, changing dietary phosphorus-protein ratio by combination of low protein rice and low phosphorus whey could effectively decrease serum phosphorus level, and improve serum albumin, as well as muscle mass and muscle strength.

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DOES VITAMIN E -COATED MEMBRANES INFLUENCE ON MARKERS OF OXIDATIVE STRESS IN HEMODIALZSIS PATIENTS WITH HOMOZYGOUS GST M1 GENE DELETION?

Petar Djuric[1], Sonja Suvakov[2], Dragana Markovic[1], Djurdja Jovanovic[2], Aleksandar Jankovic[1], Ana Bulatovic[1], Jelena Tosic Dragovic[1], Jelena Marinkovic[4], Radomir Naumovic[5], Tatjana Simic[6], Nada Dimkovic[7]

[1]Zvezdara University Medical Center, Clinical Department for Renal Diseases, BELGRADE, Serbia, [2]Faculty of Medicine, University of Belgrade, Institute of Medical and Clinical Biochemistry, BELGRADE, Serbia, [4]Faculty of Medicine, University of Belgrade, Institute of Medical Statistics and Informatics, BELGRADE, Serbia, [5]Faculty od Medicine, University of Belgrade, Internal Medicine, BELGRADE, Serbia, [6]Faculty od Medicine, University of Belgrade, Institute of Medical and Clinical Biochemistry, BELGRADE, Serbia and [7]Serbian Medical Society, Academy of Medical Sciences, BELGRADE, Serbia

Background and Aims: Increased free radicals production and down-regulated antioxidant enzymes activities contribute to protein, lipid and DNA oxidative damage particularly in HD patients lacking for GSTM1 enzyme activity. At the same time, those patients exhibit higher mortality rate than those with active GSTM1 genotype. It has been shown that vitamin E-coated membranes (VitEM) may decrease oxidative stress and inflammatory status in overall HD patients. Therefore, for the first time we analyzed VitEM dialyzers in patients who are homozygote for GSTM1 gene deletion and in whom anti-oxidative and anti-inflammatory benefit could be the greatest.

Method: GSTM1 genotypes were determined by PCR in 170 chronic HD patients. Those with GSTM1-null genotype were randomized and 80 were included in the study. Forty of them were dialyzed for three months with VitEM, while other forty were dialyzed with high-flux polysufone membranes of the same surface. Markers of protein and lipid oxidative damage, inflammation (thiol groups, malondialdehyde (MDA), Interleukin-6 (IL-6)), together with plasma antioxidant activity (glutathione peroxidase (GPX), superoxide dismutase (SOD)) were determined at the start and at the end of the study.

Results: Seventy-five patients' finished the study. There were no significant differences in baseline characteristics between the two groups (age, sex, body weight, dialysis vintage, vascular access, presence of diabetes, dialyzers surface, Kt/V and CRP). Also, there were no significant differences at baseline markers of protein and lipid oxidative damage, inflammation and plasma antioxidant activity. After three months of therapy, GPX, MDA, thiol groups increased significantly in both groups, but without statistical significance between groups (Table 1). SOD did not change significantly during three month period. IL-6 increased in control group, at the same time decreased in VitEM group, but without statistical significance.

Conclusion: Vitamin E-coated membranes did not influence markers of oxidative stress in HD patients with GSTM1-null genotype. Further studies in the field are required.

Table 1. Markers of protein and lipid oxidative damage, inflammation and plasma antioxidant activity of the analyzed patients before and after therapy

	Control group		VitEM group			
	before	After	before	after	P	P*
GPX U/L	206.7±67.2	273.7±61.6	203.7±59.1	285.7±78.7	**0.000**	0.474
SOD Ux10^3/L	55.4±11.7	60.4±22.4	53.8±9.8	55.1±21.2	0.269	0.607
MDA ng/ml	510.9±394.7	769.5±440.7	403.45±218.8	752.1±439.0	**0.000**	0.446
Thiol groups mcmol/L	6.79±1.81	8.33±2.26	7.31±2.58	8.31±2.48	**0.000**	0.445
IL-6 ng/ml	48.5±40.7	67.6±120.2	37.9±28.4	34.4±32.4	0.543	0.376

P- Within groups p*- Between groups

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LOW ANKLE BRACHIAL INDEX, AND HIGH SERUM ALBUMIN WAS INDEPENDENTLY ASSOCIATE WITH HIGHER OF ISCHAEMIC MODIFIED ALBUMIN IN CHRONIC HAEMODIALYSIS PATIENTS.

Arkom Nongnuch[1], Supawadee Sappadungsuk[1], Nathan Davies[2], Andrew Davenport[3]

[1]Ramathibodi Hospital, Medicine, bangkok, Thailand, [2]University College London, Medicine, london, United Kingdom and [3]Royal Free Hospital, Centre for Nephrology, london, United Kingdom

Background and Aims: Haemodialysis (HD) is one of the life-saving procedures which prolonged life of chronic kidney disease stage 5, however, the long-termed complications such as cardiovascular disease (CVD), immune and endothelial dysfunction are commonly occurred. The high incidence of CVD in haemodialysis patient associated with traditional and non-traditional risk factors. The novel non-traditional risk factors such as p-cresol, Advance Glycosylation End Products (AGEs), Ankle-Brachial Index (ABI), Cardio-Ankle Vascular Index (CAVI). The ischemic modified albumin (IMA) is the new marker for cardiovascular disease in various populations including haemodialysis. We aimed to explored the factors associate with higher IMA in chronic haemodialysis patients.

Method: Cross sectional study 196 chronic haemodialysis patients were collected blood sample for Ischemic modified albumin (IMA), measured Ankle-Brachial Index (ABI), Cardio-Ankle Vascular Index (CAVI), and skin autofluorescence advanced glycosylation end products (SAF).

Results: 53% were female, 21% were smoker, 57% were diabetes, 93% were hypertension, 33% were coronary artery disease, 12% on HDF. Mean Age were 69.2±13.2 year, ABI 1.1±0.15, CAVI 9.3±1.5, SAF 3.1±0.8 arbitrary unit, IMA 37.5±15.2 U/ml, and serum albumin 3.7±0.4 g/dl. In multivariate adjustment showed factors associate with higher IMA were low ABI (B co-efficiency -13.4, P=0.049) and high serum albumin (B co-efficiency 1.68, P=0.000002).

Conclusion: Lower ABI and high serum albumin associate with higher IMA. The finding underlines the association between the atherosclerosis, vascular endothelial function and cardiac injury in haemodialysis. These results should be confirmed and explored in larger and longer clinical trials.

Figure: Regression analysis of factors associate with IMA accumulation.

Parameter	Univariate			Multivariate		
	B coefficient	CI	P value	B coefficient	CI	P value
HDF	-7.14	-13.8 to -0.51	0.035	-4.4	-10.5 to 1.7	0.16
Female	-0.29	-4.5 to 4.4	0.99			
Smoker	-2.9	-8.2 to 2.3	0.26			
Diabetes	2.29	-2.2 to 6.7	0.31			
Hypertension	0.78	-8.6 to 10.1	0.17			
Frequency 3/week	-0.003	-4.4 to 4.4	0.99			
Serum albumin	15.01	9.9 to 20.1	0.0001	14.3	8.5 to 20.1	0.000002
SAF	2.46	-0.54 to 5.4	0.11			
CAVI	-1.43	-2.9 to 0.02	0.052	-0.82	-2.2 to 0.6	0.26
ABI	-12.08	-26.7 to 2.6	0.10	-13.4	-26.8 to -0.03	0.049
BMI	0.07	-0.4 to 0.5	0.77			
Age	-0.016	-0.19 to 0.15	0.85			
Hb	1.26	-0.3 to 2.8	0.12			
HbA1c	-0.75	-2.4 to 0.9	0.38			
Serum calcium	4.77	1.7 to 7.9	0.003	1.68	-1.4 to 4.8	0.29
Serum phosphate	-0.41	-2.0 to 1.2	0.61			
Log iPTH	2.52	-2.99 to 8.05	0.37			
Log B2M	5.82	-11.4 to 23.1	0.51			
Log HsCRP	-2.5	-6.8 to 1.8	0.25			
CAD	-2.07	-6.8 to 2.6	0.39			
History CAG	-1.71	-6.8 to 3.4	0.51			
History Stroke	3.52	-4.2 to 11.2	0.37			

P1579 PREVALENCE OF PROTEIN-ENERGY WASTING IN HEMODIALYSIS PATIENTS IN THE EUROPEAN REGION OF THE RUSSIAN FEDERATION

Alexander Jakovenko[1], Aleksander Rumyantsev[1]

[1]*Pavlov First Saint Petersburg State Medical University, Department of nephrology and dialysis, St. Petersburg, Russia*

Background and Aims: One of the complications of hemodialysis therapy (HD) is the development of protein-energy wasting (PEW), which is an independent predictor of morbidity and mortality in this cohort of patients. The prevalence of PEW in hemodialysis patients in different regions of the world varies from 15% to 75% but has not been practically studied in the Russian Federation.

To assess the prevalence of protein-energy wasting in hemodialysis patients in the European region of the Russian Federation.

Method: 645 hemodialysis patients were examined in 9 hemodialysis centers in 5 regions of the European part of the Russian Federation. Among the patients there were 345 women and 300 men, the average age was 56.8 $\pm$ 12.8 years. The duration of hemodialysis therapy was 8.4 $\pm$ 5.3 years. The diagnosis of PEW was established in accordance with the criteria: biochemical criteria (serum albumin $<$ 3.8 g per 100 ml; serum prealbumin (transthyretin) $<$ 30 mg per 100 ml; serum cholesterol $<$ 100 mg per 100 ml); low body weight, reduced total body fat, or weight loss; a decrease in muscle mass; and low protein or energy intakes. The level of blood albumin was determined using the BCG method (bromocresol green). Estimation of protein and calorie intake was performed using 3-day food diaries filled out by patients.

Results: Insufficient protein intake according to the International Society of Renal Nutrition and Metabolism (ISRNM) recommendations was observed in 5.5 % of patients, calories in 4.1 %, combined deficiency in protein and calorie intake in 2.7% of patients. The prevalence of PEW was 51.2 %. The relationship between age and gender was not identified. The lowest prevalence of PEW is observed in patients with a hemodialysis therapy experience of fewer than 5 years (25,4 %) and gradually increasing by 2.5 times in patients with survival rates on HD for more than 10 years ($\chi 2 = 22{,}580$ $p = 0.0001$).

Conclusion: The prevalence of protein-energy wasting in hemodialysis patients in the European region of the Russian Federation is 51,2 %.

P1580 **LONGITUDINAL CHANGES IN BODY COMPOSITION ARE ASSOCIATED WITH ALL-CAUSE MORTALITY IN PATIENTS ON PERITONEAL DIALYSIS**

Young Rim Song[1], Sung Gyun Kim[1], Hyung-Seok Lee[1], Hyung Jik Kim[1]

[1]*Hallym University Sacred Heart Hospital, Department of Internal Medicine, Division of Nephrology, Anyang-si, Korea, Rep. of South*

Background and Aims: Peritoneal dialysis (PD) is associated with a number of adverse body compositional changes, including fat gain and muscle wasting. Whether body compositional changes are associated with the long-term prognosis is uncertain. The purpose of this study was to analyze the effects of longitudinal changes in body composition on all-cause mortality in PD patients.

Method: PD patients were subjected to bioimpedance spectroscopy (BIS) and handgrip strength (HGS) at baseline and after 2 years. Among 160 patients, 131 patients were tested with a repeat BIS and HGS. Lean tissue index (LTI) loss and fat tissue index (FTI) gain were defined as a 10% decline in LTI and a 10% gain in FTI, respectively after 2 years.

Results: The prevalence of sarcopenia at baseline was 13.8%. After 2 years, LTI loss and FTI gain were observed in 40 (30.5%) and 58 (44.3%) patients, respectively. Baseline clinical factors did not predict longitudinal body compositional changes, and there was a negative association between changes in the LTI and FTI ($r = -0.574$, $p < 0.001$). Low LTI and low HGS at baseline were significant predictors of all-cause mortality after adjusting for demographic and biochemical parameters, but not when cardiovascular factors were included in the multivariate analysis. However, LTI loss and FTI gain were independent risk factors for all-cause mortality after adjusting for demographic, biochemical, and cardiovascular parameters.

Conclusion: In PD patients, longitudinal changes in LTI and FTI were more strongly associated with all-cause mortality than single values in LTI and FTI.

P1581 **IMPACT OF ACHIEVING LDL CHOLESTEROL LOWER THAN 100 MG/DL WITH STATINS, ON LIPID PROFILE AND INFLAMMATION IN END-STAGE RENAL DISEASE PATIENTS**

Susana Coimbra[1,2], Flávio Reis[3], Sara Nunes[3], Sofia D. Viana[3,4], Maria João Valente[1], Susana Rocha[5], Cristina Catarino[1], Petronila Rocha-Pereira[1,6], Elsa Bronze-da-Rocha[1], José Gerardo Oliveira[7,8], José Madureira[9], João Carlos Fernandes[10], Maria do Sameiro Faria[1,11], Vasco M.P. Miranda[12], Luís Belo[1], Alice Santos-Silva[1]

[1]UCIBIO, REQUIMTE, Laboratory of Biochemistry, Department of Biological Sciences, Porto, Portugal, [2]CESPU, Institute of Research and Advanced Training in Health Sciences and Technologies (IINFACTS), Gandra PRD, Portugal, [3]Institute of Pharmacology & Experimental Therapeutics, Coimbra Institute for Clinical and Biomedical Research (iCBR), Faculty of Medicine, & CIBB Consortium, University of Coimbra, Coimbra, Portugal, [4]Polytechnic Institute of Coimbra, ESTESC-Coimbra Health School, Pharmacy, Coimbra, Portugal, [5]LAQV, REQUIMTE, Laboratory of Applied Chemistry, Department of Chemical Sciences, Porto, Portugal, [6]Health Science Research Centre, University of Beira Interior, Covilhã, Portugal, [7]Hemodialysis Clinic of Porto, Porto, Portugal, [8]Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal, [9]NefroServe, Hemodialysis Clinic of Barcelos, Barcelos, Portugal, [10]NefroServe, Hemodialysis Clinic of Viana do Castelo, Viana do Castelo, Portugal, [11]Hemodialysis Clinic of Felgueiras, Felgueiras, Portugal and [12]Hemodialysis Clinic of Gondomar, Gondomar, Portugal

Background and Aims: Dyslipidemia is common in chronic kidney disease (CKD) and cardiovascular disease (CVD)-related events are the main causes of death in end-stage renal disease (ESRD) patients on dialysis. Concerning lipid management, clinical practice emphasized treatment escalation to achieve specific low-density lipoprotein cholesterol (LDLc) targets, which implies repeated LDLc evaluations, and enhancement of statin doses or combination of lipid-lowering therapies. However, the LDLc target is not consensual, with some entities suggesting 100 mg/dl and others a more conservative level. It has been hypothesized that lipoprotein's quality (size, composition and functionality) may be more important than their total circulating levels, as CVD risk factor. Our aim was to evaluate and compare, in ESRD patients on dialysis and under statins treatment, the levels of lipoprotein fractions and subfractions and inflammatory markers, between patients who achieved LDLc levels < 100 mg/dl and those who did not achieve that target.

Method: We studied 110 ESRD patients on dialysis (high-flux hemodialysis or hemodiafiltration) and under statin therapy; 87 presented a LDLc < 100 mg/dl (group 1) and 23 a value > 100 mg/dl (group 2); levels of high-sensitivity C-reactive protein (hsCRP), interleukin(IL)-6, lipid profile including lipoprotein fractions/subfractions, and oxidized LDL (oxLDL) were evaluated.

Results: Group 1, as compared to group 2, presented lower values of total cholesterol (TC), triglycerides, oxLDL, TC/high-density lipoprotein cholesterol (HDLc) and LDLc/HDLc ratios. Concerning lipoprotein fractions/subfractions, group 1 presented significantly higher larger and intermediate LDL, and a trend towards lower small LDL (P=0.063), higher large HDL (P=0.069) and lower small HDL (P=0.080); no significant alterations were found for very-low-density lipoprotein and intermediate-density lipoprotein. Regarding inflammatory markers, no significant differences were observed between the 2 groups.

Conclusion: Patients who achieved the LDLc < 100 mg/dl target presented a better non-conventional lipid profile, including lower oxLDL levels and an increase in larger (less atherogenic) LDL subfractions. According to our data, a lower LDLc level associates with a better lipid profile; the benefits of this improvement on HDL fractions and CVD-related events in ESRD patients on dialysis needs to be better clarified.

P1582 **THE BURDEN OF FRAILTY ON MOOD, COGNITION, QUALITY OF LIFE AND LEVEL OF INDEPENDENCE IN PATIENTS ON HEMODIALYSIS**

Bhanu Prasad[1], Maryam Jafari[2]

[1]Regina General Hospital, Saskatchewan Health Authority, Medicine, Regina, Canada and [2]Dr. T Bhanu Prasad Medical Prof Corp, Regina, Canada

Background and Aims: Frailty is an all-embracing syndrome of diminished physiological reserve to stressors resulting in reduced physical ability and increased vulnerability to hospitalization and mortality. There is data on cross-sectional frailty assessments and its subsequent relationship to mobility, quality of life, depression, cognitive decline, nursing home admissions, and disability. The most widely used definition in the literature is known as the Fried Frailty Phenotype. It is based on five physical domains that can be assessed by self-report (weight loss, low physical activity, and exhaustion) and objective measures (weakness and slow gait speed). Based on the number of deficits, individuals are characterized as robust (0), pre-frail (1-2/5) and frail ($\geq$ 3/5). The prevalence of frailty is disproportionately increased in patients with chronic kidney disease (CKD) in comparison to non-CKD counterparts and is the highest in patients on hemodialysis. While the cross-sectional measurement of frailty on hemodialysis patients has been associated with adverse clinical events, there is a paucity of data on longitudinal assessment of frailty and its relationship to outcomes. The primary objective of the study was to evaluate the change in frailty status in patients on hemodialysis over 12 months in relation to the level of independence. The secondary objective was to determine the changes in frailty and explore a relationship with mood, quality of life, and cognition.

Method: We conducted a prospective cohort study amongst 100 prevalent hemodialysis patients at the Regina General Hospital, Saskatchewan, Canada between January 2015 and January 2017. The patients underwent frailty assessments at baseline and one year later. Frailty was assessed using the Fried criteria, which included assessments of unintentional weight loss, weakness (handgrip strength), slowness (walking speed), and questionnaires for (physical activity and self-perceived exhaustion). Cognition, mood and quality of life were measured using questionnaires [Montreal Cognitive Assessment (MoCA), Geriatric Depression Score (GDS), and EuroQol (EQ-5D) utility scores and Visual Analogue Scores (VAS) respectively]. Differences across baseline and 1-year groups were assessed using McNemar's test or Wilcoxon signed-rank test, as appropriate. We assessed the differences between frail and non-frail (composite of robust and pre-frail) of groups using Mann–Whitney test or Chi-square test/ Fisher's exact test where appropriate.

Results: 97/100 had complete initial assessments. The median (Interquartile Range=IQR) duration of dialysis at baseline was 35.5 (13.75-71.75 months). One year later, 22 had died, 10 refused assessments and 3 relocated. 18/22 (82%) who died were frail. At baseline, 68% were frail, 27% were pre-frail and 5% were robust. At baseline, 69% had MoCA score$\geq$ 24, 53% had GDS score$\geq$ 2, median EQ-5D utility score was 0.80 (0.70-0.85), median EQ-VAS was 60 (44-80). 82% of the patients were independent, 17% were independent with support, and 1% required support from home care. Even though death was not a pre-specified endpoint, we found that a fifth of our patients (22/100) patients had died by the time of the next assessment in 12 months. 18/22 (82%) had been identified as frail suggesting majority of the deaths had occurred in frail patients.

Conclusion: To our knowledge, this is the first Canadian study that explores the relationship between longitudinal changes in frailty with the level of independence, mood, cognition, and quality of life. We show high prevalence (95%) of frail and pre-frail status at baseline which remained unchanged one year later. Frail patients on dialysis were older, had challenges with mobility and self-care in comparison to their non-frail counterparts. Frailty and pre-frailty is near-ubiquitous in our dialysis patients and will need to be proactively addressed to improve subsequent healthcare outcomes.

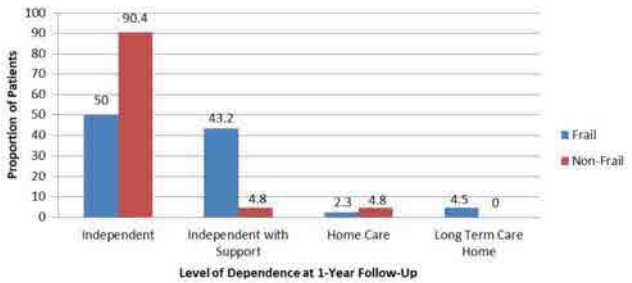


Figure:

P1583

UTILITY OF THE GLOBAL LEADERSHIP INITIATIVE ON MALNUTRITION CRITERIA FOR THE DETECTION OF MALNUTRITION AND DECLINE IN PHYSICAL FUNCTION AND ADL IN JAPANESE AMBULATORY HEMODIALYSIS PATIENTS

Haruka Ito[1], Shohei Yamamoto[1], Manae Harada[2], Takaaki Watanabe[1], Yuta Suzuki[1,2], Yusuke Isobe[1], Keigo Imamura[1], Sachi Yamabe[1], Shun Yoshikoshi[1], Atsushi Yoshida[2], Kentaro Kamiya[3], Atsuhiko Matsunaga[1]

[1]Kitasato University Graduate School of Medical Sciences, Department of Rehabilitation science, Sagamihara, Japan, [2]Sagami Circulatory Organ Clinic, Sagamihara, Japan and [3]Kitasato University, Department of Hygiene, Sagamihara, Japan

Background and Aims: In patients who undergo hemodialysis (HD), malnutrition is a frequent complication associated with higher risk of death, extended hospital stay, physical limitation, and decline of activities of daily living (ADL). Therefore, proper assessment for malnutrition in this population is important for effective disease management. The Global Leadership Initiative on Malnutrition (GLIM) released new criteria for diagnosing and grading malnutrition. Nevertheless, only very few studies have investigated malnutrition prevalence on the basis of the GLIM criteria in hemodialysis patients. Hence, the usefulness of the GLIM criteria's application in hemodialysis patients remains unclear.

The aims of this study were (1) to examine whether malnutrition diagnosed on the basis of the GLIM criteria will produce equivalent results with that diagnosed with the use of existing nutritional indicators and (2) to evaluate the association between the GLIM criteria and decline of physical function and ADL in Japanese patients on HD.

Method: This cross-sectional study included a total of 185 outpatients who undergo HD three times a week. We measured the existing nutritional indicators (GNRI, MNA-SF, phase angle, mid-arm muscle circumference, and calf circumference), physical function (Fried Scale, handgrip strength, usual gait speed, Short Physical Performance Battery, and physical activity), and ADL status (cumulative score of Barthel Index and instrumental ADL). On the basis of the GLIM criteria, the patients were classified into two groups (no malnutrition and malnutrition). In addition, in case of nutritional risk, nutritional assessment was performed by evaluation of the phenotypic (unintentional weight loss, low BMI, and/or reduced muscle mass) and etiologic (reduced intake or assimilation and/or inflammatory response) factors. Malnutrition was diagnosed if a patient has one or more of these items. The analysis of covariance (ANCOVA) was performed to examine the association between the GLIM criteria and existing nutritional indicators, physical function, and ADL status.

Results: Malnutrition was diagnosed in 41.1% of the participants based on the GLIM criteria. In contrast, on the basis of the existing nutritional indicators (GNRI, MNA-SF, phase angle, mid-arm muscle circumference, and calf circumference), malnutrition was diagnosed in 22.2%, 58.3%, 48.6%, 57.9%, and 54.6%, respectively. The ANCOVA results, adjusted for the patient's characteristics, revealed that the malnutrition group had significantly lower score than the non-malnutrition group in the existing nutritional indicators (all $P < 0.001$) (Figure). Furthermore, the malnutrition group had significantly higher Fried Scale scores, lower handgrip strength results, and lower ADL status than the non-malnutrition group, even after potential confounder adjustment (all $P < 0.05$).

Conclusion: The GLIM criteria could be one of the useful tools for screening the risk of malnutrition, frailty, lower handgrip strength, and lower ADL status in patients who undergo HD.

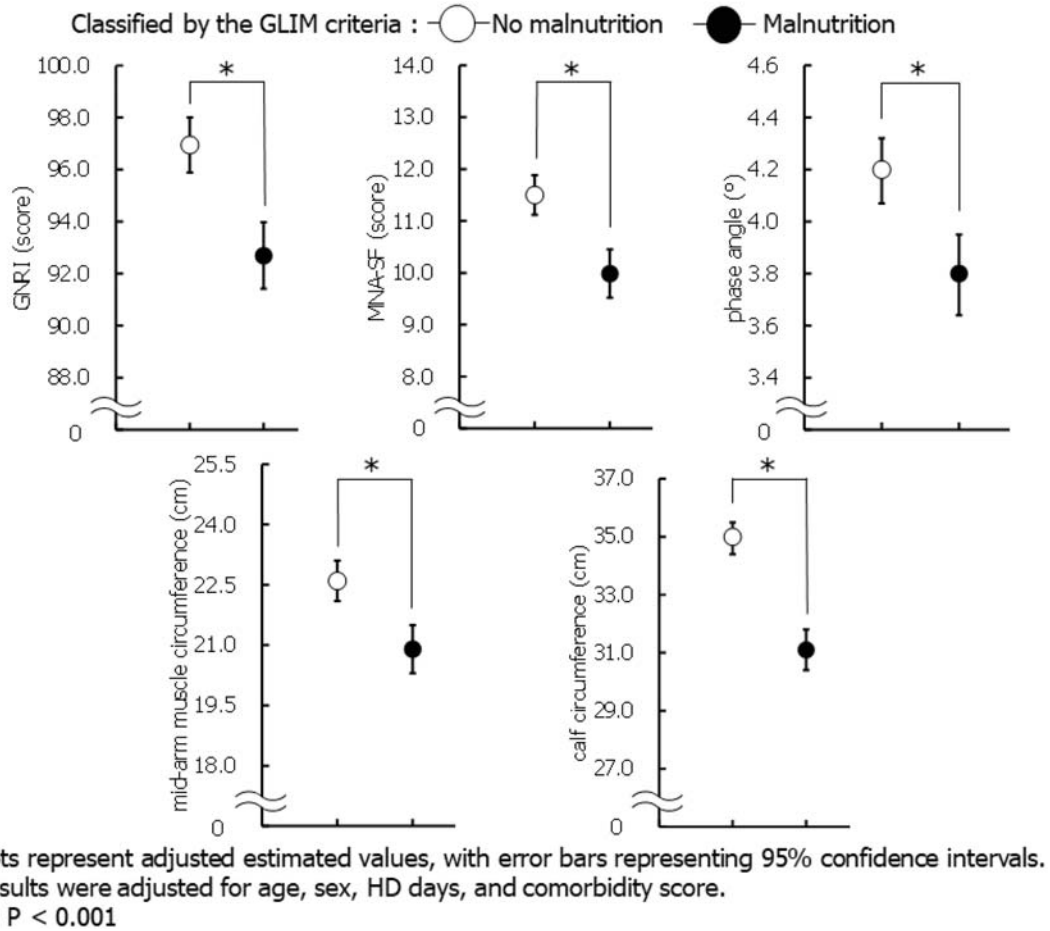


Figure: The analysis of covariance examining the adjusted associations of the GLIM criteria with existing nutritional indicators.

P1584 FRAILTY IN MAINTENANCE HEMODIALYSIS PATIENTS

Zauresh Amreyeva[1], Gulnar Chingayeva[1], Abay Shepetov[1], Assiya Kanatbayeva[1], Arina Yespotayeva[1]

[1]National Medical University, Nephrology, Almaty, Kazakhstan

Background and Aims: The population in Kazakhstan is rapidly aging, as a result the number of geriatric patients on maintenance hemodialysis (MHD) has been increasing. Frailty is prevalent in dialysis patients and is one of the common factors that can lead to increased morbidity and mortality. The primary objectives of this study were to evaluate the prevalence of frailty in elderly patients on MHD by using Edmonton Frailty Scale and assess their association with clinical and laboratory measurements. A secondary objective was to investigate the relationship between nutritional status and frailty.

Method: From July to September 2018, a total of 65 elderly patients undergoing HD in 7 dialysis facilities in Almaty, Kazakhstan were enrolled in this cross-sectional study. All participants were evaluated for the cognitive status through Mini-Mental State Examination (MMSE), nutritional status by using Mini Nutritional Assessment (MNA), Malnutrition-Inflammation Score (MIS), and anthropometric measurements (body mass index (BMI), triceps skinfold (TSF), mid-arm muscle circumference (MAMC)), functionality (Handgrip strength), as well biochemical data were collected from medical records. Frailty was defined in accordance with the Edmonton Frail scale (EFS).

Results: The study participants' median age was 69 (range: 65–88) years old, and median dialysis vintage was 36 (IQR 15–60) months, 53.8% were female. The main comorbidities were hypertension (69.2%) and diabetes (35.4%). The prevalence of frailty assessed by the EFS was 23.1% (men: 13.3%; women: 86.7), 43.1% patients were non-frail (men: 64.3%; women: 35.7%), 33.8% patients were vulnerable (men: 45.5%; women: 54.5%). Based on MIS the prevalence of PEW was 73.8% and, according to MNA, the risk of malnutrition was detected in 47.7%, and 9.2% had malnutrition. No significant difference was observed between genders in the frequency of PEW. Mean body weight was 69.1±11.3kg, the mean BMI was slightly overweight 25.6±4.29kg/m^2, while hand-grip strength was 21.33±3.36 in men and 15.5±5.51 in women, p=0.008, and it is lower than the normal population standard values. The frail patients group had a higher proportion of women 86.7% (p=0.001), worse nutritional status (93.3% and 86,7% had PEW evaluated by MIS (p=0.018) and MNA (p=0.035), respectively), more frequency of falls (p=0.01), anemia (p=0.038) when compared to group of non-frail and vulnerable patients. 66.7% of frail patients were widowed (p=0.005). The mean MMSE in this group of patients was 26.7±1.9.

Conclusion: The prevalence of frailty among elderly hemodialysis patients in this study was 23.1%, and we detected that 86.7% of them were female, as well PEW increased in frail patients. Also the study showed that protein-energy wasting is common among elderly hemodialysis patients. Its prevalence varies between 73.8% and 56.9% depending on the measurement tool used to evaluate the nutritional status. In our country with limited resources, EFS, MIS and MNA could help to follow elderly hemodialysis patients.

P1585 **FACTORS ASSOCIATED WITH PSOAS MUSCLE INDEX IN PATIENTS WITH MAINTENANCE DIALYSIS: FOR EARLY DETECTION OF SARCOPENIA**

Yoshiko Mori[1], Tomohiro Sawada[1], Keisuke Sunohara[1], Akiko Owaki[1], Hiroshi Nagaya[1], Shinichiro Inaba[1]

[1]*Tosei General Hospital, Nephrology, Seto-city, Aichi, Japan*

Background and Aims: Frailty was known to be associated with higher rates of hospitalization and mortality in dialysis patients, and sarcopenia was documented as the biological substrate of physical frailty. Therefore, early-detecting sarcopenia in dialysis patients is important for improving prognosis. The aim of our study was to investigate the factors associated with low skeletal muscle mass in dialysis patients.

Method: We recruited 134 Japanese patients (male 94, female 40; 117 maintenance hemodialysis, 11 chronic peritoneal dialysis and 6 both HD and PD) who underwent maintenance dialysis at our hospital during April 2019. Computed tomography (CT) imaging at the third lumbar vertebrae level was used to measure the psoas muscle mass index (PMI, psoas muscle area (cm2)/ height (m2)), and low skeletal muscle mass was defined as under 6.36 cm2/m2 in male and 3.92 cm2/m2 in female.

Results: The prevalence of low skeletal muscle mass was 19.4% in dialysis patients (26/134). The median values of PMI were 5.13 and 7.42 cm2/m2 in low skeletal muscle mass group and normal group, respectively. Univariate analysis identified variables associated with low skeletal muscle mass as follows: gender, age, body mass index, waist circumference, presence of coronary artery disease, total protein, albumin, asparate aminotransferase, γ-glutamyl transpeptidase, phosphorus, visceral fat area and subcutaneous fat area. Multiple logistic regression analysis using above significant factors identified independent variables associated with low skeletal muscle mass as follows: gender (male) (odds ratio [OR], 12.91; 95%confidence interval [CI], 2.50-66.57; $p<0.01$), age (per 1 year aging) (OR, 1.07; 95%CI, 1.00-1.14; $p<0.05$), waist circumference (per 1cm decrease) (OR, 1.11; 95%CI, 1.04-1.19; $p<0.01$), and albumin (per 1g/dL decrease) (OR, 5.55; 95%CI, 1.49-19.9; $p<0.05$). In sub-analysis targeting only male patients, age (per 1 year aging) (OR, 1.09; 95%CI, 1.01-1.17; $p<0.05$), waist circumference (per 1cm decrease) (OR, 1.13; 95%CI, 1.05-1.21; $p<0.01$) and albumin (per 1g/dL decrease) (OR, 5.88; 95%CI, 1.39-25.9; $p<0.05$) were independent factors associated with low skeletal muscle mass.

Conclusion: In patients who underwent maintenance dialysis, age, waist circumference and albumin could be predictive factors of low skeletal muscle mass. Dialysis patients with such factors are recommended to evaluate nutritional status and physical performance to identify sarcopenia earlier and prevent progressive course of sarcopenia and frailty.

P1586 SARCOPENIA IN HEMODIALYSIS PATIENTS

Armando Luis Negri[1], Ruben Abdala[1], Elisa Del Valle[1,2], Pablo Bridoux[2], Luciana Gonzalez Paganti[2], Marina Bravo[2], Luis Sintado[2], Paula Di Rienzo[2], Omar R Schiavelli[2], Maria B Zanchetta[1]

[1]Instituto de Investigaciones Metabolicas, Nephrology, Buenos Aires, Argentina and [2]Fresenius Medical Care Argentina, Buenos Aires, Argentina

Background and Aims: Sarcopenia is the loss of skeletal muscle mass and function that occurs with aging. These modifications lead to greater morbidity and mortality as a result of falls, hospitalization, depression and dependence among others. Chronic Kidney disease (CKD) and hemodialysis (HD) produce a favorable environment for the development of sarcopenia. Objective: to study the prevalence of sarcopenia and its different components (muscle mass, strength and physical performance) using EWGSOP 2018 proposed criteria.

Method: cross-sectional study evaluating 100 adult HD patients. We evaluated: Grip strength (GS) with Jamar Hydraulic Hand Dynamometer (three determinations in the arm without fistula); Appendicular lean mass (ALM) by DXA (GE LUNAR Prodigy Advance) and physical performance: Gait-speed (Time needed to perform a 4-meter walk on a flat surface) and the sit-stand test

Results: 58 males (M) and 42 females (F). Mean age for M was 54.3 years and 58 years for F. The prevalence of sarcopenia was 18% in the whole group, 10% in M and 20% in F. In M 33% had low GS and 26% low ALM. In M GS correlated with ALM, Albumin and weight $p<0.05$ (R^2 0.41); ALM correlated with weight r 0.75, height r 0.64 and GS r 0.46 ($p<0.05$). In F, 27% had low GS, 54% low ALM, and 17% poor physical performance. In F, GS correlated positively with ALM; ALM correlated positively with: weight r 0.78, height r 0.66, GS r 0.59 and sit-stand r 0.40 ($p<0.5$). Patients with lower grip strength had a higher prevalence of falls in the last year (40% two or more falls) $p=0.03$.

Conclusion: A significant proportion of dialysis patients had sarcopenia. Low hand grip strength was associated with a higher prevalence of falls. Recognizing sarcopenia in dialysis patients would allow us to develop strategies to prevent falls and other complications.

P1587 **EFFECT OF INTERMITTENT FASTING IN RAMADAN ON BODY COMPOSITION AND NUTRITIONAL PARAMETERS IN PATIENTS ON MAINTENANCE HEMODIALYSIS**

Mohammed Kamal Nassar[1], Ghada El-kannishy[1], Eman Abdelrazik[1], Nagy Sayed-Ahmed[1]

[1]*Mansoura Nephrology & Dialysis Unit (MNDU), Mansoura, Egypt*

Background and Aims: Intermittent fasting has been demonstrated to have many potential health-promoting effects. Intermittent fasting regimens were proven to influence metabolic regulation and chronic inflammation. Fasting during the month of Ramadan can be considered as a model of intermittent fasting among Muslims. In general, there is a shortage of studies in the context of the effect of Ramadan fasting in patients on maintenance hemodialysis (HD). The present study aimed to assess the effects of fasting in Ramadan on body composition as well as nutritional and inflammation parameters in patients on chronic HD.

Method: This prospective observational study included 68 patients on maintenance HD for more than six months in Mansoura Nephrology and Dialysis Unit (MNDU). The study was performed in Ramadan 1440 Hijri when the fasting hours ranged from 15 to 16 hours. Patients' nutritional status was assessed by malnutrition inflammation score (MIS). Anthropometric measurements, including body weight, height, mid arm circumference (MAC) and triceps skin fold thickness (TSF), were measured. Body composition was assessed by bioelectrical impedance. All of the aforementioned methods were performed before start of Ramadan and repeated three weeks after the end of the holy month in patients who fasted.

Results: Forty–five patients (66%) fasted more than 18 days during the month of Ramadan. The mean age of patients who fasted was 47.33±14.86 years with a median duration of HD of 35 months (IQR 14.5-74.5). After Ramadan, weight gain was observed in patients who fasted. However, the increase in body mass index (BMI) was statistically insignificant (28.7±6.06 vs 29.04±6.09kg/m? p=0.073). On the other hand, visceral fat was significantly reduced after Ramadan ($p<0.0001$). MIS score improved with lower score estimated after Ramadan; however, the difference was insignificant ($p=0.059$).

Conclusion: Fasting in Ramadan in HD patients was associated improvement of the metabolic profile evident by decrease in visceral fat. The effect of intermittent fasting on inflammation and nutritional parameters in patients on maintenance hemodialysis needs further investigations.

Table (1): Anthropometric measures, and Malnutrition inflammation score and body composition data of studied patient before & after Ramadan

	Before Ramadan	After Ramadan	P value
Body mass index (Kg/m2), mean±SD	28.7±6.06	29.04±6.09	0.073
Mid-arm circumference (cm), mean±SD	30.9±5.25	30.8±5.33	0.69
Triceps skin fold thickness (mm), median (Q1-Q3)	14 (12-21.5)	14 (10-20)	0.41
Mid-arm muscle circumference (cm), mean±SD	25.5±3.08	25.6±3.11	0.84
Total fat (%), mean±SD	29.4±10.96	28.2±10.64	0.36
Total body water (%), mean±SD	51.8±8.74	52.7±8.65	0.45
Visceral fat rating, median (Q1-Q3)	7 (4-10)	4 (2-8.5)	<0.0001*
Malnutrition inflammation score, median (Q1-Q3)	4 (2-5.5)	3 (2-5)	0.059

P1588

CAN L-CARNITINE SUPPLEMENTATION IMPROVE CARDIOPULMONARY FUNCTION? A RANDOMIZED CONTROLLED TRIAL IN HEMODIALYSIS PATIENTS

Fatemeh Yassari[1], Alireza Eslaminejad[2], Mehran Marashian[2], Farzaneh Dastan[2], Farzaneh Maleki Kazeri[3]

[1]NRITLD, Chronic Respiratory Diseases Research Center, Tehran, Iran and [3]SBMU, Faculty of nersing and midwifery, Tehran, Iran

Background and Aims: It is well known that L-Carnitine is a cardioprotective agent, which balances cardiac energy metabolism, by promoting mitochondrial β-oxidation and facilitating transport of long chain fatty acids into the mitochondrial matrix. It has been shown that L-Carnitine level in plasma and tissue is lower in hemodialysis patients and they may lose the benefits of this substance. As far as our knowledge, the effect of L-Carnitine on cardiopulmonary function has not been evaluated by ergospirometry up to now. The aim of this randomized clinical trial was to assess the effects of L-carnitine supplementation on cardiopulmonary Function in hemodialysis patients through ergospirometry.

Method: This randomized clinical trial was conducted on 46 chronic hemodialysis patients. The patients were divided into two groups. In both groups ergospirometry parameters (VE Max, VO2-Max, VCO2 Max, AT, VE/VCO2 Slope) were recorded for a 3-month period. During this period, one group received L-Carnitine at doses of 2 gr/day orally and the other group received only placebo. After three months, all of the mentioned parameters were rechecked and statistical analysis performed by SPSS software.

Results: Only CRP was different between the two groups increasing in placebo group significantly after 3 months ($P = 0.018$). No significant difference was detected in Cardiopulmonary factors. In terms of ergospirometry factors, PET-CO2 was the only parameter significantly increased in the treatment group ($P = 0.026$).

Conclusion: The present results indicate that L-Carnitine can improve cardiopulmonary function among hemodialysis patients.

P1589 **COMPARISON OF NUTRITIONAL STATUS IN HEMODIALYSIS PATIENTS WITH AND WITHOUT ANXIETY/DEPRESSION.**

Tulin Akagun[1], Sembol Türkmen[2], Aylin Arslan[3]

[1]*Giresun University Faculty of Medicine, Internal Medicine/Nephrology, Giresun, Turkey,* [2]*Giresun University Faculty of Medicine, Clinical Biochemistry, Giresun, Turkey and* [3]*Giresun University Faculty of Medicine, Psychiatri, Giresun, Turkey*

Background and Aims: Approximately one-third of all dialysis patients have mild to moderate malnutrition, while 6-8% have severe malnutrition. In patienst receiving maintenance hemodialysis, a low serum prealbumin is an indicator of malnutrition. Depression and anxiety are the most common psychological disorders in patients undergoing hemodialysis. The aim of this study was to evaluate the nutrional status in our hemodialysis patients and its association with anxiety and depression.

Method: In our cross-sectional study, 61 hemodialysis patients were evaluated with mini nutrional assessment (MNA) form, Beck anxiety/depression scale, clinical and laboratory data.

Results: Of 61 hemodialysis patients; 37 were male (mean age 60,8±11.7). 11.5 % of patients were malnourished. Severe depression and anxiety rates were 14.8% and 21.3% respectively. The clinical parameters of hemodialysis patients are shown in Table-1 and clinical and laboratory findings of the hemodialysis patients according to MNA scores are shown in Table-2. Malnourished patients and patients who were at risk of malnutrition; had lower urea, creatinine and prealbumin levels.

Conclusion: Anxiety was more prevalant in malnourished hemodialysis patients with lower prealbumin levels.

Age (years)	60.8 ± 11.7
Male/Female (n/n)	37/24
BMI (kg/m?	26.6±5.1
Duration of dialysis (months)	5 (3-9)
Urea (mg/dL)	131.8 ± 31.2
Creatinin	8.2±2.5
Albumin (g/dL)	4.1±0.3
C-reactive protein (mg/dL)	0.83 (0.29-2.08)
Hemoglobin (g/dL)	11.8±1.4
Prealbumin (mg/dL)	28.8±5.7
Mini Nutritional Assessment (MNA) score	
1: ≥24: well nourished (n, %)	34 (55.7 %)
2: 17-23.5: at risk of malnutrition (n, %)	20 (32.8 %)
3: <17: malnourished (n, %)	7 (11.5 %)
Urea Reduction Rate (%)	69.4±7
kt/v	1.34±0.18
Beck Depression scale (n, %)	
0: 0-9 point	20 (32.8%)
1: 10-18 point: mild depression	18 (29.5%)
2: 19-29 point: moderate depression	14 (23%)
3: 30-63 point: severe depression	9 (14.8%)
Beck Anxiety scale (n, %)	
0: 0-7 point	18 (29.5%)
1: 8-15 point: mild anxiety	18 (29.5%)
2: 16-25 point: moderate anxiety	12 (19.7%)
3: 26-63 point: severe anxiety	13 (21.3%)

Figure-1: Clinical and laboratory findings of hemodialysis patients (n=61).

	MNA score 1 n=34	**MNA score 2 + 3 n=27**	**p**
Age	62.2±13	61.2±14.4	0.982
Gender (male/female)	24/10	13/14	0.075
BMI (kg/m?	27.3±4.8	24.3±4.8	0.093
Urea (mg/dL)	133.2±30.5	118.6±21.2	**0.044**
Creatinin (mg/dL)	8.2±2.5	6.6±1.5	**0.005**
Albumin (g/dL)	4.1±0.3	4±0.4	0.483
CRP (mg/dL)	0.80 (0.19-1.53)	0.92 (0.46-3.06)	0.167
Hemoglobin (g/dL)	11.7±1.6	11.3±1.3	0.379
Prealbumin (mg/dL)	28.9±6.7	24.7±4.8	**0.019**
URR (%)	68.3±5.9	70.2±7.6	0.375
kt/v	1.31±0.16	1.40±0.26	0.182
Beck Depression scale (n, %)			
0	15(44.1%)	5 (18.5%)	0,098
1	9 (26.5 %)	9 (33.3%)	
2 + 3	10 (29.4%)	13 (48.1%)	
Beck Anxiety scale (n, %)			**0.033**
0	12 (35.3%)	6 (22.2 %)	
1	13 (38.2%)	5 (18.5%)	
2 + 3	9 (26.5%)	16 (59.3%)	

Figure-2: Clinical and laboratory findings of the hemodialysis patients according to MNA scores.

P1590 AMORPHOUS CPP AND CRYSTAL CPP OF HEMODIALYSIS PATIENTS

Kimihiko Nakamura[1], Yuki Nakayama[1], Toshiya Hiroyoshi[1], Naohito Isoyama[1], Kouki Fujikawa[1], Hideyasu Matsuyama[1], Makoto Kuro-o[2]

[1]Yamaguchi univercity, Urology, Ube, Japan and [2]Jichi Medical University, Division of Anti-Aging Medicine, Center for Molecular Medicine, Shimotsuke, Japan

Background and Aims: Serum calciprotein particles (CPP) are increased in CKD patients and correlated with vascular stiffness and calcification. CPPs are can be distinguished amorphous and crystal CPPs. Crystal CPPs are non-incubated CPPs and amorphous CPPs are the difference(Δ) incubated CPPs and non-incubated CPPs. In this study, we evaluated amorphous CPPs and crystal CPPs in hemodialysis (HD) patients.

Method: 183 end stage renal disease patients undergoing HD (57.6% men, median age 71, dialysis period; 98.4 ± 87 months) were treated in single hospital. Serum CPP levels were measured by the gel filtration method. Incubated CPPs were incubated in 24°C, 24hous then were measured similarly. We assessed the association of serum calcium (Ca), phosphorus (P), intact-PTH, FGF21, LDL-cholesterol, CRP with CPP.

Results: In multivariate analysis, P remained significant independent factors for the non-incubated CPP levels. Ca, P remained significant independent factors for the incubated CPP levels. P remained significant independent factors for the Δ CPP levels.

The association of ΔCPP levels / the incubated CPP levels with clinical variables are examined. In multivariate analysis, hemoglobin remained significant independent factors.

Conclusion: Amorphous CPPs and crystal CPPs could each be a prognostic factors.

Variable	R	P-value	β	P-value
Albumin	0.2840	***0.0001***	0.0928	0.2394
Hemoglobin	0.2669	***0.0003***	0.1584	***0.0246***
Creatinine	0.1965	***0.0082***	0.0692	0.3094
Calcium	0.2068	***0.0048***	0.0373	0.5961
Phosphorus	0.2368	***0.0013***	0.0428	0.5403
BAP	-0.2791	***0.0002***	0.1957	0.1022
FGF21	-0.3158	***0.0004***	-0.1886	***0.0155***
CRP	-0.1596	***0.0324***	0.0614	0.4160

Figure:

Association of ΔCPP levels / incubated CPP levels with clinical variables.
Univariate Multivariate

P1591 **SERUM PARAOXONASE 1 ARYLESTERASE ACTIVITY AS AN ANTIOXIDANT MARKER IN DIALYSIS PATIENTS**

Lesya Korol[1], Natalia Stepanova[2], Victoria Vasylchenko[1]

[1]State Institution «Institute of Nephrology of the National Academy of Medical Sciences», Biochemistry Laboratory, Kyiv, Ukraine and [2]State Institution «Institute of Nephrology of the National Academy of Medical Sciences», Nephrology and Dialysis, Kyiv, Ukraine

Background and Aims: Patients with chronic kidney disease (CKD) have the highest risk for cardiovascular disease associated with high-density lipoprotein deficiency, chronic inflammation and the development of oxidative stress (OS).

This study aimed to investigate serum paraoxonase 1 (PON-1) arylesterase activity in patients with end-stage renal disease (ESRD) and its association with oxidative stress markers.

Method: We conducted a cross-sectional observational study involving 58 ESRD patients. Among them, there were 20 hemodialyses (HD) patients and 38 patients treated with peritoneal dialysis (PD).

Serum PON1 arylesterase activity was determined spectrophotometrically by the number of formed phenolic complexes using phenylacetate. Also, the concentrations of malondialdehyde, serum concentrations of ceruloplasmin, thiol groups and total peroxidase activity (TPA) in erythrocyte were determined spectrophotometrically. In addition, the blood lipid spectrum (including high-density lipoproteins) was determined in all patients.

The reference group consisted of 30 conditionally healthy individuals.

For the statistical analysis, we used Kruskal-Wallis's t-test and Spearman's rank correlation test. All statistical analyses were performed using MedCalc.

Results: Serum PON1 arylesterase activity was 6.57 kU/L in reference group versus 2.25 kU/L in HD patients and 4.26 kU/L in PD patients ($p < 0.0001$) (Fig. 1). A direct association was found between serum PON1 arylesterase activity and ceruloplasmin concentration ($r = 0.38$; $p = 0.004$) and TPA ($r = 0.32$; $p = 0.02$) in HD patients. In iddition, serum PON1 arylesterase activity was associated with high-density lipoproteins ($r = 0.67$; $p < 0.0001$) in PD patients (Fig. 2).

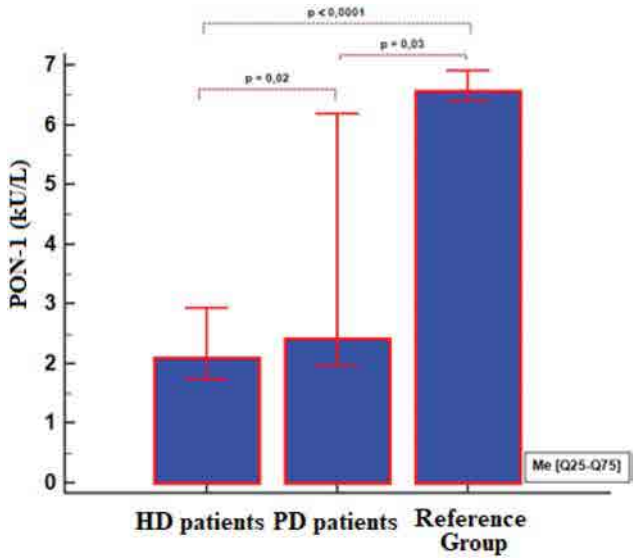


Fig. 1. Serum PON1arylesterase activity in the dialysis and reference groups.

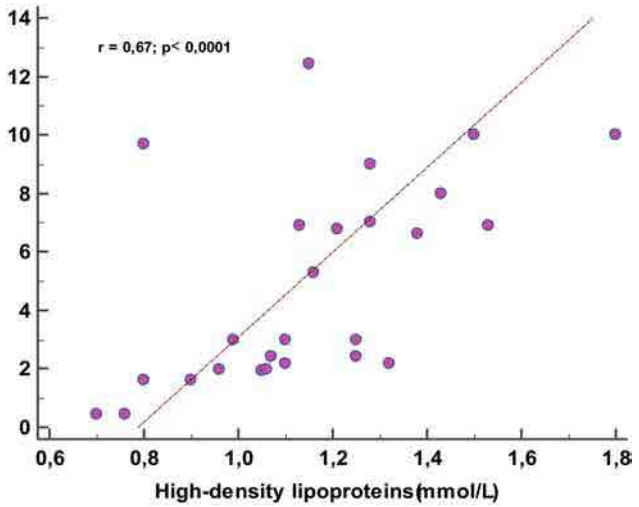


Fig. 2. Association between serum PON1 arylesterase activity and high-density lipoproteins in PD patients.

Conclusion: We observed a decrease in serum PON1 arylesterase activity in ESRD patients compared to the control group. The lowest level of serum PON1 arylesterase activity was determined in HD patients. Moreover, the association between serum PON1 arylesterase activity and a decrease in antioxidant blood markers was found.

Our results support the hypothesis that OS is an important mediator in the progression of kidney diseases and indicates a potential antioxidant role of serum PON1 arylesterase activity in ESRD patients. We suggest using serum PON1 arylesterase activity as an antioxidant marker in dialysis patients.

P1592 **HYPOCHLOREMIA AND INFLAMMATION: RELATIONSHIP BETWEEN SERUM CHLORIDE LEVELS AND NEUTROPHIL-TO-LYMPHOCYTE RATIO IN INCIDENT CHRONIC HEMODIALYSIS PATIENTS**

Francisco Valga[1], Tania Monzon[1], Fernando Henriquez[1], Gloria Anton-Perez[1]

[1]*CENTRO DE DIALISIS AVERICUM NORTE LAS PALMAS, Las Palmas de Gran Canaria, Spain*

Background and Aims: Recently the role of chloride in patients with heart failure has been reevaluated. Some studies have linked it to higher mortality in these patients, being more important, even, than sodium. On the other hand, some authors have found a higher mortality in patients with low chloride levels and sepsis. The underlying mechanisms in both cases are unknown. Some authors attribute it to concomitance with metabolic alkalosis, however, this is not a reason that fully explains these findings. Neutrophil-to-Lymphocyte Ratio (NLR) is an emerging marker of inflammation comparable to established ones such as C-reactive protein, ferritin, etc. It is also a good biomarker of mortality in certain populations such as cancer, cardiovascular and renal. Patients with chronic kidney disease on hemodialysis have high cardiovascular comorbidity and a high rate of inflammation. However, there are no studies that correlate chloride levels to inflammation markers, such as NLR, in this population. Therefore, the aim of our study was to determine if there is a relationship between chloride and NLR in our population of patients on chronic hemodialysis.

Method: Restrospective cohort study. We analyzed the values of chloride and NLR of 396 incident patients on hemodialysis over a period of 3 years (between 2016 and 2019). The patients were divided into three groups, depending on the levels of chloride (tertiles): (1: <100, 2: 100.1-103, 3> 103.1 mEq / l). In each group the average of NLR was calculated.

Results: The mean age in our sample was 64.73 ± 0.57 years, 39.7% were women (N = 157). The average of NLR was 3.84 ± 2.65 and chloride was 101.03 ± 3.91. We found that patients in the lower chloride level tertile were associated with a higher NLR levels (p <0.012). (Figure 1)

Conclusion: Incident hemodialysis patients with lower chloride levels had higher NLR values. These findings suggest a greater tendency to inflammation in these patients.

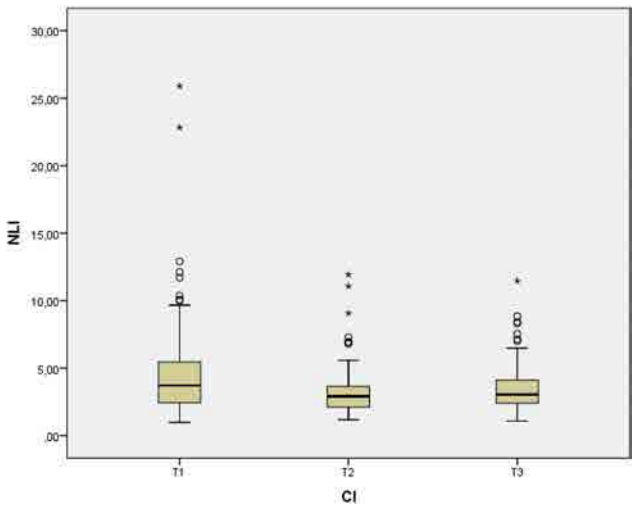


Figure 1: Chloride tertiles and NLR values

P1593

THE ASSOCIATION BETWEEN THE ANCLE-BRACHIAL INDEX AND MARKERS OF INFLAMATION IN CHRONIC HEMODIALYSIS PATIENTS

Nevi Pasko[1], Ariana Strakosha[1], Arieta Dedej[2], Loredana Kapidani[2,3], Fjona Nasto[2], Elvana Rista[4], Vilma Cadri[3], Suela Mumajesi[3], Nestor Thereska[2]

[1]University Hospital Center "Mother Thereza", Nephrology, Tirana, Albania, [2]Amerikan Hospital, [3]University Hospital Center "Mother Thereza" and [4]Hygeia Hospital

Background and Aims: Among hemodialysis patients, peripheral arterial disease (PAD) represents an important health care burden and has been associated with high mortality. The ancle-brachial index (ABI), is a reliable and noninvasive method used to asses PAD. The aim of this study was to evaluate the prevalence of PAD in patients undergoing chronic hemodialysis and the association with inflammation and malnutrition using serum C-reactive protein (CRP) and serum albumin as biomarkers.

Method: The study was conducted at different hemodialysis centers in patients receiving hemodialysis three times a week. We excluded patients with atrial fibrillation or who had been recently hospitalized. The ABI has been used as a diagnostic tool for PAD and measured before a hemodialysis session. A value of ABI less than 0.9 was considered abnormal. To better estimate the impact of malnutrition and inflammation we used the serum albumin, blood lipids values and serum C-reactive protein values defined by calculating the mean of the last three measurements.

Results: A total of 261 ESRD patients on maintenance hemodialysis were enrolled in the study. Mean age was 56.0 ($\pm$12) years, 58% were males, and 17.6% were diabetics. Mean time on hemodialysis was 5.9 ($\pm$6.7) years, with 24% of patients on dialysis for less than 3 years. Among our patients we found that the prevalence of PAD was 23.4%, of whom 58.1% were men. We found that age, diabetes, duration of hemodialysis, low serum albumin levels and high serum triglyceride levels were risk factors for PAD in hemodialysis patients. The multivariate analysis of our study has shown that a lower level of albumin and higher level of CRP were significantly associated with an ABI less than 0.9 (odds ratio, 4.54; 95% confidence interval, $P = 0.017$) after adjusting for demographic, clinical, biochemical and medication data. We did not find significant differences in serum calcium, phosphate or PTH levels between patients with PAD and those without it.

Conclusion: In conclusion, the present study showed high prevalence of PAD in patients on hemodialysis. The prevalence was higher in diabetics. Low albumin levels and C-reactive levels were independent risk factors of PAD. We found that early diagnosis and treatment of PAD could help to improve the quality of life of hemodialysed patients and postpone arterial complications in this group of patients.

P1594 INSULIN-LIKE GROWTH FACTOR-1 IS ASSOCIATED WITH MUSCLE STRENGTH IN PATIENTS ON HEMODIALYSIS

YU-KANG CHANG[1], Paik Seong Lim[2]

[1]Tungs' Taichung Metroharbour Hospital, Department of Medical Research and [2]Tungs' Taichung MetroHarbor Hospital, Division of Renal Medicine

Background and Aims: Muscle strength is a solid predictor of outcome for hemodialysis (HD) patients. In this study, our aim is to investigate the relationship between muscle strength and six potential muscle biomarkers including irisin, myostatin, myonectin, antichymotrypsin, urotensin II and insulin-like growth factor 1 (IGF-1).

Method: The cohort of prevalent HD patients in Tungs' Taichung MetroHarbor Hospital were participated in our cross-sectional clinical study. The serum muscle markers were determined using standardized enzyme-linked immunosorbent assay methods. The muscle strength was accessed by handgrip strength (HGS) on arm without vascular access before dialysis session.

Results: A total of 175 patients were enrolled in this study with an average age of 59.2 and among them 84 were males (48.0%). Among the six potentially associated with muscle strength viz HGS, we found that only IGF-1 level (r=0.180, p=0.017) correlated positively with HGS. In the multivariate regression analysis, IGF-1 was also significantly correlate with HGS after adjusted for patients' demographics [RR (95%CI)=0.091 (0.015-0.167)]. In addition, increased IGF level was correlated positively to irisin levels.

Conclusion: Our study suggested that IGF-1 was associated with HGS. The role of IGF-1 signaling in the induction of muscle atrophy in uremic patients is not fully understood.

Figure: Future research is required to obtain more detailed insight and may help to alleviate skeletal muscle atrophy in these patients.

P1595 NUTRITION AND INFLAMMATORY STATUS IN DIALYISIS PATIENTS WITH SUICIDAL IDEATION AND DEPRESSION

Neri Ruvalcaba Contreras[1], Roxana Michel Márquez Herrera[1], Rosalinda Valencia Coronado[1], Alejandro Calderón Fabián[1], Sandra Estefania López Alvarado[1], Laura Cortés Sanabria[1], Alfonso Martín Cueto Manzano[1], Enrique Rojas Campos[1]

[1]*Mexican Intitute of Social Security, Biomedical Research Unit 02, Guadalajara, Mexico*

Background and Aims: The main precursor of suicidal ideation is depression, which is the most common psychiatric disorder in dialysis patients. Studies have shown an association of depression with nutritional alterations and systemic inflammation; however, in patients with kidney disease there is no data about a possible relation between malnutrition, inflammation and suicidal ideation. Therefore, the aim of this study was to describe and compare the nutritional and inflammation statuses in dialysis patients with suicidal ideation and depression.

Methods: Cross sectional study; 36 dialysis patients >18 years old, any gender, who signed informed consent were included. Suicidal ideation was measured by one psychiatrist using the Beck Scale for Suicidal Ideation, and depression with the Beck Depression Inventory. A dietitian evaluated nutritional status by means of anthropometric and biochemical variables, and the Dialysis Malnutrition Score. Additionally, C-reactive protein and fibrinogen were measured. Results were classified as dichotomous variables for suicidal ideation (yes/no) and depression (no: normal-mild/ yes: moderate-severe).

Results: Prevalence of depression, suicidal ideation and malnutrition were 97%, 63% and 31%, respectively. Main results are shown in the table.

Conclusions: Patients with suicidal ideation and depression did not show significant differences in any of the assessed nutritional variables. However, patients with suicidal ideation and depression seemed to have higher concentrations of C-reactive protein and fibrinogen. The present study opens an opportunity for future research.

Table:

	Suicidal Ideation			Depression		
	Yes (n 23)	No (n 13)	*p*	Yes (n 21)	No (n 15)	*p*
Age (years)	34 (28-63)	32 (28-36)	0.46	33 (27-60)	33 (30-40)	0.93
PD / HD (%)	7 / 93	23 / 77		19 / 81	7 / 97	
Hemoglobin (g/dL)	10 (9-11)	11 (10-13)	0.12	11 (9-12)	10 (9-11)	0.24
Albumin (g/dL)	4.1 (3.7-4.5)	4.2 (3.8-4.4)	0.72	4.2 (3.7-4.5)	4.0 (3.7-4.3)	0.28
Creatinine (mg/dL)	10 (6-11)	10 (7-12)	0.68	10 (7-12)	10 (5-12)	0.98
Triglycerides (mg/dL)	109 (88-161)	120 (100-171)	0.74	148 (100-198)	109 (84-129)	0.11
LDL-Cholesterol	69 (61-100)	68 (49-90)	0.16	74 (56-93)	62 (55-96)	0.72
Body Mass Index (m/kg^2)	24 (21-27)	24 (23-27)	0.15	25 (22-27)	24 (22-28)	0.78
Triceps skinfold thickness (mm)	15 (10-18)	15 (12-20)	1.00	15 (12-19)	15 (8-18)	0.38
Arm muscle area (cm^2)	25 (21-50)	25 (18-35)	0.45	25 (20-42)	25 (21-41)	0.85
Nutritional status (%)*						
Malnourished	39	18	0.41	18	50	0.10
Wellnourished	61	82		82	50	
C-reactive protein (mg/l)	5.6 (3-14)	4.0 (3-5)	0.08	5.6 (3-12)	4.0 (3-9)	0.89
Fibrinogen (mg/dL)	403 (328-532)	375 (278-465)	0.26	421 (365-555)	365 (252-392)	0.02

*According to the Dialysis Malnutrition Score (wellnourished=7-10; malnourished=11-35).

PD: peritoneal dialysis; HD: hemodialysis.

P1596 **CHANGES IN INFLAMMATORY MARKERS AND NUTRITIONAL PARAMETERS IN PATIENTS RECEIVING INCREMENTAL HEMODIALYSIS:A REAL LIFE STUDY.**

Stefania Drovandi[1], Novella Conti[1], Valeria Falqui[1], Rodolfo Russo[1], Fabio Massarino[1], Enzo Moriero[1], Martina D'Ercole[1], Alessandra Civati[1], Eldi Lecini[1], Giacomo Garibotto[1], Leda Cipriani[1]

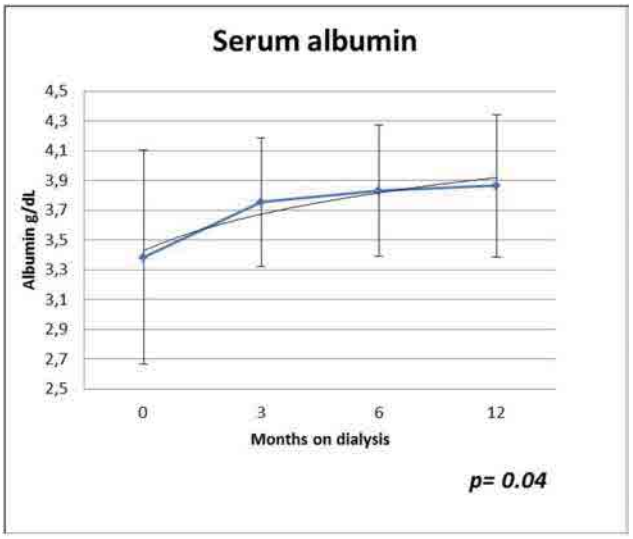
[1]Ospedale Policlinico San Martino- Università degli Studi di Genova, Nephrology, Dialysis and Transplantation Division, Genova, Italy

Background and Aims: In the last years a "personalized" hemodialysis (HD), the so-called incremental HD, has been proposed as alternative approach to the standard three-times-weekly HD. By this modality, the dose of dialysis is low at the beginning of RRT and progressively increases over time in parallel with the decrease of residual renal function. Recent studies suggested that an incremental approach to HD initiation and less frequent dialysis regimens may have several benefits, including preservation of renal function and better quality of life. However, little information is available on the effects of incremental hemodialysis on inflammation and nutritional parameters.

Method: We conducted a retrospective analysis of 92 incident adult patients (mean age 72.4±14 years) who started twice-weekly HD between January 2016 to December 2019 at our Unit. 29 patients, who were still on twice-weekly treatment at December 2019, entered the final analysis (mean follow-up 17.5±12 months). Results for C-reactive protein and ferritin, as an expression of inflammation, together with albumin, total cholesterol levels, and normalized protein catabolic rate (nPCR), that reflects nutritional status and daily dietary protein intake, were analyzed over 12 months for all patients. Results are expressed as mean ± standard deviation (SD). Patients mean age was 74±11 years; baseline eGFR 4 ± 1.99 ml/min/1.73mq; Kt/V 1.32±0.38. Males: 62% ; ethnicity: 97% White and 3% Asian. The causes of ESRD were diabetic nephropathy (24%) glomerulonephritis (24%), hypertensive nephrosclerosis (14%), obstructive nephropathy (17%), interstitial nephritis (7%), acute tubular necrosis (3%) and unknown (11%). Incident patients with a follow-up period shorter than three months were excluded from analysis. Exclusion criteria were: history of neoplasia, inflammatory bowel disease, vasculitis, major acute CV events or infections 12 months before or after the beginning of HD, patient's refusal to undergo thrice-weekly HD. Baseline characteristics at the time of initiation of twice-weekly HD were compared with characteristics at 3, 6 and 12 months. The variables were analysed using linear regression models. P<.05 values were considered to be statistically significant.

Results: Both C-reactive protein and ferritin showed a nonlinear fitting, with a decline after the first three months (54% and 46% respectively) and a further increase at 6 months (baseline vs 12 months p=0.3 and 0.08, respectively). nPCR, as a trend only, increased progressively with time. Serum albumin increased logarithmically (baseline vs 12 months p=0.04) (Figure 1) with a steep increase at 3-6 months and a moderate increase thereafter. Serum cholesterol increased also progressively over time (baseline vs 12 months p=0.03)(Figure 2).

Conclusion: This study shows that twice-weekly hemodialysis is associated with progressive increase in serum albumin and cholesterol, and, as a trend only, in nutritional intake. However, twice weekly hemodialysis does not seem to be able to control inflammation.



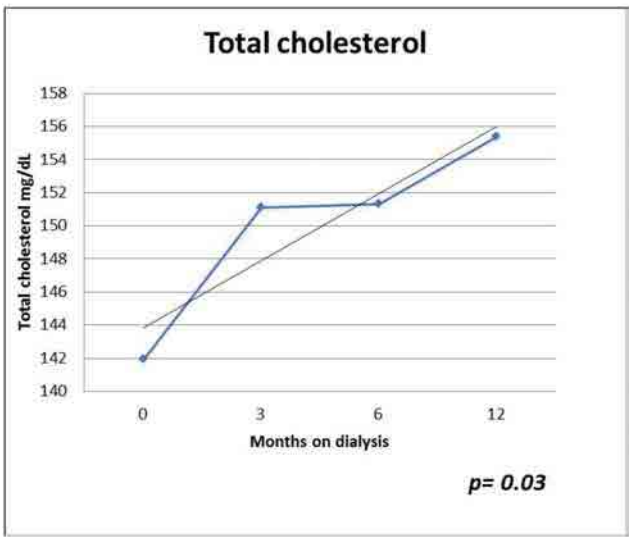


Figure:

P1597 USE OF FEBUXOSTAT IN HYPERURICEMIC PATIENTS UNDERGOING DIALYSIS: TOLERABILITY AND EFFICACY IN INDIAN POPULATION

Sourabh Sharma[1], Neha Sharma[2]

[1]Gaur Hospital, Nephrology, Sriganganagar, India and [2]Gaur Hospital, Pathology, Sriganganagar, India

Background and Aims: Hyperuricemia is associated with increased vascular events in chronic kidney disease (CKD). Febuxostat is an effective alternative treatment in this subset but there is scarcity of data on its use in patients undergoing dialysis. The aim of our study was to evaluate efficacy and safety profile of febuxostat in hyperuricemic Indian patients on dialysis.

Method: Fifty four patients with CKD stage 5D and hyperuricemia were included in the study from Jul 2018 to Mar 2019. Febuxostat was started and patients followed-up over 6 months for decline in uric acid and any adverse events.

Results: Out of 54 cases, 30 were males (55.56%). Mean age was 51.28±16.9 years. Thirty two cases were diabetic (59.26) and all cases were on two or more antihypertensives. Nine cases were suffering from gout at time of inclusion and mean serum creatinine in these cases was 10.47 mg/dl. Symptomatic cases responded to treatment within 2 weeks of therapy. Mean serum uric acid level at 3 months post-treatment (4.65±0.96 mg/dL) was significantly reduced compared from pre-treatment level (8.34± 1.18 mg/dL) [$p<0.01$]. Serum uric acid level remained significantly low for 6 months without deterioration in eGFR. Blood pressure remained well controlled during therapy period and only four cases required increment of antihypertensive medication. Out of 54 cases, five stopped medication due to adverse events. Out of them, three cases were on peritoneal dialysis. Three cases developed skin rash which subsided once drug was withheld. Most common side effect was nausea (7/54) and headache (6/54).

Conclusion: Febuxostat at a low dose of 40 mg/dl is well tolerated among dialysis population. It effectively declines serum uric acid level. Gastrointestinal side effects are most common adverse event which corresponds to non-dialysis population. There was no higher risk of skin rash or other major adverse event in this subset. It is also worth mentioning that hyperuricemia is associated with significant vascular events and all cases included in study were hypertensive.

P1598 USE EXPERIENCE OF FIRAPY (FAR-INFRARED THERAPY) TREATMENT FOR WOUND OF HEMODIALYSIS PATIENTS

Kunimi Maeda[1], Takaaki Wada[1], Shihoko Ikeda[1]

[1]*Shakujii-kouen Jin Clinic, Nephrology, Tokyo, Japan*

Background and Aims: By using far-infrared irradiation, Firapy treatment is expected to improve blood flow by expanding peripheral blood vessels and an effect of promoting wound healing due to its non-thermal effect.

The aim is to discuss the clinical effects of Firapy treatment applying to dialysis recipients with lower extremity wounds.

Method: Two dialysis patients with diabetic nephropathy who developed lower extremity wounds were included in this study. Starting from the initial stage of the wound, patients received wound rinsing at each dialysis, followed by a 30-minute Firapy treatment. The following items were observed over time from the beginning of the treatment. Evaluation and examination were then conducted.

(1) The wound healing process was evaluated over time from wound measurements, images, and records.

Results: In both cases, early initiation of Firapy treatment resulted in good healing without leaving any signs of infection or scarring. By using far-infrared irradiation, Firapy treatment has been considered to be an effective therapeutic means due to it could enhance angiogenesis and microcirculation which allows restoration of blood flow in ischemic tissue and its effect of promoting wound healing.

Conclusion: Appling Firapy treatment to the wound showed the possibility of making wound healing be faster and healed beautifully. Firapy treatment has been considered to be one of effective way to wound healing. We are looking forward to use Firapy treatment for other cases.

P1599 USE OF ASCORBATE-RICH DIALYSATE IN HEMODIALYSIS PATIENTS

IOANNIS GRIVEAS[1]

[1]*417 Army Share Fund Hospital, Nephrology, Chalandri-ATHENS, Greece*

Background and Aims: Increments of oxidative stress have been addressed as one potential cause for the accelerated atherosclerosis of chronic kidney disease patients. Ascorbate (vitamin-C) represents one of the most prominent antioxidants both in plasma and intracellulary. Unsupplemented dialysis patients have reportedly lower plasma levels of ascorbate in comparison to healthy controls, mostly due to a loss into the dialysate. Purpose of our study was the recording of the experience of the use of Ascorbate-Rich Dialysate in patients under hemodialysis (HD).

Method: 11 HD patients were recruited for the study. During a period of 8 weeks they were receiving Ascorbate-Rich Dialysate (2g/lt). Ascorbic acid levels were estimated before and at the end of the study period. We also monitored patients' anemia profile (Hb, Hct, ferritin, TSAT, rhEPO dose), lipid and nutrition status.

Results: Ascorbic acid values were towards the lower accepted levels in our patients (3.25 ± 1.01 mg/l) at the beginning of the study period. After 8 weeks receiving Ascorbate-Rich Dialysate, acorbic-acid levels were significantly increased (6.87 ± 1.50 mg/l) without transcending the upper accepted limit. During the notice period, our patients were behaved normally without any sort of adverse events. Mean Hct levels remained stable (39.10 ± 3.70% with conventional dialysate vs 39.67 ± 1.59 % with usage of ascorbate-rich dialysate). The same conclusion was noticed with Hb levels (12.85 ± 1.20 vs 13.15 ± 0.49). Mean rhEPO dose per week (epoetin- alfa) decreased (9000 ± 5200 iu vs 6250 ± 4300 iu, p=NS) and administration of Fe stopped to all of our patients. Ferritin (>700), TSAT (>35) remained stable over the whole study period. Cholesterol, triglycerides and albumin levels did not change significantly with the change of the conventional dialysate to ascorbic-rich one.

Conclusion: Although our study is limited by small numbers of subjects, short durations of follow-up, our results suggest that compared with standard care, ascorbic acid in dialysate bath is a safe choice to increase ascorbic-acid levels in traditionally vitamic C depleted HD patients within safe limits. This raise seems to favors anemia profile of HD population. Longer term studies are required to confirm these results, determine whether these changes translate into improved patient outcomes and cost-effectiveness.

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RENAL TRANSPLANTATION. EXPERIMENTAL, IMMUNE-TOLERANCE OF ALLOGENIC AND XENOGENIC TRANSPLANTS

P1600 KIDNEY PERFUSION WITH MESENCHYMAL STROMAL CELLS OR EXTRACELLULAR VESICLES PREVENTS ISCHAEMIC DAMAGE THROUGH CD73/ADO SYSTEM IN A RAT MODEL OF DCD DONATION

Maria Antonietta Grignano[1], Stefania Bruno[2], Marta Tapparo[2], Paolo Iadarola[3], Marilena Gregorini[1], Carmelo Libetta[1], Maria Antonietta Avanzini[4], Simona Viglio[5], Maddalena Cagnone[5], Eleonora Francesca Pattonieri[1], Pasquale Esposito[1,6], Teresa RAmpino[1]

[1]Fondazione IRCCS Policlinico San Matteo and University of Pavia, Unit of Nephrology, Dialysis and Transplantation, Pavia, Italy, [2]Molecular Biotechnology Centre and University of Torino, Department of Medical Sciences, Torino, Italy, [3]University of Pavia, Department of Biology and Biotechnologies "L.Spallanzani, Pavia, Italy, [4]Fondazione IRCCS Policlinico San Matteo and University of Pavia, Pediatric Department, Research Laboratory, Pediatric Oncohematology, Pavia, Italy, [5]University of Pavia, Department of Molecular Medicine, Biochemistry Unit, Pavia, Italy and [6]University and IRCCS Ospedale Policlinico San Martino, 2.Department of Internal Medicine, Nephrology, Dialysis and Transplantation Clinics, Genova, Italy

Background and Aims: Adenosine (Ado), the main substrate of ATP, is a potent endogenous anti-inflammatory nucleoside. Hypoxia induces ATP depletion, AMP extracellular increase that is phosphohydrolyzed to ADO by the enzyme ecto-5′-nucleotidase (CD73). Constitutive CD73 expression is higher in deep cortex outer medulla that is the most vulnerable region to ischemic injury. Notably CD73 is also expressed on Mesenchymal Stromal Cell (MSC) and is essential phenotypic marker.

Previously in a rat model of Donation after Circulatory Death (DCD), we demonstrated that the perfusion of ischemic kidney with MSC or MSC derived Extracellular Vesicles (EV) protects tissue up regulating mitochondrial energetic metabolism genes.

The aim of this study was to investigate the role of CD73/Ado system in MSC/EV protection from ischemia.

Method: Fisher rats were used as kidney donors and Lewis rats as MSC donors. MSC missing CD73 were produced by electroporation in the presence of specific siRNA to block CD73 expression (siMSC). EV were isolated from supernatants of MSC and siMSC (siEV) medium through differential ultracentrifugations. Size distribution and enumeration analysis were performed using NanoSight NS300. EV phenotypic characterization was performed in flow cytometer using CD45, CD49e, CD63, CD9, CD81 and CD73 monoclonal antibodies.

DCD model was obtained by renal artery clamping for 20 minutes. This warm ischemia time represents the "no touch period" imposed by the Italian law to death declaration. After nephrectomy, kidneys were perfused in hypothermia (4°C) with Belzer Solution (BS), or BS supplemented with 3x106 MSC (MSC) or BS supplemented with 28,5x109 EV/siEV (EV/siEV). The effluent fluid (EF) was collected at the beginning (T0), every hours (T1, T2, T3) and at the end of the perfusion (T4). Ado and ATP determinations in EF and tissues were performed by HPLC and ELISA, respectively.

Results: EF Ado was significantly higher in MSC vs BS from T1 and in EV vs BS from T0 to T4 ($p<0,05$). Only in EV, EF Ado concentration increased over time from T2 to T4 ($p<0,05$), while in BS, MSC and siEV there was a steady trend over time. There was a negative correlation between EF and tissue levels of Ado ($r=0,67$ $p=0,01$). Tissue ATP was higher in EV and significantly in MSC vs BS ($p<0,01$). There was a negative correlation between tissue ATP and EF ADO levels ($r= 0,79$ $p< 0,0001$). Tissue ATP/Ado ratio was significantly higher in EV vs BS ($p<0,01$). There was a negative correlation between tissue ATP/Ado ratio and EF Ado ($r= 0,84$ $p < 0.0001$). siEV cancelled EV effects on ATP and Ado levels in EF and renal tissue.

Conclusion: CD73 expressed on MSC /EV impacts on cell energy metabolism pathway and ATP generation. This is the first evidence that MSC/EV act through CD73/Ado system to prevent ischaemic damage.

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P1601 **COMPLEMENT MEMBRANE ATTACK COMPLEX DURING THE FIRST WEEK AFTER KIDNEY TRANSPLANTATION AS SEVERITY BIOMARKER TO DELAYED GRAFT FUNCTION**

Carlos Arias-Cabrales[1], Marta Riera[1,2], Maria José Pérez-Sáez[1], Javier Gimeno[3], Carla Burballa[1], Anna Buxeda[1], David Benito[1,2], Dolores Redondo Pachon[1], Marta Crespo[1], Julio Pascual[1], Eva Rodríguez-Garcia[1]

[1]Hospital del Mar, Nephrology, Barcelona, Spain, [2]IMIM, Barcelona, Spain and [3]Hospital del Mar, Pathology, Barcelona, Spain

Background and Aims: Ischemia-reperfusion (I/R) damage is a relevant cause of delayed graft function (DGF). Complement activation is involved in experimental I/R injury, but few data are available about the expression of the complement cascade final component -membrane attack complex (MAC)- and I/R injury in KT patients. We studied the dynamics of membrane attack complex (MAC) as plasma fraction (pMAC) and the histological deposit pattern of C3b, complement factor H (FH) and MAC in DGF patients.

Method: We evaluated pMAC levels in 59 recipients, 38 with immediate graft function and 21 without serum creatinine decreased at day 7 (DGF). pMAC was measured at admission for KT (day 0) and 7 days after KT (day 7). Sandwich ELISAs were used to measure MAC. Additionally, we performed imunohistoquimical stained for MAC, C3b and kidney biopsies (KB) with DGF (n=12) and a control group of one-year protocol biopsies without damage (n=4)

Results: Patients in the DGF group were older, more frequently diabetics and received kidneys from older donors and more frequently controlled cardio-circulatory death type.

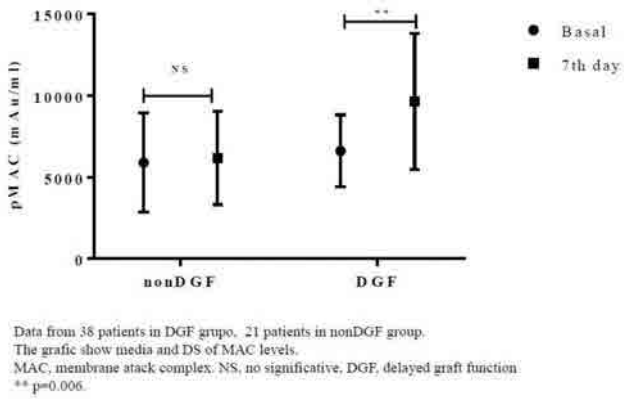
Day0 and day7 post-KT pMAC levels were similar in non-DGF patients 5902±3049 mAu/L vs 6178±2882 mAu/L; p=0.686). However, patients with DGF showed a significant increase of pMAC levels between day0 and day7 (6621±2202 mAu/L vs 9625±4142 mAu/L; p=0.006. Figure 1

Percentage pMAC levels increase (Δ0-7 pMAC%) discriminative assessment analyzed by ROC curve showed a good discriminative value for DGF with an AUC of 0.78; p<0.001 (sensitivity 81%, specificity 66% by cut-off point of 5%). In patients with DGF longer than ten days, we found more frequently patients with a Δ0-7 pMAC >5% (83% vs 17% Δ0-7 pMAC <5% ; p=0.003).Patients with DGF showed renal function at 3 and 6 months, but worse renal function 1 year after KT (serum creatinine 1.78±0.61 vs 1.35±0.30 mg/dl in non-DGF patients). DGF patients with Δ0-7 pMAC >5% displayed worse renal function 1 and 2 year after KT compared to DGF patients with Δ0-7 pMAC <5%.

MAC, C3b and FH stains were observed in tubular epithelial cells basal membrane. DGF-kidney biopsies showed more frequently high-intensity stain for MAC and FH than controls, without differences to C3b stain. DGF-kidney biopsies also showed a higher number of tubules with positive stain and larger perimeter of tubules with positive stains for MAC, C3b and FH than the controls. Figure 2.

Among the 12 patients with DGF-biopsies, three (25%) never recovered renal function, all of them presented Δ0-7 pMAC >5% and intense, diffuse and positive staining in more than 50% of tubular perimeter for MAC, FH and C3b

Conclusion: Complement activation during peritrasplant period could be related with the severity of graft injury and the presence of DGF. Therefore, the determination of MAC levels could be useful to identify patients with possible complement dependent graft injury that might benefit from complement inhibitor therapies



Data from 38 patients in DGF grupo, 21 patients in nonDGF group.
The grafic show media and DS of MAC levels.
MAC, membrane atack complex. NS, no significative, DGF, delayed graft function
** p=0.006.

Figure 1.

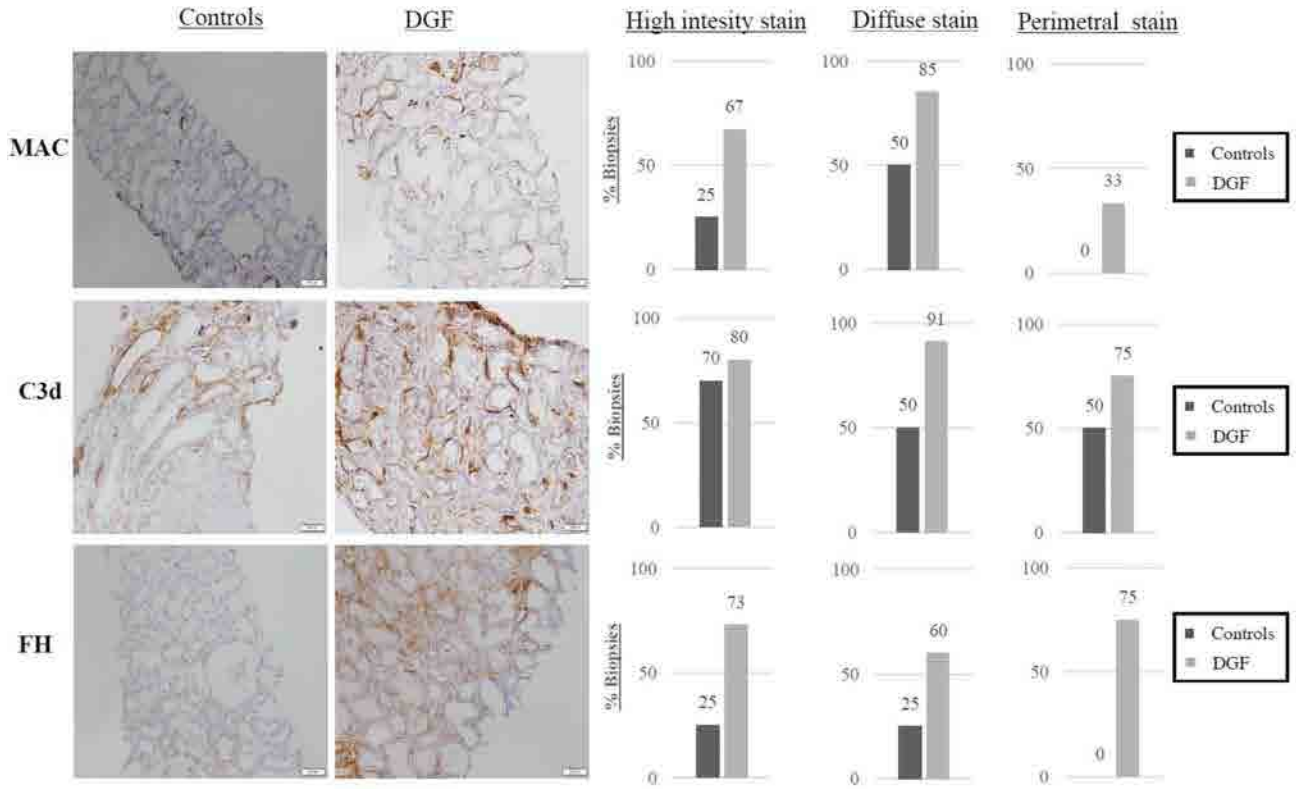


Figure 2.

P1602

MICROVASCULAR INFLAMMATION WITHOUT DSA OR C4D: AN ORPHAN CATEGORY IN BANFF CLASSIFICATION WITH INTENSE CAPILLARITIS AND CYTOTOXIC T-CELL INFILTRATION

Anna Buxeda[1,2], Laura Llinàs[2], Javier Gimeno[3], Carlos Arias Cabrales[1,2], Carla Burballa Tarrega[1], Dolores Redondo Pachon[1,2], Dàlia Raïch Regué[2], Maria José Pérez-Sáez[1,2], Julio Pascual[1,2], Marta Crespo[1,2]

[1]Hospital del Mar, Nephrology Department, Barcelona, Spain, [2]IMIM - Institute Hospital del Mar for Medical Research, Nephrology Department, Barcelona, Spain and [3]Hospital del Mar, Pathology Department, Barcelona, Spain

Background and Aims: Antibody-mediated rejection (ABMR) associated with donor-specific HLA antibodies (DSA) is the leading cause of late allograft failure after kidney transplantation. Microvascular inflammation (MVI) without detectable circulating DSA or C4d + cannot be classified as ABMR according to Banff-2017. The involvement of intragraft lymphocyte subsets in the development of humoral damage in kidney transplantation (KT) is relevant. We aimed to analyze lymphocyte subset distribution in kidney transplant biopsies (KTBx) with ABMR compared with MVI and with normal KTBx.

Method: KTBx with ABMR, MVI (g+ptc≥2, without DSA) or normal findings were included. DSA were identified with Luminex single antigen assays. Intragraft lymphocyte subsets' characterization was performed by immunohistochemistry: T-lymphocytes (CD3, CD4, CD8, Foxp3), B-lymphocytes / plasmatic cells (CD20, CD138), NK cells (CD56), macrophages / monocytes (CD68), cytotoxic cells (TIA1) and activated cells (PD1) were evaluated.

Results: We analyzed 34 KTBx: 21 ABMR, 5 MVI and 8 KTBx with normal findings. KT with ABMR and MVI had more proteinuria at the time of the biopsy compared with the normal group (575 mg/24h and 964 mg/24h *vs* 147 mg/24h, p=0.002 and p=0.005 respectively). DSA were more frequently detected in patients with ABMR (95.2% *vs* 0% and 37.5%, p<0.001 and p=0.003 respectively). KTBx with ABMR and MVI had increased cytotoxic T-cell infiltration apparently corresponding to NK cells in peritubular capillaries (ptc) compared to normal group. Moreover, both groups showed a greater number of macrophages and monocytes in glomeruli. KT with MVI but not with ABMR had a significantly increased activated cell infiltration (PD1+) in ptc compared to the normal group, and showed an increased cytotoxic T-cell infiltration in glomeruli compared to ABMR and normal groups.

Conclusion: ABMR and MVI have an increased infiltration of NK cells with cytotoxic activity in ptc that differs from the normal group. However, KT with MVI show greater infiltration of activated cells in ptc and cytotoxic T-cell in glomeruli compared to ABMR suggesting the possibility of different activation pathways.

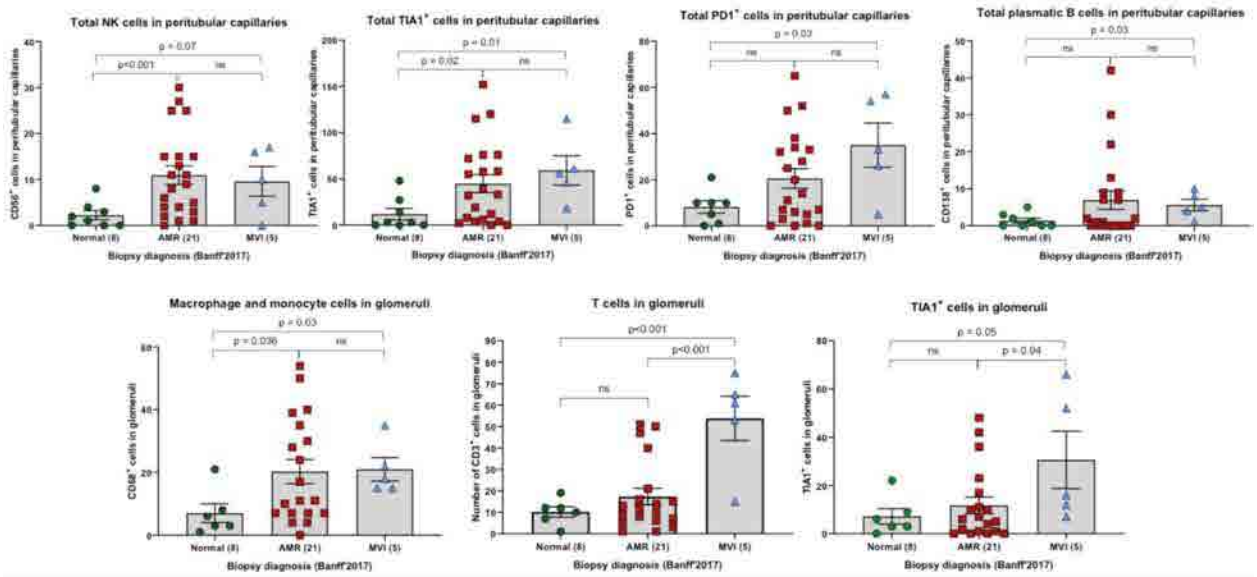


Figure:

P1603

INVOLVEMENT OF SUCCINATE DEHYDROGENASE (SDH) IN DECEASED RENAL TRANSPLANT DONORS' INFAMMATION AND FIBROSIS

Elena Guillén-Gómez[1,2,3], Irene Silva[1,1,2,3], Carla Galano[1,2,3], Yolanda Arce[1,2,3], Francisco Caballero[2,3,4], Lluis Guirado[1,2,3], Montserrat Mercedes Diaz Encarnacion[1,2,3]

[1]Fundació Puigvert, Barcelona, Spain, [2]Institut de Recerca Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [3]Universitat Autònoma de Barcelona, Bellaterra, Spain and [4]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Background and Aims: Succinate is a Krebs cycle intermediate that is converted to fumarate by succinate dehydrogenase (SDH). SDH is part of the electron-transport chain of inner mitochondrial membrane (complex II) and its activity depends indirectly on the oxygen availability. Low oxygen states, such as ischemia, can increase circulating succinate levels due to low SDH activity. In renal transplantation, ischemia and hypoxia can increase renal succinate formation and induce the infiltration of immune cells producing TNF-α, increasing inflammation, renal epithelial apoptosis, as well as leukocyte recruitment, binding and migration, which can lead to renal graft damage.

Method: Samples of pre-implantation renal tissue, 17 from living donors and 40 from deceased donors were analyzed by Real-time PCR.

Results: In kidneys from deceased donors SDH expression is downregulated before transplantation and it lasts for at least the first year. Low SDH gene expression at 4 months after kidney transplant is positively correlated with graft renal function (CKD-EPI) at 12 and 24 months (p=0.046, r= 0.6511 and p= 0.0351, r= 0.4731; respectively). In kidneys from deceased and living donors, SDHD is negatively associated with monocyte recruitment (MCP-1) and activation (IL-1β) and positively with the expression of SOD1. Moreover, only in deceased donors, SDHD gene expression correlates inversely with pro-fibrotic (TGF-β1 and vimentin) and inflammatory (TNF-α) molecules, as well as with M1 (CD80, CD86) and M2 (CD163) macrophage markers, all of which are found to be higher expressed in deceased donor kidneys than in living donor ones.

Conclusion: Our results indicate that low gene expression of SDH in kidneys from deceased donors could result in reduced activity of SDH that would reduce the ability to transform succinate to fumarate resulting in succinate accumulation, increasing inflammation and reparation through fibrosis worsening transplant outcome.

SDHD	TGF-β1	TNF-α	MCP1	IL-1β	ICAM1	CD16	CD80	CD86	CD163	VIM	SOD1
DC	p= 0.042	p= 0.0001	p= 0.008	p= 0.0007	p= 0.005	p= 0.018	p= 0.0004	p= 0.010	p= 0.0001	p= 0.003	p= 0.001
	r= -0.447	r= -0.736	r= -0.563	r= -0.682	r= -0.447	r= -0.511	r= -0.698	r= -0.547	r= -0.749	r= -0.613	r= 0.665
DV	n.s.	n.s.	p= 0.021	p= 0.010	p= 0.027	n.s.	n.s.	n.s.	n.s.	n.s.	p= 0.022
			r= -0.470	r= -0.515	r= -0.451						r= 0.465

P1604 **SIGNIFICANT DETECTION OF UNEXPLAINED HLA ANTIBODIES WITH SINGLE-ANTIGEN BEADS IN PATIENTS ON THE WAITING-LIST WITHOUT PREVIOUS SENSITIZING EVENTS**

Sara Núñez Delgado[1], Carla Burballa Tarrega[1], José Luis Caro[2], Carlos Arias Cabrales[1], Marisa Mir Fontana[2], María José Pérez Sáez[1], Eduard Palou[2], Julio Pascual Santos[1], M. Dolores Redondo Pachón[1], Marta Crespo Barrio[1]

[1]Hospital del Mar, Nephrology Department, Barcelona, Spain and [2]Blood and Tissue Bank, Histocompatibility and Immunogenetics Laboratory, Barcelona, Spain

Background and Aims: The introduction of more sensitive and specific tools as solid phase immunoasssays has improved the ability to detect HLA antibodies. The techniques based on solid phase immunoassays in Luminex system can be performed either as screening assays (with pooled antigen panels that use bead populations coated in affinity-purified class I or class II HLA molecules) or to assess the specificity with single-antigen bead (SAB) assays (single cloned allelic HLA antigen).The sensitivity of each assay Is different, and their results may be discordant. Our objective was to evaluate the potential discrepancies between tests in a cohort of patients on our waiting list with no previous sensitizing events, for their potential influence in the access to transplantation.

Method: Observational study of 184 patients included in the kidney-transplant waiting list on March 31st, 2019. All possible sensitizing events (pregnancy, transfusion and previous transplants) were registered. HLA antibodies where analyzed both by screening and SAB tests.

Results: We limited the observations to males (64.7% of the cohort), as most women (95.4%) had a known sensitizing event, not being possible to discard possible pregnancies in the remaining. Of men, 46.2% had a sensitizing event and 63.8% did not. All 63 unsensitized patients showed a negative screening test, and 49 (77,78%) had at least one SAB done being positive in 73.4% (36/49). The positive SAB yielded a cPRA >10% in 30 cases (between 21-85%), mostly (27/30) due to HLA class II antibodies (88.8% with at least one DQ antibody) with a median MFI of 1571 (range:752-17650).

A thorough review of specificities showed that 81% DQB1* and 89.6% DQA1* antibodies did not show consistency in all beads included for the same allele.

Conclusion: Screening and SAB assays show a significant discordancy in unsensitized men included in the waiting list for kidney transplantation. Automated detection of antibodies by SAB without a proper specialized interpretation may wrongly limit access to transplantation.

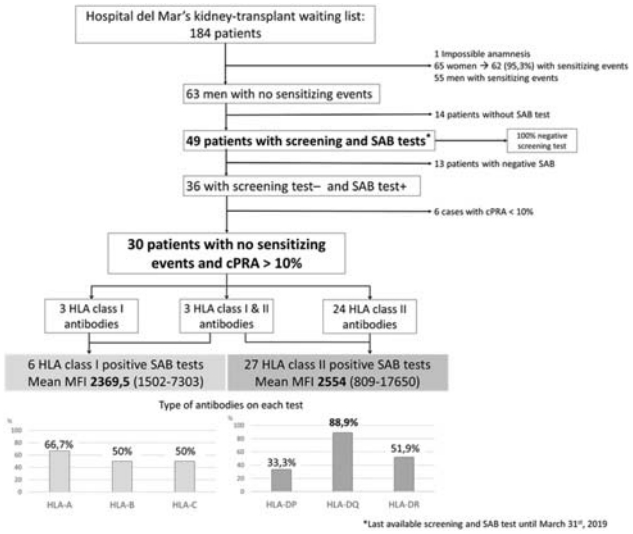


Figure:

P1605

THE EARLY RISE OF URINARY EXOSOMAL BK VIRUS MICRORNA AS A PREDICTIVE MARKER FOR BK VIRUS NEPHROPATHY IN A PROSPECTIVE KIDNEY TRANSPLANTATION COHORT

WON HEE CHO[1], Su Woong Jung[1], Jung Woo Seo[1], Ju-Young Moon[1], Kyung Hwan Jeong[2], Chan Duck Kim[3], Byung Ha Chung[4], Yeong Hoon Kim[5], Sang ho Lee[1], Jae Berm Park[6], MI JI KIM[1]

[1]Kyung Hee University Hospital at Gangdong, nephrology, Seoul, Korea, Rep. of South, [2]Kyung Hee University Medical Center, nephrology, [3]Kyungpook national University hospital, nephrology, [4]The Catholic University of Korea, Sedoul St.Mary's Hospital, nephrology, [5]Inje University busan paik hospital, nephrology and [6]Sungkyunkwan University, Samsung Hospital, transplantation surgery, seoul,

Background and Aims: BK virus nephropathy (BKVN) is one of the significant contributors to allograft dysfunction in kidney transplantation. Because of the lack of effective anti-viral medication, early detection of BKV replication and preemptive management is vital to preserving allograft function. Herein, we investigated the predictive value of urinary exosomal BKV-microRNA for BKVN in the kidney transplantation cohort.

Method: ARTKT (assessment of immunologic risk and tolerance in kidney transplantation) is a prospective observational cohort in which a total of 420 kidney transplant recipients were enrolled from 7 teaching hospitals in South Korea since 2015. Urine samples were collected at 0.5, 3, 6, 12, and 24 months after kidney transplantation in this cohort. All enrolled patients were reviewed to identify the patients diagnosed with BKVN histologically (biopsy-proven BKVN) and those experienced BK viremia defined as plasma BKV DNA load $> 4 \log_{10}$ copies per mL (presumptive BKVN). Urinary exosomal miR was quantified using real-time reverse transcription PCR.

Results: 10 patients and 14 patients developed biopsy-proven BKVN and presumptive BKVN, respectively. Because of unavailable urine samples, urinary exosomal BKV-microRNA was investigated in 8 patients with biopsy-proven BKVN and 13 patients with presumptive BKVN. 61 patients with no evidence of BKVN were selected as a negative control. Most of BKVN was developed in a median time of 3.4 months after transplantation. In line with this pattern, urinary exosomal BKV-microRNA peaked at 3 months after transplantation and decreased thereafter in biopsy-proven BKVN and presumptive BKVN, keeping higher value in biopsy-proven BKVN compared to presumptive BKVN after 3 months. At 2 weeks after transplantation, half of the patients with biopsy-proven BKVN showed an early rise of urinary exosomal BKV-microRNA, whereas patients with presumptive BKVN and no evidence of BKVN did not. However, plasma BK virus DNA was not detected in all groups at 2 weeks after transplantation. In multivariate cox proportional hazards model, urinary exosomal BKV-microRNA was significantly associated with biopsy-proven BKVN.

Conclusion: A urinary exosomal BKV-microRNA increase as early as 2 weeks after kidney transplantation predicts future BKVN development, enabling early intervention.

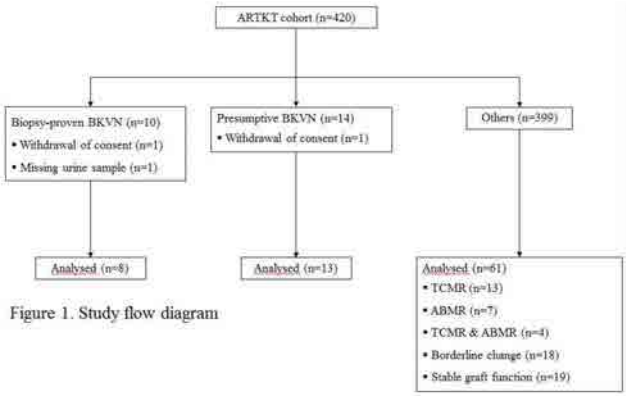


Figure 1. Study flow diagram

Figure:

	Biopsy-proven BKVN (n=8)	Presumptive BKVN (n=13)	Others (n =61)	*p* value
Age (year)	50.4 ± 10.7	49.5 ± 13.6	49.1 ± 11.1	0.90
Male gender, n (%)	7 (87.5)	7 (53.8)	36 (59.0)	0.27
BMI (kg/m^2)	21.7 ± 2.9	22.5 ± 2.6	23.2 ± 3.1	0.23
DM, n (%)	1 (12.5)	2 (15.4)	25 (41.0)	0.18
HTN, n (%)	8 (100.0)	11 (84.6)	54 (88.5)	0.60
Cold ischemia time (minute)	128.1 ± 94.6	103.9 ± 109.3	102.9 ± 117.6	0.47
ABO incompatible KT, n (%)	2 (25.0)	4 (30.8)	12 (19.7)	0.60
HLA mismatch number	4.0 ± 1.5	3.3 ± 2.3	3.4 ± 1.6	0.56
Induction immunosuppression				
Antithymocyte globulin, n (%)	2 (25.0)	3 (23.1)	17 (27.9)	1.00
Basiliximab, n (%)	6 (75.0)	10 (76.9)	44 (72.1)	1.00
Maintenance immunosuppression				
Steroid, n (%)	8 (100)	12 (92.3)	60 (98.4)	0.45
Tacrolimus, n (%)	7 (87.5)	12 (92.3)	60 (98.4)	0.12
MMF or MPA, n (%)	7 (87.5)	11 (84.6)	55 (90.2)	0.11
Desensitization				
Rituximab, n (%)	2 (25.0)	4 (30.8)	21 (34.4)	0.73
Intravenous immunoglobulin, n (%)	1 (12.5)	3 (23.1)	19 (31.1)	0.57
Plasmapheresis, n (%)	1 (12.5)	3 (23.1)	21 (34.4)	0.48
Donor				
Donor age (year)	52.0 ± 11.9	51.4 ± 9.5	46.7 ± 11.3	0.09
Male donor, n (%)	4 (50.0)	7 (53.8)	27 (44.3)	0.81
Deceased donor, n (%)	5 (62.5)	2 (15.4)	7 (11.5)	<0.01

Figure 2. Time course urine exosomal bkv-miR-B1-5p and plasma BK virus DNA load after kidney transplantation.

P1606 **TIM-3/GAL-9 AS PREDICTORS OF COMPOSITE OUTCOMES AFTER KIDNEY TRANSPLANTATION: A COHORT STUDY**

Lin Yan[1], Yangjuan Bai[1], Yamei Li[1], Yi Li[1], Xianding Wang[2], Yunying Shi[3], Lanlan Wang[1]

[1]West China Hospital of Sichuan University, Laboratory Medicine, Chengdu, P.R. China, [2]West China Hospital of Sichuan University, Urology, Chengdu, P.R. China and [3]West China Hospital of Sichuan University, Nephrology, Chengdu, P.R. China

Background and Aims: T cell immunoglobulin and mucin domain (Tim-3) and its ligand, galectin-9 (Gal-9), play an important role in immune regulation. Serum soluble Tim-3 (sTim-3) and Gal-9 (sGal-9) were observed to be correlated with renal function after kidney transplantation in our previous study, but whether these two could predict the adverse outcomes after transplantation is unknown.

Method: 91 recipients receiving kidney transplantation were enrolled in this cohort study. 20 of all recipients suffered composite outcomes after kidney transplantation within two years. 71 recipients had stable renal function during this period. The expressions of sTim-3 and sGal-9 before and one month after transplantation were measured by ELISA.

Results: The level of sTim-3 before transplantation was significantly higher in recipients with stable renal function than composite outcomes (Median: range, 2275: 840-4236 pg/ml vs 1589: 353-3094 pg/ml, P=0.002, shown in Figure 1). The level of sGal-9 after transplantation was significantly lower in stable group than composite outcome group (Median: range, 4869: 1418-13080 pg/ml vs 6852: 4128-10760 pg/ml, P=0.003, shown in Figure 1). Area under curve (AUC) of sTim-3 before transplantation was 0.737 (P=0.002, shown in Figure 2) through the analysis of receiver operating characteristic curve (ROC curve). AUC of sGal-9 after transplantation was 0.751 (P=0.003, shown in Figure 2). After survival analysis, the percentage of recipients free from composite outcomes was significantly lower in patients with low level of sTim-3 than high sTim3 (P<0.0001, shown in Figure 3), so was in patients with high sGal-9 than low sGal-9 (P=0.0004, shown in Figure 3).

Conclusion: Serum sTim-3 and sGal-9 could predict the adverse outcomes within two years after kidney transplantation.

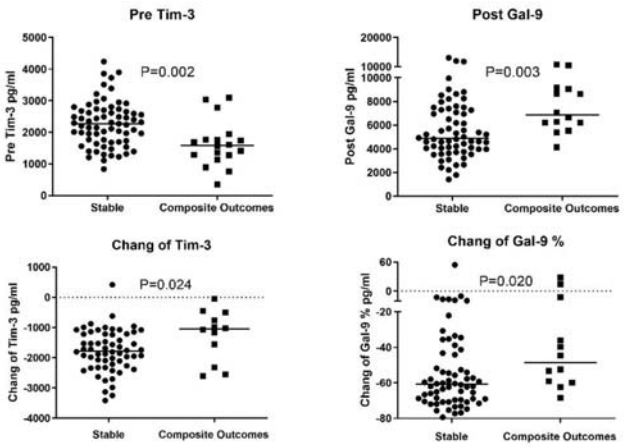


Figure 1

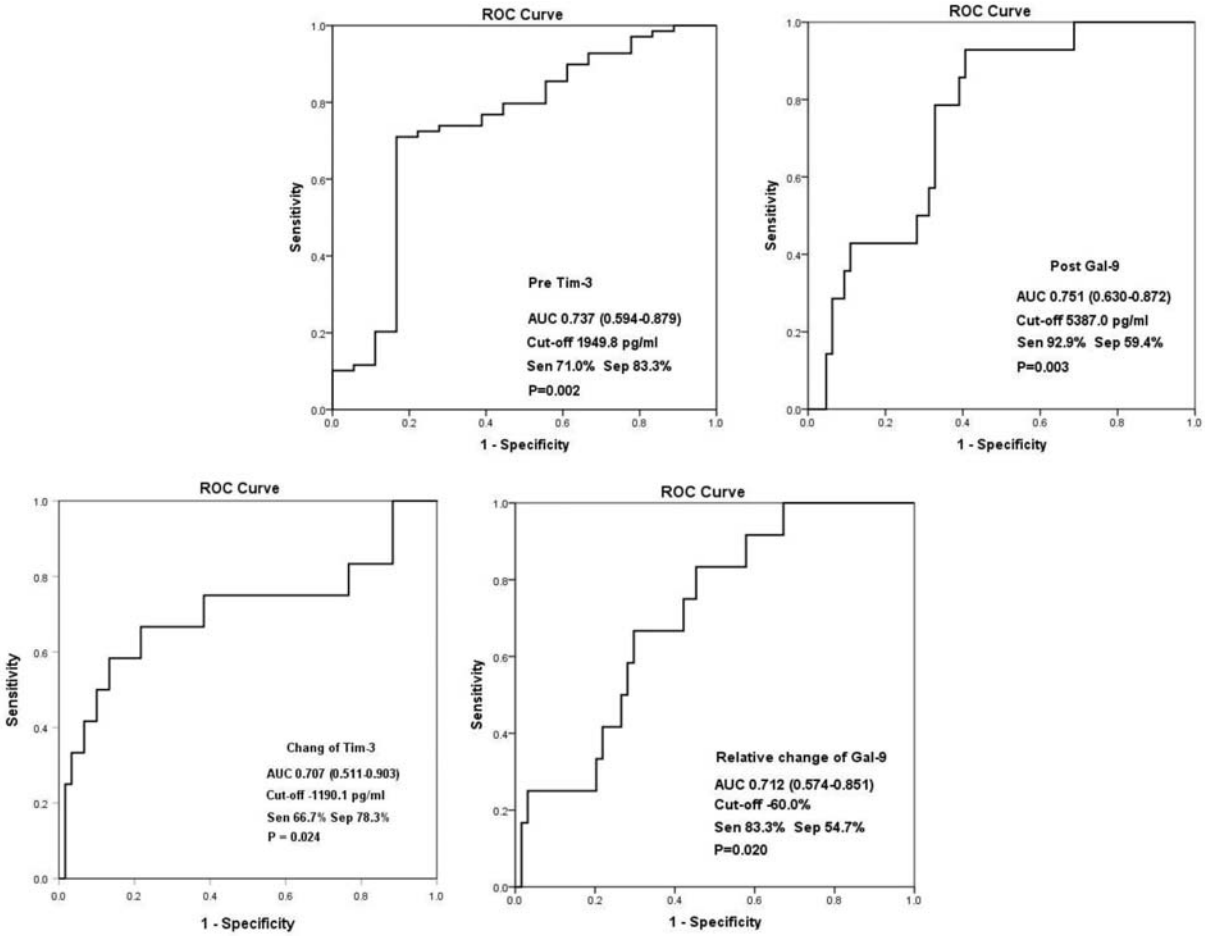


Figure 2

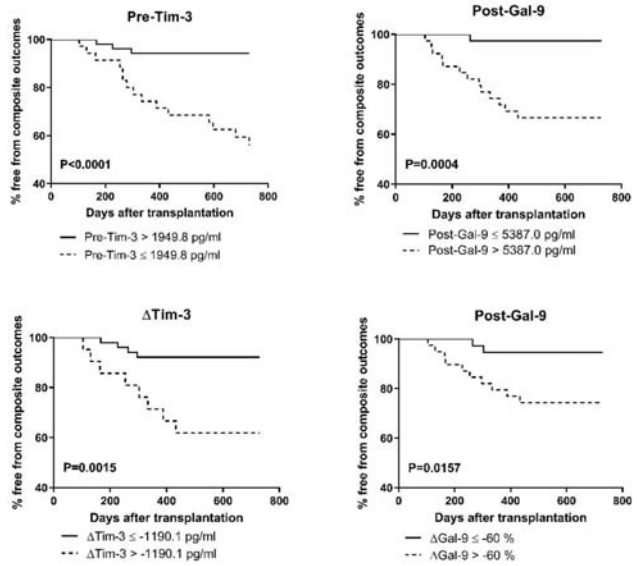


Figure 3

P1607 **CD 137 SIGNALING IN REGULATORY DENDRITIC CELLS IS REQUIRED FOR SUPPRESSING A SYSTEMIC INFLAMMATION IN THE BM12-INDUCIBLE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS.**

Jong Soo Lee[1], Hong Rae Cho[2], Jongha Park[1], Kyung Don Yoo[1], Byungsuk Kwon[3], Hojong Park[2], Sang Jun Park[2], Kyungsun Park[1]

[1]Ulsan University Hospital, Internal medicine, Ulsan, Korea, Rep. of South, [2]Ulsan University Hospital, General Surgery, Ulsan, Korea, Rep. of South and [3]Ulsan University Hospital, Biomedical institute, Ulsan, Korea, Rep. of South

Background and Aims: Although CD137 is well known as a costimulatory receptor in T cells, limited information is available for its immunoregulatory function. Here, we report that CD137 signaling maintains $CD11b^+$ regulatory dendritic cells (DCs) that can suppress activation of donor T_H1 and T_H17 $CD4^+$ T cells in chronic graft-versus-host disease (GVHD).

Method: Chronic GVHD can be induced by mouse BMT models in which donor and recipient strain combination is MHC class I identical but MHC II mismatched. This chronic GVHD model recapitulates human SLE.

Results: : The deletion of CD137 in recipient mice shifted the disease phenotype toward acute GVHD, which was caused by the activation of donor T cells. $CD137^{-/-}$ recipients had had characteristic changes associated with acute GVHD: 1) there were defects in differentiation of T follicular helper (T_{FH}) cells, germinal-center B cells, and plasma cells, and production of anti-DNA IgG_1 autoantibody; 2) their splenic DCs showed dys-regulated expression of DC-specific transcription factors and pro-inflammatory genes, and 3) there were strong activation of donor T cells but decreased Treg cells in the $CD137^{-/-}$ recipient spleen. $CD11b^+$ splenic DCs stimulated with agnostic anti-CD137 antibody and CpG markedly increased expression of immunomodulatory genes, and such regulatory DCs inhibited acute GVHD in $CD137^{-/-}$ recipients. Their suppressive action was mediated through IL-10 that is indispensable for the induction and expansion of peripheral Treg cells.

Conclusion: Our study identifies CD137 signaling in DCs as an important braking point to prevent systemic inflammation, and this control system may be considered as a therapeutic strategy for a variety of inflammatory and autoimmune diseases.

P1608 **CXCL13 IS STRONGLY INDUCED BY RENAL ISCHEMIA REPERFUSION INJURY AND CORRELATES WITH SEVERITY OF RENAL INFLAMMATION**

Mi-Sun Jang[1], Kirill Kreimann[1], Robert Greite[1], Song Rong[1], Sibylle Von Vietinghoff[1], Roland Schmitt[1], Oliver Dittrich-Breiholz[2], Jan Hinrich Bräsen[3], Vijith Vijayan[4], Hermann Haller[1], Stephan Immenschuh[4], Faikah Gueler[1]

[1]Hannover Medical School, Department of Nephrology, Hannover, Germany, [2]Hannover Medical School, Core Unit Genomics, Hannover, Germany, [3]Hannover Medical School, Pathology, Hannover, Germany and [4]Hannover Medical School, Transfusion medicine, Hannover, Germany

Background and Aims: Ischemia reperfusion injury (IRI) is a strong trigger of inflammation and is tightly linked to renal allograft damage and function. CXCL13 or B lymphocyte chemoattractant (BLC) is a chemokine that controls B cell organization in lymphoid tissues and has recently been described as a biomarker for B cell involvement in acute kidney allograft rejection.

Method: To show, that CXCL13 is already induced by IRI alone we used renal IRI models in mice with different ischemia times and a kidney transplantation model. We measured serum CXCL13 and characterized cell infiltrates by immunohistochemistry and performed single cell RNA sequencing. Allogenic and isogenic kidney transplantation (KTX) in mice was done to evaluate these findings in the transplant setting.

Results: Systemic CXCL13 levels increased within hours after surgery in a time dependent manner, both after induction of IRI and KTX. Levels of CXCL13 increased with duration of ischemia time and were higher in allogenic than isogenic transplantation with equal duration of ischemia. CXCR5, the receptor for CXCL13, is mainly expressed on B lymphocytes but also on a subset of T lymphocytes and macrophages. CXCR5 positive infiltrates were detected in IRI kidneys seven days after injury. In kidney allografts interstitial B cell infiltrates were observed as early as seven days and increased further towards three weeks after KTX.

Conclusion: The current findings indicate that IRI is a strong trigger of CXCL13 expression in the kidney and release into the circulation, which is followed by B lymphocyte infiltration into damaged tissue in ischemic and renal allografts.

P1609 HLA EPITOPE MATCHING IN KIDNEY TRANSPLANTATION AND PRACTICAL APPLICATION

Irena Rambabova Bushljetikj[1], Goce Spasovski[1], Koco Dimitrovski[2]

[1]*University Clinic of Nephrology, Nephrology, Skopje, Republic Of North Macedonia and* [2]*Institute of Transfusion Medicine, Skopje, Republic Of North Macedonia*

Background and Aims: HLA compatibility between donor and recipient is an important factor that influences graft outcomes after kidney transplantation. Increasing number of class I (HLA-AB) and class II (HLA-DR) mismatches are associated with an increased risk of acute rejection and graft loss. Recent developments have increased our understanding of the structural basis of HLA antigenicity and may allow accurate evaluation of the immunogenic potential of broad antigen HLA mismatches.

The immunogenicity of HLA antigens is determined by continuous and discontinuous short sequences of amino acids that form the antibody-accessible regions within each HLA allele known as epitopes. HLAMatchmaker, a computer algorithm that calculates the number of epitope mismatches between donors and recipients by considering each HLA allele as a combination of distinct epitopes known as triplets (continuous amino acid sequences) or eplets (closely located contiguous amino acid sequences).

Method: A total number of 55 adult patients with LDKT were included in the study. The inclusion criteria: first transplantation of one organ - kidney, use of living donor related or unrelated, emotionally related (spouses) donor. Data concerning donor - sex, age of the donor, type of donation (related or unrelated donor), and data concerning the recipients: sex, age, hemodialysis vintage, underlying disease, type of immunosuppressive therapy, were analyzed. The number of eplet HLA mismatches for each recipient and donor pair at HLA class I (HLA-AB) and class II (HLA-DR) loci was calculated using HLAMatchmaker (Version 1.2)

Results: In our study we have included 55 patients. 44 patients have related and 11 have unrelated donors. From the group of related donors 31 patients were haploidentycal, with 3 HLA miss match, in the group of unrelated donors-recipients 5 of them have 6 miss match. According HLA MM triplets Class $1 + 2 <$ or > 20 we have devided 2 groups, but no statistical difference on the graft function was observed in the follow up period.

Three acute rejections were reported in the group of patients with HLA miss match triplets Class $1 + 2 > 20$.

Conclusion: An increasing number of epitope HLA mismatches is associated with an increased risk of acute rejection. Triplet HLA mismatches may provide better risk stratification for acute rejection and graft survival among those who are otherwise classified as low immunological risk at the broad antigen level.

P1610 THE PERSPECTIVE APPROACH TO ASSESING THE DONOR-RECIPIENT HISTOCOMPATIBILITY IN CADAVERIC KIDNEY TRANSPLANTATION

Aleksei Zulkarnaev[1], Vadim Stepanov[1], Andrey Vatazin[1]

[1]*Moscow Regional Research and Clinical Institute, Surgical department of transplantation and dialysis, Moscow, Russia*

Background: In Russia, each transplant center has its own separated waiting list. This significantly reduces the ability to select the optimal recipient in terms of tissue compatibility. **Aim**: to perform a multivariate analysis of the effect of the number of epitope mismatches on transplant survival.

Method: An observational retrospective cohort study was performed, which included 824 adult recipients. All patients underwent transplantation of a cadaveric kidney compatible by blood group. The endpoint was considered transplant loss. The death-censored graft survival was evaluated. The calculation of the number of epitope mismatches (EpMM) was carried out using information from publicly available resources about the population frequency of haplotypes and the repertoire of epitopes with confirmed immunogenicity. All possible combinations of the donor and recipient genotypes were compiled, and the probability of each combination was calculated. Then, for each combination with nonzero probability the number of donor epitopes absent in the recipient was determined. After that, the weighted average EpMM was calculated, where the weighted coefficient was the normalized probability of occurrence of each combination.

Results: All recipient donor pairs had HLA incompatibilities (HLA MM): 1.9% - 1 HLA MM, 6.7% - 2 HLA MM, 29.9% - 3 HLA MM, 38.5% - 4 HLA MM, 18, 1% - 5 HLA MM, 4.9% - 6 HLA MM. EpMM increased with increase of the HLA MM count, but not linearly: 6 [interquartile range – IQR 4; 7] (from 2 to 7), 12 [IQR 7.74; 17.25] (from 4 to 20), 18 [IQR 14; 22] (from 8 to 28), 24 [IQR 20; 30] (from 10 to 33), 30.5 [IQR 25; 37] (from 13 to 35) and 36 [IQR 26.5; 44.5] (from 15 to 40) for 1, 2, 3, 4, 5, and 6 HLA MM, respectively.

Significant risk factors for graft loss in the adjusted multivariate model were: HLA MM (1 – HR 1; 2– HR 1.24 [95% confidence interval - 95% CI 0.7; 2.15], p = 0.344; 3– HR 1, 48 [95% CI 0.86; 2.33], p = 0.251; 4– HR 1.88 [95% CI 1.32; 2.52], p <0.001; 5– HR 2.41 [95 % CI 2; 2.93], p <0.001; 6– HR 2.98 [95% CI 2.59; 3.46], p <0.001) p <0.001; duration of conservation HR 1.08 per hour [95% CI 1.02; 1.16], p = 0.01; panel-reactive antibodies (PRA) HR 1.24 per every 10% [95% CI 1.06; 1.58], p = 0.01; but not the type of donor, age and gender of the recipient.

When included EpMM in the model, significant risk factors were: EpMM (<10– HR 1; 10-19– HR 1.71 [95% CI 1.09; 2.49], p = 0.021; 20-29– HR 2,11 [95% CI 1.59; 2.68], p <0.001; 30-39– HR 2.4 [95% CI 1.96; 2.86], p <0.001; 40-49– HR 2, 59 [95% CI 2.17; 3.04], p <0.001; ≥50– HR 2.71 [95% CI 2.31; 3.15], p <0.001) p <0.001; PRA HR 1.18 for every 10% [95% CI 1.09; 1.5], p = 0.007; but not the duration of conservation, donor type, age and gender of the recipient. However, HLA MM was no longer a significant risk factor for HR graft loss 1.19 [95% CI 0.88; 1.55], p = 0.451. Increasing the EpMM from <10 to 10-19 significantly increases the risk of graft loss. This is an important aspect in the context of our study, since the number of EpMM 10-19 can correspond to 2-6 HLA MM.

Validation of this method of assessing immunological load on a larger sample of patients is required. The list of immunogenic epitopes is constantly updated. The accumulation of this knowledge can improve results of transplantation.

Conclusion: The number of epitope mismatches remains an important factor in long-term transplant survival even when adjusted for other risk factors: the number of HLA mismatches, the donor type and the level of presensitization. This determines the possibility of using this method as an adjuvant in the donor-recipient pair selection. At the same time, there is a theoretical possibility of using this method as an alternative to the traditional assessment of tissue compatibility of a donor and a recipient.

P1611 **PRE-ANALYTICAL CONSIDERATIONS IN STUDYING CIRCULATING MICRORNA EXPRESSION: COMPARISON BETWEEN PAIRED EDTA PLASMA, EDTA WHOLE BLOOD AND PAXGENE BLOOD RNA TUBES**

Veerle Wijtvliet[1], Amaryllis Van Craenenbroeck[1,2], Annemieke Smet[1], Steven Van Laere[3], Annick Massart[1,4], Benedicte De Winter[1], Daniel Abramowicz[1,4], Kristien Ledeganck[1]

[1]University of Antwerp, Laboratory of Experimental Medicine and Paediatrics and member of the Infla-Med Centre of Excellence, Antwerp, Belgium, [2]University Hospitals Leuven, Department of Nephrology, Leuven, Belgium, [3]University of Antwerp, Translational Cancer Research Unit, Department of Medical Oncology, Antwerp, Belgium and [4]Antwerp University Hospital, Department of Nephrology and Hypertension, Antwerp, Belgium

Background and Aims: microRNA (miRNA) dysregulations have been related to pathological processes, including kidney disease. Relative stability in blood makes miRNAs attractive biomarkers. The current recommendation is to use fresh EDTA plasma samples (i.e. processed within 30 min. from sampling) to study circulating miRNA. However, cumbersome logistics might preclude broad implementation. Therefore, we investigated the potential of whole blood EDTA and PAXgene blood RNA tubes as alternative sources to study circulating microRNA expression profiling.

Method: Paired EDTA plasma, EDTA whole blood and PAXgene blood RNA tubes were obtained from 10 healthy adults (50% male). EDTA plasma samples were processed within 30 min. after sampling and immediately stored at -80°C. EDTA whole blood tubes and PAXgene tubes were kept at room temperature for 48 hours after sampling. Subsequently, the content of the EDTA whole blood samples was transferred to a 15 mL Falcon tube and stored at -80°C. PAXgene tubes were transferred to -20°C following the manufacturer's protocol. Within 1 month of storage, all samples were thawed and miRNA was extracted using the Qiagen miRNeasy serum/plasma kit and subjected to RNA-sequencing (Oxford Genomics Centre). Based on the raw data, a count table was created using the online tool miRDeep* for the identification of both novel and known microRNAs. Subsequent downstream bio-informatic analyses approaches consisted of 1) unsupervised hierarchical clustering with principal component analysis (PCA); 2) calculation of differential miRNA expression using generalized linear models with differences considered significant if the false discovery rate-adjusted p-value was inferior to 10%.

Results: Initial assessment of the count table showed significant differences in the number of detected microRNAs. A median of 220 different microRNAs was detected in EDTA plasma samples versus 661 in PaxGene samples ($p < 0.05$) and 490 in EDTA whole blood samples ($p < 0.05$) (Figure 1A). We also found fewer novel miRNAs in EDTA plasma samples than in PAXgene samples ($p < 0.001$) and EDTA whole blood samples ($p < 0.05$). Low count microRNAs, defined as below 10 reads in more than 20% of the samples, were more abundant in Paxgene samples versus EDTA plasma samples ($p = 0.0039$), but this difference was not significant when comparing EDTA whole blood samples with EDTA plasma samples (Figure 1B). PCA analysis (Figure 1C) showed a clear separation of samples according to the blood collection method, strongly suggesting that the blood collection method predominantly determines the miRNA expression profile.

Conclusion: Bio-informatic analyses demonstrated different miRNA expression profiles according to three different blood collection methods, underpinning the importance of a standardized method for the collection of blood aimed at studying circulating miRNAs. As such, this study has important implications for the design of novel studies aiming to investigate circulating miRNAs.

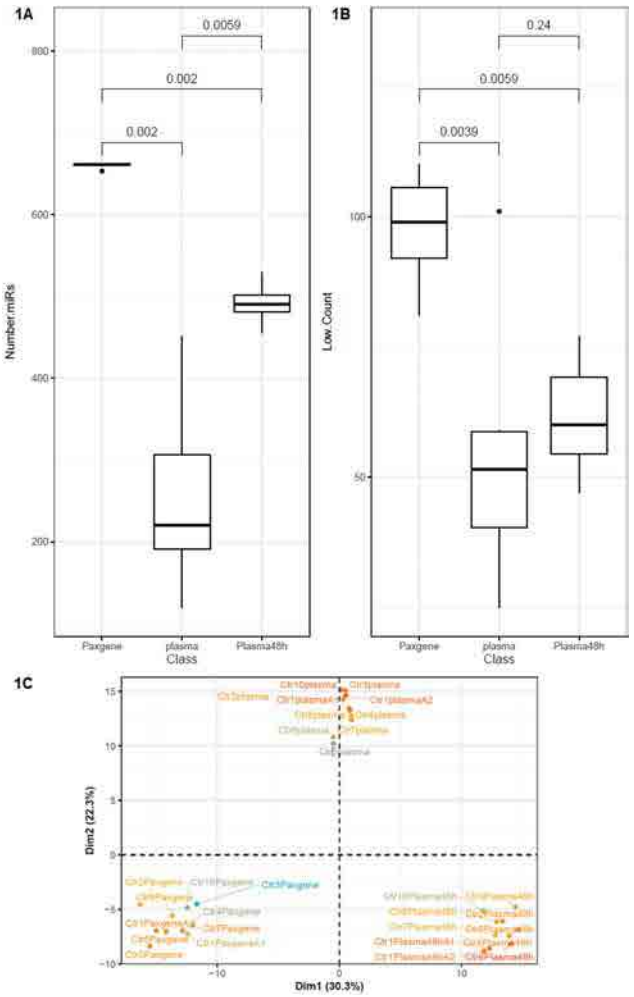


Figure 1: A median of 220 different microRNAs was detected in EDTA plasma samples versus 661 in PaxGene samples ($p < 0.05$) and 490 in EDTA whole blood samples ($p < 0.05$) (Figure 1A). Low count microRNAs were more abundant in Paxgene samples versus EDTA plasma samples ($p = 0.0039$) (Figure 1B). PCA analysis showed a clear separation of samples according to the blood collection method (Figure 1C). Paxgene = Paxgene blood RNA tube; Plasma48h = EDTA whole blood and; plasma = EDTA plasma.

P1612

CAN THE URINARY NITRATE TO CREATININE RATIO BE USED AS A MARKER FOR KIDNEY TRANSPLANT REJECTION?

Amy Riddell[1], John Kirkwood[2], Miranda Smallwood[1], Paul Winyard[1], Bridget Knight[1], Karen Steer[2], Lynette Puddicombe[2], Lidia Romanczuk[2], Angela Shore[1], Mark Gilchrist[1]

[1]University of Exeter and [2]Royal Devon and Exeter NHS Trust

Background and Aims: Early identification and treatment of kidney transplant rejection episodes is vital to limit loss of function and prolong the life of the transplanted kidney and recipient. Current practice depends on detecting a creatinine rise. A biomarker to diagnose transplant rejection, either at an earlier time point, or to inform earlier decision making to biopsy, could be transformative. Urinary nitrate concentration is elevated in renal transplant rejection. Nitrate is a nitric oxide (NO) oxidation product. Transplant rejection upregulates NO synthesis via inducible nitric oxide synthase leading to elevations in urinary nitrate concentration. Historically, assays for measurement of inorganic nitrate in biological fluids have been too time consuming to be useful in a clinical setting. We have recently validated a urinary nitrate concentration assay which could provide results in a clinically relevant timeframe. Our aim was to determine whether urinary nitrate concentration is a useful tool to predict renal transplant rejection in the context of contemporary clinical practice.

Method: We conducted a prospective observational study, recruiting renal transplant participants over an 18 month period. We made no alterations to the patients' clinical care including medications, immunosuppression, diet and frequency of visits. We collected urine samples from every clinical attendance including routine attendances, unscheduled attendances for acute clinical indications, and on the day of attendance for biopsy, for those who underwent biopsy. We measured the urinary nitrate to creatinine ratio (uNCR) between patient groups including routine attendances, biopsy proven rejection and biopsy proven "no rejection". uNCR was examined over time for those with transplant rejection. Groups were compared using a 2 tail t-test of unequal variance, for statistical significance.

Results: A total of 2656 samples were collected. uNCR during biopsy proven rejection, median 49 μmol/mmol, IQR 23-61, was not significantly different from that of routine samples, median 55 μmol/mmol, IQR 37-82 (p=0.56), or biopsy proven "no rejection", median 39 μmol/mmol, IQR 21-89, (P=0.77). Overall uNCR was highly variable; median 52 μmol/mmol, IQR 31-81, with no diagnostic threshold for kidney transplant rejection. Furthermore, within-patient uNCR was highly variable over time, and thus it was not possible to produce individualised patient thresholds to identify rejection.

Conclusion: The urinary nitrate to creatinine ratio is not a useful biomarker for renal transplant rejection.

P1613 INFLUENCE OF GENETIC POLYMORPHISM IN MMPS AND TIMPS ON ALLOGRAFT OUTCOME IN RENAL TRANSPLANT RECIPIENTS

Mansi Bhatt[1]

[1]SGPGIMS, Nephrology, Lucknow, India

Background and Aims: Renal transplantation (RT) is currently the most effective replacement therapy and believed as a boon for patients with end-stage renal disease (ESRD). Allograft rejection remains to be one of the crucial impediments in successful renal transplantation. Matrix metalloproteinases (MMPs) and their natural inhibitors (tissue inhibitors of matrix metalloproteinases; TIMPs) play an important role in immune-mediated tissue destruction of the allograft by allowing influx of leucocytes and mononuclear cells into the graft. The study of MMPs and TIMPs in transplant rejection may also lead to novel approaches in the therapy of rejection processes. To investigate the association of functional polymorphisms in MMP-1 (-1607 1G/2G), (-519 A/G); MMP-3(5356 A/G), (1161 A/G); MMP-9 (1721G/C), (Q279R A/G), (R668Q G/A); TIMP1(+536 C/T) and TIMP3(-1298 C/T gene with risk of allograft rejection in renal transplant recipients of North India.

Method: A total of two hundred live related renal transplant donors and recipients pairs blood sample was collected and were genotyped for MMP-1 (-1607 1G/2G), (-519 A/G); MMP-3(5356 A/G), (1161 A/G); MMP-9 (1721G/C), (Q279R A/G), (R668Q G/A); TIMP1(+536 C/T) and TIMP3(-1298 C/T) gene polymorphisms by polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP) methodology. All two hundred renal transplant recipients were categorized into 162 non-rejecters and 32 rejecters and were analyzed further. All the statistical analysis was done using SPSS software.

Results: The genotype frequencies of MMP1 (-1607 1G/2G) [2G/2G; odds ratio (OR) = 2.97, 95% confidence intervals (95% CI) = 1.69-5.20, $P \leq 0.05$]; MMP9 (Q279R) [RQ; odds ratio (OR) = 0.47, 95% confidence intervals (95% CI) = 0.25-0.99, P = 0.02 & QQ; odds ratio (OR) = 0.49, 95% confidence intervals (95% CI) = 0.25-0.94, P = 0.03]; MMP9 (P574R) [PR; odds ratio (OR) = 2.70, 95% confidence intervals (95% CI) = 1.77-4.13, $P \leq 0.05$ & RR; odds ratio (OR) = 2.70, 95% confidence intervals (95% CI) = 1.09-6.71, P = 0.03]; TIMP1(+536 C/T) [CT; odds ratio (OR) = 15.41, 95% confidence intervals (95% CI) = 9.12-26.05, $P \leq 0.05$ & TT; odds ratio (OR) = 7.01, 95% confidence intervals (95% CI) = 3.39-14.49, $P \leq 0.05$] and TIMP3(-1298 C/T) [CT; odds ratio (OR) = 0.31, 95% confidence intervals (95% CI) = 0.19-0.50, $P \leq 0.05$] was significantly associated with allograft rejection. On comparison of genotypic frequencies for MMP-1, MMP-3, MMP-9, TIMP1 and TIMP3 gene polymorphisms between rejecters and non-rejecters no significant difference was found while comparing genotypic frequencies of non-rejecters with donors a significant association was observed in MMP1 (-1607 1G/2G) [$P \leq 0.05$]; MMP9 (Q279R) [P = 0.02]; MMP9 (P574R) [$P \leq 0.05$]; TIMP1 [$P \leq 0.05$] and TIMP 3 [$P \leq 0.05$] respectively. Therefore, MMP1 (-1607 1G/2G), MMP9 (Q279R), MMP9 (P574R), TIMP1 and TIMP3 demonstrated significantly reduced risk for allograft rejection. MMP1 (-1607 1G/2G) [$P \leq 0.02$]; MMP9 (P574R) [$P \leq 0.05$]; TIMP1 [$P \leq 0.05$] and TIMP3 [P =0.01] was also found significantly associated on comparison between rejecters and donors.

Conclusion: Mutant genotypes/ alleles for MMP1 (-1607 1G/2G); MMP9 (Q279R); MMP9 (P574R); TIMP1 (+536 C/T) and TIMP3 (-1298 C/T) are associated with reduced risk for allograft rejection and improved allograft survival in North Indian transplant recipients and could serve as an ideal marker to predict pre-transplant allograft outcome.

P1614 **ANTIAPOPTOTIC EFFECS OF CATECHIN AND GEMIGLIPTIN ON TACROLIMUS-INDUCED RENAL INJURY IN MICE**

Hyun Lee Kim[1], BYUNG CHUL SHIN[1], JONG HOON CHUNG[1]

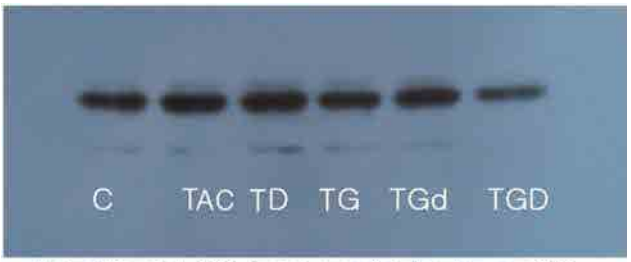
[1]*Chosun University Hospital, Internal Medicine, Divison of Nephrology, Gwangju, Korea, Rep. of South*

Background and Aims: The aim of this study was to investigate the anti-apoptotic effects of catechin (CA) and dipeptidyl peptidase IV (DPP IV) inhibitor gemigliptin on tacrolimus (TAC)-induced nephropathy in mice.

Method: The mice (n=30) were divided into 5 groups (n=6/group); control group were intraperitoneally (IP) injected 0.9% saline, TAC group were IP injected TAC 2.5 mg/kg, DPP IV inhibitor group were given in addition gemigliptin 20 mg/kg (G20) by oral gavage. TAC-CA group were given TAC by IP injection and CA 100 mg/kg by subcutaneous injection. TAC-TA-G20 group were given with same dosages.

Results: The 24 hours urine protein amounts were significantly increased in TAC group (46.1±10.9mg/day) compared to control group (11.3 ±4.4mg/day) and significantly decreased in TAC-CA-G20group (13.1 ±5.9mg/day, P <0.01) compared to TAC group. Serum creatinine levels were significantly increased in TAC group (1.03 ± 0.26 mg/dL) compared to control group (0.17 ± 0.02 mg/day) and significantly decreased in TAC-CA-G20group (0.23 ± 0.05 mg/day, p=0.008) compared to TAC group. In Western blot analysis of apoptotic protein, the BCL-2 protein expression by TAC was significantly suppressed by CA and gemigliptin injection but, the p53 protein expression by TAC was significantly resolved by CA and DPP IV inhibitor. There are proximal tubular edema and mild interstitial inflammation in the kidney of mice after TAC injection but no significant pathologic changes by CA injection and DPP IV inhibitor injected group.

Conclusion: Catechin and DPP IV inhibitor gemigliptin treatment has beneficial antiapoptotic effects on acute TAC-induced renal injury in mice.



Western blot analysis of BCL-2 protein expression In Tacrolimus group (TAC) group, BCL-2 protein expression was higher than that of control group(C). In TD group, TG group, TGd group, and TGD group, BCL-2 protein expression was decreased than that TAC group.

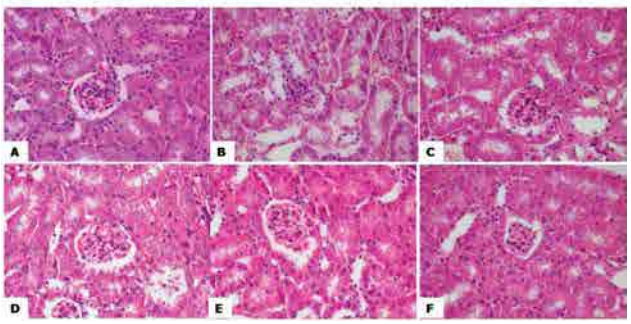


Figure: Western blot analysis of BCL-2 protein expression In Tacrolimus group (TAC) group, BCL-2 protein expression was higher than that of control group(C). In TD group, TG group, TGd group, and TGD group, BCL-2 protein expression was decreased than that TAC group.

P1615 **IDENTIFICATION OF URINARY PROTEOMIC PROFILE OF PATIENTS WITH CHRONIC ALLOGRAFT NEPHROPATHY**

Amr Khalifa[1], Hala El-Wakil[1], Hayam El-Aggan[1]

[1]*Faculty of Medicine Convention Center, Nephrology Department, alexandria, Egypt*

Background and Aims: Chronic allograft nephropathy (CAN) is a major complication that occurs post-transplantation. At present, the diagnosis of chronic allograft nephropathy (CAN) is based on renal biopsy. Therefore, there is an ultimate need to identify more specific and sensitive noninvasive methods for the early diagnosis of CAN. Recently, proteomic-based modalities have been developed to discover biomarkers of CAN.

Method: Urine samples from 75 participants were collected. Participants were divided into 3 groups: Group I: 25 patients with chronic allograft nephropathy, group II: 25transplanted patients with stable renal functions, and group III: 25 healthy control subjects matched for age and sex. Each group was divided into training set and test set. Specimens were purified with magnetic beads-based weak cation exchange chromatography and analyzed in a MALDI-TOF MS.

Results: A Genetic Algorithm (GA) was used to set up the classification models. Five peaks represented the proteomic profile that differentiates between the CAN patients and the control group with sensitivity of 100%, specificity of 100%, recognition capability of 100 % and cross-validation91.7 % and five peaks differentiate between the transplant patients with normal renal functions and the control groups with sensitivity of96.8 %, specificity of 95.5 %, recognition capability of 98 % and cross-validation of 100 %.

Conclusion: We identified a pattern for CAN and transplant patients with normal renal functions by proteomic profiling using MALDI-TOF-MS and magnetic beads.

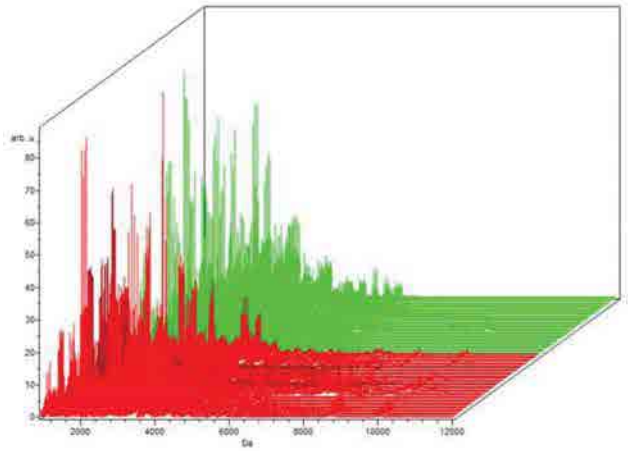


Figure:

The colored stack view in ClinProTools in group 1. It shows the spectra of class 1 (CAN patients) in red color against spectra of class 2 (controls) in green

P1616 **ASSESSMENT OF SEQUENTIAL CHANGES OCCURRING IN THE BODY FLUID COMPOSITION BY BIO-IMPEDANCE ANALYSER IN PRE AND EARLY POST RENAL TRANSPLANT PATIENTS**

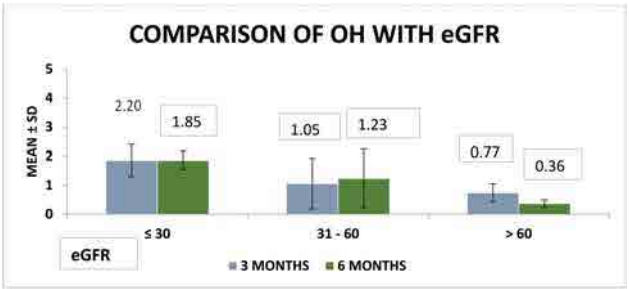
Lalithambika devi B.N[1], Sanjay Maitra[1]
[1]Apollo Hospital Jublihills, Nephrology, Hyderabad, India

Background and Aims: Chronic kidney disease is now recognized as major causes of death in India. The Global Burden of Disease (GBD) study 2015, ranked chronic kidney disease as 17th among the causes of deaths globally (age standardized annual death rate of 19·2 deaths per 100 000 population). Deaths due to renal failure constituted 2·9% of all deaths in 2010–13 among 15–69 year-olds, an increase of 50% from 2001–03. These are varies metabolic derangements in CKD patients, among which volume overload is the major problem contributing uncontrolled hypertension and increases cardiovascular mortality. There will be increased total body water (TBW) and extracellular water (ECW) at the expense of reduced intracellular water (ICW). Renal replacement therapies such as dialysis or kidney transplantation are the major treatment modalities. Renal transplantation is the treatment of choice for end stage renal failure patients. Despite improving renal dysfunction, patients are at risk for existing or new onset of conditions after transplantation and may alter the body fluid physiology. Till date, renal transplant patients received little attention towards fluid balance and nutritional status. There are many studies supporting the use of bioimpedance analyzer as a reliable tool in assessing the fluid status in haemodialysis patients, but there are very few studies done in post renal transplant patients to know their fluid status with single functioning kidney where Glomerular filtration rate are generally much lower than normal.

Method: fifty renal transplant recipients were followed in our centre for 6 months (68 males, maximum were in 31-45years of age). Biochemical parameters like haemoglobin, urea, creatinine, electrolytes, albumin, estimated glomerular filtration rate (eGFR); TBW, ECW, ICW and over hydration (OH) measured using bioimpedance analysis (BCM, Fresenius) were evaluated at baseline (pre-transplant) and after transplant at 3 and 6 months. Baseline biochemical and bio-impedance values were compared with 3 and 6 months post transplant. Patients were divided into 3 sub-groups based on eGFR: **good graft function** (eGFR >60 ml/min), **borderline graft function** (eGFR 30-60 ml/min) and **severe graft dysfunction** (eGFR >30 ml/min/1.73m2). TBW, ECW, OH and ICW were compared between the sub groups of eGFR at 3 and 6 months post transplant.

Results: Comparing before transplant with 3 and 6 months post-transplant, TBW, ECW and OH were reduced while ICW increased significantly with good graft function. On comparing 3 months to 6 months post-transplant, ECW, TBW, OH reduced further but there was not much difference in ICW. OH at 6 months post-transplant was 0.6 L (within normal range of gender-matched individuals from the reference population, that is, −1.1 to 1.1 L). In patients with severe graft dysfunction (<30ml/min), TBW, ECW and OH were remained high when compared to borderline (31-60ml/min) and with good graft function group (>60ml/min). Biochemical improvement was comparable with bio-impedance parameters at 3 months and 6 months post transplant with good graft function.

Conclusion: The BIA showed significant reduction in TBW, ECW and OH by 6 months post transplant and ICW increased as graft function improved post transplantation by 3 months and thereafter, change was not significant. Parameters of Bio-impedance analyzer of well-functioning kidney transplant recipients showed that the altered body water compartments quickly normalizes which is never achieved by a hemodialysis session. We found that Bio-impedance analyzer was useful to know the changes in body fluid composition in post renal transplant patients.



Graph 1: OH was significantly high in low GFR group (<30ml/min) when compared to higher GFR groups at 3 and 6 months post transplant.



Graph 2: TBW was found to be high in low GFR subgroup (<30ml/min) when compare to borderline and good eGFR sub groups at 3 months and 6 months.

P1617 **RENAL TRANSPLANT PATIENTS HARBOR NEUTROPHILS SECRETING B-CELL ACTIVATING FACTOR (BAFF) WHICH CAN BE SUPPRESSED BY MTOR INHIBITORS**

Hannah Steinberg[1], Sebastian Dolff[2], Andreas Kribben[1], Xin Ma[1], Oliver Witzke[2], Benjamin Wilde[1]

[1]University of Duisburg-Essen, University Hospital Essen, Department of Nephrology, Essen, Germany and [2]University of Duisburg-Essen, University Hospital Essen, Department of Infectious Diseases, Essen, Germany

Background and Aims: B cell activating factor (BAFF) is a cytokine which drives B cell survival and maturation. Several studies have shown that elevated BAFF levels in renal transplant patients are associated with increased risk for the development of donor specific antibodies and antibody mediated rejection. It was the aim of this study to investigate neutrophils as cellular source of BAFF in renal transplant patients.

Method: Neutrophils (NT) were freshly isolated from whole blood of healthy controls (HC) and renal transplant patients (RTX). After isolation, purity of neutrophils was usually above 98%. Neutrophils were stimulated with LPS or TNFα in presence of Granulocyte-colony stimulating factor (GCSF) or Granulocyte macrophage colony-stimulating factor (GMCSF). In selected conditions, FK506 or rapamycin was added. Supernatants were harvested after 20 hours of culture and BAFF levels were determined by ELISA.

Results: GCSF/TNFα and GCSF/LPS were the most potent stimuli leading to BAFF secretion of NT in HC (403 ±64 pg/ml and 421 ±69 pg/ml). NT derived RTX showed similar capacity to secrete BAFF as compared to HC (GCSF/TNFα: 515 ±31 pg/ml and GCSF/LPS: 539.4 ±36 pg/ml). Treatment of cultures with rapamycin reduced BAFF levels (515 ±100 pg/ml vs. 348 ±27 pg/ml, $p<0.001$). Treatment with FK506 was less efficacious (515 ±31 pg/ml vs. 465 ±31 pg/ml, $p=0.01$).

Conclusion: NT may enhance of B cell maturation and survival via BAFF. BAFF-secretion by NT can be suppressed with mTOR inhibitors. In renal transplantation, NT might promote formation of allo-antibodies and drive antibody mediated rejection.

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RENAL TRANSPLANTATION. EPIDEMIOLOGY AND OUTCOME

P1624 TORQUE TENO VIRUS FOR RISK STRATIFICATION OF GRAFT REJECTION AND INFECTION IN KIDNEY TRANSPLANT RECIPIENTS - A PROSPECTIVE OBSERVATIONAL TRIAL.

Konstantin Doberer[1], Georg A. Böhmig[2], Elisabeth Puchhammer-Stöckl[2], Gregor Bond[1]

[1]Medical University Vienna, Nephrology and Dialysis, Vienna, Austria and [2]Medical University Vienna, Center for Virology, Vienna, Austria

Background and Aims: The non-pathogenic and ubiquitous Torque Teno virus (TTV) is associated with immunosuppression in solid organ transplant recipients. Studies in kidney transplant patients proposed TTV quantification for risk stratification of graft rejection and infection. This prospective observational trial was designed to assess the potential of TTV load for risk prediction of both, infection and rejection in the first year after transplantation. The objective of this trial was to provide TTV cut-off level to define an optimal TTV range as a basis for a randomised controlled interventional trial to test the efficacy of TTV-guided immunosuppression.

Method: Within this trial (DRKS00012335) all 386 adult ($\geq$18 years of age) consecutive kidney graft recipients transplanted at the Medical University Vienna, Austria, between January 1st 2016 and June 31st 2018. were subjected to longitudinal per protocol TTV monitoring. In total 3265 TTV measurements were taken and 71 biopsy proven graft rejections (defined by BANFF classification) and 472 clinically relevant infections were documented in the first year post-transplant. After reaching steady state at the end of post-transplant month 3, peripheral TTV plasma load was analyzed in the context of subsequent rejection and infection by rt-PCR.

Results: Patients with allograft rejection had lower levels of TTV compared to patients without rejection (median $3.5x10^6$ c/mL, IQR $1.7x10^5$-$1.3x10^8$ c/ml vs. median $2.5x10^8$ c/mL, IQR $5.8x10^6$-$9.3x10^8$ c/mL; $P = .028$) in subsequent biopsies. TTV load in individuals experiencing an infectious event in the subsequent observation period was higher compared to patients without infection (median $3.9x10^8$ c/mL, IQR $7.9x10^6$-$3.3x10^9$ c/mL vs. median $2.6x10^7$ c/mL, IQR $1.3x10^6$-$9.2x10^8$ c/mL; $P < .001$). Of note, TTV was quantified several weeks before rejection diagnosis and infection onset. Each log increase in TTV load decreased the odds for rejection by 22% (OR 0.78, 95% CI 0.62-0.97; P = .027) and increased the odds for infection by 11% (OR 1.11, 95% CI 1.06-1.15; P < .001). The association of TTV and infection and rejection, respectively was not altered by confounding or effect modification. A TTV load between 10^6 and 10^8 copies/mL was defined as optimal range to minimize the risk for rejection and infection.

Conclusion: These data support the initiation of an interventional trial assessing the efficacy of TTV-guided immunosuppression to reduce infection and graft rejection in kidney transplant recipients.

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P1625 **HIGHER DIETARY ACID LOAD IS ASSOCIATED WITH INCREASED RISK FOR KIDNEY FUNCTION DECLINE AND GRAFT FAILURE IN KIDNEY TRANSPLANT RECIPIENTS**

Stanley Ming Hol Yeung[1], António W Gomes-Neto[1], Maryse C.J. Osté[1], Else Van den Berg[1], Jenny E Kootstra-Ros[1,2], Jan-Stephan Sanders[1], Stefan P. Berger[1], Juan Jesus Carrero[3], Martin De Borst[1], Gerjan Navis[1], Stephan Bakker[1]

[1]University Medical Center Groningen, Internal Medicine, Division of Nephrology, Groningen, Netherlands, [2]University Medical Center Groningen, Laboratory Medicine, Groningen, Netherlands and [3]Örebro University, School of Medicine, Department of Medical Epidemiology and Biostatistics, Sweden

Background and Aims: Dietary acid load is associated with low grade metabolic acidosis and might accelerate kidney function decline in patients with chronic kidney disease (CKD). We investigated whether dietary acid load, estimated as net endogenous acid production (NEAP), is associated with kidney function decline in kidney transplant recipients (KTR) and to what extent this association is mediated by variation in venous bicarbonate (HCO_3^-).

Method: We used data from 642 KTR with a functioning graft $\geq$1 year after transplantation who were enrolled in the Transplantlines Food & Nutrition Cohort Study between 2008-2011. We applied the Frassetto equation (NEAP = (54.5 X protein (g/d) / potassium (mEq/d) - 10.2)) to calculate $NEAP_{FFQ}$ using intake reported in food frequency questionnaires and $NEAP_{Urine}$ from assessments of 24 hours urinary urea and potassium excretion. Patients were divided into tertiles of NEAP and differences across tertiles were analyzed by ANOVA, Kruskall-Wallis and Chi-Square tests, as appropriate. Cox regression models were used to study the associations between $NEAP_{FFQ}$ and $NEAP_{Urine}$ (both continuous variables and categories) with the composite endpoint kidney function decline, defined as doubling of serum creatinine or graft failure. Mediation analyses were performed to evaluate whether these associations were explained by venous bicarbonate.

Results: Mean age was 53$\pm$13 years, 56.1% were men, and mean eGFR was 52$\pm$20 ml/min/1.73m^2. Patients within the highest tertile of $NEAP_{FFQ}$ were younger (P=0.04), more recently transplanted (P=0.002), consumed less fruit and vegetables (P<0.001), more fish (P=0.001), less alcohol (P=0.01), more meat (P<0.001) and had lower serum HCO_3^- concentration (P=0.02). During a median follow-up time of 5.3 (4.1-6.0) years, 121 (18.8%) patients developed kidney function decline. In multivariable Cox regression analysis, higher $NEAP_{FFQ}$ (per SD increase) was associated with increased risk of kidney function decline, independent of potential confounders, including age, sex, BMI, time after transplantation, primary kidney disease, eGFR and proteinuria (adjusted HR 1.30; 95%CI 1.10-1.53, P=0.002). Compared to patients in the lowest $NEAP_{FFQ}$ tertile, those in the highest tertile had a >1.5 higher risk of kidney function decline (adjusted HR 1.67; 95%CI 1.07-2.62, P=0.03). We observed similar results using $NEAP_{Urine}$ as the study exposure (adjusted HR 1.46 per SD increase; 95%CI 1.24-1.73, P<0.001; adjusted HR 1.99; 95%CI 1.24-3.18, P=0.004 for patients in the highest versus lowest tertile of $NEAP_{Urine}$). These associations between $NEAP_{FFQ}$ (Figure A) and $NEAP_{Urine}$ (Figure B) with kidney function decline were visualized by fitting multivariable Cox regression models based on restricted cubic splines.

Mediation analyses estimated that venous HCO_3^- at baseline mediated 19.3% (P=0.008) of the association between $NEAP_{FFQ}$ and kidney function decline and 26.5% (P=0.002) of the association between $NEAP_{Urine}$ with kidney function decline.

Conclusion: Higher NEAP is associated with a higher risk for kidney function decline in KTR, and this association was in part mediated by venous HCO_3^-. We speculate that reducing dietary acid load might mitigate the risk of kidney function decline in KTR.

P1626 **LIQUID BIOPSY IN RENAL TRANSPLANT: THE ROLE OF DONOR-DERIVED CELL-FREE DNA TO DETECT REJECTION**

Mattia Rossi[1], Vincenzo L'Imperio[2], Meghan Kapp[3]

[1]University and Hospital of Verona, Renal Unit, Department of Medicine, verona, Italy, [2]University of Milano-Bicocca, Medicine and Surgery, Pathology, monza, Italy and [3]Vanderbilt University Medical Center, Pathology, Microbiology and Immunology, Nashville, Italy

Background and Aims: Circulating donor-derived cell-free DNA (dd-cfDNA) has recently been proposed as an early non-invasive marker for renal allograft rejection (Bloom et al, J. Am. Soc. Nephrol. 2017;28, 2221–2232). Recent studies demonstrated its potential role in the detection of any kind of rejection with better performance in detecting antibody-mediated rejection (ABMR) (Huang et al, Am J Transplant. 2019;19:1663–1670). However, at the current cutoff value for a positive test, the test seems to be affected by low sensitivity for T-cell mediated rejection (TCMR) and false positive results in the setting of non-rejection related damage. In the present study, the performance of dd-cfDNA is assessed on a retrospective series of transplant renal biopsies.

Method: Sixty-three renal biopsies from 52 allograft recipients with available dd-cfDNA results, evaluated between November 2017 and December 2019 at Vanderbilt University Medical Center, Nashville, Tennessee, were reviewed. Clinical and histological features along with the final diagnosis were recorded. Renal allograft rejection was classified following Banff 2013 criteria. Pearson's chi-squared test was used to compare cases positive and negative for dd-cfDNA. Receiving operator curve (ROC) analysis was used to assess the performance of the test in detecting any rejection and ABMR. A p-value of <0.05 was considered statistically significant.

Results: The patients were 53 ± 12.5 years old, 43% were men, 51% and 49% were Caucasian and African-American, respectively. The median value of dd-cfDNA was 2.6% for ABMR and 2.4% for any kind of rejection, statistically different from the group without rejection (0.56%, $p = 0.002$ and 0.0003, respectively). TCMR failed to demonstrate a statistically significant difference in dd-cfDNA levels vs controls (1.8% vs 0.56%, $p = 0.627$). The comparison of groups with positive and negative dd-cfDNA test is reported in Figure (panel A). Positive patients demonstrated a higher rate of findings associated with ABMR such as DSA positivity, moderate microcirculation inflammation, and transplant glomerulopathy, in addition to diagnostic ABMR and chronic/active ABMR. Moreover, a significant difference was found between the two groups in the rate of any kind of rejection. ROC analysis for any ABMR (Figure, panel B) demonstrated an AUC of 0.76 (95% CI 0.61-0.91) with a sensitivity (Sn) of 92.3%, a specificity (Sp) of 60%, a positive predictive value (PPV) of 37.5% and a negative predictive value (NPP) of 96.8%. ROC analysis for any kind of rejection (Figure, panel C) demonstrated an AUC of 0.84 (95% CI 0.74-0.94) with a Sn of 94.1%, a Sp of 65.2%, a PPV of 50% and a NPP of 96.8%. Among the patients with positive dd-cfDNA and without rejection (n=16, 51%), allograft biopsy demonstrated borderline TCMR in 4, acute tubular injury in 8, chronic pyelonephritis in 1, mild interstitial fibrosis in 1, and 2 with minimal histological abnormalities. Notably, none of the cases with a positive test were diagnosed with polyomavirus nephropathy.

Conclusion: Similar to previous studies, dd-cfDNA represents a sensitive test for detection of ABMR, with high performance in any rejection setting with the Banff 2013 criteria. However, the high rate of false positive results and the presence of undetected T-cell mediated events (e.g. borderline cases) at the current recommended cut-off value for positivity limits its employment as a surrogate for the renal biopsy.

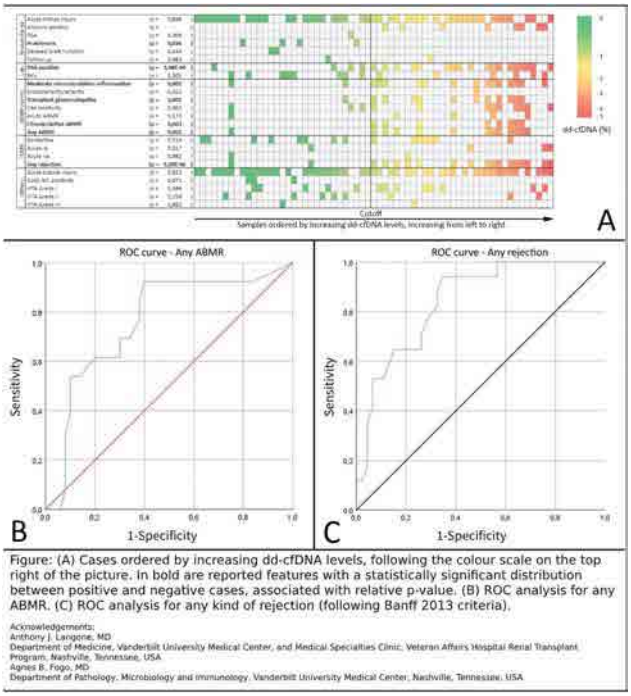


Figure: (A) Cases ordered by increasing dd-cfDNA levels, following the colour scale on the top right of the picture. In bold are reported features with a statistically significant distribution between positive and negative cases, associated with relative p-value. (B) ROC analysis for any ABMR. (C) ROC analysis for any kind of rejection (following Banff 2013 criteria).

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Department of Medicine, Vanderbilt University Medical Center, and Medical Specialties Clinic, Veteran Affairs Hospital Renal Transplant Program, Nashville, Tennessee, USA
Agnes B. Fogo, MD
Department of Pathology, Microbiology and Immunology, Vanderbilt University Medical Center, Nashville, Tennessee, USA

Figure:

P1627 **KIDNEY TRANSPLANT OUTCOMES FOR CHILDREN AND YOUNG ADULTS IN THE UK.**

Alexander Hamilton[1], Lucy Plumb[1], Anna Casula[2], Manish D. Sinha[3]

[1]University of Bristol, Population Health Sciences, Bristol, United Kingdom, [2]UK Renal Registry, Bristol, United Kingdom and [3]Evelina London Children's Hospital, Paediatric Nephrology, London, United Kingdom

Background and Aims: Multiple international studies report young adulthood is associated with kidney transplant loss. However, there are few published UK graft survival data for children and young adults. To our knowledge, no studies assess initial transplant function or examine declining function, when interventions may improve outcomes.

We aimed to report graft survival for UK children and young adults and to explore the importance of donor and recipient variables on graft loss and rate of decline.

Method: Retrospective cohort study using UK Renal Registry and NHS Blood and Transplant data, including patients aged <30 years who underwent kidney transplantation between 1998-2016. Univariate analyses included Kaplan-Meier survival curves and log-rank tests. Multivariable analyses used Cox proportional hazards to investigate variables associated with death-censored graft failure in a conditional risk-set model for multiple failure data. Age group was time-varying. We used the Efron method for ties, stratification by graft number and clustering at participant level.

We calculated estimated glomerular filtration rate (eGFR) using the Schwartz formula if aged <18 years and the 4-variable Modification of Diet in Renal Disease formula otherwise. For participants with ≥4 values outside the first 6 months, individual regressions of eGFR against time were performed. We undertook multivariable linear regression to establish associations with eGFR slope gradients.

Results: We studied 5121 individuals. Of these, 371 received a further transplant during the study period. There were 1371 graft failures and 145 deaths with a functioning graft over a 39541-year risk period. The cohort was 61% male and 80% white. Most (36%) had structural kidney problems, followed by glomerulonephritides (29%). Live donation occurred in 48%, donation after brainstem death in 46% and after circulatory death in 6%. Mean initial eGFR was 62 mls/min/1.73m^2.

Median graft survival was 7 years. One-year survival was 94.4% (95% confidence interval (CI) 93.7, 95.0), 5-year survival 84.0% (95% CI 82.9, 85.0), 10-year survival 71.1% (95% CI 69.6, 72.5), 15-year survival 60.2% (95% CI 58.1, 62.3) and 20-year survival 51.2% (47.6, 54.7). Survival at 15 years was least at 54.4% (95% CI 49.9, 58.7) in those transplanted at age 15-19 years and most in those transplanted at age 0-4 years at 71.7% (95% CI 63.4, 78.5).

Figure 1 displays hazard ratios for graft loss. Protective associations were male gender (p=0.04), living donation (p=0.02) and higher initial eGFR (p<0.0001). Risk associations included adverse human leucocyte mismatches (p=0.001), black ethnicity (p=0.001), young adulthood and glomerulonephritides. Risk associations for faster eGFR decline included female gender (p<0.0001), age group 15-19 years (p=0.04), higher initial eGFR (p<0.0001), additional graft (p=0.003) and transplants during 2011-2014 (p=0.03).

Conclusion: This study reports long-term graft survival for UK children and young adults and evaluates associations with declining transplant function. It contributes up to 20 years of follow-up and considers initial graft function in addition to established co-variates. Graft survival was ≈60% at 15 years. The study highlights the changing survival by age group over time. Those aged <5 years at transplant had the least initial survival, but best long-term graft survival relative to other age groups. Initial transplant function is strongly associated with graft performance. Similar associations with gender, ethnicity and age group are seen compared with other studies. Young adulthood is a high-risk period for UK patients and interventions are needed to improve outcomes during transition and young adulthood.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
KIDNEY					
Kidney disease	Etiology unknown	Multiple causes (HCV, diabetes, pre-renal kidney disease)	HCV-related cryoglobulinemia	Obstructive nephropathy	Mesangial proliferative glomerulonephritis
Months in dialysis	5	21	7	33	13
LIVER					
Liver transplant indication	HCV-cirrhosis	HCC, HCV-cirrhosis	HCV-cirrhosis	HBV/HDV-cirrhosis	HCV-cirrhosis
HCV-genotype	1b	4	4	NA	4a
MELD at SLKT	28	21	21	22	24
Child-Pugh at SLKT	B9	B9	B7	B7	C10
HIV					
HIV infection duration at SLKT (years)	24.8	24.4	24.9	24.8	26.8
CD4+ nadir (cells/microL)	90	218	96	1	73
CD4+ at SLKT (cells/microL)	308	601	135	110	329
ART at SLKT	3TC+ABC+ATV	LPV+RTV	ABC+3TC+LPVr	3TC+fosAPV+RAL	RAL+DRV+RTV
SIMULTANEOUS LIVER AND KIDNEY TRANSPLANT					
Age at SLKT (years)	38	50	48	49	54
SLKT year	2007	2009	2010	2013	2014
Months in waiting list	4.5	11	2.9	9.6	4
Years of follow-up	12.2	10.1	9.5	6.2	0.1

Figure 1: Coefficient plot of multivariable associations with graft loss in UK children and young adults.
Abbreviations: eGFR – estimated glomerular filtration rate; HLA – human leucocyte antigen; CI – confidence interval

P1628 **ASSESSING CORONARY HEART DISEASE IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION - IS THERE SPACE FOR A RISK SCORE MODEL?**

Joana Marques[1], Luisa Pereira[2], Ana Messias[1], Nuno Moreira Fonseca[1], Patrícia Cotovio[1], Francisco Remédio[1], Manuel Anibal A. Ferreira[1], Fernando Nolasco[1]

[1]Hospital Curry Cabral, Nephrology Department, Lisboa, Portugal and [2]Centro Hospitalar Universitário do Algarve, Nephrology Department, Faro, Portugal

Background and Aims:

Type 1 diabetes mellitus (DM1) is associated with an increased risk of coronary heart disease (CHD), which is generally more aggressive and frequently asymptomatic. This risk substantially increases for those with nephropathy. In selected patients, simultaneous pancreas-kidney transplantation (SPKT) is the renal and pancreatic replacement therapy of choice, as it increases longevity and stabilizes diabetic complications. Despite essential, universal screening protocols for silent CHD in this population are still debatable. As so, Gowdak recently developed a simple clinical risk score to determine the pre-test probability of significant CHD in single kidney transplant candidates.

Our aim was to identify potential risk factors associated with the presence of significant lesions on pre-SPKT coronary angiography (CA) and test the utility of Gowdak score in SPKT candidates.

Method: 77 patients submitted to SPKT between 2011 and 2018 were retrospectively included in this study. All subjects underwent CA as screening method for CHD during the eligibility evaluation. Demographic, clinical, laboratory, therapeutic and imaging characteristics were studied. Continuous variables are presented as means or medians; categorical variables as frequencies. Univariate analysis (Qui2 or Fisher test) and multivariate analysis (logistic regression) were performed. Comparison between groups of patients with and without CA injury was performed using SPSS statistics version 23 and a $p < 0.05$ was considered significant.

Results: In the past 8 years, 99 SPKT were performed; 78% of these patients (N=77) were submitted to preoperative CA; mean age was 36±5.9 years and 64% were male. The mean duration of DM1 was 25 years and 97% had retinopathy, 43% neuropathy, 31% dysautonomia, 19% peripheral arterial disease and 7% cerebrovascular disease. We excluded 1 due to missing data. A minority of SPKT (3%, N=2) was preemptive. The mean time on dialysis was 37 months. Only one patient had angor, wh0 was excluded of Gowdak risk score assessment. Most patients (87%, N=67) were hypertensive; 56% (N=43) were on statin; 48% (N=37) had smoking habits, and 5% (N=4) had a BMI>30 kg/m2. CA identified at least one lesion in 48% (N = 37) of the patients, of which 30% (N=11; 14% of all CA) underwent intervention; none had complaints of angor. Based on Gowdak risk score, mean probability for CHD was 30.8% and 19 patients had a risk >40% - the recommended cut off to pursuit CA as screening method - but only 2 required intervention. In a univariate analysis, we found that the only distinguishing feature between the group of patients with and without CA lesions was smoking (p=0.005). DM1 with 20 or more years of evolution was found to have a significant association with coronary artery disease development (identifiable by any diagnostic test) (p=0.048). In our population of SPKT recipients Gowdak risk score did not predicted those with significant CHD.

Conclusion: In our study, CA was positive for lesion in almost half of the patients, all of them asymptomatic. Despite the fact that Gowdak probability score failed to identify those with significant CHD before CA (probably because all of our patients were diabetic), in our population for every seven patients submitted to CA, one needed coronary intervention. We highlight that asymptomatic patients with long-term DM and smokers should be carefully evaluated. The task of correctly ascertaining the presence of CAD can be more overwhelming when we take into account that there is a high prevalence of asymptomatic patients with extensive CAD. Facing the importance of an unmissed diagnosis we encourage the use of CA as an initial screening method, even if it is invasive. Further studies should be encouraged to create screening algorithm for SPKT candidates. Finally, medium- and long-term follow-up studies are needed to evaluate the effects of preoperative selection on posttransplant cardiac events and survival rates.

P1629

THE COMBINATION OF KDRI AND THE HISTOLOGICAL SCORE IMPROVES THE RISK STRATIFICATION OF MARGINAL ORGANS IN KIDNEY TRANSPLANTATION

Marco Fiorentino[1], Francesco Pesce[1], Simona Simone[1], Giuseppe Castellano[2], Pasquale Gallo[1], Michele Battaglia[3], Loreto Gesualdo[1]

[1]University of Bari Aldo Moro, Department of Emergency and Organ Transplantation, Nephrology, Dialysis and Transplant Unit, Bari, Italy, [2]University of Foggia, Department of Medical and Surgical Sciences, Foggia, Italy and [3]University of Bari Aldo Moro, Department of Emergency and Organ Transplantation, Urology Andrology and Kidney Transplantation Unit, Bari, Italy

Background and Aims: The organ shortage has led to increase the procurement of kidneys from marginal donors, but the risk of graft failure is still object of debate. The aim of the study is to assess whether using both clinical and histological scores can better assess the risk for worse outcome for marginal organs.

Method: We analyzed 210 kidney transplant recipients from donors aged >50 years. We retrospectively calculated the Kidney Donor Risk Index (KDRI) for each donor and we divided the population according to the KDRI (-, if KDRI ≤ median; +, if KDRI > median) and the histological score (HS, -, if HS ≤ 3; +, if HS > 3) in 4 groups: KDRI-HS- (low KDRI and HS), KDRI-HS+ (low KDRI and high HS), KDRI+HS-(high KDRI and low HS) and KDRI+HS+ (high KDRI and HS). We compared graft function between groups at 2 years and Cox regression analysis was performed to assess the risk for end stage renal disease (ESRD) between groups.

Results: Overall, median KDRI was 1.44 (1.25-1.65), while mean total HS was 3.04±1.62. Median follow-up was 51.9 (26.4 – 99.4) months. Graft function at 2 years was significantly worse in groups with high KDRI (KDRI+HS- and KDRI+HS+) compared to those with low KDRI ($p<0.001$), while no differences were found according to the HS. By contrast, the best ROC curve in predicting the development of ESRD is for the model that included both KDRI and histological score (AUC 0.81, 95%CI 0.708-0.914, $p<0.001$). A Cox model adjusted for recipient age, gender, acute rejection, DGF and chronic allograft dysfunction, patients with high KDRI and high HS are more likely to develop ESRD compared to the other groups (OR 5.6, 95%CI 1.3 to 24.5, p=0.02)(**Figure 1**).

Conclusion: Patients with high KDRI and HS have worse outcome compared to patients with high KDRI but better histology. The integration of histology to clinical score may improve the assessment of the risk for graft failure in patients receiving organs from marginal donors.

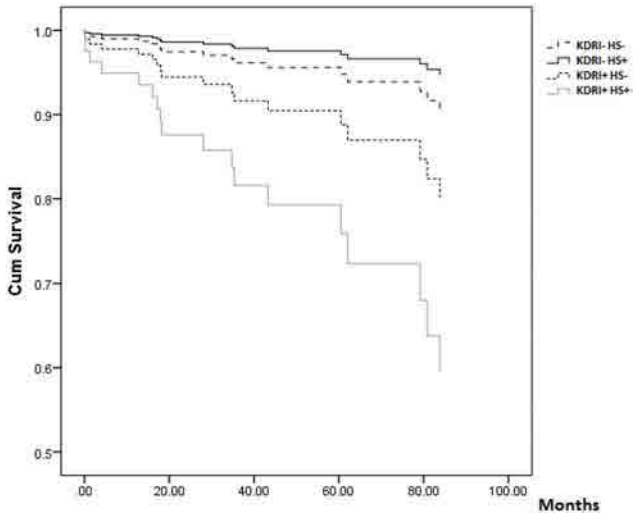


Figure 1: Cox regression model (outcome: ESRD)

P1630 **IS THERE ALWAYS A SURVIVAL BENEFIT WITH KIDNEY TRANSPLANTATION? RESULTS FROM A BELGIAN COHORT.**

Rachel Hellemans[1], Anneke Kramer[2], Johan De Meester[3], Dirk Kuypers[4], Michel Jadoul[5], Wim Van Biesen[6], Alain Le Moine[7], Jean-Marie Krzesinski[8], Karl Martin Wissing[9], Kim Luyckx[1], Marieke Van Meel[10], Erwin De Vries[10], Ineke Tieken[10], Serge Vogelaar[10], Undine Samuel[10], Daniel Abramowicz[1], Vianda Stel[2], Kitty J Jager[2]

[1]University Hospital Antwerp, Nephrology, Edegem, Belgium, [2]Amsterdam UMC, locatie AMC, ERA-EDTA Registry, Amsterdam, Netherlands, [3]A.Z. Nikolaas, Nephrology, Sint-Niklaas, Belgium, [4]UZ Leuven, Nephrology, Leuven, Belgium, [5]UCLouvain, Nephrology, Ottignies-Louvain-la-Neuve, Belgium, [6]Ghent University Hospital, Nephrology, Gent, Belgium, [7]Université Libre De Bruxelles / Campus Érasme, Nephrology, Anderlecht, Belgium, [8]Chu De Liège, Nephrology, Liège, Belgium, [9]UZ Brussel, Nephrology, Jette, Belgium and [10]Foundation Eurotransplant International Foundation, Leiden, Netherlands

Background and Aims: Older studies have shown a survival benefit with kidney transplantation compared to dialysis, even for patients older than 60 years. However, due to important evolutions such as older recipient age and the use of less-than-optimal quality donors, it is unclear if the survival benefit with transplantation still holds true nowadays.

Method: Patient survival was analyzed for 3808 Belgian patients waitlisted for a first deceased donor kidney transplant between 2000 to 2012. Patients were divided into age categories (20-44y, 45-64y, ≥65y). Primary outcome was the comparison of mortality during median waiting time *plus* 3 years follow-up, either after transplantation or when remaining on dialysis. Outcomes were analyzed separately for those receiving a standard criteria donor (SCD) or an expanded criteria donor (ECD) transplant. The survival analyses were adjusted for age, sex and primary renal disease.

Results: Among patients ≥ 65 years old, only SCD transplantation provided a significant survival benefit compared to dialysis: mortality was 16.3 % (95 % CI: 13.2–19.9 %) with SCD transplantation, 20.5 % (16.1–24.6 %) with ECD transplantation, and 24.6 % (19.5–29.5 %) when remaining on dialysis. Relative mortality risk was increased in the first months after transplantation compared to dialysis, with equal risk levels being reached earlier for SCD than ECD transplantations in all age groups.

Conclusion: This study suggests that older patients have a survival benefit with SCD transplantation versus dialysis, but the survival benefit with ECD transplantation versus dialysis may be small or non-existent.

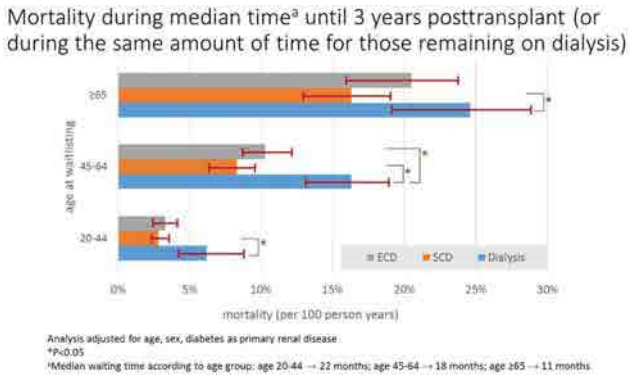


Figure:

P1631 EFFECT OF DONOR TYPE ON 3-MONTH HOSPITAL READMISSION AFTER KIDNEY TRANSPLANTATION

Yiman Wang[1], Martin Heemskerk[2], Aiko De Vries[3], Wieneke Michels[3], Friedo W. Dekker[1]

[1]Leiden University Medical Center (LUMC), Clinical Epidemiology, Leiden, Netherlands, [2]Dutch Transplant Foundation, Leiden, Netherlands and [3]Leiden University Medical Center (LUMC), Internal Medicine - Division of Nephrology /Transplant Center, Leiden, Netherlands

Background and Aims: Hospital readmission after kidney transplantation remains a burden not only for the kidney transplant recipients (KTRs) but also for the healthcare system. Therefore, it can also indicate the quality of care. The causes of hospital readmission in KTRs mainly include problematic graft function and complications caused by the invasive procedure or immunosuppressive regime. In the Netherlands, almost 1000 kidney transplantations are performed annually with an aging recipient population. In spite of the benefit of living donor transplantation, roughly half of the patients will receive a graft from a donor donating after cardiac death(DCD) or brain death(DBD). From 2000 to 2017 the DCD procedure accounted for 43% of all deceased donors in the Netherlands, which is the highest worldwide. With this analysis, we aim to investigate the effect of donor type on 3-month hospital readmission after kidney transplantation and also investigate this effect in different age groups.

Method: Our study was conducted with data abstracted from the Netherlands Organ Transplant Registry (NOTR). We retrieved data for all first-time KTRs over 18 years old from 1st Jan 2016 to 31st Dec 2018. A multivariate logistic regression model with multiple imputation for missing values was used to estimate the hazard ratio (HR) of post-transplant 3-month hospital readmission for different donor types and control for confounding. KTRs with living or deceased donors and KTRs with DCD or DBD donors were compared, respectively. Subgroup group analysis was conducted to investigate the effect of different donor types on 3-month hospital readmission within different recipient age groups(age below 65 vs 65 years or older).

Results: Among 1917 first-time KTRs surviving 3 months with a functioning graft, 941 (49,1%) had no hospital readmission, 371 (19,4%) had one readmission in this period, and 244 (12,7%) had two or more readmissions (361 (18,8%) with missingness in readmission). Within the cohort, 1163(60,7%) received a graft from a living donor, 281(14,7%) from DBD donors and 473(24,7%) from DCD donors. 259(23,3,%) recipients with living donor kidney transplantation were 65 years old or older while it is 104 (43,3%) for recipients with DBD donors and 172(41,5%) for recipients with DCD donors. KTRs with living donors were at lower risk of 3-month hospital readmission after transplantation compared to those with deceased donors (HR, 0,77; 95%CI, 0,61 to 0,95). The difference was consistent in KTRs under 65 years old (HR, 0,70; 95%CI, 0,53 to 0,92) but disappeared in KTRs above 65 years old(HR, 0,90; 95%CI: 0,60 to 1,35) in subgroup analysis. KTRs with DCD and DBD donors had a similar risk of 3-month hospital readmission.

Conclusion: Kidney transplant recipients younger than 65 years of age with a living donor have a lower risk of post-transplant 3-month hospital readmission compared to those with a deceased donor. KTRs at an age of 65 or above KTRs with either a DCD or DBD donor are similar with regard to 3-month hospital readmission across different age groups.

P1632 **IMPACT OF RENAL TRANSPLANTATION ON THE FUNCTIONAL STATUS OF PATIENTS WITH END-STAGE RENAL FAILURE IN TACROLIMUS ERA**

Hatem Kaies Ibrahim Elsayed Ali[1], Ahmed Daoud[2], Karim Soliman[3]

[1]University Hospitals of Birmingham, United Kingdom, [2]Medical institute, Houston, United States of America and [3]university of south carolina, United States of America

Background and Aims: Survival after renal transplantation has improved significantly over the past 20 years. On the contrary, surprisingly little is known about the functional status post-transplant. A fundamental understanding of the functional status of patients surviving renal transplantation is of primary importance to clinicians and families alike, who often pursue renal transplantation with a principal hope that functional status will improve. The aim of our study is to assess the effect of renal transplantation on functional status of the patients in tacrolimus era

Method: Using data from the United States organ procurement and transplantation network, all renal transplant patients maintained on tacrolimus-based immunotherapy and had functional assessment at time of transplant and five-years post-transplant were retrospectively reviewed. Data including age, sex, gender, ethnicity, functional status, diabetes, body mass index, cold ischemia time, number of previous transplants, panel reactive antibodies, donor type, donor age, HLA-mismatches, number of acute rejection episodes, induction therapies, maintenance immunotherapy on discharge were collected. Functional status was defined according to Karnofsky score measurements. Descriptive analysis was used to assess effect of renal transplantation on functional status. Outcome measured was functional status five-years post-transplant. Multiple logistic regression analysis was used to assess factors affecting functional status post-transplant.

Results: 19704 patients were included in the study. Among patients with mild impairment at time of transplant, only 13.55% showed worsening of functional status. Among patients with moderate impairment at time of transplant, 65.5% showed improvement of functional status while only 3.92% showed worsening of functional status. Among patients with severe impairment at time of transplant, 88.56% showed improvement in functional status (64.57% showed improvement to mild impairment and 23.99% showed improvement to moderate impairment). Multiple logistic regression analysis showed that steroid withdrawal protocol is associated with improvement in functional status (OR=1.24, P=0.007, CI ranges from 1.06 to 1.45), while dialysis maintenance before transplantation was associated with abnormal functional status post-transplant (OR=0.73, P=0.003, CI ranges from 0.59 to 0.89).

Conclusion: This study revealed that renal transplantation is associated with substantial improvement in functional status of the patients. Steroid withdrawal protocols is associated with significant improvement in functional status while maintenance dialysis before transplantation is associated with worse outcomes. This study recommends using steroid withdrawal protocols and performing transplantation for the patients at the pre-dialysis state. Functional status at time of transplant shouldn't be a hindrance to performing transplantation.

P1633 STANDARDIZED REVIEW OF DONOR AFTER BRAIN DEATH KIDNEY OFFERS; A QUALITY IMPROVEMENT PROJECT

Amy Riddell[1], Deborah Munro[1], Lins Varughese[1], Anusha Edwards[2], Samuel Turner[2], Dominic Taylor[1]

[1]North Bristol Trust, Renal and [2]North Bristol Trust, Transplant surgery

Background and Aims: Transplanting renal centres have a duty to use the finite resource of the deceased-donor kidney pool to benefit potential recipients without exposing them to excessive risk. However, there is known variation in centre and clinician practice. This may relate to clinicians' attitude to risk, knowledge of the recipient and unit culture. Centre differences in acceptability of donor organs is evidenced by variation in NHS blood and transplant registry data. Use of marginal donors has become more frequent, especially for older recipients with higher comorbidity. In the UK this year we will see whether switching to an 'opt out' donation law further increases this proportion of donors.

We developed a systematic method to retrospectively review donation after brain death (DBD) kidney offers declined by our centre, with the intention of reducing variation in practice between clinicians, and identifying cases where offer acceptance may have been appropriate

Method: All DBD kidney offers declined by the Richard Bright Renal Service between June 2018 and May 2019 were reviewed. Data were collected by casenotes review and by contact with other transplanting units to establish the outcome of donor kidneys and recipient progress. Reasons for offer decline were recorded. Donor and recipient risk indices (DRI and RRI) were calculated. For patients now transplanted, the DRI of the declined offer was compared to the DRI of the transplanted kidney.

Results: During the study period, 98 DBD kidneys were declined. A donor organ identifier was not available in 8 cases, so 90 are considered here. Average donor age was 57 years with 52% having a Donor Risk Index (DRI) score of 4, and 74.7% a DRI score $\geq$3. The most common reasons for organ decline were donor related (65%), of which 27% were due to poor kidney function and 22% age mismatch; or recipient related (35%), where 30% were deemed inadequate quality for the recipient and 30% were unavailable or unwell. Of those kidneys which were transplanted elsewhere, 88% were functioning at 6 months with a median creatinine of 119 (IQR 106-148).

There were 60 potential recipients, 61% of whom had a RRI score $\geq$3; 44% had a RRI equal to or less than the DRI of the declined organ. Those who have still not been transplanted have accrued a median of 352 extra days on dialysis. 31 recipients (52%) have been transplanted since their declined offer. The median change in DRI score from the declined offer to the accepted offer was -1 (IQR -2 to 1), and offers were accepted after a median of 45 (IQR 14-143) additional dialysis days. Of those who were transplanted after declining a donor offer, 11 (39%) received a kidney from a donor with equal or worse DRI than the original offer, after a median of 49 further days on dialysis.

Conclusion: This review process highlights the effect of kidney offer decline on future progress of the potential recipient, as well as differences in our centre practice compared to other centres. Key to this review is to highlight the risks involved with DBD organ decline- 18% of recipients ultimately received an equal or inferior kidney while accruing additional time on dialysis. Alongside this review we have implemented strategies including a policy on AKI in donors and monthly multidisciplinary meetings to discuss individual DBD decline cases. We aim to standardize decision making and increase our utilization of all as well as marginal DBD organs, and expect to show a reduction in variation in practice in future reviews. Use of this process in other units or at a national level could reduce unwarranted variation in the utilization of the donor organ pool.

P1634

TIME-UPDATED SERUM CALCIUM AND PHOSPHATE ARE ASSOCIATED WITH GRAFT AND PATIENT OUTCOMES AFTER KIDNEY TRANSPLANTATION

Willemijn Van der Plas[1], António W Gomes-Neto[2], Stefan P. Berger[2], Schelto Kruijff[1], Stephan Bakker[2], Martin De Borst[2]

[1]University Medical Center Groningen, Surgery, Groningen, Netherlands and [2]University Medical Center Groningen, Internal Medicine, Division of Nephrology, Groningen, Netherlands

Background and Aims: Disturbances in calcium-phosphate homeostasis are common after kidney transplantation. The clinical implications of changes in calcium-phosphate homeostasis after transplantation are unclear. The aim of this study was to assess the relationship between time-updated serum calcium and phosphate levels and subsequent graft and patient outcomes.

Method: Kidney transplant recipients with ≥2 serum calcium and phosphate measurements were included from a large single-center cohort; only first transplants were considered. Patients with graft failure <3 months were excluded, as were measurements obtained when eGFR was <15 mL/min/1.73m^2 or during intensive care unit admission. Normocalcemia was defined as (albumin-corrected) calcium between 2.20 and 2.60 mmol/L (8.8-10.4 mg/dL), and normophosphatemia as 0.70-1.50 mmol/L (2.17-4.64 mg/dL). Time-updated multivariable Cox regression analyses and time-updated restricted cubic splines analyses were performed to assess the relationship between post-KTx serum corrected calcium and phosphate levels and mortality and death-censored graft failure (DCGF). Final models were adjusted for recipient age, sex, BMI, eGFR, proteinuria, systolic BP (all time-updated), antihypertensive drug use, recipient CMV status, donor age, sex, and status (living or post-mortal), cold and warm ischemia times, HLA mismatches, primary kidney disease, and serum phosphate (in calcium analyses) or corrected calcium (in phosphate analyses).

Results: A total of 2,769 patients with 138,496 serum corrected calcium and phosphate levels post-KTx were included (median [IQR] 43 [31-61] measurements per patient). Mean age was 47 ± 14 yrs, 42.3% was female, and 19% underwent a pre-emptive transplantation. Hypercalcemia was more common in the first year (15%) and declined to ∼5% during long-term follow-up; hypocalcemia occurred in ∼10% throughout. Hypophosphatemia (24.3%) and hyperphosphatemia (15.5%) were particularly common during the first 30 days post-transplant, and stabilized at ∼10% and ∼5% after the first year. During median follow-up of 16.3 (8.7 – 25.2) years, 477 patients (17.2%) developed DCGF and 1050 (37.9%) patients died. In multivariable regression analyses, post-transplant hypocalcaemia was associated with an increased risk of DCGF (fully adjusted hazard ratio [HR] 2.01 [95% CI 1.61-2.50], P<0.0001; Figure 1A), but not mortality (HR 1.06 [95% CI 0.88-1.27], P=0.55; Figure 1B). Post-transplant hypercalcaemia was associated with an increased risk of mortality (HR 1.77 [95% CI 1.44-2.17], P<0.0001), but not DCGF (HR 0.79 [95% CI 0.48-1.32], P=0.37). Patients with post-KTx hyperphosphatemia were at increased risk of both DCGF (HR 37.12 [95% CI 30.33-45.42], P<0.0001; Figure 1C) and mortality (HR 3.17 [95% CI 1.65-3.86], P<0.0001; Figure 1D). Patients with hypophosphataemia had a lower risk of developing DCGF (HR 0.48 [95% CI 0.28-0.81], P<0.01), but not mortality (HR 0.92 [95% CI 0.72-1.18], P=0.42). Similar results were obtained in sensitivity analyses in a subgroup with parathyroid hormone data available (N=1,412) or after exclusion of the highest and lowest 0.5% of calcium or phosphate levels.

Conclusion: Post-transplant hypocalcaemia and hyperphosphatemia are associated with an increased risk of DCGF, while hypophosphataemia was linked with a lower DCGF risk. Hypercalcaemia and hyperphosphataemia were associated with an increased mortality risk. These findings underline the relevance of keeping calcium and phosphate within normal range after kidney transplantation.

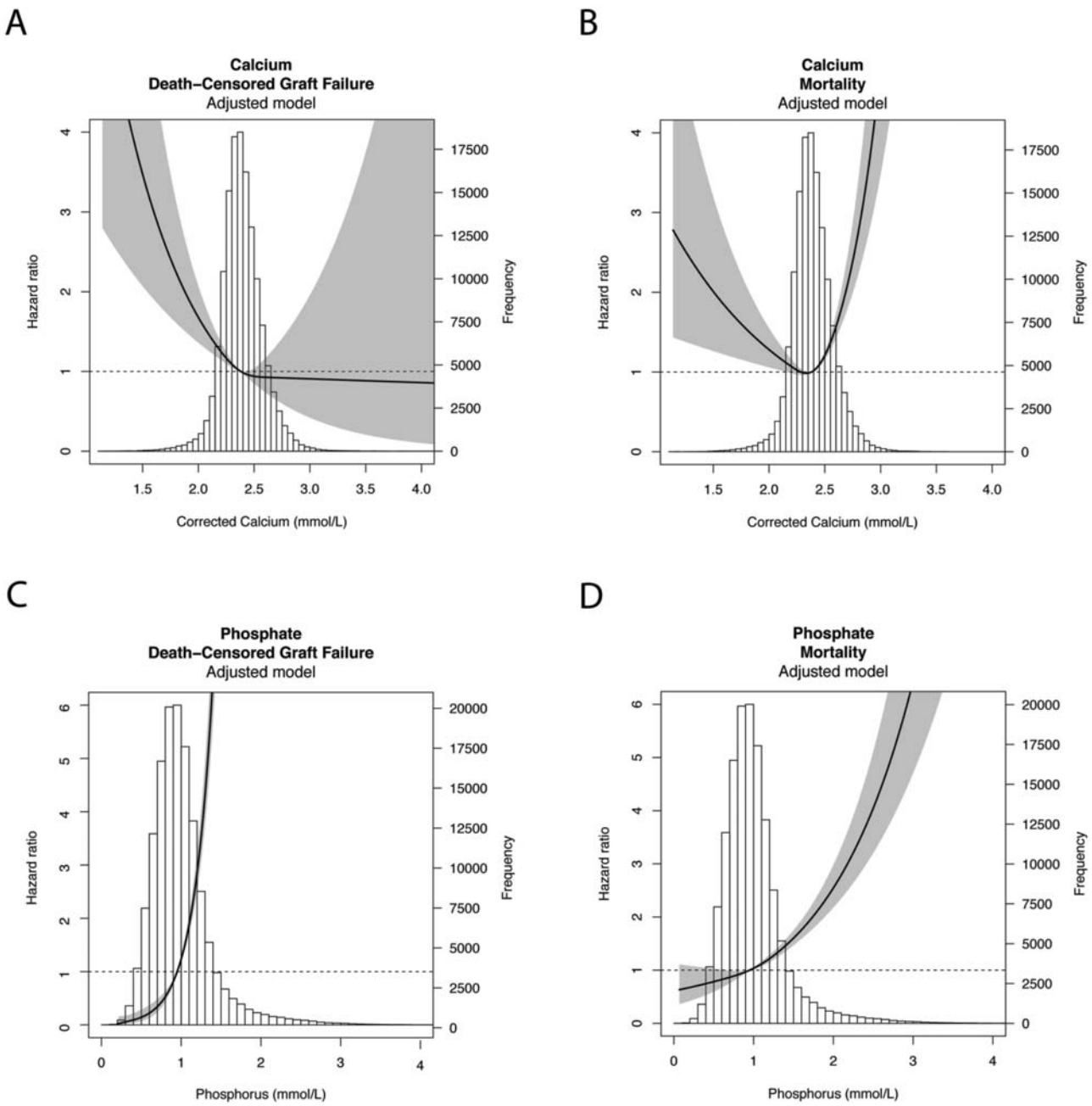


Figure:

Figure 1 – Cubic spline curves depicting the relationship between serum calcium or phosphate and death-censored graft failure or all-cause mortality

P1635 **INVESTIGATING REASONS FOR ETHNIC INEQUITY IN LIVING-DONOR KIDNEY TRANSPLANTATION IN THE UK: A MIXED METHODS ANALYSIS OF A MULTICENTRE QUESTIONNAIRE-BASED STUDY**

Katie Wong[1,2], Yoav Ben-Shlomo[1], Amanda Owen-Smith[1], Fergus Caskey[1,2], Stephanie MacNeill[1], Charles R.V. Tomson[3], Frank Dor[4], Pippa Bailey[1,2]

[1]University of Bristol, United Kingdom, [2]Southmead Hospital, United Kingdom, [3]Newcastle University, United Kingdom and [4]Imperial College London, United Kingdom

Background and Aims: A living-donor kidney transplant (LDKT) is one of the best treatments for kidney failure, yet in the UK there is evidence of ethnic inequity in access. We designed this questionnaire-based mixed-methods study to investigate the patient-reported reasons that family members of Black, Asian and Minority Ethnic group (BAME) individuals were not able to become living kidney donors.

Method: This questionnaire-based case-control study included 14 UK hospitals. Participants were adults transplanted between 1/4/13-31/3/17. Participants provided data on all relatives aged >18 years who could have been potential living kidney donors. Participants were asked for the reasons why relatives could not donate: individuals were asked to tick all options that applied from a list of reasons (Age; Health; Weight; Location; Financial/Cost; Job; Blood group; No-one to care for them after donation), and a box was provided for free-text entries following the option of 'Other – please give details'. Multivariable logistic regression was used to analyse the association between the likelihood of selecting each reason for non-donation and the participant's ethnicity (binary variable White versus BAME). 56/171 BAME respondents provided free text responses and all were analysed. Qualitative responses were analysed using thematic analysis.

Results: 1,240 questionnaires were returned from 3,103 patients (40% response). There was strong evidence that after adjustment for potential confounders sex, age and socio-economic position, BAME individuals were more likely than White respondents to indicate that family members lived too far away to donate (adjusted odds ratio (aOR) 3.14 [95% CI 2.10-4.70]), were prevented from donating by financial concerns (aOR 2.25 [95% CI 1.49-3.39]), were not able to take time off work (aOR 2.05 [95% CI 1.36-3.09]), and were not the right blood group (aOR 1.47 [95% CI 1.12-1.94]). Four qualitative themes were identified from free-text responses from BAME participants: i) Burden of disease within the family ii) 'Unorthodox' religious beliefs iii) Specific geographical concerns (healthcare provision, visa difficulties) iv) Knowledge handling. The theme 'Knowledge Handling' incorporated three subthemes: a) Need for more detailed knowledge, b) Protected disclosure of health status, and c) Recipient assumptions about potential donor knowledge.

Conclusion: We have identified multiple barriers to living kidney donation in the UK BAME population, which should be further investigated and addressed. BAME transplant recipients were more likely to report that potential donors were not the right blood group to donate: work should be undertaken to ascertain if this reflects true ABO-incompatibility or perceived incompatibility. Potential donors living outside the UK is a major barrier, related to difficulties with accessing visa and concerns about a specific country's healthcare system's capacity for longer-term post-donation care. The financial barriers reported may disproportionately affect overseas donors who, although entitled to reimbursement for travel, accommodation and visa costs, may incur large "up-front" costs which may be prohibitive. No respondents reported that a major religion's position on living donation was a barrier to donation. However, there were several references to family members holding beliefs that were described as 'distorted' religious beliefs: this highlights the need to understand the beliefs of potential donors who belong to non-mainstream religions, which may be out of the remit of denominational faith leaders.

P1636 **THE IMPACT OF CALCINEURIN INHIBITOR WITHDRAWAL ON DE NOVO DSA PRODUCTION IN LIVING DONOR KIDNEY TRANSPLANTATION**

Takahisa HIRAMITSU[1], Akiko Kanda[1], Kenta Futamura[1], Toshihide Tomosugi[1], Manabu OKADA[1], Goto Norihiko[1], Shunji Narumi[1], Yoshihiko Watarai[1]

[1]*Nagoya Daini Red Cross Hospital, Transplant and endocrine surgery, Nagoya, Japan*

Background and Aims: Chronic antibody mediated rejection caused by de novo donor specific antibody (dnDSA) is one of the biggest reasons for graft failure. At present, because it is difficult to treat CAMR, prevention of de novo DSA production is important. We investigated the risk factor for dnDSA production in living donor kidney transplantation.

Method: 807 patients underwent living donor kidney transplantation between January 2008 and December 2016. 159 recipients were excluded because of preformed DSA (58 recipients), pediatric transplantation (35 recipients), pancreas transplantation after kidney transplantation (4 recipients), and insufficient data on DSA after transplantation (62 recipients). 648 recipients were enrolled in this study. In 84 out of 648 recipients, dnDSA were detected until December 2018. With cox regression analysis, the risk factors for de novo DSA production were investigated between dn DSA positive and negative groups. The impact of donor characteristics including age and sex, and recipient characteristics including age, sex, hemodialysis vintage, cold ischemic time, past history of transfusion, pregnancy, and transplantation, HLA mismatch, pre-operative Flow PRA results, ABO incompatibility, rituximab induction, splenectomy, pre-operative plasmapheresis, transplantation from first-degree relatives, conversion of calcineurin inhibitor (CNI), conversion of mycophenolate mofetil, mizoribin, and everolimus, CNI used for induction, induction with mycophenolate mofetil, mizoribin, and everolimus, CNI withdrawal, withdrawal of mycophenolate mofetil, mizoribin, and everolimus, and rejection within 6 months after transplantation were investigated.

Results: In the univariate analysis, male recipient, male donor, and CNI withdrawal were the significant risk factors (P=0.020, HR 1.795, 95%CI 1.095-2.942; P=0.027, HR 0.568, 95%CI 0.344-0.938; P<0.001, HR 6.346, 95%CI 2.560-15.730, respectively). In the multivariate analysis, calcineurin inhibitor withdrawal was significant risk factor with P<0.001, HR 6.374, 95%CI 2.567-15.828.

Conclusion: Calcineurin inhibitor withdrawal was the significant risk factor for de novo DSA production in living donor kidney transplantation

P1637 **UK KIDNEY ALLOCATION SCHEME: APPROPRIATE MATCHING BUT RESOURCE IMPLICATIONS.**

Eleanor Murray[1,2], Robert Pearson[1,2], Peter Thomson[1], Marc Clancy[1], John Asher[1]

[1]*Glasgow Renal and Transplant Unit, NHS GGC, Glasgow, United Kingdom and* [2]*University of Glasgow, United Kingdom*

Background and Aims: UK NHSBT kidney matching scheme changed in September 2019, aiming to better match graft and patient survival through stratification of donors and recipients into risk quartiles. We present data on two years of transplants aiming to highlight discrepancies between our unit and the model on which the scheme is based, and the potential implications on service provision of its' introduction.

Method: We reviewed all deceased donor transplants in our centre in 2015 and 2016. Recipients and donors were re-classified into the risk index quartiles and endpoint data included inpatient days in first year, 1 year eGFR, survival, imaging, and infection episodes. Comparisons were made with NHSBT literature.

Results: 196 deceased donor transplants were performed. Distribution of D1-4 kidneys to R1-4 recipients in our cohort did not reflect those presented in the allocation scheme models, with our population skewed toward higher risk R4 category (73.4%), including 55 D4R4 (83% of D4 kidneys), see Figure 1. 2.0% had an age difference between donor and recipient of >25years, and 12.8% 15-25 years, compared with the NHSBT proposed targets of 8% and 20% respectively.

Within the R4 group, recipients receiving a D4 graft were associated with a higher rate of DGF (41.7%, vs 23.2% D1-D3 grafts, p=0.009), longer index admission (median 11 days vs 8 days, p=0.038) and more readmissions within the first post-operative year (median 18 vs 11 days, p = 0.005) – Figure 2.

D4 grafts demonstrated lower mean eGFR at one year (35.7, vs. 54.8 ml/min, p<0.001), Figure 3. R4 recipients experienced graft loss more frequently (HR 3.4 vs R1-3 (95%CI 0.8-13.9, p=0.12). One-year survival in R4 cohort was 97.8% (four deaths), and 93.8% at 4 years; R1-3 cohort had 100% survival to 4 years; there was no significant impact on R4 patient survival with D4 kidneys vs. D1-D3.

Day ward attendances, bacteraemia, and CT imaging events did not differ by R or D category; D4 was associated with higher rates of transplant ultrasound (5.6 vs R1-3 4.25, p=0.009), and R4 with higher rates of urinary tract infection (3.6 vs R1-3 1.5, p=0.03).

Conclusion: Firstly, our transplant population is weighted to higher risk R4 recipients; secondly, intended principals of the allocation scheme are already largely being observed. Thirdly, our data does suggest that increasing R4D4 transplants will have a significant impact on transplant centres, with resource burden primarily within the first year. But despite poorer graft function, patient survival appears to be equivalent and improved matching may in the longer term reduce need for re-implantation as the scheme intends.

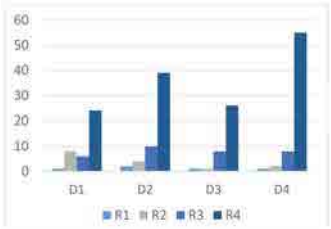


Figure 1: Current graft numbers by Donor (D) and Recipient (R) category

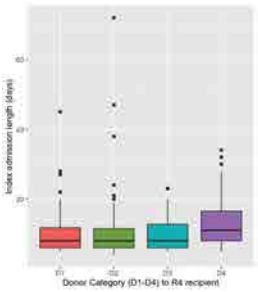


Figure 2: Length of transplant admission for 'R4' recipients for each donor risk category

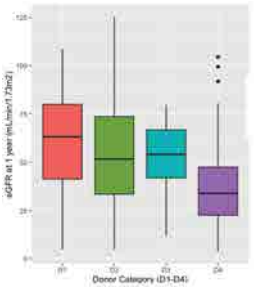


Figure 3: eGFR at one year in 'R4' recipients for each donor risk category

P1638

EARLY RENAL FUNCTION TRAJECTORIES, CYTOMEGALOVIRUS SEROSTATUS AND LONG-TERM GRAFT OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS: A BAYESIAN ANALYSIS STUDY

Jonathan Law[1,2], Richard Borrows[2], David McNulty[2], Adnan Sharif[2], Charles Ferro[1,2]

[1]University of Birmingham, Institute of Cardiovascular Sciences, Birmingham, United Kingdom and [2]University Hospitals Birmingham NHS Foundation Trust, Department of Renal Medicine, Birmingham, United Kingdom

Background and Aims: Despite significant improvements in short-term kidney transplant survival, long-term graft survival has not improved to the same degree with transplant failure being a top four cause of end-stage renal disease. We previously showed in a prevalent kidney transplant population that most patients do not experience linear renal function trajectories[1]. Many, instead, have periods of stability whilst others experience rapid progression. We also showed that episodes of rapid progression are associated with graft loss. Understanding trajectories of kidney allograft function is, therefore, key to defining the mechanisms underpinning allograft dysfunction. In this study, we evaluated the allograft function trajectories and associated factors, in an unselected, incident population of kidney allograft recipients in the early period post-transplantation. We also investigate whether episodes of rapid progression or non-progression are associated with graft loss in an extended follow-up period

Method: Demographic and clinical data were obtained from electronic health records. We used Bayesian smoothing techniques[1] to create 10,000 Monte Carlo sample curves for 310 kidney transplant recipients for estimated glomerular filtration rates from 3-27 months after transplantation. This technique produces a smooth curve for each patient that reflects the gradual, longer term changes in eGFR values, rather than the rapid, short-term changes because of clinical and biologic variation as well as other interference including measurement error. The estimated trajectory is a smooth curve, allowing its slope to be calculated month by month. The probability of having an episode of rapid progression (decline greater than 5 ml/min/1.73m^2/year in any 1-month period) and non-progression (decline no greater than -1ml/min/1.73m^2/year) were calculated. Overall follow-up period was 8 years. Factors associated with having an episode of rapid progression, non-progression, and associations with long-term graft loss were explored.

Results: A median of 54 eGFR measurements per patient were available from 3-27 months for analysis. 65 patients (21%) had a probability of rapid progression greater than 0.8. During the follow-up period, 34 patients (11%) lost their graft. In multivariable Cox Proportional Hazard analysis, a probability greater than 0.8 of rapid progression was associated with long-term death-censored graft loss (Hazard ratio, 2.17; 95% CI, 1.04-4.55). In separate multivariable logistic regression models, cytomegalovirus serostatus donor positive to recipient positive (Odds ratio [OR], 3.82; 95% CI 1.63-8.97), CMV donor positive (OR 2.06; 95% CI 1.15-3.68), and CMV recipient positive (OR 2.03; 95% CI 1.14-3.60) were associated with having a greater than 0.8 probability of an episode of rapid progression. Having a probability greater than 0.8 of non-progression was not associated graft loss.

Conclusion: Early episodes of rapid progression are associated with long-term death-censored graft loss and are associated with cytomegalovirus seropositivity. Possible mechanisms include adverse cytomegalovirus-related immunomodulatory effects resulting in increased infections, glomerular injury and allograft vasculopathy. Further investigation into these factors may yield potentially modifiable risk factors and improve graft survival.

P1639 **DEVELOPMENT OF SELF-LIMITED LOW-LEVEL BK VIREMIA/VIRURIA SUGGESTS IDEAL IMMUNOSUPPRESSION TO SUPPRESS T-CELL AND ANTIBODY-MEDIATED REJECTION AND PRESERVE KIDNEY ALLOGRAFT FUNCTION**

Bettina Näf[1], Thomas Müller[1], Rudolf Peter Wuthrich[1], Thomas Schachtner[1]

[1]*UniversitätsSpital Zürich, Nephrology, Zürich, Switzerland*

Background and Aims: Polyomavirus BK (BKV) viremia has been suggested as a surrogate marker of overimmunosuppression. Due to recent advances in monitoring strategies and pre-emptive therapy, progression to BKV-associated nephropathy (BKVN) has been reduced. Reduction of maintenance immunosuppression during BKVN, however, has been associated with both T-cell mediated rejection (TCMR), antibody-mediated rejection (ABMR), and inferior kidney allograft outcomes. Although the administration of intravenous immunoglobulins (IVIG) failed to treat BKVN, IVIG may have properties to reduce allosensitization.

Method: We studied 860 kidney transplant recipients (KTRs) predominantly under tacrolimus-based triple-drug maintenance immunosuppression from 2009 to 2018. We identified 130 KTRs (15.1%) with high-level BK viremia >10,000 copies/mL (presumptive BKVN), 180 KTRs (20.9%) with low-level BK viremia <10,000 copies/mL, 85 KTRs (9.9%) with isolated BK viruria, and 465 KTRs (54.1%) with no BK viruria/viremia. Kidney allograft outcomes with respect to TCMR, ABMR, development of *de novo* donor-specific antibodies (DSA), kidney allograft survival, and estimated glomerular filtration rate (eGFR) slope were analysed. Due to the increased incidence of TCMR and ABMR among KTRs with presumptive BKVN, 48 of 130 KTRs (36.9%) with high-level BK viremia starting from 2015 received IVIG (0.5 g/kg of body weight) on a biweekly basis during BKV replication.

Results: Very interestingly, KTRs with low-level BK viremia/viruria showed a significantly lower incidence of TCMR compared to KTRs with no BK viremia/viruria and KTRs with high-level BK viremia ($p<0.05$). In addition, KTRs with low-level BK viremia/viruria showed a significantly lower incidence of ABMR compared to KTRs with high-level BK viremia ($p<0.05$). No differences were observed with respect to the development of *de novo* DSA (MFI>5000) between KTRs with low-level BK viremia/viruria, KTRs with no BK viremia/viruria, and KTRs with high-level BK viremia ($p>0.05$). KTRs with low-level BK viremia/viruria showed superior kidney allograft survival and lower eGFR slope compared to KTRs with no BK viremia/viruria and KTRs with high-level BK viremia ($p<0.05$). The administration of IVIG during high-level BK viremia didn't impact the development of TCMR, ABMR, development of *de novo* DSA, eGFR slope, and kidney allograft survival ($p<0.05$).

Conclusion: Our results show that low-level BK viremia/viruria is associated with suppression of TCMR and ABMR in the early period posttransplantation, and preservation of kidney allograft function in the long-term. The administration of IVIG didn't prove beneficial to reduce allosensitization among KTRs with high-level BK viremia.

P1640

COLONIZATION AND INFECTION WITH ESBL-PRODUCING AND CARBAPENEM-RESISTANT ENTEROBACTERIACIEAE IN KIDNEY TRANSPLANT RECIPIENTS: RISK FACTORS, IMPACT OF RENAL GRAFT FUNCTION AND USE OF HOSPITAL RESOURCES

Alessandra Palmisano[1], Eleonora Salsi[2], Paride Fenaroli[1], Anna Maria Degli Antoni[2], Ilaria Gandolfini[1], Carlo Ferrari[2], Enrico Fiaccadori[1], Umberto Maggiore[1]

[1]Nephrology Unit;, Department of Medicine and Surgery, Parma University Hospital, Parma, Italy and [2]Infectious Diseases and Hepatology Unit, Department of Medicine and Surgery, Parma University Hospital, Parma, Italy

Background and Aims: ESBL-producing and carbapenem resistant (CR) Enterobacteriaceae are a common cause of severe infection, morbidity and mortality in kidney transplant recipients (KTR). Few studies have investigated the risk factors for ESBL-producing/CR Enterobacteriaceae colonization and infection in this group of patients, the effect of colonization and infection on KTR's renal graft function, and the use of hospital resources.

Method: Retrospective follow-up study on a consecutive series of patients undergoing kidney transplantation at Parma University Hospital (Italy) between January-2016 and December-2018. We performed a multivariable-adjusted analysis of the predictive factor associated with MDR infection/colonization via general linear models for prevalence- and risk- ratio. Renal function (eGFR) decline was compared by mixed-effects random-coefficients models, hospital resources by negative binomial regression.

Results: We enrolled 180 KTR (mean recipient's age: 52.4 [SD 12.4]; males 65%; mean donor's age: 54.6 [SD 15.6]) and followed them up for 2-years post transplantation. Cumulative prevalence of colonization 3-months post-transplantation and cumulative incidence of infection were 26.1% and 9.4% for ESBL, and 4.4% and 1.6% for CR. ESBL colonization was associated with hemodialysis vs peritoneal dialysis (93% vs 70% non-colonized; adjusted RR 0.21 [95% CI: 0.06 to 0.98]), dialysis vintage (mean months: 65 vs 42; adjusted associated with being above the median, RR 2.17 [95% CI: 1.32 to 3.55]) and retention of ureteral stent for more than one month after transplant (28% vs 12%; adjusted RR 2.09 [95% CI: 1.27 to 3.44]) ; ESBL infection was associated with retention of ureteral stent (47% vs 13%; adjusted RR 4.89 [95% CI 2.11 to 11.35]) whereas CR colonization was associated with surgical complication during transplant admission (50% vs 15%; adjusted RR 4.61 [95% CI 1.28 to 16.66]). Two patients (both with CR) died over the study follow-up, whereas none of the patients lost the graft.

CR infection was associated lower baseline (3-months post-transplantation) eGFR compared to the other groups (-28.4mL/min/1.73m2 [95% CI: -50.5 to -6.3]); a numerically more rapid decline (up to - 5mL/min/year) of eGFR, albeit not statistically significant, was observed in patients with CR colonization compared to non-colonized at 2 years of follow-up.

In comparison with non-colonized patients, adjusted mean days of carbapenem treatment in ESBL/CR colonized/infected was 5.7 vs 0.7 (P=0.003); length-of-hospital stay 5.8 vs 1.0 (P=0.055); days on drug-resistant-infection intravenous-outpatient-therapy 20.7 vs 0.1 (P= 0.008).

Conclusions: The study shows that ESBL and CR colonization and infection in KTR are statistically associated with longer hemodialysis vintage, urological procedures, and surgical complications. They cause an increase in the hospital resources use and may jeopardize transplant outcomes.

P1641 DONOR ACUTE KIDNEY INJURY HAS A DELETERIOUS IMPACT ON KIDNEY GRAFT SURVIVAL: THE DON-AKI STUDY

Rémi Lenain[1], Camille Prouteau[1], Nicolas Chatauret[2], Aurélie Deshayes[2], Yohann Foucher[3,4], Magali Giral[4,5], Aghilès Hamroun[1], Mehdi Maanaoui[1], Marc Hazzan[1]

[1]CHU Lille, Nephrology, Lille, France, [2]Agence de la Biomédecine, Saint-Denis La Plaine, France, [3]INSERM UMR 1246 -SPHERE, Nantes, France, [4]Nantes University Hospital, Nantes, France and [5]Centre de Recherche en Transplantation et Immunologie INSERM, UMR1064, Nantes, France

Background and Aims: Acute kidney injury (AKI) during organ procurement represents an important cause of discarded kidneys. In the context of organ shortage, the evaluation of such grafts is needed in order to enlarge the donor pool. Although many studies showed an increased risk of delayed graft function when donors present with AKI, long-term impact on graft survival remains controversial. A recent large US registry study concluded that AKI during organ procurement had no deleterious effect on graft survival. However the definition of AKI in this latter study is questionable. Indeed the donor baseline serum creatinine (SCr), according to KDIGO recommendations, is often not available. In this situation, the KDIGO guidelines suggest to estimate the baseline SCr using the MDRD equation, assuming a baseline glomerular filtration rate at 75 mL/min/1.73m?

This method was applied in the present study to assess the impact of donor kidney failure on long term kidney allograft survival.

Method: We analyzed the French national allocation system CRISTAL (Agence de la Biomédecine) data of all the recipients who received a deceased donor kidney graft from 2006 to 2017. 26786 transplant patients from 14899 deceased kidney donors were included. The donors were categorized into four groups. Ongoing AKI at the time of kidney procurement: n=1880 (3373 transplantations, AKI group), AKI with total recovery (normal SCr) at the time of kidney procurement: n=1332 donors (2392 transplantations, recovery group), elevated SCr all along the procedure: n=952 donors (1745 transplantations, unclassified AKI/CKD group) and normal SCr all along the procedure: n=10735 donors (19276 transplantations, no-AKI group). The main outcome was death censored graft survival.

Results: 4458 graft losses occurred during the study period (648 in the AKI group, 411 in the recovery group, 297 in the unclassified AKI/CKD group and 3102 in the no-AKI group) after a median follow-up time of 5.7 years (3 - 8.9). Multivariate analysis showed a significant increase risk of graft loss for each group when compared to the no-AKI group: HR 1.18 (1.04-1.34), HR 1.15 (1.04-1.28) and HR 1.22 (1.12-1.34) for the unclassified AKI/CKD, recovery and AKI groups, respectively. Regarding the AKI group, the risk of graft loss increased according to the AKI stage (KDIGO 2012): HR 1.20 (1.08-1.32) for stage I AKI and HR 1.31 (1.13-1.53) for stage II-III AKI.

Conclusion: Donor AKI represents a significant risk factor of graft loss, independently of SCr at the time of procurement. Stage II-III AKI carries a higher risk than stage I AKI suggesting a "dose-effect". However, considering organ shortage, further studies are required to better allocate these sub-optimal kidneys.

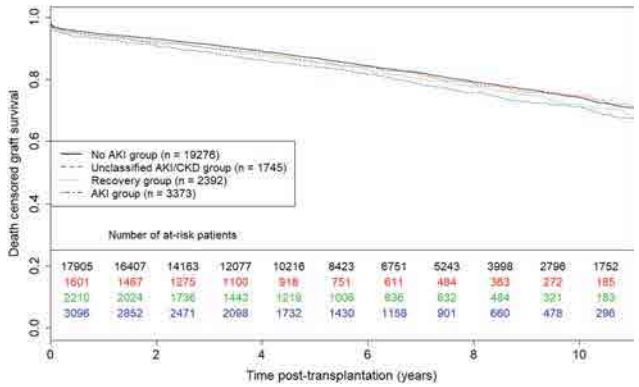


Figure:

P1642 **CORONARY ARTERY CALCIFICATION AMONG RENAL TRANSPLANT RECIPIENTS**

Mohamed Osama[1], Medhat Mahmoud[2], Salem El Deeb[2], Ahmed Elmowafy[1], Hussein Sheashaa[1], Ahmed Donia[1], Ayman Refaie[1], Ashraf Fouda[1]

[1]Urology & Nephrology center Mansoura university, Nephrology, Mansoura, Egypt and [2]Faculty of Medicine, Internal Medicine, Zagazig, Egypt

Background and Aims: Bone-mineral disease and vascular calcification are common complications in hemodialysis. The harmony between parathyroid hormone, calcium and phosphorus is impaired during hemodialysis and it supposed to be reversed by kidney transplantation but it is not known if the effect on vascular calcification will be reversed. Our aim is to study renal transplantation effect on hemodialysis associated vascular calcification and the risk factors for development and progression of vascular calcification.

Method: Transplant registry in Mansoura Urology and Nephrology Center, Egypt was reviewed for kidney transplant recipients (KTRs) who received renal allo-transplantation between January 2016 and December 2017 (149 KTRs). Patients were divided according to the presence of vascular calcification using non-contrast CT into 2 groups. Group I: 58 KTRs with pre-transplant vascular calcification, Group II: 91 KTRs without pre-transplant vascular calcification. Group I then were subdivided into 3 groups according to Agatston score (coronary calcium score) to 3 groups: Mild calcification (11-100), Moderate calcification (101-400), Severe calcification (>400). All patients were screened for coronary vascular calcification 2 years after transplantation using multi-slice coronary CT. Patients with detectable CAC at baseline and a CAC score change was $\geq$25% and patient with CAC score of 0 and follow up $\geq$ 4 were considered as progressors.

Results: The recipients` age in both group ranged from 18 years to 55 years. Older age is associated with higher incidence of vascular calcification (p value: 0.048) with male predominance and mean body mass index is 32.5$\pm$2.3.

Majority of patients underwent hemodialysis before transplantation (90%). The longer hemodialysis duration, the more severe the degree of vascular calcification (p value: 0.003). There was no difference among both groups regarding CKD bone-mineral biomarkers except for intact PTH which was higher among vascular calcification patients (p value: 0.023).

The majority of our patients received induction therapy; Basiliximab and received tacrolimus based immunosuppressive regimen. There was no significant difference regarding rejection episodes or post-transplant medical disorders. Presence of vascular calcification did not affect graft outcome over 2 years.

Despite significant improvement in CKD-bone disease biomarkers (p value: 0.001; calcium, phosphorus, alk. phosphatase and intact PTH changes), Vascular calcification incidence increased after transplantation from 38.9% to 40.9% especially for severe form with rise of median agatston score from 258.85 (21,813) to 354.55(20, 1198.8). Patients were divided according to progression into 2 groups: progressors (59 KTRs) and non-progressors (90 KTRs). On comparison of both groups, there were 3 independent risk factors for CAC progression: pre-transplant Calcium score (Figure 1), dialysis duration (Figure 2) and pre-transplant PTH level (Figure 3) with significant p value: <0.001, <0.001 and 0.05 respectively. Pre-emptive transplantation is inversely proportional in determining CAC progression with p value: 0.02. ROC curve analyses were performed to evaluate the discriminatory power of the three parameters.

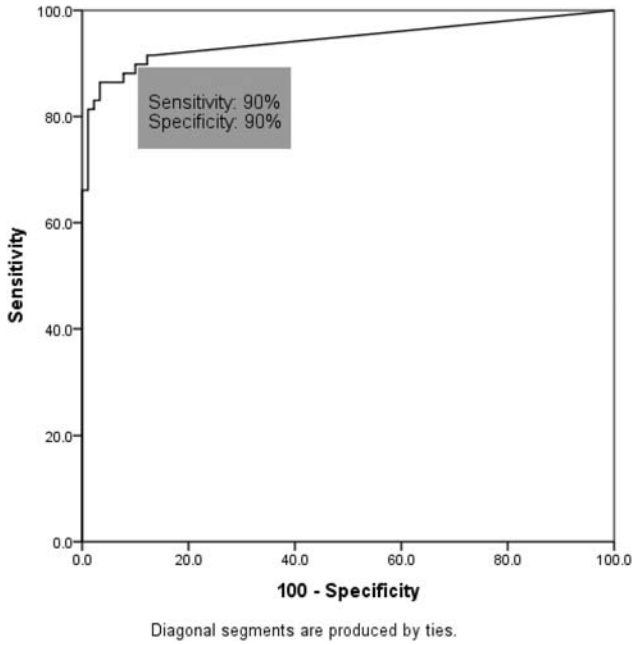


Figure (1): ROC for CAC progression, Dependent variable pre-transplant CAC

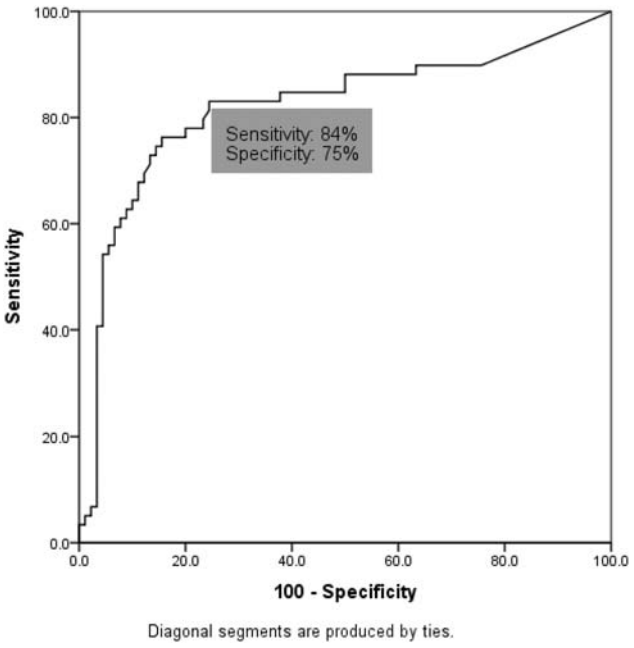


Figure (2): ROC for CAC progression, Dependent variable dialysis duration

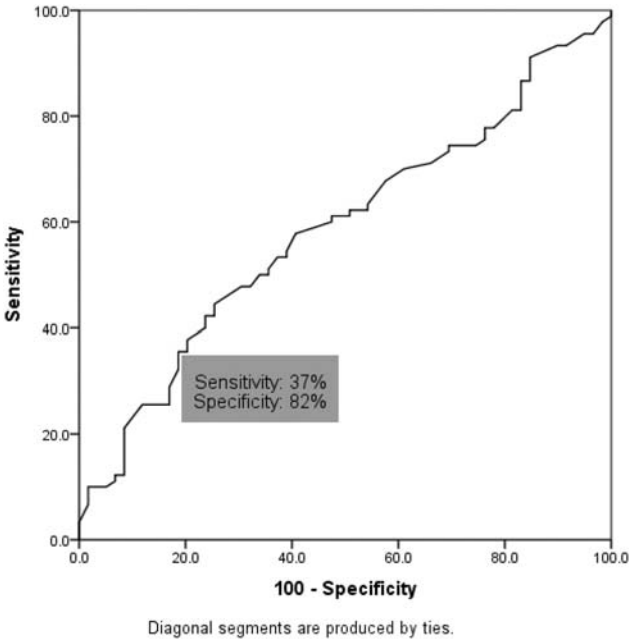


Figure (3): ROC for CAC progression, Dependent variable pre-transplant PTH level

Conclusion: Baseline CAC, duration of dialysis and pre-transplant serum PTH level are factors associated CAC progression. Renal transplantation does not stop or reverse CAC. Progression of CAC is the usual evolution pattern of CAC in renal transplant recipients. Very important was the finding that the follow-up calcium Score was significantly related to the baseline score., which emphasizes the importance of primary prevention of CAC development.

P1643 TORQUE TENO VIRUS FOR RISK STRATIFICATION OF SUBCLINICAL GRAFT REJECTION AFTER KIDNEY TRANSPLANTATION- A PROSPECTIVE STUDY

Konstantin Doberer[1], Georg A. Böhmig[1], Elisabeth Puchhammer-Stöckl[2], Gregor Bond[1]

[1]Medical University Vienna, Medicine III, Vienna, Austria and [2]Medical University Vienna, Center of Virology, Vienna, Austria

Background and Aims: Non-invasive monitoring strategies are insufficient to detect patients at risk for subclinical graft rejection after kidney transplantation. The highly prevalent and non-pathogenic Torque Teno virus (TTV) reflects the immunocompetence of its host: high level viraemia indicates strong and low level viraemia weak immunosuppression, respectively. Thus TTV replication might serve as a candidate for immunologic monitoring.

Method: To analyze the association between TTV and subclinical kidney graft rejection, an interim analysis of the prospective "TTV POET" cohort study (DRKS00012335) was performed including data available until 31/01/2019. All consecutive kidney graft recipients transplanted at the Medical University Vienna since 01/12/2016 (n=308) with a protocol biopsy 12 months after transplantation (n=47; median 12.4 months) and stable graft function were included. Biopsy results according to current BANFF classification were analyzed in the context of peripheral blood TTV levels quantified by PCR.

Results: Graft function was excellent (median eGFR MDRD: 57 ml/min/1.73m2, urinary PKR: 92 mg/g). Twenty recipients (43%) had subclinical rejection (borderline TCMR, n=16; ABMR, n=3; TCMR type I, n=1). TTV level quantified at the date of biopsy was lower in recipients with rejection compared to recipients without rejection. The risk for rejection increased by 11% with each log level decrease in TTV copies/ml (RR 0.89, 95% CI 0.85-0.93; $p<0.001$). Differences in TTV levels were evident not only at the date of biopsy, but already 6 weeks earlier. Patients with biopsies showing chronic leasons, suggesting ongoing allo-reactivity, had a longer period of time with TTV levels $<$1x106 copies/ml.

Conclusion: Our data suggests an association between TTV level and subclinical graft rejection at 12 months after kidney transplantation. Future clinical trials are necessary to test the potential of TTV guided immunosuppression to reduce subclinical rejection.

P1644 **SAPS AND EPTS SCORES AS PREDICTORS OF RENAL FUNCTION IN RECENT RENAL TRANSPLANTATION**

Jimmy Reinaldo Sanchez Gil[1], Armando Coca[1], Guadalupe Rodriguez Portela[1], Carmen Aller Aparicio[1], Alicia Mendiluce[1]

[1]Valladolid, HOSPITAL CLÍNICO UNIVERSITARIO DE VALLADOLID, Valladolid, Spain

Background and Aims: The risk scores used in Critical Care Units estimate the severity and mortality of patients. The SAPS (Simplified Acute Physiologic Score) and its SAPS II and SAPS III variants calculate the severity by collecting the values recorded in the first 24 hours. The EPTS (Estimated Post-Transplant-Survival) is used as a reference for the allocation of organs in the US by the OPTN. The objective is to determine its use in recent renal transplant units as estimator of subsequent renal function, in services where patients move from the operating room to a nephrological intermediate care unit.

Method: The SAPS (II and III) and OPTN scores were applied in 87 (N = 87) consecutive renal transplanted patients. The point value of each of the scales was evaluated with the creatinine values at hospital discharge, and one month after the transplant. The scores obtained on the SAPS scales were divided as follows (SAPSIIA <20 points, SAPSIIB ≥20 points) (SAPSIII A <30 points, SAPSIIIB ≥30 points). In the EPTS scale, two cut-off points were used to divide the groups (20% Score; EPTS-IA ≤20%, EPTS-IB> 20%), (Score 40%; EPTS-IIA ≤40%, EPTS -IIB> 40). The sérum creatinine means of each of the groups were compared. Data were analyzed with SPSS 20.0.0

Results: Significant differences were found in serum creatinine levels in renal function at the first month of transplantation in the SAPS II groups (SAPS IIA 1.38 mg / dl, SAPS IIB 1.79 mg / dl; P = 0.017 95% CI). With an area under the ROC curve of 0.65 (P = 0.017 95% CI). In the SAPS III groups no significant differences were found. In the EPTS scales, there were also significant differences in creatinine one month after the transplant in the group with a score of 40% (EPTS-IIA ≤40% 1.42 mg / dl, EPTS-IIB> 40 1.81 mg / dl; P = 0.024 95% CI) With an Area under the ROC curve of 0.64 (P = 0.037 95% CI).

Conclusion: The SAPSII and EPTS scores can be a useful tool in estimating renal function one month after renal transplantation, giving a prognosis of renal graft function. The combined use of these scales together with other functional graft tests could have an important relevance in the management and follow-up of recent renal transplantation. Other studies with larger sample sizes are necessary to establish the appropriate cut-off points for the scales.

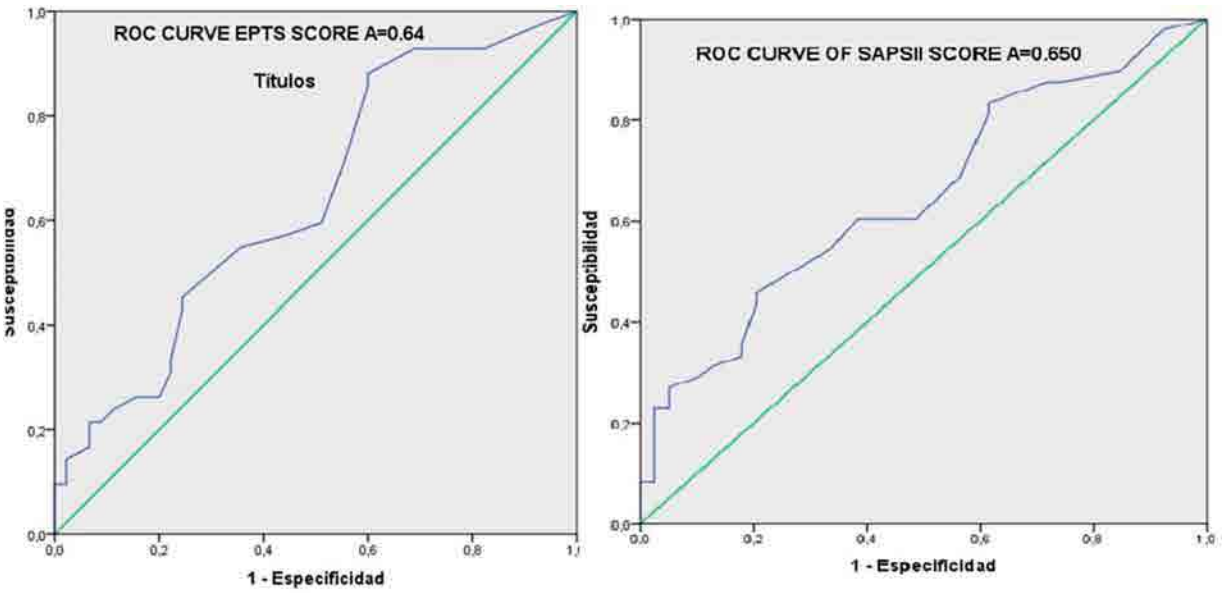


Figure:

P1645 VITAMIN K DEPENDENT PROTEINS AFTER KIDNEY TRANSPLANTATION: RESULTS FROM PROSPECTIVE STUDY.

Maria Fusaro[1,2], Pascale Khairallah[3], Andrea Aghi[4], Mario Plebani[5], Martina Zaninotto[5], Chiara Cosma[5], Maria A. Aponte Farias[3], Natalia E. Cortez[6], Giovanni Luigi Tripepi[7], Thomas Nickolas[3]

[1]National Research Council (CNR), Institute of Clinical Physiology (IFC), Pisa, Italy, [2]University of Padua, Padova, Italy, [3]Columbia University Medical Center, New York, United States of America, [4]Clinica Medica 1, University of Padua, Padova, Italy, [5]Laboratory Medicine Unit, University of Padua, Department of Medicine, Padova, Italy, [6]University of California, Davis, Davis, United States of America and [7]Consiglio Nazionale Delle Ricerche, Reggio Calabria, Italy

Background and Aims: Two Vitamin K-dependent proteins (VDKPs) link bone and vasculature in CKD-MBD: Bone Gla Protein (BGP) and Matrix Gla Protein (MGP). In ESKD, Vitamin K deficiency is highly prevalent and leads to increased levels of inactive VKDPs (undercaboxylated (ucBGP and dephosphorylated (dp)-uMGP), which are linked to greater risk of fractures and severity of vascular calcification. We hypothesized that kidney transplantation (KT) would improve Vitamin K status and lower levels of inactive VKDPs.

Method: Between 2014-2017, we conducted a study in 34 patients to assess changes in VKDPs during the 1st year of KT. In a specialized lab we determined VKDPs pre- and 1-year post-KT: total BGP, uc BGP, total MGP, and dp-uc MGP. We determined the prevalence of Vitamin K deficiency based on levels of uc BGP and dp-uc MGP.

Results: Our cohort had a mean +/- SD age of 48+/-14 years, 32% were female and 97% were Caucasian. 1 year post-KT, there was a decrease in the levels of all VKDPs and the prevalence of Vitamin K deficiency (**Table 1** and **Figure 1**). Patients with greatest severity of Vitamin K deficiency pre-KT had the largest decreases of inactive VDKPs post-KT.

Conclusion: KT was associated with improvement in Vitamin K status as manifested by decreased levels of inactive VKDPs. These are the first prospective data on VKDPs in CKD patients pre- and post-KT. Studies are needed to assess the impact of improvement in VKDP status after KT on CKD-MBD outcomes.

Variable	Pre-KT	Post-KT	p-value
uc-BGP ng/mL (median; IQR)	8.56 (5.45, 9.55)	3.41 (1.24, 4.80)	**< 0.001**
Vitamin K deficient by uc-BGP – n (%) (Cut-Off: uc-BGP>=4.5 ng/ml) *	26 (76.5%)	11 (32.4%)	**<0.001**
Total BGP ng/mL (median; IQR)	132 (79.85, 279.5)	22.55 (18.85, 30.6)	**<0.001**
Total MGP nmol/L (median; IQR)	29.19 (26.67, 32.30)	20.15 (14.68, 23.23)	**<0.001**
dp-ucMGP pmol/L (median; IQR)	910.5 (653.3, 1396.5)	637 (517, 777.5)	**<0.001**
Vitamin K deficient by dp-ucMGP- n (%) (Cut-Off: dp-uc MGP>500 pmol/L)	33 (97.1%)	27 (79.4%)	**0.012**

Figure 1. Total BGP and MGP levels in patients Pre and Post-KT.

P1646 **SURVIVAL OF KIDNEY TRANSPLANTS ACCORDING TO PRESENCE OF HLA ANTIBODIES WHEN DONORSPECIFIC ANTIBODIES ARE SCREENED DURING POSTTRANSPLANT FOLLOW-UP**

Inge Derad[1], Johanna Busch[1], Martin Nitschke[1], Malte Ziemann[2]

[1]*Universität zu Lübeck, Nephrology and Transplantation, Luebeck, Germany and*
[2]*Universität zu Lübeck, Transfusionsmedizin, Luebeck, Germany*

Background and Aims:

Posttransplant kidney survival depends on several risk factors. A careful immunogenetic matching and the absence of HLA donor specific antibodies (DSA) seem to determine the longevity of the transplant.

Method:

Screening the presence of donor specific HLA antibodies in our posttransplant outpatients was implemented in 2010 (every 6 months in case of DSA free patients for two years, then yearly, and every 3 months in case of DSA + patients for two years, then twice a year). At the same time a treatment protocol was implemented, omitting reduction of immunosuppressive drugs in case of newly detected DSA, and most important with preventing steroid withdrawal in this case.The present single center study reports the long-term survival and kidney function from patients undergoing HLA-screening after transplantation between 2010 and 2016 with a follow-up until 2018. Using a Kaplan-Meier analysis patients without HLA antibodies (no HLA-ab), with HLA antibodies but without DSA (NDSA), and with donor-specific HLA antibodies (DSA) were compared by logrank-testing.

Results:

A full dataset was obtained from 318 patients. The mean overall survival (patients and organ function) didnt differ between the three groups, p=0.318: no HLA-ab 7.2 years (95%confidence interval 6.7;7.6), NDSA 6.6 (5.9;7.2), DSA 6.8 (6.1;7.5), overall 7.0 (6.6;7.3), events are given in Table1. Whereas the mean patient survival didnt differ between the groups (p=0.715), the mean death-censored graft survival differed significantly, p=0.008, with a reduced transplant survival in the patients with HLA antibodies but without donorspecific antibodies: no HLA-ab 8.0 years (95%confidence interval 7.7;8.3), NDSA 7.0 (6.4;7.6), DSA 7.6 (7.1;8.2), overall 7.7 (7.4;8.0), numbers are given in Table1.

Conclusion:

In conclusion, the presence of HLA antibodies was associated with a reduced transplant survival. Patients with HLA antibodies had a worse survival than patients with DSA undergoing HLA screening with a personalised immunosuppressive regimen. Immunosuppressive regimen of the groups, as well as other known risk factors of graft survival have to be further analysed. The results of these multivariate analyses have to be awaited to determine whether the risk for graft loss inferred by HLA antibodies is independent from other factors.

Table 1. Summary of case processing

A		**Tx Survival and Death**	**censored**	
HLA antibodies post tx	total number	number of events	N	percent
no HLA antibodies	149	21	128	85,9%
NDSA	84	19	65	77,4%
DSA	85	17	68	80,0%
in total	318	57	261	82,1%
B		**Tx survival**	**censored**	
HLA antibodies post tx	total number	number of events	N	percent
no HLA antibodies	149	5	144	96,6%
NDSA	84	13	71	84,5%
DSA	85	8	77	90,6%
in total	318	26	292	91,8%

P1647 **CHANGES IN CAUSES OF EARLY GRAFT LOSS IN LIVING DONOR KIDNEY TRANSPLANT RECIPIENTS, 1972-2018**

Kenta Futamura[1,2], Goto Norihiko[1], Hiroki Fukuhara[3], Takaaki Nawano[1], Akiko Kanda[1], Toshihide Tomosugi[3], Manabu OKADA[3], Makoto Tsujita[4], Takahisa HIRAMITSU[3], Shunji Narumi[3], Yoshihiko Watarai[3]

[1]Japanese Red Cross Nagoya Daini Hospital, Transplant Nephrology, Nagoya, Japan, [2]Nagoya University Graduate School of Medicine, Department of Nephrology, Nagoya, Japan, [3]Japanese Red Cross Nagoya Daini Hospital, Transplant Surgery, Nagoya, Japan and [4]Masuko Memorial Hospital, Transplant Nephrology, Nagoya, Japan

Background and Aims: In living donor kidney transplantation, the progress of immunosuppressants in recent decades has led to an average graft survival period more than 15 years. However, the rate of graft loss (GL) within 5 years is still about 5%. Since the incidence of early GL is low, clinical evidence of causes and risk factors are limited and it remains unclear whether early GL was predictable before transplantation. Our purposes were to characterize a patient population with GL, to identify risk factors associated with early (<5 years) GL.

Method: The subjects were 1,779 patients who underwent living donor kidney transplantation at Japanese Red Cross Nagoya Daini hospital and Masuko Memorial Hospital from January 1, 1972 to December 31, 2018 (former group (1972-1999) : 503, latter group (2000-2018) : 1,276). We retrospectively examined patient characteristics, timing and causes of GL in 445 cases with GL by December 31, 2019 (GL cases in former group : 335, GL cases in latter group : 110).

Results: The 5- and 10-year graft survival rates were on an increasing trend, with 74.7% and 58.3% in former group and 95.2% and 88.7% in latter group, respectively. In latter group, T cell-mediated rejection and recurrence of primary diseases were significantly more frequent in GL cases within 5 years after transplantation than over 5 years (10% vs 0%, p=0.02 and 6% vs 0%, p=0.04). Although not significant, GL due to antibody-mediated rejection tended to more frequent in over 5 years after transplantation (22% vs 45%). Compared the causes of GL within 5 years after transplantation between GL cases in former group and latter group, rate of allograft rejection significantly reduced (88% vs 44%, p<0.001), and infections (especially BK polyomavirus infection), medication nonadherence and recurrence of primary diseases tended to increase (0%, 4% and 3% vs 8%, 16% and 8%, respectively).

Conclusion: Our analysis suggests that management of infections, medication nonadherence and recurrence of primary diseases have become more important for living donor kidney transplant recipients in recent years with improved immunosuppressants.

Table Ca uses of graft loss (GL) in latter group (2000-2018)

N=110	GL within 5 years after transplantation (n=50)	GL over 5 years after transplantation (n=60)	Univariate
Category n, (%)			p-value
Death with functioning graft	14 (28)	25 (42)	0.83
Antibody-mediated rejection	11 (22)	27 (45)	0.68
T cell-mediated rejection	5 (10)	0 (0)	0.02
Recurrence of primary diseases	3 (6)	0 (0)	0.04
Infections	3 (6)	2 (3)	0.12
Medication nonadherence	6 (12)	2 (3)	0.19
Others	8 (16)	4 (7)	0.50

P1648 **CLINICAL OUTCOMES OF LIVING DONOR KIDNEY TRANSPLANTATION FROM MARGINAL DONORS**

Yoshitaka Kinoshita[1], Takashi Yagisawa[1], Toru Sugihara[2], Saki Takeshima[1], Taro Kubo[1], Takahiro Shinzato[1], Toshihiro Shimizu[1], Jun Kamei[2], Fujisaki Akira[2,3], Satoshi Ando[2], Motofumi Suzuki[3], Haruki Kume[3], Tetsuya Fujimura[2]

[1]Jichi Medical University Hospital, Surgical Branch, Institute of Kidney Diseases, Shimotsuke, Tochigi, Japan, [2]Jichi Medical University Hospital, Department of Urology, Shimotsuke, Tochigi, Japan and [3]The University of Tokyo, Department of Urology, Tokyo, Japan

Background and Aims: Evidence demonstrating the outcomes of living donor kidney transplantation (LDKT) from marginal donors (MDs) is limited. We retrospectively investigated the clinical outcomes of LDKT from MDs in both recipients and donors.

Method: Clinical data on patients who received LDKT in Jichi Medical University Hospital between 2006 and 2019 were extracted from the medical records. Based on the Japanese guideline for preoperative conditions of donors, they were classified as standard donors (SDs) or MDs, the latter including the elderly and patients with obesity, hypertension, diabetes mellitus, and reduced renal function. Multivariate Cox proportional hazard regression analysis for graft survival was performed using explanatory variables of the donor conditions (MD vs SD) and recipient conditions, including age, gender, duration of dialysis, ABO compatibility, and presence of donor specific antibodies. The estimated glomerular filtration rates (eGFRs) of the donors were compared using an unpaired t-test.

Results: Of the 293 donors, 195 were SDs and 98 were MDs.

Demographics and baseline characteristics of recipients and donors

	Marginal Donor (n = 98)	Standard Donor (n = 195)
Recipient characteristics		
Age, year, Mean (SD)	48.5 (13.0)	47.5 (13.3)
Male, n (%)	55 (56.1)	119 (61.0)
Primary disease leading to transplantation, n (%)		
Glomerulonephritis	37 (37.8)	75 (38.5)
Diabetes mellitus	27 (27.6)	37 (19.0)
Plycystic kidney disease	4 (4.1)	14 (7.2)
Hypertension/nephrosclerosis	3 (3.1)	10 (5.1)
Unknown	9 (9.2)	24 (12.3)
Others	18 (18.2)	35 (17.9)
Duration of dialysis, year, median (IQR)	1.22 (0.24–2.94)	1.56 (0.63–4.02)
ABO incompatible, n (%)	25 (25.5)	65 (33.3)
Donor specific antigens positive, n (%)	10 (10.2)	15 (7.7)
Donor characteristics		
Age, year, Mean (SD)	63.9 (9.6)	55.0 (9.8)
Male, n (%)	47 (48.0)	75 (38.5)
Marginal factors, n (%)		
Hypertension	66 (67.3)	
Elderly	30 (30.6)	
Diabetes mellitus	22 (22.4)	
Reduced renal function	6 (6.1)	
Obesity	5 (5.1)	
Number of marginal factors, n (%)		
1	76 (77.6)	
2	19 (19.4)	
3	5 (5.1)	

Recipients of kidney transplants from MDs were associated with a higher incidence of death-censored graft loss than recipients of kidney transplants from SDs.

Kaplan-Meier plots for overall and death-censored graft survival.

Multivariate Cox proportional hazard regression analyses for overall and death-censored graft survival

	Overall graft survival Hazard ratio (95% CI)	*p* value	Death-censored graft survival Hazard ratio (95% CI)	*p* value
Marginal Donor (vs. standard donor)	1.79 (0.95–3.38)	0.070	2.46 (1.10–5.47)	0.028
Age(year, continuous)	1.02 (1.00–1.05)	0.070	0.98 (0.95–1.02)	0.297
Male(vs. female)	2.73 (1.31–5.66)	0.007	2.44 (1.00–5.93)	0.050
Duration of dialysis (year, continuous)	1.00 (0.99–1.02)	0.676	1.01 (0.98–1.03)	0.676
ABO incompatible (vs. compatible)	0.68 (0.33–1.43)	0.312	0.39 (0.11–1.33)	0.132
Donor specific antigens positive (vs. negative)	4.20 (1.19–14.88)	0.026	1.78 (0.22–14.31)	0.588

The eGFRs of MDs before transplantation were significantly lower than those of SDs, while no significant differences were observed between the two groups 3- and 5-years after transplantation.

Comparison of estimated glomerular filtration rates of donors

	Marginal donor mean (SD), n	Standard donor mean (SD), n	Difference (95% CI)	*p* value
Highest eGFR Pre-transplantation	85.3 (17.3), 98	90.0 (19.5), 195	-4.7 (-9.3 to -0.2)	0.043
< 1 year	51.5 (10.5), 98	55.1 (11.5), 195	-3.6 (-6.2 to -0.8)	0.011
1 – 3 years	51.8 (12.9), 88	54.7 (11.5), 183	-2.9 (-6.0 to 0.1)	0.062
3 – 5 years	53.5 (12.2), 53	55.7 (11.1), 140	-2.3 (-5.8 to 1.4)	0.24
5 years or later	56.3 (13.4), 34	56,1 (11.2), 90	0.2 (-4.7 to 5.0)	0.92

Conclusion: While the renal prognosis of recipients of kidneys from MDs is poorer than that of recipients from SDs, donating a kidney has no adverse effects on the renal health of MDs. The present study is the most comprehensive study that examined that the outcomes of LDKT from MDs according to the Japanese guideline.

P1649 **IS BK VIRUS CARCINOGENIC?!**

Ahmed Saleh[1,2], Ahmed Halawa[2,3]

[1]Suez Canal University, Internal Medicine and Nephrology, Ismailia, Egypt, [2]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield Kidney Institute, Sheffield, United Kingdom and [3]University of Liverpool, Transplantation Science, Liverpool, United Kingdom

Background and Aims: The role of polyomaviruses (PyV) in malignancy is controversial, this can be demonstrated in three ways; Firstly, hit and run mechanism where polyomaviruses contribute to the early phases of oncogenic progression. The second way, where PyV act as a passenger as polyomaviruses neither necessary nor contribute to the oncogenic progression. The third way, where PyV acts as (bystander) as PyV is not related to the malignancy, but PyV could be detected in the anatomically connected sites or neighbouring cells. BKV has been classified as a possible carcinogenic to humans (2b) as there is sufficient evidence that it is carcinogenic to animals, however, BKV carcinogenicity evaluation to humans was inadequate. There are inconsistent data regarding the contribution of BKV to tumors that occur in both animals and humans.

Method: Retrospective analyses of 492 consecutive renal transplant recipients in a single-center, 2010-2018. Data Source: prospectively managed electronic patient records. Malignancy data in both control and BKV infected groups were assessed.

Results: A total of 492 cases were studied, were categorized into 2 groups the BKV infected group (n:73) patients and BKV non-infected group (n: 419) patients, then an assessment of different malignancies in both groups. The BKV infected group had 15 cases out of 73 who had malignancy, while the BKV non-infected group had 28 cases out of 419 totally (Table 1). The association between malignancy in BKV was statistically significant (P-value of 0.038). Moreover, the risk factors involved in the development of malignancy in renal transplant recipients were older age, BK virus infection and maintenance immunosuppression agents (Table 2). Lastly, Logistic regression analysis was used to assess predictors of malignancy among renal transplant recipients. For every one-year increase in age among renal transplant recipients, the odds of having a malignancy increase by 4.6% (p=0.003). Meanwhile, there is a 4 times increase in the odds of having malignancy for recipients who are BK virus-positive vs. those who are BK virus negative (p=0.001). Furthermore, there is a 10 times increase in the odds of having malignancy for recipients who are on sirolimus as a maintenance immunosuppressant vs. those who are on TAC/PRED/MMF (p=0.007).

Conclusion: Our study highlights the statistically significant correlation between BK virus infection and the development of malignancy in renal transplant recipients. However, statistical correlation doesn't mean causation which makes the potential oncogenic role of BKV is unclear. Also, there is increased reporting of malignancy in patients infected with BKV. Increased vigilance is required for early detection of malignancy in patients infected with BKV not only the patients who are heavily immunosuppressed.

Table 1. Types of malignancies associated with each group:

No	Malignancy types		
	Malignancy	BKV negative (n=419)	BKV positive (n=73)
1.	Skin Squamous Cell carcinoma	8 (1.9)	4 (5.5)
2.	Skin Basal Cell Carcinoma	5 (1.2)	4 (5.5)
3.	Mixed (Squamous + Basal)	1(0.2)	2 (2.7)
4.	PTLD	0	1 (1.4)
5.	Lung Ca (NSCLC))	0	1 (1.4)
6.	GIT (Malignancy)	0	1 (1.4)
7.	Melanoma	1 (0.2)	1 (1.4)
8.	Renal Cell Ca	1 (0.2)	1 (1.4)
9.	Breast Ca	2 (0.5)	1 (1.4)
10.	B. Cell Lymphoma	1 (0.2)	0
11.	Bronchus Associated Lymphoid Tissue Lymphoma (Baltoma)	1 (0.2)	0
12.	Ovarian Adenocarcinoma	1 (0.2)	0
13.	Urothelial Ca	1 (0.2)	0

Table 2. Baseline characteristics of kidney transplant recipients according to their malignancy status

Variables		Total (n= 492)	transplantation associated malignancy Present (n=39)	Absent (n=453)	p-value
Gender, n (%)	Male	337 (68.5)	27 (69.2)	310 (68.4)	0.92 [a]
	Female	155 (31.5)	12 (30.8)	143 (31.6)	
Age (year), mean ± SD		54.12 ± 13.69	61.15 ± 12.26	53.55 ± 13.66	**0.001** [b]
BKV infection					
	Negative	419 (85.2)	24 (61.5)	395 (87.2)	**<0.001** [a]
	Positive	73 (14.8)	15 (38.5)	58 (12.8)	
Race, n (%)					
	White	444 (90.2)	37 (94.9)	407 (89.8)	
	Asian	8 (1.6)	1 (2.6)	7 (1.5)	
	Pakistani	18 (3.7)	0	18 (4)	0.59 [c]
	Black	8 (1.6)	1 (2.6)	7 (1.5)	
	Mixed	3 (0.6)	0	3 90.7)	
	Others*	11 (2.2)	0	11 (2.4)	
Diabetes Mellitus, n (%)		95 (19.3)	11 (28.2)	84 (18.6)	0.14 [a]
No. of renal transplantations, n (%)					
	One time	416 (84.6)	29 (74.4)	387 (85.4)	
	two time	62 (12.6)	8 (20.5)	54 (11.9)	0.13 [c]
	Three times	14 (2.8)	2 (5.1)	12 (2.6)	
Type of Transplant, n (%)					
	DBD	250 (50.8)	24 (61.5)	226 (49.9)	
	DCD	92 (18.7)	5 (12.8)	87 (19.2)	0.36 [a]
	Alive	150 (30.5)	10 (25.6)	140 (30.9)	
Induction Immunosuppressant, n (%)					
	Basiliximab	425 (89.9)	28 (80)	397 (90.6)	
	Campath	35 (7.4)	5 (14.3)	30 (6.8)	0.11 [c]
	ATG	10 (2.1)	2 (5.7)	8 (1.8)	
	Rituxmab	3 (0.6)	0	3 (0.7)	
Maintenance Immunosuppressant, n(%)					
	TAC PRED MMF	404 (82.3)	33 (84.6)	371 (82.1)	
	Without MMF	44 (9)	2 (5.1)	42 (9.3)	
	without prednisolone	22 (4.5)	0	22 (4.9)	**0.033** [c]
	Sirolimus	7 (1.4)	3 (7.7)	4 (0.9)	
	AZA	14 (2.9)	1 (2.6)	13 (2.9)	
DR mismatch, n (%)		226 (54.1)	22 (56.4)	244 (53.9)	0.75 [a]
Sensitization, n (%)		203 (41.3)	15 (38.5)	188 (41.6)	0.70 [a]
Acute rejection, n (%)		32 (6.5)	3 (7.7)	29 (6.4)	0.59 [c]
Delay graft function, n (%)		172 (35)	17 (43.6)	155 (34.2)	0.24 [a]
Graft failure, n (%)		41 (8.3)	4 (10.3)	37 (8.2)	0.26 f

*others: Afro Carribean, Somali and Mixed White and Asian
[a] P values are based on Chi Square test. Statistical significance at P < 0.05
[b] P values are based on Mann Whitney U test. Statistical significance at P < 0.05
[c] P values are based on Fisher Exact test. Statistical significance at P < 0.05

Figures:

P1650

HIGH-DENSITY LIPOPROTEIN PARTICLES AND THEIR RELATIONSHIP TO POSTTRANSPLANTATION DIABETES IN RENAL TRANSPLANT RECIPIENTS

Sara Sokooti Oskooei[1], Tamas Szili-Torok[1], Jose L Flores-Guerrero[1], Maryse C.J. Osté[1], António W Gomes-Neto[1], Hiddo Lambers Heerspink[2], Margery A. Connelly[3], Stephan Bakker[1], Robin P.F. Dullaart[1]

[1]University Medical Center Groningen, Internal Medicine, Groningen, Netherlands, [2]University Medical Center Groningen, Clinical Pharmacy and Pharmacology, Groningen, Netherlands and [3]LabCorp, Burlington, United States of America

Background and Aims: It is established that high concentrations of High-Density Lipoprotein (HDL) are associated with low risk of type 2 diabetes and posttransplantation diabetes mellitus (PTDM). However, HDL particles vary by size, density, and biological action. The aim of our study was to determine the association between different HDL particles with the development of PTDM in renal transplant recipients (RTRs).

Method: We included 351 stable outpatient adult RTR with a functioning graft $\geq$1 year from the Tranplantlines Food and Nutrition Study(NCT02811835). HDL particle concentration and size were measured by ^{1}H-NMR spectroscopy using a Vantera® NMR Clinical Analyzer (LabCorp, Raleigh, NC). HDL size was weighted averages derived from the sum of the diameter of each subclass multiplied by its relative mass percentage. Estimated ranges of HDL diameter for the HDL subclasses were as follows: large HDL particles, 9.6–13 nm; medium HDL particles, 8.1–9.5 nm; and small HDL particles, 7.4–8.0 nm. PTDM was defined according the American Diabetes Association's diagnostic criteria for diabetes. Multivariable-adjusted Cox proportional-hazards regression analyses were performed to assess the prospective association of HDL particles with PTDM.

Results: During 5.2 (IQR, 4.1–5.8) years of follow-up, 39 (11%) RTR developed PTDM. In a multivariable Cox regression analysis, higher HDL cholesterol was associated with a lower risk of PTDM development, after adjustment for age, sex and BMI (hazard ratio[HR] 0.55, 95% CI 0.36-0.83 per 1SD mg/dL; *P*=0.005). Moreover, among different HDL indices; HDL size, and large HDL were inversely associated with PTDM, after adjustment for age, sex, and BMI ([HR 0.48, 95% CI 0.31-0.76 per 1SD nm; *P*=0.002], and [HR 0.63, 95% CI 0.47-0.84 per 1SD µmol/L; *P*=0.002], respectively). However medium HDL and small HDL were not associated with risk of developing PTDM ([HR 0.88, 95% CI 0.64-1.23 per 1SD µmol/L; *P*=0.48], and [HR 1.14, 95% CI 0.85-1.52 per µmol/L; *P*=0.37], respectively). In additional models, the association remained significant for HDL cholesterol, HDL size, and large HDL after adjustment for other confounders including, the lifestyle, use of medication, kidney function and transplantation-specific parameters. In the last model after adjustment for age, sex, BMI, triglycerides, systolic blood pressure, and fasting plasma glucose, association were similar for HDL cholesterol, HDL size, and large HDL ([HR 0.61, 95% CI 0.40-0.94 per 1SD mg/dL; *P*=0.024], [HR 0.58, 95% CI 0.36-0.93 per 1SD nm; *P*=0.025], and [HR 0.68, 95% CI 0.50-0.93 per 1SD µmol/L; *P*=0.017].

Conclusion: In this study, we found that higher concentrations of HDL cholesterol, large HDL, and higher HDL size were associated with a lower risk of developing PTDM in RTRs, independent of established risk factors for PTDM development.

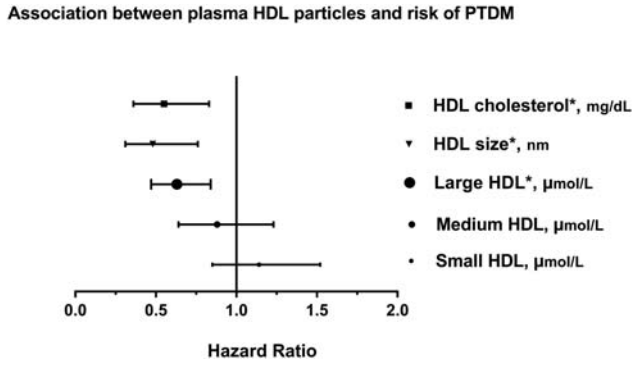


Figure:

P1651

HLA CW12 IN KIDNEY TRANSPLANT RECIPIENTS IS A NOVEL RISK FACTOR FOR THE DEVELOPMENT OF POST-TRANSPLANTATION DIABETES: A SINGLE-CENTRE RETROSPECTIVE STUDY

Nuvreen Phagura[1], Alice Culliford[2], Felicity Evison[3], Suzy Gallier[3], Jay Nath[2], David Briggs[4], Adnan Sharif[1,2]

[1]College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom, [2]Department of Nephrology and Transplantation, University Hospitals Birmingham, Birmingham, United Kingdom, [3]Department of Health Informatics, University Hospitals Birmingham, Birmingham, United Kingdom and [4]H&I Birmingham, NHS Blood and Transplant, Birmingham, Birmingham, United Kingdom

Background and Aims: Counselling kidney transplant candidates for their personalised risk of developing post-transplantation diabetes mellitus (PTDM) requires an understanding of risk factors. While some risk factors are well defined (e.g. age, ethnicity, body mass index), others like HLA typing are heterogeneously reported and lack consistency. The aim of this study was to investigate the association between HLA alleles and PTDM risk.

Method: Data was retrospectively extracted from hospital informatics systems for all kidney transplant recipients at a single-centre between 2007 and 2018, with patients excluded if they had pre-existing diabetes. Electronic patient records were then manually searched and records linked to various sources (e.g. NHS Blood and Transplant tissue typing, Hospital Episode Statistics, national death registry) to create a well-phenotyped cohort. Standard immunosuppression for all kidney transplant recipients during this study period was basiliximab induction with maintenance immunosuppression consisting tacrolimus, mycophenolate mofetil and low-dose corticosteroids. PTDM classification was aligned with International Consensus recommendations.

Results: Data was extracted for 1,560 kidney allograft recipients, with median follow up 5.4 years (IQR 2.7-8.7 years) up to October 2018. PTDM developed in 243 kidney transplant recipients (incidence 15.6%). A range of HLA alleles were examined (e.g. HLA-A, HLA-B, HLA-Cw, HLA-Bw, HLA-DR and HLA-DQ) but only the presence of HLA-Cw12 allele was associated with risk for PTDM (27.4% versus 14.3%, $p<0.001$) along with a selection of predominately recipient- and transplant related variables. In a logistic regression model, adjusted for all variables with a p-value <0.15 on univariate analysis, recipient HLA-Cw12 was found to be an independent risk factor associated with development of PTDM (Odds Ratio 1.793 [95% confidence interval 1.070-3.002], $p=0.027$) along with recipient female sex, recipient age, recipient BMI and recipient non-white ethnicity.

Conclusion: HLA-Cw12 allele in the kidney transplant recipient is independently associated with development of PTDM, although it is important to acknowledge association does not imply causality. This association has not been previously reported and requires validation and further investigation to understand any possible underlying biological mechanisms.

P1652 **IMPACT OF HEPATITIS C VIRUS AND DIRECT ACTING ANTIVIRALS ON JAPANESE RENAL ALLOGRAFT RECIPIENTS**

Kazuaki Okino[1], Keita Yamazaki[1], Keiichiro Okada[1], Keiji Fujimoto[1], HIROKI ADACHI[1], Furuichi Kengo[1], Hitoshi Yokoyama[1]

[1]*Kanazawa Medical University, Nephrology, Uchinada, Japan*

Background and Aims: The impact of hepatitis C virus (HCV) infection on patient survival after renal transplantation was worse. Previously, we found that continuous HCV infection was a significant independent risk factor for actuarial survival (especially at ≥20 years after the transplant procedure) among Japanese renal allograft recipients. This study evaluates the impact of HCV and of the new direct acting antivirals (DAAs) on patient outcomes in renal allograft recipients.

Method: We studied 46 cases (28 males, 18 females; 37 living-donor cases, 9 deceased-donor cases; mean follow-up period 305 months ranging from 2 to 420 months) out of the 315 renal transplanted patients who underwent the first renal transplantation in Kanazawa Medical University since 1974. They had antibodies against HCV: 11 were positive for HCV RNA and received DAAs (Group A, all of them genotype 1b); 27 were HCV RNA positive and did not receive any treatment (Group B); 8 were negative for HCV RNA (Group C) (Fig.1).

Results: All Group A patients had HCV RNA negativity after 2-12 weeks of treatment started, and 11 (100%) achieved a sustained virological response (SVR) at 24 weeks. All of them had no adverse effects by the use of DAAs. In this cohort, no patients in Group A died. On the other hand, 15 (55.5%) of 27 in Group B and 3 (37.5%) of 8 in Group C died. Causes of death among Group B were liver cirrhosis (5 cases), hepatocellular carcinoma (2 case), infections complicated with chronic hepatitis (6 cases) in chronic phase, fibrosing cholestatic hepatitis due to HCV (1 case) after surgery, and cardiovascular disease (1 case). The patient survival rate was significantly higher in Group A patients who received DAAs by Kaplan- Meier life table method (Log Rank test, Kay-square 11.7, p=0.004) (Fig.2).

Conclusion: Our results support the notion that continuous HCV infection was a harmful and that new DAAs were efficient and safe to treat HCV infection after renal transplantation.

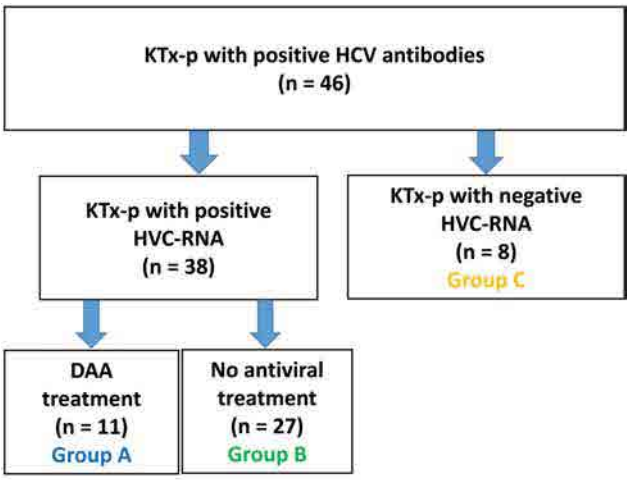


Fig.1 Graphical representation of the studied HCV positive cohort. KTx-p, kidney transplanted patients

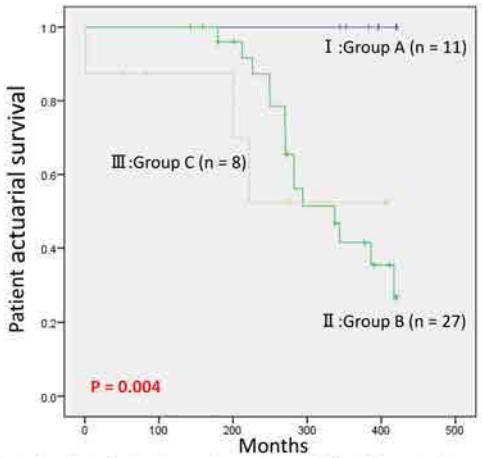


Fig.2 Survival analysis for death according to HCV-Ab(+)/RNA(+) received DAAs (Group A) vs. HCV-Ab(+)/RNA(+) not received any treatment (Group B) vs. HCV-Ab(+)/RNA(-) (Group C).

P1653 METABOLIC SYNDROME-RELATED DIETARY PATTERN AND RISK FOR MORTALITY IN RENAL TRANSPLANT RECIPIENTS

Qingqing Cai[1], Maryse C.J. Osté[1], Louise H. Dekker[1], António W Gomes-Neto[1], Stephan Bakker[1], Martin De Borst[1], Gerjan Navis[1]

[1]*University Medical Center Groningen, Groningen, Netherlands*

Background and Aims: The metabolic syndrome (MetS) is an important risk factor for premature mortality in renal transplant recipients (RTR). Diet plays an important role in MetS development. Although an unhealthy diet may affect the long term outcome in RTR, no specific dietary patterns have been established that are linked with MetS in RTR. Reduced rank regression (RRR) has emerged as a method that identifies linear functions of predictor variables (food groups) that explain maximized variation in the response variables (biomarkers). We aim to identify a MetS-related dietary pattern (MetS-DP) in RTR, and to test its association with all-cause mortality.

Method: We included 432 adult RTR who had a functioning graft $\geq$1 year and were free of diabetes at baseline. The MetS-DP was constructed at baseline using dietary information derived from a 177-item food frequency questionnaire by reduced rank regression (RRR). In the RRR model, six components of MetS were used as response variable (age- and sex- adjusted waist circumference, systolic blood pressure, diastolic blood pressure, serum triglycerides, HbA1c, and HDL cholesterol), and 48 food groups were made as predictor variables. Using Cox proportional regression, we evaluated the association between the Met-DP score and all-cause mortality in RTR.

Results: The MetS-DP was characterized by a high intake of fat processed meat and desserts, and a low intake of vegetables, tea, rice, fruits, milk and vegetarian products. During a mean follow-up of 5.2 $\pm$1.2 year, 64 RTRs (14.8%) died. Multivariate analysis showed that RTR in the highest tertile of MetS-DP score had a higher risk of all-cause mortality (hazard ratio [HR]=2.38; 95% confidence interval [CI],1.16-4.91, P=0.018) compared to the lowest tertile, independent of potential confounders.

Conclusion: The results suggest that the MetS-DP is significantly associated with all-cause mortality in RTR. Dietary measures may be useful to prevent MetS and reduce mortality in RTR.

P1654 **INCIDENCE AND RISK FACTORS OF THROMBOTIC MICROANGIOPATHY AFTER KIDNEY TRANSPLANTATION**

Kenta Futamura[1,2], Goto Norihiko[1], Hiroki Fukuhara[3], Takaaki Nawano[1], Akiko Kanda[1], Toshihide Tomosugi[3], Manabu OKADA[3], Makoto Tsujita[4], Takahisa HIRAMITSU[3], Shunji Narumi[3], Yoshihiko Watarai[3]

[1]Japanese Red Cross Nagoya Daini Hospital, Transplant Nephrology, Nagoya, Japan, [2]Nagoya University Graduate School of Medicine, Department of Nephrology, Nagoya, Japan, [3]Japanese Red Cross Nagoya Daini Hospital, Transplant Surgery, Nagoya, Japan and [4]Masuko Memorial Hospital, Transplant Nephrology, Nagoya, Japan

Background and Aims: Thrombotic microangiopathy (TMA) is characterized by mechanical hemolytic anemia, thrombocytopenia, and renal impairment. TMA that occurs in kidney transplant recipients has multiple etiologies and may be de novo or recurrent. Main causes of TMA among recipients are atypical hemolytic uremic syndrome (aHUS), immunosuppressive drugs, ischemia-reperfusion injury (IRI), viral infections, and antibody-mediated rejection (ABMR). Pathological findings of TMA with thrombosis in glomeruli and arterioles are not rare in graft biopsies, but the clinical signs vary widely by etiologies, and incidence and risk factors for each are uncertain. The purpose of this study is to clarify the current status of TMA after kidney transplantation.

Method: The subjects were 1,336 patients (5,425 biopsy specimens) who underwent kidney transplantation (851 ABO-compatible and 485 ABO-incompatible) at Japanese Red Cross Nagoya Daini Hospital and Masuko Memorial Hospital from January 1, 2000 to June 30, 2018. We investigated patient characteristics and graft survival in 69 patients with pathological findings of TMA (12 with symptomatic TMA and 57 with asymptomatic TMA) and 1,207 patients without findings of TMA. Sixty patients were excluded because of incomplete data or biopsy specimens. TMA patients with acute kidney injury (AKI) were defined as symptomatic TMA in this study.

Results: The incidence of post-transplant TMA was 5.2% (symptomatic TMA : 0.9%, asymptomatic TMA : 4.3%) in our cohort. Multivariate analysis revealed significant risk factors for TMA were presence of donor specific antibodies (DSA) and use of cyclosporine (odds ratio [OR] 3.52; 95% confidence interval [CI] 1.58-7.88; p=0.002 and OR 3.70; 95% CI 1.68-8.11; p=0.001, respectively). Causes of symptomatic TMA were ABMR : 66.7% (5 patients with ABO-incompatibility, 3 with preformed DSA), aHUS : 16.7%, cytomegalovirus and adenovirus infection : 8.3%, and causes of asymptomatic TMA were drug-induced: 40.4% (21 patients with calcineurin inhibitor, 2 with everolimus), ABMR: 31.6% (10 with ABO-incompatibility, 8 with de novo DSA), IRI : 14.0 %. Onset of post-transplant TMA was significantly associated with lower graft survival (Figure A), with a stronger correlation in symptomatic TMA than in asymptomatic TMA (Figure B and C).

Conclusion: TMA with AKI that occurred after kidney transplantation had a poor graft prognosis. Therefore, avoiding transplantation, changing donors or using tacrolimus instead of cyclosporine should be considered for patients with DSA or ABO-incompatibility.



Figure:

P1655 HYPERKALAEMIA IN PREVALENT KIDNEY TRANSPLANT RECIPIENTS

Toby Humphrey[1,2,3], Nicholas Torpey[2], Thomas Hiemstra[1,2,3]

[1]Department of Medicine, University of Cambridge, Cambridge, United Kingdom, [2]Department of Nephrology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom and [3]Cambridge Clinical Trials Unit, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

Background and Aims: Hyperkalaemia is a common and life-threatening medical emergency present in up to 10% of acute hospital admissions. End-stage Kidney Disease (ESKD) patients undergoing transplantation are at increased risk of hyperkalaemia, a potentially life-threatening medical emergency. Although the prevalence of hyperkalaemia in ESKD is well described, few studies have assessed the incidence and associations of hyperkalaemia in kidney transplant recipients. We evaluated post-transplant hyperkalaemia in a single centre using a large electronic health record dataset of emergency admissions.

Methods: Prevalent kidney transplant recipients were identified using ICD-10 codes from a complete Electronic Health Records database of all emergency admissions to Addenbrooke's Hospital, Cambridge between April 2015 and August 2018. We abstracted demographics, comorbidities, concomitant medications, biochemistry results including all blood potassium values, in-hospital prescribing and admission and discharge dates.

Data were summarised as frequency (%), mean± standard deviation (SD) or median with interquartile range (IQR) as appropriate. Categorical variables were compared by Chi-squared test and continuous variables by Student's *t*-test or Mann–Whitney *U*-test based on their distribution. Factors associated with developing hyperkalaemia were explored using mixed-effects logistic regression and odds ratios (OR) are reported.

Results: 421 prevalent kidney transplant recipients were admitted a total of 1,065 times via the Emergency Department and a further 475 times direct to the Transplant ward. 324 (77%) were deceased-donor recipients with 83 (20%) living-donor recipients and 14 (3%) simultaneous pancreas kidney (SPK) recipients.

Median age of admitted recipients was 56 (IQR 44-65) years and 87% were of white ethnic origin. Mean serum potassium was 4.56±0.72 mmol/L compared to 4.21±0.61 mmol/L amongst the 170,913 non-kidney transplant patients admitted over the same time period ($p<0.001$). 376 (89%) recipients were prescribed a calcineurin inhibitor.

Hyperkalaemia >5.5mmol/L occurred in 282 (67%) of 421 prevalent kidney transplant recipients with 203 (48%) patients including all SPK recipients experiencing moderate-severe hyperkalaemia (K >=6.0mmol/L). Of these, 110 (39%) received emergency treatment with insulin/dextrose. Potassium concentration immediately (≤ 60 min) pre-treatment was 6.26±0.76 mmol/L. The mean reduction in potassium at 4-hours post treatment was 0.89±0.90 mmol/L. Twenty-five of 110 (23%) patients developed hypoglycaemia (glucose <4mmol/L) within 6 hours of treatment and 37/110 (34%) required retreatment with insulin/dextrose within 24 hours.

Kidney transplant recipients were at significantly increased risk of developing hyperkalaemia (OR 19.8, 95% Confidence Interval (CI) 16.2-24.4, $p<0.001$) compared with all admitted patients and this risk persisted after adjustment for age, sex and co-morbidity (OR 3.6, 2.9-4.5, $p<0.001$). Associations with hyperkalaemia amongst transplant recipients included receiving a deceased-donor kidney (OR 1.96, 1.13-3.40, $p=0.017$) and exposure to beta-blockers (OR 2.26, 1.36-3.59, $p=0.001$) and calcineurin inhibitors (OR 6.39, 2.81-14.5, $p<0.001$).

Conclusion: Kidney transplant recipients are at greatly increased risk of developing hyperkalaemia. Recipients who become hyperkalaemic are more likely to have received a deceased-donor transplant and be prescribed beta-blockers and calcineurin inhibitors than those who do not. Insulin/dextrose for hyperkalaemia is associated with hypoglycaemia in almost 1 in 4 recipients treated and re-treatment is required in one third of recipients.

P1656

THE IMPACT OF PRE-TRANSPLANT DIALYSIS MODALITY ON EARLY POST-TRANSPLANT PERIOD ADVERSE EVENTS : A PROSPECTIVE COHORT STUDY WITH PROPENSITY SCORE MATCHING.

Hyo Jin Boo[1], Wooseong Huh[1], Yon su Kim[2], Chul-Woo Yang[3], Yong-Lim Kim[4], Jong Soo Lee[5], Joong Kyung Kim[6], Seung Hyeok Han[7], Jung-Won Hwang[8]

[1]Samsung Medical Center, Department of Medicine, [2]Seoul National University Hospital, Department of Medicine, [3]Seoul St. Mary's Hospital, Department of Medicine, [4]Kyungpook National University Hospital, Department of Medicine, [5]Ulsan University Hospital, Department of Medicine, [6]Bongseng Memorial Hospital, Department of Medicine, [7]Severance Hospital, Department of Medicine and [8]Seoul National University Bundang Hospital, Department of Anesthesiology and Pain Medicine

Background and Aims: Among peritoneal dialysis (PD) or hemodialysis (HD) while waiting for a kidney transplant (KT), which is better in terms of KT outcomes has long been of interest. Nowadays it is difficult to agree on which modality is better. The primary objective of this study was to compare the incidence of composite outcomes (delayed graft function, primary non-function, biopsy-proven acute rejection) within 1 year after primary adult KT between recipients taken PD and HD before KT (PD group vs. HD group, respectively).

Method: This study was a prospective, multi-sites cohort study. We used a propensity score matching to control for patients characteristics.

Results: Total 1040 patients were enrolled consecutively. Among them, 1030 patients (248, PD group; 782, HD group) were included in the final analysis. The HD group was older and had higher prevalence of diabetes, higher Charlson comorbidity index score, higher prevalence of positive PRA and more prescription of rituximab than the PD group significantly. After propensity score matching (246, PD group; 476, HD group), there were no differences in baseline characteristics between the two groups. In the whole population, there was no difference in the risk of the composite outcomes between the PD and HD groups (19% vs. 17%, hazard ratio [HR] 1.25, 95% confidence interval [CI] 0.88 ~ 1.77, p = 0.21). There were also no differences in the risk of each component in the composite outcomes between the two groups. Primary non-function, a component of the composite outcomes did not occur in the both groups. There were no differences in the risks of death, frequency and total duration of re-hospitalization after KT for 1 year, and the changes of eGFR for 1 year between the two groups. The results from the propensity score matched population were consistent with those from the whole population. There was no difference in the risk of the composite outcomes between the PD and HD groups (19% vs. 17%, HR 1.17, 95% CI 0.80 ~ 1.74, p = 0.43).

Conclusion: The pre-transplant dialysis modality does not affect the incidences of delayed graft function and acute rejection in early period of KT. (NCT01513707)

This study was supported by Baxter Incorporated.

P1657 GRAFT- AND PATIENT-SURVIVAL IN TRANSPLANT KIDNEY PATIENTS UNDERGOING TRANSPLANT BIOPSIES

Björn Peters[1,2], Johan Mölne[3], Salmir Nasic[4], Marie Felldin[5], Lars Mjörnstedt[5], Bernd Stegmayr[2]

[1]Skaraborg Hospital, Nephrology, Skövde, Sweden, [2]Umeå University, Public Health and Clinical Medicine, Umeå, Sweden, [3]Sahlgrenska University Hospital, Pathology, Gothenburg, Sweden, [4]Skaraborg Hospital, Research Center (FoU), Skövde, Sweden and [5]Sahlgrenska University Hospital, Transplantation Center, Gothenburg, Sweden

Background and Aims: Kidney transplantation is a frequent treatment in uremic patients. However, long term patency is limited. The aim of this study was to investigate the histological findings in transplant biopsies in relation to clinical outcome in patients.

Method : 1542 patients (36.4 % women) were included if they had a first kidney transplant registered in a quality assessment registry (period October 24, 1968 and August 28, 2017) and also had registered a first transplant kidney biopsy during the period January 1, 2007 until Mars 2, 2018. Graft- and patient-survival analysis was performed by Kaplan-Meier- and Cox-regression-analysis (adjusted for age and gender). Data are presented as Hazard Ratio (HR) and 95% Confidence Intervals (CI). A two-sided p-value of <0.05 was considered as statistically significant.

Results: Patients with primary and recurrent glomerulonephritis (GN) found in the biopsy had a worse graft- (70% at 5-year) and patient-survival (85% at 5-year) compared to all other diagnoses ($p<0.05$). Comparing with GN as reference group with respect to graft-loss the risk was lower if biopsies revealed infections (HR 0.3, CI 0.1-0.9), chronic damages (HR 0.38, CI 0.2-0.6), CNI-toxicity (HR 0.3, CI 0.2-0.6) or rejection (HR 0.5, CI 0.3-0.9). Looking at patient-survival, compared to those with GN a lower risk for early death was found for those with tubulointerstitial diseases (HR 0.35, CI 0.1-0.9), chronic damages (HR 0.35, CI 0.2-0.7), CNI-toxicity (HR 0.4, CI 0.2-0.9) and rejection (HR 0.4, CI 0.2-0.9) while those with hematological diseases (HR 14, CI 3.7-53.6) had higher risk for early death. Comparing subgroups within rejections, there was a significant ($p<0.01$) better graft-survival in patients with cellular rejection or borderline changes (90% at 5-year) versus those with humoral (65% at 5-year), chronic humoral and cellular rejection (60% at 5-year), and transplant-glomerulopathy (TGP) (70% at 5-year). The patient-survival was worse for patients with a TGP (70% at 5-year) compared to cellular rejections ($p=0.04$). Patients with humoral (HR 4.4, CI 2.3-8.4), chronic humoral and cellular rejection (HR 5.8, CI 2.9-9.9) and TGP (HR 3.7, CI 1.6-8.8) had higher risk for graft-loss and patients with TGP (HR 3.5, CI 1.2-10.5) had higher risk for early death compared to cellular rejection as reference. In addition, it was found that the median time between the graft-loss and death (25 patients) was 76 days (mean 304 days) and 44% of these patients died within 30 days after graft-loss. The median age of these patients was 62 years. Between the patients who died within 30 days and the others, no differences were found in cause of death, findings in the transplant kidney biopsies or type of transplant kidney (living versus deceased).

Conclusion: Patients with GN and patients with TGP had a worse outcome in both graft- and patient-survival. Awareness should focus on the patients who die soon after graft-loss.

P1658

RENAL RECOVERY AFTER LIVER TRANASPLANTATION ALONE IN PATIENTS WITH LIVER CIRRHOSIS AND SEVERE CHRONIC KIDNEY DISEASE WITH NORMAL KIDNEY SIZE

EUN HYE YANG[1], Soon Bae Kim[1], Sung-Gyu Lee[2]

[1]Asan Medical Center, University of Ulsan College of Medicine, Division of Nephrology, Seoul, Korea, Rep. of South and [2]Asan Medical Center, University of Ulsan College of Medicine, Division Of Kidney and Pancreas Transplantation, Department of Surgery, Seoul, Korea, Rep. of South

Background and Aims: Most guidelines recommend simultaneous liver-kidney transplantation (SLKT) in patients with liver cirrhosis (LC) and severe chronic kidney disease (CKD) over liver transplantation alone (LTA). CKD, however, is not irreversible. This study evaluates the reversibility of kidney disease after LTA based on kidney size.

Method: In this single-center retrospective study, we classified 90 patients with LC and severe CKD into 3 groups: normal kidney-LTA (NK-LTA, n=39), small kidney [both <9cm]-LTA (SK-LTA, n=40), and small kidney-SLKT (SK-SLKT, n=11). Baseline characteristics and renal recovery and survival outcomes were compared among 3 groups.

Results: The NK-LTA group had a lower percentage of hepatocellular carcinoma, a higher pre-LT eGFR, and a shorter duration of eGFR at <60 ml/min and pre-LT dialysis. This group, however, was older, received livers from a higher percentage of deceased donors and had a higher Child-Pugh score. Renal recovery, defined as no hemodialysis (HD) after LT, was found in 79% of those in the NK-LTA group, which was higher than 7.5% of those in the SK-LTA group. Renal survival, defined as patient survival without progression to HD or kidney transplant was found in 56% of patients in the NK-LTA group, which was higher than 2.5% of those of the SK-LTA group.

Conclusion: Patients with LC and severe CKD with normal kidney size may experience reversible kidney disease after LTA. Therefore, kidney after liver transplantation is recommended over SLKT for these patients.

P1659 **SURVIVAL OF PATIENTS WAITING FOR KIDNEY TRANSPLANTATION IN TERMS OF COMPETING RISKS**

Aleksei Zulkarnaev[1], Vadim Stepanov[1], Andrey Vatazin[1]

[1]*Moscow Regional Research and Clinical Institute, Surgical department of transplantation and dialysis, Moscow, Russia*

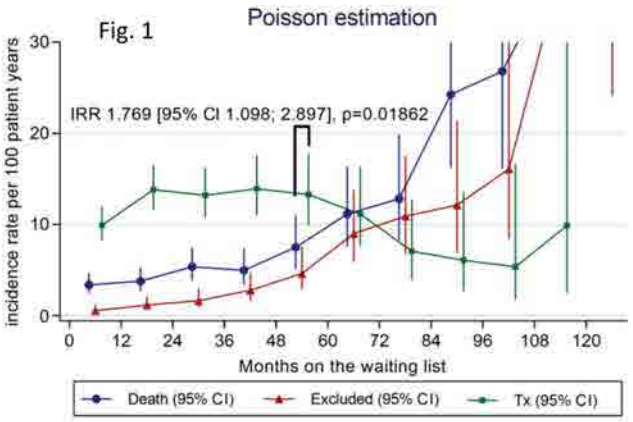
Background and Aims : In Russia, when choosing a donor-recipient pair, the "waiting time" factor has very little weight. Aim: to analyze the survival of patients on the waiting list for kidney transplantation and the results of transplantation depending on the duration of waiting.

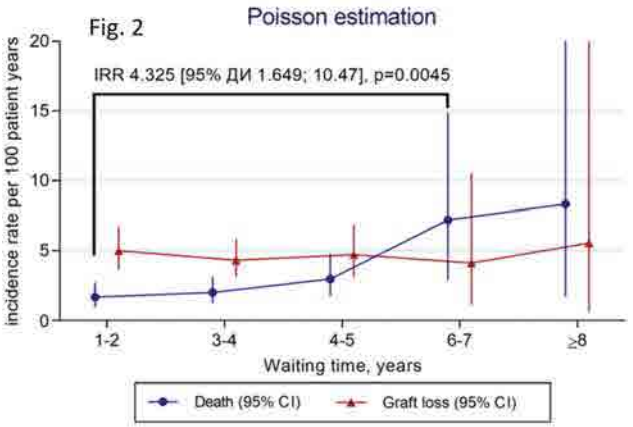
Method : We performed a retrospective observational analysis that included 1,197 patients on the waiting list. The end point was exclusion from the waiting list (WL). The causes for exclusion (death, exclusion due to deterioration of the comorbid background or transplantation) were considered in terms of competing risks.

Results : In total, 72.5% of patients reached the end point: 21.1% of them died, 11% were excluded, and 40.4% underwent transplantation. Kaplan-Meier estimate showed that cumulative risk of death was 80.4% [95% CI 77.9; 88.6], of exclusion – 77.9% [95% CI 65.4; 88.2], of transplantation – 63.6% [95% CI 58.3; 69] after 10 years on the waiting list. However, such an assessment cannot be directly interpreted as a prediction of the relevant event risk for the patient in the WL, because it does not take into account competing events.

According to a balanced assessment of the competing risks (Fine and Gray regression model), cumulative incidence was 30.9% [95% CI 27.7; 34.2] for death, 18.2% [95% CI 15.5; 21.1] for exclusion and 49.4% [95% CI 46; 52.6] for transplantation after 10 years on WL.

The probability of transplantation was significantly higher than the risk of death up to and including 5 years of waiting (incidents rate ratio – IRR 1.769 [95% CI 1.098; 2.897]). When waiting 7 to 8 years, the probability of transplantation was less than the risk of death: IRR 0.25 (95% CI 0.093; 0.588; p=0.0009) – fig 1.





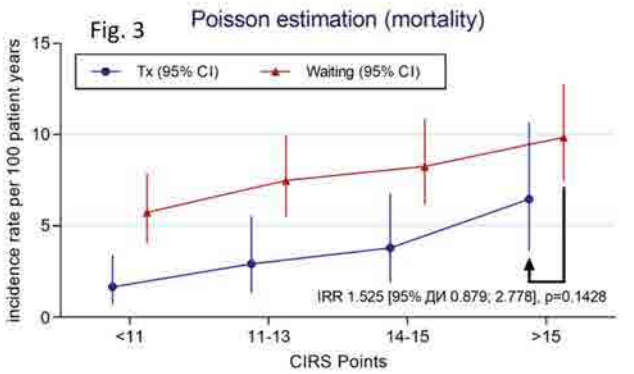


Figure:

Of the 483 recipients, 61 died and 119 returned to dialysis. The risk of graft loss after 10 years was 68.5% [95% CI 57.5; 79.1] and the risk of death of a recipient with a functioning graft was 48.3% [95% CI 34.7; 63] according to Kaplan-Meier estimate. The cumulative incidence was 30.8% [95% CI 23.3; 38.5] and 55.7% [95% CI 46.6; 63.5] according to Fine and Gray estimate, respectively. The risk of death after transplantation increases significantly when waiting for more than 6 years – IRR 4.325 [95% CI 1.649; 10.47], p=0.0045 relative to a shorter waiting period – fig 2.

With an increase in the waiting period, the comorbid background (CIRS scale) deteriorates significantly, even adjusted for the initial patient condition: the partial correlation r=0.735; p<0.0001. The deteriorating comorbid background reduces the expediency of transplantation – fig 3 (the potential patient's benefit is significantly reduced).

Conclusion : 1. In the context of competing risks, the Fine and Gray estimate gives a more balanced risk assessment compared to the Kaplan-Meier method.

2. Increasing the waiting time for transplantation significantly increases the risk of death of the candidate on the waiting list and reduces the probability of transplantation, as well as increases the risk of death of the recipient after transplantation. Apparently, this is mainly due to the deterioration of the comorbid background.

P1660 ACCESS TO KIDNEY TRANSPLANTATION IN THE UK CHINESE POPULATION: A UK RENAL REGISTRY ANALYSIS

Katie Wong[1,2], Fergus Caskey[1,2], Yoav Ben-Shlomo[1], Anna Casula[3], Pippa Bailey[1,2]

[1]University of Bristol, United Kingdom, [2]Southmead Hospital, United Kingdom and [3]United Kingdom Renal Registry, Bristol, United Kingdom

Background and Aims:

Previous UK Renal Registry (UKRR) analyses and the Access to Transplantation and Transplant Outcome Measures (ATTOM) study have shown ethnic disparity in access to kidney transplants in the UK, but access to transplantation for the UK Chinese population has not been investigated

In this UKRR analysis, we compared the likelihood of kidney transplantation between the UK White and UK Chinese renal populations, aiming to investigate whether there was evidence of ethnic disparity in access to kidney transplantation for this specific ethnic group.

Method:

Data on all adult patients >=18 years who started renal replacement therapy (RRT) between 1/1/97 and 31/12/16 were extracted from the UKRR. Patients with ethnicity recorded as anything other than "Chinese" or "White" were excluded from analysis. Patients with ethnicity data missing were also excluded. Patients aged >= 75 years at the start of RRT were excluded because of the high prevalence of comorbidity which decreases the likelihood of transplantation and the very small proportion of patients receiving a kidney transplant in the UK in this age group. Socioeconomic status (SES) was measured using country-specific Index of Multiple Deprivation (IMD) quintiles derived from patient postcodes (1= most deprived, 5= least deprived).

The independent variable of interest was Chinese ethnicity (Chinese vs White). Multivariable logistic regression models were used to investigate the relationship between Chinese ethnicity and being listed on the deceased donor transplant waiting list i) at start of RRT ii) 2 years after start of RRT iii) pre-emptive kidney transplantation, iv) kidney transplantation at 3 years after start of RRT, and v) living-donor kidney transplantation. The models were run unadjusted and then adjusted for the confounders, specified a priori, age, sex, primary renal disease and SES. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using robust standard errors to account for clustering by renal centre.

Results:

The dataset comprised of 92,857 incident RRT patients. 0.5% (n=501) were of Chinese ethnicity, 76% (n=70,575) were White. The findings of the multivariable logistic regression analyses are presented in Table 1. Even after adjustment for potential confounders UK Chinese patients had lower odds of being waitlisted at the start of RRT (OR 0.71, [95% CI 0.54-0.94]) but were more likely to be waitlisted at 2 years (OR 1.28, [95% CI 1.02-1.61]) compared to White patients. UK Chinese individuals were also less likely to receive a pre-emptive kidney transplant (OR 0.47, [95% CI 0.29-0.78]), less likely to be transplanted within 3 years of starting RRT (OR 0.69, [95% CI 0.52-0.92]) or have a living-donor kidney transplant(LDKT) (OR 0.39, [95% CI 0.26-0.59]) compared to White patients.

Conclusion:

This is the first study that has shown that UK Chinese renal patients are less likely to have the opportunity to receive a living or deceased kidney transplant. Future research needs to test whether later presentation or more rapid progression of renal disease could explain these observations. The higher odds of transplant listing at 2 years suggests fitness for transplantation is not a significant barrier. The reasons why this ethnic group are less likely to receive a LDKT is also not well understood. Understanding whether these disparities reflect modifiable policy, health system or donor/recipient level barriers will help ensure equitable access to transplantation.

Table 1: Results of multivariable logistic regression analyses investigating Chinese ethnicity and access to kidney transplantation

	Unadjusted analysis Chinese vs White OR, (95% CI), P-value	Adjusted analysis* Chinese vs White OR, (95% CI), P-value
Waitlisted at RRT start	0.76 (0.58-0.99), P=0.04	0.71 (0.54-0.94),P=0.02
Waitlisted at 2 years from RRT start	1.33 (1.09-1.61), P=0.005	1.28 (1.02- 1.61), P=0.03
Pre-emptive transplant	0.51 (0.32-0.82), P=0.005	0.47 (0.29-0.78), P=0.003
Transplanted within 3 years of RRT start	0.79 (0.63-0.99), P=0.04	0.69 (0.52-0.92), P= 0.01
Living donor kidney transplant	0.40 (0.27-0.59), P<0.001	0.39 (0.26-0.59), P<0.001

*Adjusted for potential confounders age, sex, primary renal disease and socioeconomic status
OR=odds ratio
RRT=Renal Replacement Therapy

Figure:

P1661

EVOLUTION OF RENAL FUNCTION IN RENAL TRANSPLANTED DONORS PATIENTS IN ASYSTOLE TYPE II. IS THERE A CORRELATION BETWEEN HISTOPATHOLOGY PARAMETERS OF THE DONOR BIOPSY AND THE GRAFT SURVIVAL? EXPERIENCE IN OUR CENTER

Cristina Andrades Gómez[1], Francisco Manuel González Roncero[1], Alejandro Suárez Benjumea[1], Blanca Gascó Martos[1], Carmen González Corvillo[1], María del Carmen De gracia Guindos[2]

[1]Hospital Universitario Virgen del Rocío, Nephrology, Sevilla, Spain and [2]Hospital Virgen de las Nieves, Nephrology, Granada, Spain

Background and Aims: With the aim of increasing the number of kidney transplant donors (RT), the use of organs from cadaver donors in asystole (DA) type II of Maastricht has been enhanced in recent years.The important ischemia that this type of donation entails makes it especially complex, resulting in a higher incidence of delayed renal function and non-primary graft function, compared to the TR from donor in brain death.We present our experience with the Mastricht DA type II TR since the beginning of our program in 2013

Method: 108 patients with type II performed between January 2010 and June 2019, median follow-up 30 months.

Results: : mean age of the donor 42 years, 65% blood group A, mean Cr at the first month of 3 mg/dl, at the 3rd month of 1.9 mg/dl and currently 1.6 mg/dl. Mean ange of the receptor 46 years, time on dialysis 30 months, 1st transplant all, except 1. PRAc pre TR was $<$ 25%, initial immunosuppression with thymoglobulin, steroids, mycophenolate, and delayed introduction of tacrolimus. 10% never function; 73.5% delayed renal function. 7.2% acute rejection. Survivors of the 1st, 3rd and 5th year recipients are 98%, 98% and 86% respectively. In a innovative way, it has been registered the correlation between histopathology parameters of the donor biopsy and the graft survival.

Conclusion: RT with type II DA has more incidence of delayd renal function and non-primarygraft function, however results in survival and kidney function in our center are very acceptable, comparable to donors in brain death.

P1662 **COMMERCIAL KIDNEY TRANSPLANTATION: PARTICIPANTS' ATTITUDES AND PERCEPTIONS.**

Fatma AlRahbi[1,2,2], Issa Alsalmi[2]

[1]Ministry of Health/Royal Hospital, Nephrology, Muscat, Oman and [2]Ministry of Health/Royal Hospital, nephrology, Muscat, Oman

Background and Aims: Kidney transplantation is the gold standard for patients with end-stage kidney disease. In view of shortages of available organs, long wait times for possible transplantation, and strict regulation, many patients opt for commercial transplantation. The national diseased program must be a priority with full financial and administrative support. All government agencies including religious affairs must work together to support the program and to provide the citizens with a good transplantation service and ameliorate the impact of commercial transplantation.

This study elicits the reasons and motivations for patients with end-stage kidney disease to elect for commercial transplant.

Method: A questionnaire-based evaluation was conducted during the period from July 2015 until late December 2015. It consisted of 28 multiple choice questions and was distributed to all patients who underwent commercial kidney transplantation.

Results: One hundred and fifty patients were approached to participate and 106 agreed. Of the participants, 60% were male with an average age of 41.5 (SD 14.8) years and ranged from 18 to 83 years. The majority (82%) of our participants were educated ranging from primary to college level. The major reason (71%) for these participants to obtain commercial transplants was stated as the unavailability of a live related donor. Thirteen percent stated that they objected to getting a kidney donated from a family member, and 9% stated that they were worried about taking a kidney from a family member. Finally, 3% of participants stated that they needed prompt transplant and could not wait for a long time for transplant investigations and the workup associated with this program.

Conclusion: Even considering the ongoing ethical debates, number of patients undergoing commercial transplantation is on the rise. The study showed that the most common underlying cause for seeking commercial transplantation is the unavailability of a national transplant program, particularly transplantation from cadaveric sources.

Operation Cost	**No=106**
$15,000-$30,000	3 (2.8%)
$30,000-$45,0000	33 (31.1)
More than $45,000	52 (49%)
Not sure	12 (11.3%)

Table 2: Patient's experience after transplantation

Variables	**Yes**	**No**	**Not sure**
Would you repeat this experience again	40 (38%)	27 (25.4%)	33 (31.1%)
Would you advice other ESKD patients for the same	59 (56%)	36 (34%)	5 (6%)
Would you sell your kidney to other ESKD patients	21 (20%)	50 (47.1%)	29 (27.3%)

P1663 CLINICAL AND PATHOLOGICAL FACTORS INFLUENCING RESIDUAL RENAL FUNCTION AFTER LIVING DONOR NEPHRECTOMY

Akihiro Okubo[1], Hideki Yokoi[1], Kaoru Sakai[1], Takeshi Matsubara[1], Motoko Yanagita[1]

[1]*Kyoto University Hospital, Department of Nephrology, Kyoto, Japan*

Background and Aims:

Renal function decreases with aging. Aging is associated with significant changes in structure and function of the kidney. On the macrostructural level, kidney cortical volume decreases, therefore total kidney volume (TKV) also decreases with aging. On the microstructural level, the number of glomerulosclerosis increases, therefore nephron number decreases with aging. Some reports show that the decline of TKV and nephron number is accompanied by a reduction in renal function.

However, in the field of living kidney transplantation, TKV and glomerulosclerosis are not fully evaluated as factors influencing the donor's post-transplant renal function.

Living kidney transplantation is an established renal replacement therapy for end-stage renal disease patients. To predict living kidney recipient's renal function, one-hour protocol biopsy is conducted during the operation. From one-hour protocol biopsy, donor's pathophysiological findings such as glomerulosclerosis can be evaluated. In this study, we evaluated the correlation of potential influencing factors including TKV and glomerulosclerosis with pre- and post-transplant renal function in living kidney donors.

Method:

This is a retrospective study including all 37 living related kidney donors seen at Kyoto University Hospital from January 2013 to April 2019. Estimated glomerular filtration rate (eGFR) was calculated using equation for Japanese population from serum creatinine levels at pre- and post-transplant. TKV was calculated from the 3D volume-rendered images of enhanced CT (=$\pi/6\times$length$\times$width$\times$thickness), and adjusted to standard body surface area (BSA) by individual BSA. The ratio of number of non-glomerulosclerosis per that of whole glomeruli (non-GS) was evaluated by protocol renal biopsy at one hour after renal reperfusion. This study protocol was approved by the Ethics Committee on human research of the Graduate School of Medicine, Kyoto University.

Results:

We evaluated 37 living kidney donors (35.1% male, mean age 58.2 $\pm$ 12.0 years). Mean pre-transplant eGFR was 75.7 $\pm$ 12.1 ml/min/1.73m2, mean post-transplant eGFR; 44.9 $\pm$ 7.75 ml/min/1.73m2, adjusted TKV (aTKV); 349.3 $\pm$ 58.4 ml, and non-GS; 0.892 $\pm$ 0.086. Pre-transplant eGFR was associated with aTKV and aTKV$\times$nonGS ($r=0.525$, 0.569 respectively, $p<0.01$). Post-transplant eGFR was associated with age ($\geqq$65 years old, $p<0.01$), aTKV, non-GS, and aTKV$\times$non-GS ($r=0.527$, 0.344, 0.626 respectively, $p<0.05$). The rate of eGFR decline was associated with age ($\geqq$65 years old, $p=0.044$), but not with aTKV and non-GS, aTKV$\times$non-GS.

Conclusion:

These results suggest that non-GS and age are correlated with post-transplant renal function but not pre-transplant renal function in living kidney donor, and the decline rate of eGFR are correlated with age.

P1664 ASSOCIATED WITH SERUM MYOSTATIN LEVEL WITH GAIT SPEED IN RENAL TRANSPLANT RECIPIENTS

Chi-Chong Tang[1], Jia-Sian Hou[1], Yu-Chi Chang[1], Chia-Wen Lu[1], Ming-Che Lee[2,3], Bang-Gee Hsu[1,3]

[1]Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Division of Nephrology, Hualien, Taiwan, R.O.C., [2]Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Department of Surgery, Hualien, Taiwan, R.O.C. and [3]Tzu Chi University, School of Medicine, Hualien, Taiwan, R.O.C.

Background and Aims: Walking speed test is a usefulness tool for cardiovascular risk stratification in older adults. The inhibition of myostatin in adult significantly increases muscle mass and confers benefits upon measures of performance and metabolism. The present study evaluated the relationship between walking speed test and serum myostatin levels in renal transplant recipients.

Method: Fasting blood samples were collected from 84 renal transplant recipients. Handgrip strength (HGS) was measured using a Jamar Plus Digital Hand Dynamometer for assessment of muscle strength. Gait speed was measured by walking 6 meters at the usual speed. Gait speed < 1 m/s was defined as low gait speed group according to the European Working Group on Sarcopenia in Older People (EWGSOP) criteria. Serum myostatin levels were measured using a commercial enzyme-linked immunosorbent assay.

Results: Thirty-one renal transplant recipients (36.9%) had low gait speed, and they included a lower percentage of use of mycophenolate mofetil ($p = 0.003$), higher percentage of use of steroid ($p = 0.037$), older age ($p = 0.0090$, higher body weight ($p = 0.044$), body mass index ($p = 0.017$), skeletal muscle index ($p = 0.027$), serum triglyceride ($p = 0.029$), glucose ($p = 0.007$), blood urea nitrogen ($p = 0.041$), cystatin C ($p = 0.015$), while lower estimated glomerular filtration rate from serum creatinine (eGFRcre, $p = 0.047$) and estimated glomerular filtration rate from serum cystatin C (eGFRcys, $p = 0.006$) compared with renal transplant recipients with normal gait speed. After adjusting for cofounders associated with low gait speed in these patients by multivariable logistic regression analysis, serum myostatin levels (Odds ratio (OR): 0.943, 95% confidence interval (CI): 0.898–0.990, $p = 0.018$), and mycophenolate mofetil used (OR: 0.199, 95% CI: 0.050–0.795, $p = 0.022$) were independently associated with low gait speed in renal transplant recipients. The area under the receiver-operating characteristic (ROC) curve indicates the diagnostic power of serum myostatin levels at predicting low gait speed of renal transplant recipients was 0.769 (95% CI: 0.664-0.854, $p < 0.001$). Multivariable forward stepwise linear regression analysis also showed that serum myostatin levels ($\beta = 0.353$, adjusted R^2 change: 0.245, $p = 0.001$) was positively associated with gait speed values in renal transplant recipients.

Conclusion: In this study, serum myostatin levels is found to be positively correlated with gait speed values and is identified as serum low myostatin levels is associated with low gait speed in renal transplant patients.

P1665 STUDY OF CORRELATION OF DONOR KIDNEY VOLUME AND WEIGHT WITH GRAFT OUTCOMES FOLLOWING LIVE DONOR KIDNEY TRANSPLANTATION

Prasad Dandekar[1], Manish Jain[1], Ashish Nandwani[1], Kulbir Ahlawat[1], Shyam Bansal[1], Pranaw Jha[1], Dinesh Kumar[1], Dinesh Bansal[1], Amit Mahapatra[1], Ashwini Gadde[1], Vijay Kher[1]

[1]*Medanta- medicity, Nephrology, India*

Background:

Impact of organ quality in long-term graft function in living kidney transplantation is less well understood. Potential markers of donor organ quality in living kidney donation may include donor kidney volume and weight. There have been some studies done which correlated individually graft volume with its outcome. Trials have also explored in the fact that graft mass also influences the recipient eGFR. But no study so far has combined these two variables and correlated with the graft outcome.

Aims: To study the association between baseline graft kidney volume and weight matched with recipient body surface area and graft function by serum creatinine. Secondarily the association with proteinuria, graft survival at 1 year and episodes of acute rejection was also studied.

Method: Prospective observational single centre study conducted at our centre. Total 60 live donor renal transplants from period of October 2018 to December 2018 were assessed for the donor kidney volume and its weight and then correlated with creatinine at post-transplant day 7 and 1 year after transplant. Cadaveric, paediatric and second transplants were excluded. Whole renal parenchymal volume was obtained from the delayed phase CT data excluding the renal sinus fat using Syngo Volume Calculation. According to common procedure recommendations, kidney grafts were prepared first then weighed by the surgeon.

Results: 45 were female donors and 15 were male donors. Mean donor age was 46.60 +/- 12.04 years with minimum donor age of 19 years and maximum donor age of 75 years. The donated graft GFR was 48.86 ml/min/1.73 m^2 with a S.D. of 42.77 ml/min/1.73 $m^{2.}$ .Mean transplanted graft volume (donated kidney volume X 1.73 m^2/ recipient BSA) was 137.49 mm^3/1.73m^2 with a S.D. of 28.34 mm^3/1.73m^2 (Minimum 95 mm^3/1.73 m^2 and maximum 227.23 mm^3 /1.73 m^2). Mean total kidney volumes of females was 254.45 +/- 46.57 mm^3 and males was 293.37 +/- 42.99 mm^3 (p value < 0.05). Donor kidney volume and donor age showed negative co-relation (r-0.25) (p-0.08.) Donor kidney volume and donor GFR showed a positive co-relation (r 0.38) and it was statistically significant $p < 0.001$. **Graft volume and serum creatinine on post-transplant day 7 had negative co-relation (r=-0.19), not statistically significant**. **Graft volume had negative co-relation with creatinine at 1 year (r= -0.49), statistically significant (p < 0.01). Hence lower the graft volume, higher the creatinine.**

Mean transplanted graft weight was 170 grams (+/- 34 grams)- Minimum 119.5grams, maximum 204 grams. **Donor kidney weight showed a positive correlation with the donor's body surface area**. No correlation with age was seen. Donor kidney weight and donor GFR showed a positive correlation (r 0.26). **Graft weight and serum creatinine on post-transplant at 7 day showed negative co-relation(r=-0.25) but it was not statistically significant. Graft weight and creatinine at 1 year (r= -0.49) had negative co-relation and it was statistically significant (p < 0.01).**

Hence higher the transplanted graft volume and weight, better is the e-GFR at one year post-transplant. No significant association was found with proteinuria at 1 year with either graft volume or weight (p-0.07). In present study 3 patients had an acute cellular rejection. There was no statistically significant co-relation found between kidney volume and acute cellular rejection. None of the patients had an acute humoral rejection till 1 year of follow up period. None of the patients had graft loss till 1 year follow up.

Conclusion: The present study shows that during pre-operative donor evaluation, the donor kidney volume and weight estimation helps us in predicting the outcome of the renal transplant. Better kidney volumes matched to the body surface area of recipient predict better outcomes. Hence kidneys with higher graft volume and weight that is matched to recipient have better e-GFR at 1year post-transplant. This will help us in finding the suitable donors wherever feasible.

P1666 **ASSOCIATION OF TACROLIMUS TROUGH LEVEL AND DAILY DOSE RATIO WITH OUTCOMES IN A PROSPECTIVE PREVALENT COHORT OF KIDNEY TRANSPLANT RECIPIENTS**

Orsolya Cseprekal[1], Adrienn Marton[1], Szilárd Török[1], Istvan Mucsi[2], Laszlo Wagner[1], Adam Remport[1], Miklos Zsolt Molnar[3,4]

[1]Semmelweis University, Department of Transplantation and Surgery, Budapest, Hungary, [2] University Health Network, Kidney Transplant Program Toronto General Hospital, Toronto, Canada, [3]James D Eason Transplant Institute, Methodist University Hospital, Memphis, United States of America and [4]University of Tennessee Health Science Center, Department of Surgery, Memphis, United Kingdom

Background and Aims: Tacrolimus is an integral part of the immunosuppressive regimen after solid organ transplantation. Due to its narrow therapeutic window, it requires frequent serum trough level (C0) monitoring and dose adjustment. Both over- and under treatment may have harmful effects regarding overall mortality and graft survival due to increased risk of cardiovascular diseases, malignancies, new onset diabetes and rejection. C0 and total daily dose ratio (CD) has recently been suggested as a potential predictor of worse graft outcome in the early period after transplantation, however, long term prospective studies are lacking. We hypothesized the association between lower CD ratio and increased risk of death with functioning graft (DWFG), graft loss (GL) and overall death (D) in our prospective cohort study.

Method: Our study included 386 prevalent kidney transplant recipients (205(53%) males, median and IQR age of 47.5 (13.2) years, eGFR 53.5 (22.5) ml/min/1.73m2, time since last transplant 51 (26-79) months) out of a total of 993 enrolled between 2006-2007. Sociodemographic, past medical history, clinical and laboratory data were collected and CD was recorded at baseline and 1 year after the enrollment. The associations between CD and CD2 ratios and above mentioned outcomes were examined using survival models..

Results: The median and IQR of CD was 2.1(1.4-3.2) at baseline and 2.0 (1.3-3.0) 1 year later (CD2). There was 46 (11.9%) DWFG, 79 (20.5%) GL and 68 (17.6%) D, respectively. After adjustment for important confounders (age, gender, eGFR, Charlson score, dialysis duration, donor age, rejection), neither CD (DWGL: HR 0.56(0.30-1.03) p=0.06; GL: HR 0.82(0.50-1.36) p=0.46; D: HR 0.79(0.48-1.32) p=0.38) nor CD2 (DWGL: HR 1.12(0.54-2.31) p=0.74; GL: HR 0.76(0.61-1.97) p=0.78; D: HR 1.19(0.64-2.20) p=0.59) found to be predictors of the outcomes.

Conclusion: CD ratio was not associated with increased risk of death with functioning graft, graft loss or overall death in our prevalent kidney transplant recipients.

P1667 ANALYSIS OF RISK FACTORS FOR CMV DISEASE IN KIDNEY TRANSPLANT PATIENTS - SINGLE CENTER STUDY

Vladimir Hanzal[1], Janka Slatinska[2], Petra Hruba[3], Ondrej Viklicky[1]

[1]Institute for Clinical and Experimental Medicine, Nephrology, Prague, Czech Republic, [2]Institute for Clinical and Experimental Medicine, Nephrology, Pragie, Czech Republic and [3]Institute for Clinical and Experimental Medicine, Transplant Laboratory, Prague, Czech Republic

Background and Aims:

Cytomegalovirus (CMV) disease and infection negatively influence outcome of kidney transplantation. The aim of this retrospective study was to analyze risk factors for CMV disease and its influence on kidney graft function and survival.

Method:

1050 patients underwent kidney transplantation from January 2014 to December 2018 and received calcineurin inhibitor, mycophenolate mofetil and steroid-based immunosuppression. Recipients with PRA>20% received rATG while others had received basiliximab as induction. 825 out of 1050 patients (78.6%) received CMV prophylaxis (D+/R-, n=173; R+, n=652). Patients were followed up to 71 months /median 38 months/.

Results:

CMV tissue invasive disease occurred in 49 out of 1050 patients (4.7%), while CMV infection in 87 patients (8.3%). CMV disease, but not CMV infection, had significant negative influence on graft survival at 5 years post transplantation (p=0.0029). Patients with CMV disease had significantly worse graft function at 4 years post transplantation (p<0.0001). CMV disease occurred in 31 out of 173 patients (17.9%) in D+/R- group vs. 18 out of 652 patients (2.8%) in R+ group. Incidence of CMV infection was 30/173 patients (17.3%) in D+/R- group vs. 57/652 patients (8.7%) with induction therapy. Shortening of CMV prophylaxis was found in 82 patients (9.9%). Leukopenia ($\leq$ 2.0 x 10^9/L) was observed in 97 (11.7%) patients from those who received CMV prophylaxis, Its shortening significantly increased risk for both CMV infection (20,7% vs. 7.2%, p<0,0001) and CMV disease (8,5% vs. 4,2%, p=0,04). Among most significant risk factors for CMV disease in univariable analysis were CMV mismatch (OR 11, 95% CI: 5,9-20,4; p<0,0001), delayed graft function (OR 2,8, 95% CI: 1,6-5,1; p<0,0001, cadaveric donor (OR 6, 95% CI: 1,5-25,1; p=0,00013) and shortening of CMV prophylaxis (OR 2.1, 95% CI: 0,91-4,86; p=0,08). Multivariable analysis revealed as independent significant predictors of CMV disease DGF (OR 2,29, 95% CI: 1,2-4,3; p=0,01) and CMV mismatch (OR 10,8, 95% CI: 5,7-20,6; p<0.0001) in a model adjusted for type of donor, prophylaxis shortening and leukopenia.

Conclusion:

CMV mismatch is the main independent predictor of CMV disease after kidney transplantation in multivariable analysis.

P1668 **SIMULTANEOUS LIVER-KIDNEY TRANSPLANTATION IN PEOPLE LIVING WITH HIV: A CASE-SERIES WITH LONG TERM FOLLOW-UP**

Giovanni Dolci[1], Giovanni Guaraldi[1], Franceschi Erica[1], Gaetano Alfano[2,2], Francesco Fontana[2], Fabrizio Di Benedetto[3], Gianni Cappelli[2]

[1]Infectious Disease Unit, University of Modena and Reggio Emilia, Modena, Italy., Modena, Italy, [2]3 Nephrology Dialysis and Kidney Transplantation Unit, University of Modena and Reggio Emilia, Modena, Italy., Modena, Italy and [3]Hepato-Pancreato-Biliary Surgery and Liver Transplantation Unit, University of Modena and Reggio Emilia, Modena, Italy, Modena, Italy

Background and Aims: The number of simultaneous liver-kidney transplants (SLKT) has been constantly increasing in the past two decades. In the US, the relative proportion of liver transplants performed as part of SLKT augmented from 2.7% in 2000 to 9.3% in 2016. In this rapidly evolving scenario, people living with HIV (PLWH) have been substantially excluded from SLKT. The poor prognosis of SLKT in people living with HIV (PLWH) has refrained transplant centers to perform this procedure.

Method: We retrospectively describe indications, clinical characteristics and survival of HIV-infected patients who underwent SLKT at the Transplant Centre of Modena, Italy.

Results: Since 2001 five SLKTs were performed in HIV-affected subjects. With regards to medical eligibility criteria for SLKT all the patients were on hemodialysis and had liver end-stage disease or HCC at time of transplantation (Table 1A). Mean age at transplantation was 47.8± 5.93 years and all patients were Caucasian males. Mean duration of HIV was 25 years and all patients had undetectable HIV-viral load at SLKT. The causes of end-stage renal disease were different in all recipients and only one had biopsy-proven kidney disease. Dialysis vintage was 15.8±10.2 months. Four patients had HCV-related cirrhosis and one had hepato-carcinoma (HCC).

Mean HCV-RNA at SOT was 464,327 copies/ml; in three HCV patients, the sustained virologic response to HCV therapy was obtained after transplant with peg-INF in one case (pre-direct antiviral agent era) and with a combination of sofosbuvir, daclatasvir and rifampicin in the other two. Only one patient had HBV-HDV-related cirrhosis and did not experience HBV or HDV relapse during the follow-up.

At the end of a mean follow up of 7.6±4.71 years, four out of five patients are still alive One patient died on post-transplant day 41 for disseminated candidiasis with cerebral involvement (Table1 b). During the follow-up period, HIV-VL remained undetectable over nearly 10 years. Clinical outcome was characterized by the reverse of frailty in all the patients. All of them are conducting an independent living with quality of life exceeding 90% using the EUQoL 5D-5L questionnaire. The liver function was normal and remained stable during the observation period. Bile duct stricture and bile duct calculi were the main surgical complications.

Regarding renal function, mean serum creatinine was 1.7±0.4mg/dl corresponding to a mean estimated GFR of 47.7±5.9 ml/min. Only one patient had proteinuria (0.8 gr/daily) after 10 years of transplantation. Contrary to our expectations, no cases of graft rejections occurred during this long-term follow-up despite mean HLA mismatches of 5.75 and underexposure to the immunosuppressive agents. Withdrawn of steroids occurred after 1.8±2.5 years from SLKT. Thereafter, immunosuppressive therapy continued with monotherapy: calcineurin inhibitor in three recipients and inhibitors of the mammalian target of rapamycin in the other one.

Conclusion: Contrary to the previously published data, this case series describes a favorable clinical outcome in PLWH who received SLKT. The absence of graft rejection despite the reduced immunosuppressive therapy highlights the concept that the liver is able to induce tolerance in kidney transplantation. These results could lead other transplant programs to consider SLKT as a reliable clinical option in PLWH with liver and kidney failure.

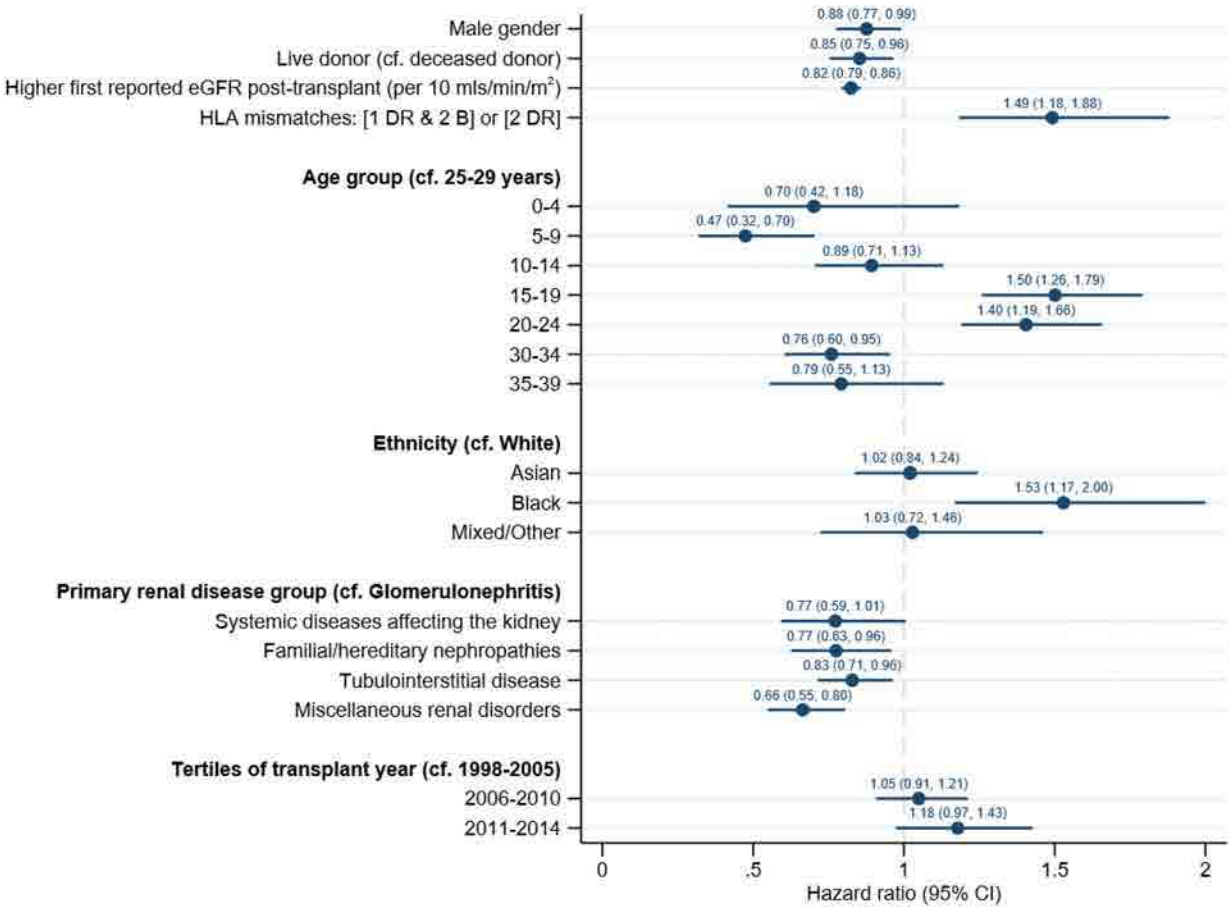


Figure 1: Coefficient plot of multivariable associations with graft loss in UK children and young adults.
Abbreviations: eGFR – estimated glomerular filtration rate; HLA – human leucocyte antigen; CI – confidence interval

P1669 **PROGNOSTIC IMPORTANCE OF BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) IN RENAL TRANSPLANTATION**

Agnes Molnar[1,2], Edgar Szkibinszkij[2,3], Lilla Lenart[1,2], Adam Hosszu[1,2], Illes Kovacs[4], Laszlo Wagner[3], Fruzsina Rimaszombati[2], Soma Novozanszki[2], Attila Szabo[1,5], Andrea Fekete[1,2]

[1]Semmelweis University, 1st Department of Pediatrics, Budapest, Hungary, [2]Hungarian Academy of Sciences, "Lendület" Diabetes Research Group, Budapest, Hungary, [3]Semmelweis University, Department of Transplantation and Surgery, Budapest, Hungary, [4]Semmelweis University, Department of Ophtalmology, Budapest, Hungary and [5]Hungarian Academy of Sciences, Pediatrics and Nephrology Research Group, Budapest, Hungary

Background and Aims: The prevalence of end-stage renal disease (ESRD) has increased ten times higher in the past twenty years, where renal replacement therapy (dialysis or kidney transplantation (KTx)) is the sole life-saving treatment. KTx is the preferred option as it is associated with improved survival and quality of life as well. Delayed graft function (DGF) is one of the main problems affecting long-term kidney survival. Brain-derived neurotrophic factor (BDNF) signalling pathways play pivotal role in mitigating cerebral ischemia/reperfusion injury (IRI), however the relation of BDNF and IRI in KTx is unknown. The aim of our human clinical study was to explore the relationship between serum BDNF concentration, BDNF gene polymorphism and renal graft function after KTx.

Method: Study characteristics: We enrolled 59 ESRD patients with average age of 54.8±12 years who received KTx. Proportion of male patients was 57%. Average cold ischemic time was 927±310 min, warm ischemic time was 54.5±39 min. DGF occurred in 5 cases. Baseline triple immunosuppression therapy consisted of tacrolimus, mycophenolate or everolimus, and prednisolone. Until now, 44 patients completed the 2 years follow-up. For a comparable control group, we collected blood samples from 79 healthy volunteers with average age of 53.9±16 years and with male gender proportion of 52%. Serum BDNF, creatinine, blood urea nitrogen, haemoglobin, blood glucose level and thrombocyte numbers were measured before KTx and 1 week, 1-, 3-, 6 months, and 1-, 2 years after transplantation, as well as in controls. GFR was estimated based on the CKD-EPI formula. BDNF Val66Met polymorphism was determined by PCR-RFLP.

Results: There was no difference in genotype or allele distribution between any of the groups, and no correlation could be observed between serum BDNF and different genotypes either. Serum BDNF level was lower in ESRD patients than healthy controls ($p=0.03$). There was a weak correlation and marginal significance ($p=0.056$) between eGFR and serum BDNF level in controls, while in KTx recipients this correlation reached higher significance ($p=0.01$). Above median BDNF values at 1 month after KTx were predictive for better graft function during the 2 observed years.

Conclusion: Our preliminary human study proposes that BDNF could be a novel biomarker of posttransplant graft function, however further clinical studies with significantly larger population are definitely needed to confirm these results.

P1670

GLOMERULAR C4D IN POST-TRANSPLANT IG-A GLOMERULONEPHRITIS IS ASSOCIATED WITH DECREASED ALLOGRAFT SURVIVAL

Željko Kikić[1], Haris Omic[1], Georg A. Böhmig[1], Nicolas Kozakowski[2], Michael Eder[1]

[1]Medical University of Vienna, Internal medicine III, Div. of Nephrology and Dialysis, Wien, Austria and [2]Medical University of Vienna, Institute of Pathology, Wien, Austria

Background and Aims: Post transplant (pTX) glomerulonephritis (GN) is an important factor contributing to early and late allograft failure. De novo or recurrent IgA GN are the most frequent pTX-GN forms, however little is known about the optimal risk and therapeutic assessment. Recently, immunopathological evidence of glomerular C4d staining has been suggested as a prognostic tool in native glomerular kidney disease, in particular IgA GN. While peritubular capillary C4d is an accepted diagnostic criterion for antibody mediated rejection (ABMR), the role of glomerular C4d in pTX-GN is unkown. The primary hypothesis was that the finding of immunohistochemical glomerular C4d may be associated renal graft survival in post TX IgA GN.

Method: This large retrospective cohort study included all indication biopsies performed for cause in 885 kidney allografts from 1999-2006. Cases were screened for biopsy verified de novo or recurrent pTX-GN. GN cases were re-assessed by a single nephropathologist (NK). Primary endpoint was death-sensored graft survival followed until 01.01.2017.

Results: The prevalence of pTX-GN was 9.6% (n=85/885). De novo or recurrent IgA-GN was the most common pTX GN form with 40%. Of the 34 cases with pTX IgA GN, 27 had adequate material for interpretation of immunohistochemical glomerular C4d in the biopsy specimen. Eighteen of the 27 cases (66%) with pTx-IgA GN showed positive immunohistochemical C4d staining along glomerular capillary walls. There was no difference in renal function at biopsy or after one year comparing glomerular C4d positive vs. C4d negative pTX IgA GN. In univariate KM analysis glomerular C4d positive pTX-IgA GN showed significantly worse renal allograft survival rates (28%) compared to glomerular C4d negative pTX IgA GN (50%) or cases without GN (66%), $p<0.001$, respectively. In a multivariate Cox-Regression analysis including baseline covariates as well C4d+ABMR, Borderline lesion and TCMR, C4d+pTX IgA-GN remained independently associated with death censored graft-loss (HR 2.92, 95% CI 1.51-5.64, p=0.001).

Conclusion: Glomerular C4d staining in post transplant IgA glomerulonephritis is an independent risk factor for worse allograft survival and may provide a valuable risk assessment tool for prognostic and therapeutic decisions in post transplant glomerulonephritis.

P1671 **CHALLENGES AND OUTCOMES OF A KIDNEY TRANSPLANT PROGRAM IN LOW INCOME SETTINGS - THE EXPERIENCE OF THE REPUBLIC OF MOLDOVA**

Elena CUIBAN[1], Igor CODREANU[2], Adrian Tanase[3], Tatiana TIMBALARI[2], Sergiu Iacob[1], Sergiu Gaibu[1]

[1]Republican Clinical Hospital, Haemodialysis and Kidney Transplantation Unit, Chisinau, Moldova, [2]Transplant Agency, Chisinau, Moldova and [3]State University of Medicine and Pharmacy, Urology and Surgical Nephrology Department, Chisinau, Moldova

Background and Aims: During the last decade, the development of kidney transplantation in the Republic of Moldova took a new course due to the adoption of the new transplantation law, and was strongly marked by the first transplant from a brain death donor. The implementation of a transparent organ allocation policy, the development of donation after brain death and the upgrade of the transplant infrastructure, based on European good practices, are the strengths of the new program.

Method: Since 2014, all the kidney grafts from deceased donors have been allocated based on the electronic allocation system (Renal Score), which includes the following variables: compatibility in ABO and HLA systems, dialysis vintage, time on waiting list, renal graft accessibility score, age difference between recipient and donor. All the living donors were evaluated based on a National Protocol. This is a retrospective analysis of the kidney transplant program during a period of five years, focused on recipient and donor demographics, donor-recipient matching, medical outcomes.

Results: During 2014-2018, there were performed 75 kidney transplantations: 23 (30,7%) from living donors and 52 (69,3 %) from brain-death donors. Among the kidney transplant recipients, there were 24 women (32,4%) and 50 men (67.6%). From 23 living kidney donors there were 10 (43,5%) males and 13 (56,5%) females, 21 (91,3%) were related donors and 2 (8,7%) emotionally related. The mean age of living donors was 50,45, ranging from 23 to 67, with 6 donors (20,1%) older than 60 years old.

During this period, from 110 evaluated potential brain death donors 48 (43,6%) became effective brain-death donors and kidneys were procured in 36 (75%) cases (from 15 men (41,7%) and 21 women (58,3%)). The mean recipients age was 41,13, ranging from 23 to 67, while the mean donor age was 54,72, ranging from 19 to 72 years old. 18 donors (50%) were older than 60, the mean age of male donors were 49,4 and 59,14 for female donors. The mean donor-recipient age difference was 17,09 years (min- 0, max- 40). The mean cold ischemia time was 17,31 hours, with a minimum of 6,33 hours and a maximum of 25,8 hours. The majority of donors were blood type 0-14 (38.8%) and A-13 (36,1%) and only 6 donors (16.6%) blood type B and 3 (8.3%) type AB. Regarding the outcomes, we noticed a rate of delayed graft function in 43,6% cases, 2,6% of slow graft function and 53,9% recipients with immediate graft function

Conclusion: Despite social and economic challenges in our country, the joint efforts of the kidney transplant team, the Transplant Agency and the government support ensure a growing kidney transplant program. The strengths of our program are the good legal framework and the respect for the main ethical and medical principals: transparency and traceability, ensured by the informational platform, equity and utility ensured by the use of the automated allocation system, accessibility ensured by the fool coverage of transplant related services by the public health insurance. We still face many challenges, as the high rate of marginal donors compared to younger recipients and donor-recipient age disparities, a long cold ischemia time and a sub-optimal organ discard rate, which is mainly due to the shortage of transplant professionals, the direct effect of the migration of health care personnel. Our next goal is to identify and to improve the factors impacting on kidney graft outcomes in order to achieve better results.

P1672 **IMPACT OF ISLET TRANSPLANTATION VERSUS INSULIN ALONE AFTER KIDNEY TRANSPLANTATION IN TYPE 1 DIABETES PATIENTS.**

Mehdi Maanaoui[1,2,3], Mikael Chetboun[2,3,4], Julie Kerr-Conte[2,3], Valery Gmyr[2,3], Thomas Hubert[2,3], Robert Caiazzo[2,3,4], Arnaud Jannin[2,3,5], Kristell Le Mapihan[2,3,5], Marie-Christine Vantyghem[2,3,5], Marc Hazzan[1], François Pattou[2,3,4]

[1]CHU Lille, Department of Nephrology, Lille, France, [2]INSERM, U1190, Lille, France, [3]Univ.Lille, U1190 – EGID, Lille, France, [4]CHU Lille, Department of General and Endocrine Surgery, Lille, France and [5]CHU Lille, Department of Endocrinology, Diabetology, and Metabolism, Lille, France

Background and Aims: In patients with type 1 diabetes and end-stage renal disease, kidney transplantation improves both quality of life and survival. When simultaneous kidney-pancreas transplantation appears too invasive, or after failure of the pancreatic graft, an islet after kidney transplantation (IAK) may be considered to restore a stable endocrine function. The aim of our work was to assess the impact of islet transplantation on kidney transplantation outcomes versus insulin alone.

Method: In this retrospective parallel-arm cohort study in Lille, we included all type 1 diabetes patients who received a kidney graft from 2000 to 2017, followed by an islet transplantation after kidney (IAK) or not (kidney alone, KA). The primary study endpoint was the change of renal function (estimated glomerular filtration rate, eGFR). Secondary endpoints were glycemic control-related markers, such as HBA1c.

Results: During the period of study, 14 patients were included in the KA group versus 15 in the IAK group (including 5 after failure of a simultaneous pancreatic graft) were enrolled. At baseline, kidney donor sex, BMI, cause of death, cold ischemia time and recipient sex, waiting time on dialysis, type of dialysis, and number of previous kidney transplantation, were similar between the two groups. Yet, there were significant differences between KA and IAK, considering donor age (resp. 56.0±15.0 vs 35.2±13.7 years, $p<0.001$), use of perfusion machine (resp. 7 vs 0, $p= 0.002$), recipient age (resp. 55.7±5.7 vs 42.1±6.1, $p<0.001$), and recipient BMI (24.7± 1.8 vs 21.9±2.5 k/m? $p=0.004$). In IAK, the median (IQR) time between islet and kidney transplantation was 21.8 months (19.0 – 29.4). eGFR was not significantly different at baseline (IAK: 57.8±17.7 vs KA: 48.9±21.4 ml/min, $p=0.22$) but the decrease was significantly lower up to 5 years in the IAK group (IAK: 0.05±1.99 ml/min/year vs KA: -2.42±3.43 ml/min/year, $p=0.03$). HBA1c was similar at baseline in both groups (IAK: 7.8±1.6% versus KA: 7.9±1.1%, $p=0.31$), but significantly lower in the IAK group up to 5 years (IAK: 6.6±0.97% versus KA: 7.8±1.12%, $p<0.001$).

Conclusion: In patients with type 1 diabetes and a functioning kidney graft, IAK was associated with a better glucose control and a slower decrease of eGFR than standard insulin therapy. Our results suggest that IAK should be proposed to type 1 diabetes patients with a functional kidney graft.

P1673 ANEMIA AND DECREASED MUSCLE MASS AND MUSCLE STRENGTH IN KIDNEY TRANSPLANT RECIPIENTS

Joanna Sophia Jacoline Vinke[1], Hanneke Wouters[2], Adriaan Post[1], Suzanne Stam[1], Rianne M. Douwes[1], António W Gomes-Neto[1], Gerwin Huls[2], Stefan P. Berger[1], Stephan Bakker[1], Martin De Borst[2], Michele Freerk Eisenga[1]

[1]University Medical Center Groningen, Department of Nephrology, Groningen, Netherlands and [2]University Medical Center Groningen, Department of Hematology, Groningen, Netherlands

Background and Aims: Post-transplant anemia is highly prevalent in kidney transplant recipients (KTRs). It is known that anemia impairs health-related quality of life, especially physical functioning. Although surmised, data about the latter are scarce. Hence, we aimed to investigate the association between anemia and muscle mass and muscle strength in KTRs.

Method: We used the TransplantLines Biobank and Cohort study, a prospective cohort study among all types of solid organ transplant recipients. For the current study, we used stable KTRs with a functional graft for more than 1 year post transplantation and with data available on hemoglobin levels and muscle mass (n=824). Muscle mass was assessed using 24-hour urinary creatinine excretion. Muscle strength was determined by means of hand grip strength using a dynamometer. Hand grip strength was tested three times with 30 seconds recovery time between attempts. For current analyses, the mean overall hand grip strength was calculated. Anemia was defined as hemoglobin $<$12 g/dL for women and $<$13 g/dL for men, according to WHO definitions. We used multivariable linear regression analyses to assess associations between anemia and muscle mass and strength.

Results: We included 824 KTRs (age 56$\pm$13 years, 60% males), with a mean hemoglobin of 13.5$\pm$1.8 g/dL. Anemia was present in 28% (n=277) of KTRs. Serum hemoglobin was associated with creatinine excretion, independent of age, sex, eGFR, BMI, hs-CRP, smoking status, alcohol use, and the use of RAAS-inhibitors, calcineurin inhibitors, proliferation inhibitors, or prednisolone (β=0.13, $P<0.001$). Similarly, the presence of anemia was independently associated with a lower creatinine excretion (β=-0.09, P=0.002). In line with creatinine excretion, hemoglobin levels (β=0.15, $P<0.001$) and the presence of anemia (β=-0.09, P=0.002) were also associated with handgrip strength independent of potential confounders.

Conclusion: Low hemoglobin levels and anemia are both strongly associated with lower muscle mass and muscle strength in KTRs, likely impairing physical functioning. Future research is needed to address whether correction of anemia improves physical performance in KTRs.

P1674 **KIDNEY TRANSPLANTATION FROM HBSAG+ LIVING DONORS TO HBSAG- RECIPIENTS: CLINICAL OUTCOMES AT A HIGH-VOLUME CENTER**

Xianding Wang[1], Jinpeng Liu[1], Tao Lin[1]

[1]*West China Hospital, Sichuan University, Urology, Chengdu, P.R. China*

Background and Aims: Data on kidney transplantation (KTx) from hepatitis B surface antigen (HBsAg)+ donors to HBsAg- recipients [D(HBsAg+)/R(HBsAg-)] are limited. We aimed to report the outcomes of D(HBsAg+)/R(HBsAg-) KTx in recipients with or without hepatitis B surface antibody (HBsAb).

Method: Eighty-three D(HBsAg+)/R(HBsAg-) living KTx cases were retrospectively identified. The 384 cases of KTx from hepatitis B core antibody (HBcAb)+ living donors to HBcAb- recipients [D(HBcAb+)/R(HBcAb-)] were used as the control group. Primary endpoint was post-transplant HBsAg -→+.

Results: Before KTx, 24 donors (28.9%) in the D(HBsAg+)/R(HBsAg-) group were hepatitis B virus (HBV) DNA+, and 20 recipients were HBsAb-. All eighty-three D(HBsAg+)/R(HBsAg-) recipients received HBV prophylaxis, while no D(HBcAb+)/R(HBcAb-) recipients received prophylaxis. After a median follow-up of 36 months (range 6-106) and 36 months (range 4-107) for the D(HBsAg+)/R(HBsAg-) and D(HBcAb+)/R(HBcAb-) groups, respectively, 2/83 (2.41%) D(HBsAg+)/R(HBsAg-) recipients and 1/384 (0.26%) D(HBcAb+)/R(HBcAb-) became HBsAg+, accompanied with HBV DNA+ (P=0.083). The three recipients with HBsAg-→+ were exclusively HBsAb-/HBcAb- before KTx. Recipient deaths were more frequent in the D(HBsAg+)/R(HBsAg-) group (6.02% vs. 1.04%, P=0.011), while liver and graft function, rejection, infection, and graft loss were not significantly different. In univariate analyses, pre-transplant HBsAb-/HBcAb- combination in the D(HBsAg+)/R(HBsAg-) recipients carried a significantly higher risk of HBsAg-→+, HBV DNA-→+, and death.

Conclusion: Living D(HBsAg+)/R(HBsAg-) KTx in HBsAb+ recipients provides excellent graft and patient survivals without HBV transmission. HBV transmission risks should be more balanced with respect to benefits of D(HBsAg+)/R(HBsAg-) KTx in HBsAb-/HBcAb- candidates.

P1675 BONE DENSITOMETRY IN RENAL TRANSPLANTED PATIENTS

Ana Carina Ferreira[1,2], Marco Mendes[1,2], Cecília Silva[1], Patrícia Cotovio[1], Inês Aires[1,2], David Navarro[1], Fernando Correia Caeiro Pereira[1,2], Rute Salvador[3], Bruna Correia[3], Guadalupe Cabral[3], Fernando Nolasco[1,2], Manuel Anibal A. Ferreira[1,2]

[1]Hospital Curry Cabral, Nephrology, Lisboa, Portugal, [2]Nova Medical School, ., Lisboa, Portugal and [3]CEDOC, Tissue Repair and Inflammation Lab, Lisboa, Portugal

Background and Aims: Renal transplant and associated immunosuppression can influence bone volume. Presently, the data is conflicting with older studies showing bone loss after transplant, while recent ones didn't conclude the same. The aim of this study was to analyse the relations between bone-related molecules [phosphorus (Pi), Calcium (Ca), Magnesium (Mg), parathyroid hormone (PTH), bone alkaline phosphatase (bAP), calcitonin, vitamin D (vitD), alpha-klotho, fibroblast grow factor (FGF) 23, sclerostin] and bone densitometry findings in renal transplanted patients.

Method: We performed a prospective cohort study of a consecutive sample of *de novo* single renal transplanted patients in our unit. At inclusion, demographic, clinical and transplant-related data were collected, X-ray of the pelvis and hands (Adragão score) and echocardiographic findings were recorded. All patients were submitted to a laboratorial evaluation and a bone biopsy at baseline (time 0). Patients were followed for 12 months, after which performed laboratorial evaluation, 2nd bone biopsy, echocardiogram, X-ray of pelvis and hands, bone densitometry (DXA) and non-contrast cardiac CT for Agatston score (time 1). Continuous variables are presented as medians and categorical variables as frequencies. Associations between variables were performed using Wilcoxon matched-pairs test and Spearman correlation test. STATA software was used and $p < 0.05$ was considered statistically significant.

Results: We recruited 85 patients from 1st October 2015 to 1st March 2018. At the end of 12 months, 6 patients refuse to perform the 2nd evaluation, 5 had primary non-function of the kidney graft, 1 had no 1st bone biopsy sample in time 0 and 4 patients died. We performed a 2nd evaluation in 69 patients and included those in this study.

Mean age 50.2±12.4 years, 48 men, 53 caucasian (78.8%), median BMI 24.5 (22.7 – 27.8), median dialysis vintage 55 months (42 – 84). Patients had a median cumulative steroid dose of 5692.5 (5260 – 7250) mg. At 12 months, the median FRAX value for osteoporotic fracture was 3.5 (2.2 – 6.2) and for femoral neck fracture was 0.8 (0.2 – 2.7). The DXA findings are shown in Table 1.

We found a negative correlation between vascular calcifications (Agatston Score and respective calcium percentile) and T and Z score of femoral neck (p=0.04), but not with the other DXA variables. Total femur variables (DMO, T-score, Z-score) were correlated with sclerostin values in time 1 ($p<0.01$), and there was a trend for correlation between the spine DXA variables (DMO, T-score, Z-score) and sclerostin in time 1 (p=0.08, p=0.07, p=0.04). Spine DXA variables were negatively associated with alpha-klotho in time 0 (p=0.04, p=0.05, p=0.06). We didn't found correlations with Pi, Ca or bAP. There was a negative correlation between FRAX osteoporotic and femoral neck fracture values and alpha-klotho in time 1 (p=0.002; p=0.003).

Conclusion: We found an inverse correlation between T and Z scores of femoral neck and coronary vascular calcifications. Regarding bone-derived hormones, Spine T and Z scores and FRAX values negatively correlated with alfa-klotho. Sclerostin seems to be associated with high mineral density.

Table 1

DMO Spine	1.1 (1 – 1.2)
T-score Spine	-1.1 (-1.9 - -0.1)
Z-score Spine	-0.8 (-1.8 – 0.4)
DMO femoral neck	0.9 (0.8 – 1)
T-score femoral neck	-1.4 (-2.2 - -0.6)
Z-score femoral neck	-0.7 (-1.5 – 0)
DMO femur	0.9 (0.8 – 1)
T-score femur	-1 (-2.1 - -0.4)
Z-score femur	-1 (-1.4 – 0.2)
FRAX – osteoporotic fracture (%)	3.5 (2.2 – 6.2)
FRAX – femoral neck fracture (%)	0.8 (0.2 – 2.7)

P1676 **LONG TERM RENAL FUNCTIONS IN LIVING KIDNEY DONORS AND ITS RELATIONSHIP WITH TRANSFORMING GROWTH FACTOR ßETA-1GENE POLYMORPISMS**

Betül Kübra Tüzün[1], Özant Helvacı[2], Hasan Haci Yeter[2], BURAK ÖZBAŞ[2], Berfu Korucu[2], Sevim GÖNEN[3], Galip GÜZ[2]

[1]Gazi University School of Medicine, Department of Internal Medicine, ANKARA, Turkey, [2]Gazi University School of Medicine, Department of Nephrology, ANKARA, Turkey and [3]Gazi University School of Medicine, Department of Medical Biology and Genetics, ANKARA, Turkey

Background and Aims: Renal transplantation is the optimal treatment choice for most patients with end-stage renal disease. Despite the efforts to increase cadaveric transplantation, the primary source of kidneys is still living donors. Donating a kidney is associated with lower than expected GFR especially in the presence of hypertension and proteinuria. Increased risk of ESRD and cardiovascular disease are small and controversial.

TGF-β1 is an essential regulator of fibroblast phenotype and function, hence the main driver in most healthy/pathogenic fibrotic processes. TGF-β1 overexpression has been accused of poor results in chronic nephropathies. Single nucleotide polymorphisms (SNP) in the TGF-β1 gene may accelerate chronic allograft nephropathy and chronic kidney disease progression. In this study, we aimed to assess two TGF-β1 polymorphisms' effect on long term renal function in kidney donors.

Method: This cross-sectional, single-center study was conducted in a tertiary referral center. Seventy-two living kidney donors who had donated between January 1999 and May 2018 were included in the study. The age, body mass index, and sex-matched control group consisted of 100 volunteers without systemic disease. GFR was calculated with CKD-EPI formula. Renal functions were compared between donors and controls. TGF-β1 gene polymorphism status of donors was evaluated with RT-PCR. Namely, +869T/C at codon 10 (rs1800470) and +915G/C at codon 25 (rs1800471) abbreviated as codon 10 SNP and 25 SNP respectively. TGF-β1 gene polymorphism effect on renal functions was assessed with a proper statistical approach.

Results: The study included 72 (53 female, 19 male) kidney donors, and 100 (69 female, 31 male) healthy controls. The mean age of the donor group was 50 ± 12 years, and the mean age of the control group was 47 ± 11 years.The mean creatinine levels of donors were significantly higher than the mean creatinine levels of the control group (0.96±0.2 vs. 0.72±0.2 mg/dL p <0.001). The mean GFR values of donors were markedly lower than the GFR values of the control group (76±20 vs. 107±22 mL/min). Regarding codon 10 SNP status, 34/18/20 donors had C/C, T/C, and T/T phenotypes. The preoperative and final GFR were similar between all groups. Regarding codon 25 SNP status, 61/6/5 donors had G/G, G/C, and C/C phenotypes. The preoperative GFR was statistically similar between all groups. The final GFR was highest for donors with G/G phenotype and lowest for those with C/C phenotypes (Table1). Donors with C/C phenotype were at 4.7 fold increased risk for GFR< 60 ml/min compared to those with G/G phenotype (HR:4,74 %95 CI: 1,482-15,212; p:0,009).

Conclusion: Kidney donation is associated with lower GFR compared to healthy individuals. The more profound decline in some cases may be explained with TGF-β1 SNP at codon 25. Our study shows C/C phenotype is associated with lower final GFR in renal transplant donors. We propose this particular finding might be useful for eligibility, especially for marginal donors after validation with studies including a higher number of participants.

Table1: Association of TGF β1 polymorphisms at codon 25 with renal function

	G/G	G/C	C/C	p-value
# of donors	61	6	5	NA
Age	50 ±12	50±12	49±13	0,9
Sex: F/M	46/15	5/1	2/3	NS
Age at transplant	44 ± 10	46±12	45±11	0,8
Months post transplant	51 (6-237)	49 (6-74)	47(12-168)	0,6
Proteinuria (mg/day)	86 (48-1697)	120 (54-188)	172 (56-208)	0,2
BMI	27,4 ± 4,3*	32,1 ± 5,9	24,5 ± 3,2*	**0,04**
Pre-operative GFR	109 ± 19	111 ± 24	106 ± 15	0,9
Final GFR	79 ± 20	64 ± 8	56 ± 10	**0,006**

Risk of GFR< 60 ml/min, regression analysis

	Hazard ration	%95 C. Interval	p-value
G/G	Reference	Reference	Reference
G/C	1,463	0,183-11,669	0,7
C/C	**4,748**	1,748-15,212	**0,009**

NA: not applicable, NS nonsigni˚cant at all levels, * p= 0,169 between G/G and C/C groups

Figure:

P1677 **KIDNEY ALLOGRAFT HISTOLOGY IN RECIPIENTS WITH TRANSPLANTATION VINTAGE LONGER THAN 10 YEARS**

Tomoko Namba-Hamano[1], Takayuki Hamano[2], Masahiro Kyo[3], Yutaka Yamaguchi[4], Kawamura Masataka[5], Taniguchi Ayumu[5], Shigeaki Nakazawa[6], Kato Taigo[5], Toyofumi Abe[5], Miyaji Kyakuno[7], Imamura Ryoichi[5], Nonomura Norio[5], Yoshitaka Isaka[1]

[1]Osaka University Graduate School of Medicine, Nephrology, Suita, Osaka, Japan, [2]Nagoya City University Graduate School of Medical Sciences, Nephrology, [3]Osaka Umeda Iseikai Dialysis Clinic, [4]Yamaguchi's Pathology Laboratory, [5]Osaka University Graduate School of Medicine, Urology, [6]University of Alabama at Birmingham, Microbiology and [7]Takatsuki General Hospital, Kidney transplantation

Background and Aims: Few studies have evaluated long-term graft histology. The aims of this study were to reveal the histological characteristics peculiar to long-term graft and to identify clinical manifestations and histological findings predicting graft survival after biopsy.

Method: In this retrospective study, we enrolled all allograft biopsies conducted in two institutions between 2002 and 2018 in recipients who had underwent transplantation 10 years before (n=107). The revised Banff criteria were used to evaluate histological findings. For a baseline cress-sectional study, we employed logistic regression analyses, to explore clinical factors associated with each histological parameter. Restricted cubic spline functions were used for non-linear associations. In longitudinal study, log-rank test and Cox proportional hazards models were used to evaluate the death-censored graft loss.

Results: Median (IQR) of time after transplantation, recipient age at biopsy, and donor age were 13 (11, 19), 49 (42, 59), and 51 years (43, 58), respectively. Median (IQR) eGFR and proteinuria at biopsy was 29 (24,40) mL/min/1.73m^2 and 0.46 (0.18,0.80) g/day, respectively. Seventeen patients (16%) had FSGS lesion, which was the most common glomerular abnormality in this cohort. Figure 1 shows the distribution of histological parameters. Donor age, in addition to proteinuria, was found to be associated with the presence of FSGS lesion [Odds ratio 2.37 (95%CI 1.16-4.88) per 10-year]. When constructing a non-linear model, estimated prevalence of FSGS lesion was increased in grafts from donors of > 40 years old (Figure 2). Logistic regression analyses revealed that eGFR at biopsy and transplantation vintage were associated with the presence of ci [Odds ratio 0.48 (95%CI 0.32-0.71) per 10 mL/min/1.73m^2, and 1.17 (1.05-1.30) per 10-year, respectively]. We also found that eGFR at biopsy and proteinuria were associated with the presence of ct [Odds ratio 0.40 (95%CI 0.26-0.63) per 10 mL/min/1.73m^2, and 2.02 (1.07-3.84) per 1g/day, respectively]. Figure 3 shows Kaplan-Meier curves for death-censored graft survival after biopsy. During 3.5 years of observation, 33% of patients lost their graft functions. Log rank tests revealed that the risk of graft loss is increased in the groups with the presence of ct (p=0.001), and FSGS lesion (p=0.0001), and higher score of cg (p<0.0001). In multivariate Cox proportional hazards model, the highest score of cg in addition to grater proteinuria and lower eGFR at biopsy showed higher risk of graft loss after biopsy [Hazard ratio 3.26 (95% CI 1.25-8.53) as compared to cg0, 1.64 (1.09-2.46) per g/day, and 0.39 (0.24-0.64) per 10 mL/min/1.73m^2, respectively].

Conclusion: The grafts from older donors, especially older than 40 years old, have FSGS lesion more frequently. Only cg score, not ct score or FSGS lesion, predicts graft survival after biopsy in patients with long transplantation vintage, independently from clinical information.

Figure 1.

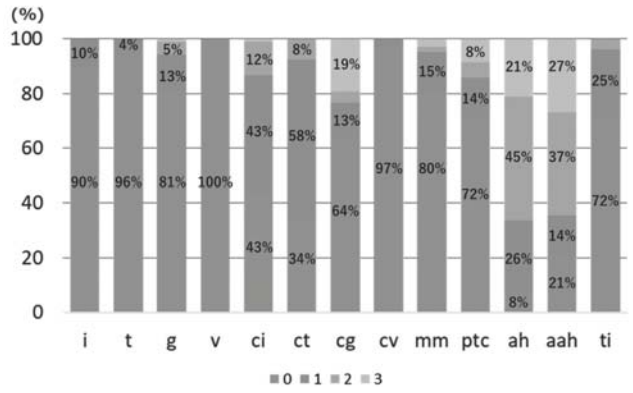


Figure 1:

Figure 2.

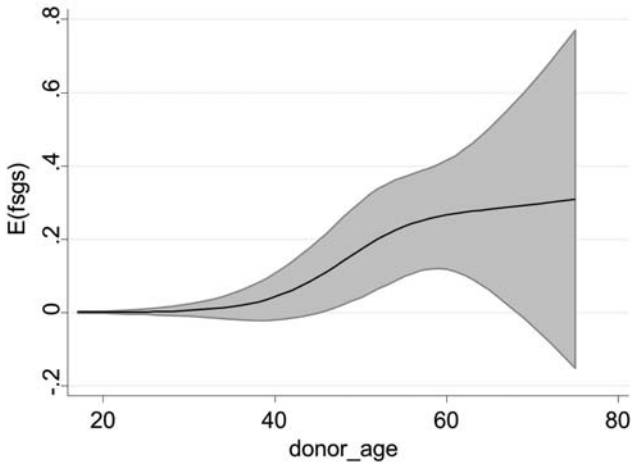


Figure 2:

Figure 3.

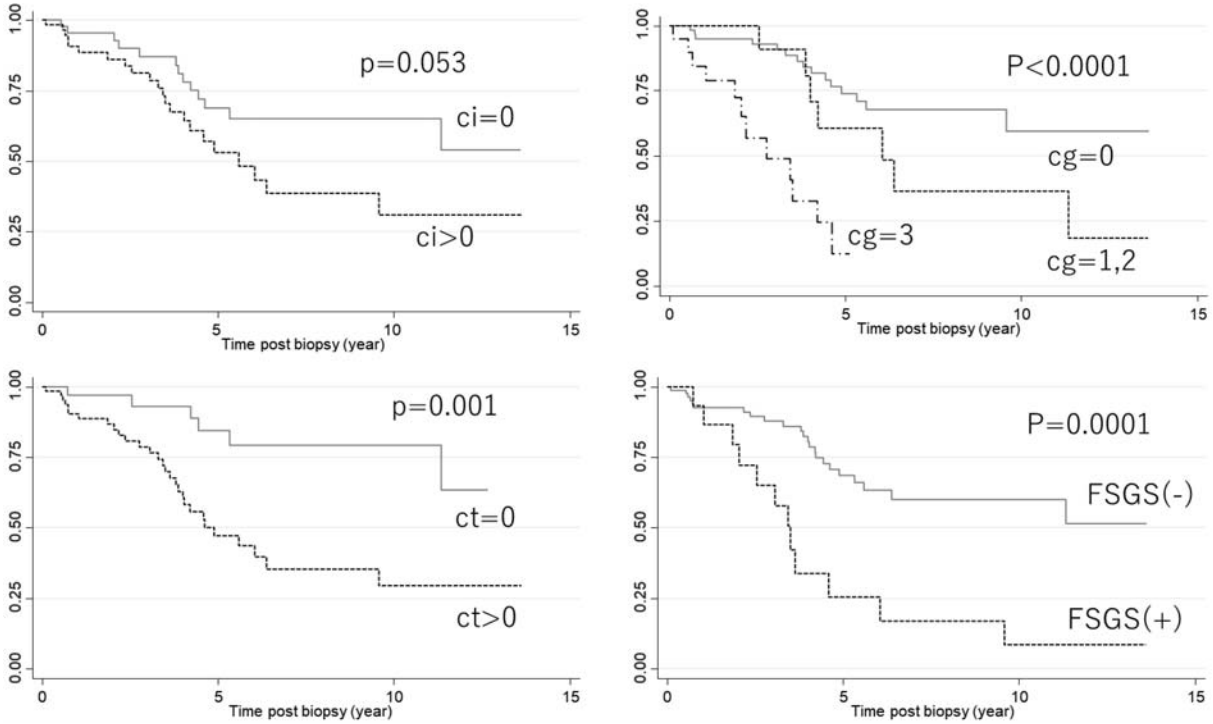


Figure 3:

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ASSOCIATION OF EPIDERMAL GROWTH FACTOR(EGF) AND EGF RECEPTOR POLYMORPHISMS WITH END STAGE RENAL DISEASE AND ACUTE RENAL ALLOGRAFT REJECTION IN KOREAN POPULATION

Sunwoo Kang[1], Byeong Woo Klm[2]

[1]*Inje University Pusan Paik Hospital, Nephrology, Busan, Korea, Rep. of South and*
[2]*Haeundae Bumin Hospital, Nephrology, Busan, Korea, Rep. of South*

Background and Aims: Epidermal growth factor (EGF) has been found to be associated with development and repair mechanisms of several renal diseases. In this study, we hypothesized that single nucleotide polymorphisms (SNPs) of the EGF or its receptor genes might have association with end stage renal disease (ESRD) or acute renal allograft rejection (AR) in Korean patients.

Method: 347 recipients of the first renal transplants for ESRD including 63 AR patients among them and 289 healthy adults were included in the study. Five EGF gene SNPs (rs11568835, rs11568943, rs2237051, rs11569017, rs3756261) and four EGFR gene SNPs (rs1140475, rs2293347, rs1050171, rs6965469) were analyzed. The genotypes of these SNPs were analyzed using AxiomTM genome-wide human assay. For statistical analysis we used SNPStats and Haploview version 4.2. Multiple logistic regression models (codominant, dominant, recessive and Log-additive) were produced to obtain odds ratio (OR), 95% confidence interval (CI), and p value.

Results: One SNP (rs11569017) in EGF gene showed significant association with ESRD but not with AR. Another SNP (rs11568835) in EGF gene showed significant association with susceptibility to AR but not with ESRD. One SNP (rs1050171) in EGFR gene showed significant association with susceptibility to AR but not with ESRD.

Conclusion: We suggest that genetic polymorphisms of EGF and EGFR gene may be associated with the risk of development of ESRD and AR in the Korean population.

P1679 **HYPOMAGNESAEMIA AND HYPERGLYCAEMIA AFTER KIDNEY TRANSPLANTATION**

Rasmus Carlsen[1], My Svensson[2], Kåre Birkeland[3], Iain Bressendorff[4], Hanne Gulseth[5], Anders Åsberg[1], Karsten Midtvedt[1], Trond Geir Jenssen[1]

[1]Oslo University Hospital, Norway, [2]Akershus University Hospital, Norway, [3]University of Oslo, Norway, [4]Herlev and Gentofte Hospital, Department of Medicine and Department of Nephrology, Herlev, Denmark and [5]Norwegian Institute of Public Health, Department of Chronic Diseases and Ageing, Norway

Background and Aims: Hypomagnesaemia has been associated with increased insulin resistance and decreased insulin secretion. Recent data suggest that early post-engraftment hypomagnesaemia may play a role in development of post-transplant diabetes mellitus (PTDM). This single-centre study investigated the association between hypomagnesaemia 8 weeks post-engraftment and glucose metabolism changes 1 year after kidney transplantation.

Method: The study included 425 renal transplantation recipients, transplanted at Oslo University Hospital between March 2015 and May 2018. All included patients had functioning grafts with valid blood sampling and oral glucose tolerance tests 8 weeks and 1 year after transplantation. Patients with known pretransplant diabetes and those developing PTDM the first 8 weeks after transplantation were excluded. The association between plasma magnesium 8 weeks after transplantation and HbA_{1c}, fasting plasma glucose and 2-hr glucose after 1 year was tested using both unadjusted and multiple linear regression, adjusted for: gender, age, body mass index (BMI), systolic blood pressure (SBP), tacrolimus (trough), measured glomerular filtration rate (mGFR; iohexol clearance) and plasma triglycerides.

Results: Patients had a median age of 54 (range 18-83) years, 65% were men and mean mGFR 1 year after transplantation was 56 (SD±14) ml/min/1.73m^2. Median plasma magnesium was 0.72 (0.46-0.94) mmol/L 8 weeks after Tx and patients with hypomagnesaemia (Mg< 0.7 mmol/L) (n=169) were not different compared to patients with normal plasma magnesium (n=256) regarding age, gender, BMI, tacrolimus, mGFR, SBP or plasma triglycerides after 1 year.

In unadjusted linear regression 1 mmol/L higher plasma magnesium at 8 weeks was associated with the following glycaemic endpoints 1 year after transplantation (β-coefficient, CI 95%, p-value); fasting glucose: HbA_{1c}: +9 mmol/mol (1;16, *P*=0.02); +0.5 mmol/L (-0.7;1.7, *P*=0.39); 2-hour glucose: +0.74 mmol/L (-2.5;3.9, *P*=0.65). In multiple linear regression the following numbers were: Fasting glucose: HbA_{1c}: +8 mmol/mol (0.3;16, *P*=0.042); +0.7 mmol/L (-0.5;2.0, *P*=0.26); 2-hour glucose: +2.8 mmol/L (-0.6;6.2, *P*=0.11).

Conclusion: In both unadjusted and multiple linear regression there was a positive correlation between 8-week plasma magnesium and HbA_{1c} 1 year after transplantation. A similar trend was found for fasting and 2-hour glucose, although this was not statistically significant.

P1680 MINERAL METABOLISM CHANGES AFTER RENAL TRANSPLANTATION

Ana Carina Ferreira[1,2], Marco Mendes[1,2], Cecília Silva[1], Patrícia Cotovio[1], Inês Aires[1,2], David Navarro[1], Fernando Correia Caeiro Pereira[1,2], Rute Salvador[3], Bruna Correia[3], Guadalupe Cabral[3], Fernando Nolasco[1,2], Manuel Anibal A. Ferreira[1,2]

[1]Hospital Curry Cabral, Nephrology, Lisboa, Portugal, [2]Nova Medical School, ., Lisboa, Portugal and [3]CEDOC, Tissue Repair and Inflammation Lab, Lisboa, Portugal

Background and Aims: Successful renal transplant restores many physiologic abnormalities, including improvement of chronic kidney disease-mineral and bone disorder (CKD-MBD) syndrome, and modifications of bone-related molecules in disease and health can help to understand pathophysiology of this syndrome.

The aim of this study was to analyse the evolution of some of the new CKD-MBD players [alpha-klotho, fibroblast grow factor (FGF) 23, sclerostin] pre and post transplantation and the associations between those and the usual markers of the CKD-MBD disease [parathyroid hormone (PTH), bone alkaline phosphatase (bAP), calcitonin, vitamin D (vitD), phosphorus (Pi), Calcium (Ca) and Magnesium (Mg)] pre and post transplant. We also looked at the differences between values in the two time-points (delta).

Method: We performed a prospective cohort study of a consecutive sample of *de novo* single renal transplanted patients in our unit. At inclusion, demographic, clinical and transplant-related data were collected, X-ray of the pelvis and hands (for Adragão score) and echocardiographic findings were recorded. All patients were submitted to a bone biopsy and laboratorial evaluation at baseline (time 0). Patients were followed for 12 months (time 1), after which performed laboratorial evaluation, a second bone biopsy, echocardiogram, X-ray of pelvis and hands, bone densitometry and non-contrast cardiac CT (Agatston score). Continuous variables are presented as medians and categorical variables as frequencies. Associations between variables were performed using Wilcoxon matched-pairs test and Spearman correlation test. STATA software was used and $p < 0.05$ was considered statistically significant.

Results: We recruited 85 patients from 1st October 2015 to 1st March 2018. At the end of 12 months, 6 patients refuse to perform the 2nd evaluation, 5 had primary non-function of the kidney graft, 1 had no sample on bone biopsy in time 0 and 4 patients died. We performed a 2nd evaluation in 69 patients and included those in this study.

Mean age 50.2 ± 12.4 years, 48 men, 53 caucasian (78.8%), median BMI 24.5 (22.7 – 27.8), median dialysis vintage 55 (42 – 84). We observe a significant reduction on phosphorus (delta: -1.1 mg/dl), magnesium (delta: -0.5 mg/dl), PTH (delta: -297.7 pg/ml), Calcitonin (delta: -0.9 ng/L), sclerostin (delta: -1.1 ng/ml), bone alkaline phosphatase (delta: -11.5 U/L) and FGF23 (delta: -1656.5 RU/ml). Both calcium (delta: 0.7 mg/dl) and alpha-klotho (delta: 265.7 pg/ml) serum levels increase, with no significant changes in vitamin D levels.

With restoring renal health (time 1) and comparing with time 0, PTH maintain the negative correlation with sclerostin (p=0.02) and the positive correlation with FGF23 (p=0.0002) as in time 0; modify the correlation with Pi, becoming a negative correlation instead of positive (p=0.001) and gain new correlations with Ca (p=0.001) and vitamin D levels (p=0.03). Also, PTH correlated with the delta FGF23 (rho=-0.4, p=0.003) and sclerostin correlated with delta PTH (p=0.01). FGF23 didn't associate with delta PTH, neither PTH associated with delta sclerostin. FGF23 didn't reveal statistical association with Pi or Ca levels after transplant, contrasting with positive associations in pre transplant (p=0.002, p<0.0001). On the contrary, sclerostin developed a new correlation with Pi (p=0.0004) and a negative correlation with Ca (p=0.01). We didn't find correlations between these molecules and alpha-klotho.

Conclusion: In conclusion, it seems that sclerostin influences PTH levels and that PTH is the stimulus for the increase or decrease of FGF23 serum levels (as we found a positive association between those two molecules in both time-points and a negative association between PTH and the difference of FGF23 pre and post transplant). Levels of Ca and Pi seemed to be directly influenced by the level of PTH in post transplant, and those minerals seemed to be key factors for sclerostin secretion.

P1681

12-MONTH SURVEILLANCE BIOPSIES IN RENAL TRANSPLANT PATIENTS AT LOW IMMUNOLOGICAL RISK. ARE THEY STILL WORTH OF BEING DONE?

Roberta Cortinovis[1], Nicola Bossini[1], Simona Fisogni[2], Francesca Valerio[1], Camilla Maffei[1], Franco Nodari[3], Alberto Malagoli[4], Silvio Sandrini[1], Francesco Scolari[1]

[1]University of Brescia and Spedali Civili General Hospital, Nephrology, Brescia, Italy, [2]University of Brescia and Spedali Civili General Hospital, Pathology, Brescia, Italy, [3]University of Brescia and Spedali Civili General Hospital, Vascular Surgery, Brescia, Italy and [4]University of Brescia and Spedali Civili General Hospital, Rheumatology and Clinical Immunology, Brescia, Italy

Background and Aims: In renal transplant field, the progressive increase both of donor and recipient age has led further challenges in patient management. In this setting, the personalization of immunosuppressive therapies (IT) has been strongly suggested. We have investigated renal histology at 12 months after transplantation to assess whether surveillance biopsies (SB) could be considered an additional tool to further improve management of immunosuppression.

Method: Monocentric retrospective analysis of SB performed 12 months post-transplant (Tx) between 2009-2018. For each SB were collected recipient and donor demographic data, HLA mismatch, induction and maintenance IT, DGF, cold ischemia time, PRA, DSA and nDSA, previous episodes of acute rejection (AR), serum creatinine (Cr) at the time of SB and 1, 3 and 5 years later, histological score according to Banff classification in force at the time of SB. Statistics included comparison between groups and Cox regression.

Results: We analyzed 209 SB in as many pts, most of them at low immunological risk (first Tx in 94.3%, PRA <30% in 88%, DSA at time of Tx in 5.4%). All pts received induction therapy; maintenance IT included calcineurine inhibitors in 97%, mycophenolate mofetil in 49%, mTOR inhibitors in 30%, azathioprine in 10% and corticosteroids in 33%.

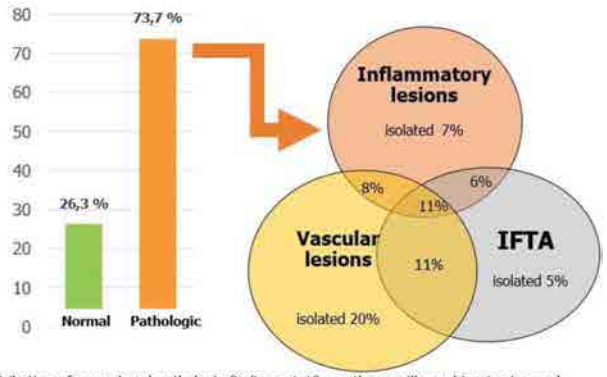
SB showed normal histology in only 26.3% of cases. There were no differences in renal function between normal and pathological biopsies (Cr 1.40 vs 1.46 mg/dl, p=NS). Major histologic findings, isolated or associated with each other [Fig. 1], were vascular lesions (VL, 40%), IFTA (33%) and inflammatory lesions (IL, 32%).

VL correlated with donor age (OR 1.07, p<0.001), whereas IFTA with both donor age (OR 1.03, p=0.04) and DGF (OR 1.07, p=0.04). IFTA was the only histological pattern associated with a lower renal function (Cr 1.58 vs 1.39 mg/dl, p=0.016). IL included interstitial infiltrates (14.8% of specimens), tubulitis (9.6%), glomerulitis (19.6%) and capillaritis (ptc, 13.9%). Both glomerulitis and capillaritis were associated with the presence of DSA, both at Tx (OR 4.35, p=0.037) and at biopsy (OR 5.45, p<0.001).

All types of lesions were found to be related with previous AR (VL with OR 3.08, p= 0.003, IFTA with OR 2.15, p=0.04, IL with OR 4.71, p<0.001) and to be more frequent in the last 5 year biopsies, according to an older donor age (59.5 vs. 52.3 ys, p< 0.001) and a lower HLA-matching (mismatch AB >2: 50.5% vs 32%, p=0.045).

Indipendent histological variables that predicted a worsening of renal function were glomerulitis/capillaritis (HR 6.996, P<0.001) and VL (HR 2.229, p=0.038).

Conclusion: Our data confirm that stable renal function does not exclude the presence of subclinical histological lesions, even in patients at low immunological risk. Abnormal findings are present in 73.7% of our SB. Glomerulitis/capillaritis and VL can affected renal function, so their recognition should be considered for immunosuppression optimization. Patients with previous AR are at higher risk for all types of histologic lesions and may require a closer monitoring.



Distribution of normal and pathologic findings at 12-month surveillance biopsies in renal transplant patients.

Figure:

P1682 **POST-TRANSPLANT VISIT-TO-VISIT PULSE PRESSURE VARIABILITY AND RISK OF RENAL ALLOGRAFT FUNCTION DECLINE**

Ekamol Tantisattamo[1,2], Natnicha Leelaviwat[3], Chawit Lopimpisuth[4], Natchaya Polpichai[5], Possawat Vutthikraivit[6], Sakditad Saowapa[3]

[1]Division of Nephrology, Hypertension and Kidney Transplantation, Department of Medicine, University of California Irvine School of Medicine, Orange, United States of America, [2]Multi-Organ Transplant Center, Section of Nephrology, Department of Internal Medicine, William Beaumont Hospital, Oakland University William Beaumont School of Medicine, Royal Oak, United States of America, [3]Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, [4]Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [5]Faculty of Medicine Songklanagarin Hospital, Prince of Songkla University, Songkhla, Thailand and [6]Phramongkutklao College of Medicine, Mahidol University, Bangkok, Thailand

Background and Aims: Pulse pressure (PP) is associated with risk of kidney disease. Association between visit-to-visit PP variability (VVPPV) and renal allograft outcomes is unknown.

Method: VVPPV, variation of PP between each consecutive BP measurement at 4, 12, 24, 36, and 48 weeks after kidney transplantation (KT), was determined by using coefficient of variation (CV = SD/Mean x 100%). VVPPV was then categorized into 12 strata (<5, 5 - <10, 10 - <15, 15 - <20, 20 - <25, 25 - <30, 30 - <35, 35 - <40, 40 - <45, 45 - <50, 50 - <55, and ≥55). Association between the categorized VVPPV and progression of renal allograft function, which was defined by a decrease in estimated glomerular filtration rate (eGFR) after 12-week post-KT, was examined by Cox proportional hazard regression analysis.

Results: Of all 102 renal transplant recipients from a single kidney transplant center, mean age±SD was 54.16±11.73 years and 63 patients (62%) was female. An incidence rate of worsening renal allograft function after 12-week post-KT was 0.017 person-weeks with a median survival time of 36 weeks (Figure 1). Every 5% increase in CV of PP was associated with a 14% increased risk of worsening post-transplant eGFR (hazard ratio (HR) 1.142431, 95% confidence interval (CI) 0.9999617 to 1.305199, and p value 0.050). After adjusted for age, gender, types of induction immunosuppressive medications, pretransplant body mass index category, every increase in 5% CV of PP was significantly associated with a 16% greater risk of worsening post-transplant eGFR (HR 1.160975, 95% CI 1.007967 to 1.337209, and p value 0.038).

Conclusion: VVPPV is an independent predictor of worsening renal allograft function.

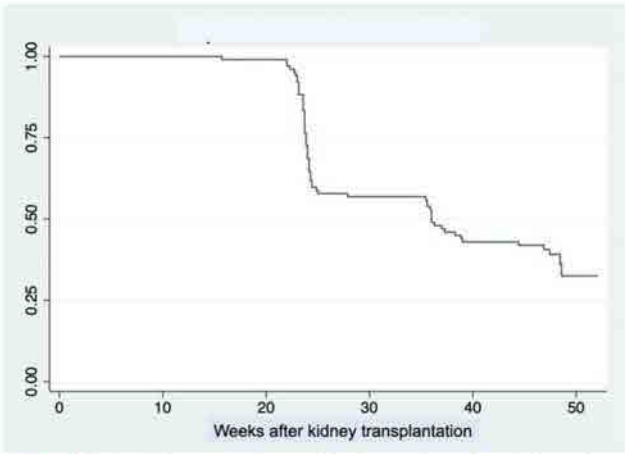


Figure 1: Kaplan-Meier curve estimates risk of worsening estimated glomerular filtration rate after kidney transplantation

Figure:

P1683 INFLUENCE OF BIOPSY PROGNOSIS ON GRAFT SURVIVAL

Cristina Andrades Gómez[1], Miguel Ángel Pérez valdivia[2], Jorge Calvillo Arbizu[3], Rocío Cabrera López[4], Marta Suñer Poblet[2], Carmen González Corvillo[2]

[1]Hospital Universitario Virgen del Rocío, Neprhology, Seville, Spain, [2]Hospital Universitario Virgen del Rocío, Nephrology, Seville, Spain, [3]Universidad de Sevilla, Ingeniería de Telecomunicaciones, Sevilla, Spain and [4]Hospital Universitario Virgen del Rocio, Anatomical pathology, Sevilla, Spain

Background and Aims: Renal transplantation is the best alternative renal replacement option for patients with advanced chronic kidney disease. However, the supply of young donors is limited, and does not cover the demand of patients on the renal transplant waiting list, for this reason are being used older donors and exists a high discard rate of those organs base on pathological results (score) of the preimplant renal biopsy.

There are several methods to evaluate the quality of the kidneys and the Kidney Donor Profile Index (KDPI) has acquired special relevance to decide the perform of preimplant renal biopsy. Based on the score, a preimplant renal biopsy is performed, which is decisive in certain cases.

However, there is poor evidence to support this decision, which can be described as "conservative," since there is not enough certainty that there is influence of the preimplant biopsy score score on graft survival.

Method: 389 biopsies of kidney transplant donors of cadaver donors in brain death and asystole type III were included. Donors in asystole type II, combined and live, were excluded. Samples examined by the same pathologist and in paraffin (no case by freezing). A graft survival analysis was performed based on the results of the renal biopsy (score). Likewise, a multivariate analysis of graft survival was carried out including, in addition to the results of the renal biopsy, results such as the age of the donor and recipient and the KDPI.

Results: graft survival was compared between two transplant subpopulations in our hospital based on whether a preimplant biopsy was performed. According to the data used there are no significant differences in graft survival between transplants in which biopsy has been performed and those that have not.

Conclusion: our work shows, as is currently the case in the literature, the absence of influence on the score of the preimplant biopsy score on graft survival.

P1684

MULTI-NATIONAL SURVEY AMONG NEPHROLOGISTS AND TRANSPLANT SURGEONS ABOUT THE SUITABILITY AND ACCEPTANCE OF MARGINAL LIVE KIDNEY DONORS WITH HEAVY SMOKING OR INTERMITTENT DRUG ABUSE

Ziad Arabi[1], Abdullah Hamad[2], Kaysi Saleh[3], Mohammad Bukhari[4]

[1]King Abdulaziz Medical City, King Abdullah International Medical Research Center & King Saud Bin Abdulaziz University for Health Sciences, Adult Transplant Nephrology, Organ Transplant Center, Riyadh, Saudi Arabia, [2]The Regional Medical Center, Department of Nephrology, Orangeburg, SC,, United States of America, [3]CHU Clermont-Ferrand,, Saint Pryv/ Saint Mesmin, France and [4]University of Taif, Department of Nephrology, Taif, Saudi Arabia

Background and Aims: Potential kidney donors who actively smoke heavily or had intermittent illegal drug use (IIDU) are mostly excluded from donating a kidney. Tobacco use in kidney donor has been linked to worse outcomes for donors and while less evidence exists for IIDU as they mostly excluded from donation. We conducted a short survey about the suitability of these marginal living kidney donors. The purpose of this survey is to form a consensus on live kidney donor with using smoking or illegal drugs.

Method: This is a cross-sectional survey of nephrologists and transplant surgeons about suitability and acceptance of marginal live kidney donors. We asked physicians about accepting kidney donors who are actively smoking or using illegal drugs. The survey was mainly distributed through AST and ERA-EDTA. The role of these organization is limited to facilitate the distribution of the survey as an external study. We excluded in-training nephrologists or transplant surgeons.

Results: One hundred twenty-two physicians from 22 countries (80% nephrologists and 20% transplant surgeons (TS)) participated in the survey. Most physicians were experienced in pre-transplant evaluation (72% over 6 years' experience and 68.5% of responders perform donors' evaluation on weekly or monthly bases). Interestingly, most physicians would allow donation in active smoker with advice to quit later (56.2%) (62% of nephrologists versus only 29% of TS (p=0.002). TS would decline active smoker patients than nephrologists (42% versus 25%, p=0.09). Less physicians considered donors with IDU (after psychiatric counselling) than active smoking (30% versus 56.2%, p=0.00003). There was no difference in acceptance rate for donors with IIDU between TS and nephrologists (33.3% versus 29% respectively, p=NS) or in declining these donors (37.5% versus 45.3%, p=0.4). TS would accept more active smokers to donate if no alternative donor available than nephrologists (29.2% vs. 12.3%, p=0.04) but not IDU (29.2% vs. 25.8%, p=ns).

Conclusion: Active heavy smoking and intermittent illegal drug use are not viewed as solo contraindications for kidney donation by most physicians. Nephrologists and TS did not differ in attitude regarding donors with IIDU. Nephrologist seems more confident to accept donors who are actively smoking with advice to quit afterward while TS would accept them more if no alternative donor available or would decline them completely.

Figure:

P1685 **POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD): SINGLE INSTITUTIONAL EXPERIENCE OF TWO DECADES**

Inês Coelho[1], Sofia Cerqueira[2], Catarina Romãozinho[3], Luís Rodrigues[3], Rita Leal[3], Maria Guedes Marques[3], Lidia Santos[3], Rui Alves[3,4], Arnaldo Figueiredo[5,6]

[1]Amato Lusitano Hospital, Department of Nephrology, Castelo Branco, Portugal, [2]Centro Hospitalar Trás-os- Montes e Alto Douro, Department of Nephrology, Vila Real, Portugal, [3] Coimbra Hospital and University Center, Department of Nephrology, Coimbra, Portugal, [4]Faculty of Medicine, University Clinic of Nephrology, Coimbra, Portugal, [5]Coimbra Hospital and University Center, Department of Urology and Kidney Transplantation, Coimbra, Portugal and [6]Coimbra University, Faculty of Medicine, Coimbra, Portugal

Background and Aims: Post-transplant lymphoproliferative disorders (PTLD) are a group of heterogeneous lymphoid proliferations in chronic immunosuppressed recipients of solid organ and hematopoietic stem cell transplantation. Due to rarity of this disease, retrospective studies from transplant centers have been the main source to provide knowledge and treatment guidelines, which are still in evolution. This study examined the clinical outcomes and identified the predictors of mortality in adult renal transplant recipients who developed PTLD.

Method: We have studied the incidence of PTLD in adult renal transplant recipients who were transplanted in our hospital from 1996 to 2019. Data was collected for demographics, transplant and immunosuppression history, EBV and CMV serostatus, diagnosis, treatment and outcomes of PTLD. We performed univariate and multivariate analysis to identify prognostic factors. PTLD was classified according to 2018 WHO lymphoma classification.

Results: Twenty-four patients (12 males and 12 females) were eligible for the analysis. Mean age at time of the transplant was 43.1 ± 16.9 years, with a time between grafting and PTLD of 66 months (IQR 36-98 months). Mean follow-up time was 87 months (IQR 61-117 months). 25% of patients received a living donor renal transplant. 12,5% of patients received induction therapy with thymoglobulin. Mean age at time of PTLD diagnosis was 48,8 ± 17,9 years. Five cases were from Epstein-Barr virus (EBV) mismatched (D+/R-) transplants and there was seroconversion at time of PTLD diagnosis. 25% of patients had central nervous system involvement. 19 patients have monomorphic PTLD and the most common histological diagnosis was diffuse large B cell lymphoma. We identified that age >30 years at time of the transplant was predictor of mortality (HR 33.01; 95% CI: 3.24-336.14; p=0.003). Surprisingly, presence of B symptoms at time of PTLD diagnosis confer a better prognosis (HR 0,143; 95% CI: 0,035-0,579; p=0.006). All cases were managed with reduction in immunosuppression and converted to everolimus. 8 patients were treated with rituximab and there was no significant difference in the survival of these patients. By the end of follow-up, 7 patients went into remission, 1 returned to chronic dialysis, and 16 patients died (15 of them due to the disease). Mean time between PTLD and death was 3 months (IQR 1-6 months).

Conclusion: PTLD is an infrequent disease with a poor prognosis in renal transplant patients. Some cases have a close relationship with EBV, but it can also develop in the absence of the classical risk factors. The factor affecting mortality in our population was age >30 years at time of the transplant. Presence of B symptoms at time of PTLD diagnosis seems to confer a better prognosis probably due to early investigation and diagnosis of the disease.

P1686 **MULTI-NATIONAL SURVEY AMONG NEPHROLOGISTS AND TRANSPLANT SURGEONS ABOUT THE SUITABILITY AND ACCEPTANCE OF MARGINAL LIVE KIDNEY DONORS WITH MICROSCOPIC HEMATURIA**

Ziad Arabi[1], Kaysi Saleh[2], Abdullah Hamad[3], Mohammad Bukhari[4]

[1]King Abdulaziz Medical City, King Abdullah International Medical Research Center & King Saud Bin Abdulaziz University for Health Sciences, Adult Transplant Nephrology, Organ Transplant Center, Riyadh, Saudi Arabia, [2]CHU Clermont-Ferrand,, Saint Pryv/ Saint Mesmin, France, [3]The Regional Medical Center, Orangeburg, SC,, United States of America and [4]University of Taif, Taif, Saudi Arabia

Background and Aims: Potential kidney donors with isolated hematuria are often excluded from donating although there is a wide controversy about the definition and threshold of investigations or exclusion form donation. Many centers use the cut off of > 3 RBC in men and > 5 RBC in women. Some centers consider positive dipstick on urinalysis as the definition of microscopic hematuria. Kidney biopsy in these donors can be borderline and inconclusive. We conducted a short survey about the suitability of these marginal living kidney donors with microscopic hematuria.

Method: This is a cross-sectional survey of nephrologists and transplant surgeons (TS) about suitability and acceptance of marginal live kidney donors with isolated microscopic hematuria. The question was about a 35-yr. old man non-smoker with isolated microscopic hematuria (4 RBC on repeated UA and trace hematuria on dipstick) and negative imaging. The survey was mainly distributed through American Society of Transplantation, American Society of Transplant Surgeons and European Renal Association-European Dialysis and Transplant Association. In-training nephrologists or transplant surgeons were excluded.

Results: A total of (n= 122 from 22 countries, 80% nephrologists and 20% TS) responded to the survey. Most respondents were experienced in donor evaluation (72% of physicians have over 6 years' experience and 68.5% of them perform donors' evaluation on weekly or monthly bases). Interestingly, at this low level of microscopic hematuria (4 RBC on repeated UA and trace hematuria on dipstick) only very limited number of respondents (7.5%) would allow donation without further work up. Instead, most respondents (n= 75, 63%) would ask for kidney biopsy prior to taking further steps. Many physicians (n=35, 29%) choose to ask for an alternative donor to avoid the hassle of kidney biopsy which may not change the management. There was no difference in acceptance rate for donors between TS and nephrologists (7.2% versus 8.3% respectively, p=NS), requesting kidney biopsy (63.9% vs. 62.5%) or in declining these donors (28.8% versus 29.1%, p=NS).

Conclusion: Young kidney donors with persistent isolated microscopic hematuria (even at mild degree) require further evaluation with kidney biopsy before donation. However up to one third of the nephrologist and transplant surgeon will ask for an alternative donor to avoid the hassle of kidney biopsy which can be borderline or inconclusive.

Figure:

P1687

ASSOCIATION OF URINARY MICRORNA-21-5P WITH INTERSTITIAL FIBROSIS AND TUBULAR ATROPHY (IFTA) IN RENAL TRANSPLANT RECIPIENTS

Michal Gniewkiewicz[1], Izabela Paszkowska[1], Jolanta Gozdowska[1], Katarzyna Czerwinska[1], Anna Sadowska-Jakubowicz[1], Dominika Deborska-Materkowska[1], Agnieszka Perkowska-Ptasinska[1], Maciej Kosieradzki[2], Magdalena Durlik[1]

[1]Medical University of Warsaw, Department of Transplantation Medicine, Nephrology and Internal Medicine, Warsaw, Poland and [2]Medical University of Warsaw, Department of General and Transplantation Surgery, Warsaw, Poland

Background and Aims: One of the most limiting factors of long-term graft survival is chronic renal allograft dysfunction (CAD). The major hallmarks of CAD are interstitial fibrosis and tubular atrophy (IFTA).

MicroRNAs (miRNAs) are 19-25 nucleotides, small, noncoding molecules involved in the regulation of gene expression. MiRNAs have a role in various immunological processes, including inflammation and fibrosis. Particularly, microRNA-21-5p (miR-21) is reported to be strongly associated with pathogenesis regarding tubulointerstitium.

The aim of this study was to analyse expression levels of urinary miR-21 in the renal transplant recipients and evaluate their application in the assessment of IFTA and kidney allograft function.

Method: The expression levels of urinary miR-21 were measured in 31 renal transplant recipients with biopsy-evaluated IFTA (IFTA 0+I: n=17; IFTA II+III: n=14) by quantitative PCR. Protocolar biopsies were performed 1 or 2 years after renal transplantation. Urine samples were collected at the time of biopsy procedure. MicroRNA-191-5p was used as reference gene. Correlations between the clinicopathological parameters and the level of expression of miR-21 were assessed.

Results: Relative expression level of miR-21 was significantly increased in IFTA II+III group compared to IFTA 0+I group. MiR-21 correlated positively with serum concentration of creatinine and negatively with eGFR. ROC analysis showed diagnostic value of miR-21 with an area under curve (AUC) of 0.80, high sensitivity and specificity.

Conclusion: MiR-21 is associated with IFTA and dysfunction of kidney allograft. It may be considered as potential non-invasive biomarker of renal allograft function.

P1688

THE IMPACT OF KIDNEY DONOR PROFILE INDEX (KDPI) AND KIDNEY DONOR RISK INDEX (KDRI) ON KIDNEY TRANSPLANT FUNCTION: A MONOCENTRIC ANALYSIS AFTER ONE YEAR OF FOLLOW UP

Andrea Solazzo[1], Giacomo Mori[1], Gianni Cappelli[1], Laura Tonelli[1], Francesca Facchini[1], Francesco Fontana[1], Gaetano Alfano[1], Stefano Baroni[2]

[1]AOU Modena - University Hospital of Modena, Surgical, Medical and Dental Department of Morphological Sciences, Section of Nephrology, Modena, Italy and [2]Ospedale Civile di Baggiovara, Intensive Care Unit, Baggiovara, Italy

Background and Aims:

Evaluation of kidney donors is a complex process based on the elaboration of clinical, laboratory and imaging data.

Until 2014, the quality of kidney transplant (KTx) was assessed considering standard donation criteria (SCD) or extended donation criteria (ECD).

ECD kidneys (kECD) defined subjects older than 65 years without comorbidities or younger, but with comorbidities, such as hypertension, cerebral stroke, high creatinine level (above 1.5 mg/dL).

The Kidney Donor Risk Index (KDRI) is an estimate of the relative risk of post-transplant kidney graft failure from a particular deceased donor compared to a reference donor.

The value obtained is than converted in a percentage called KDPI (KDPI ≥85% is considered as similar of a kidney from ECD), which represent the percentage of utilized donor in the last year better than the considered.

Italian experience in Donor Cardiac Death (DCD) is growing and doubled last KTx year, reaching 1.1 pmp in 2018, with the 22.5% of donors procured at our center.

Our DCD KTx protocol has been active since November 2017, with promising results. We considered only controlled DCD (cDCD) Maastricht Class III.

Methods:

We compared all DCD and DBD KTx performed in the Nephrology Unit of the University Hospital of Modena, Italy, from November 2017 to December 2018. We excluded living donor transplantation and combined liver–kidney transplantation. In this study, only cDCD are considered.

We studied KDPI and KDRI score for both DBD and DCD KTx .

Comparison between data from DCD and DBD was performed with t – Student and Chi Square test, survival analysis according to Kaplan-Meier and a Pearson correlation between KPI-KDRI and one year graft function was elaborated.

ROC curve analysis was performed for KDPI – KDRI and DGF for both groups.

A p lower than 0.05 was considered significant.

Results:

A total of 28 DBD KTx, 18 double (64.3%) and 10 single (35.7%) and 7 DCD KTx, 3 double (42.8%) and 4 single (57.2%) were observed during the study. Donors and recipients clinical and immunological characteristics are reported in table1.

All of DCD and 64.3% of DBD donors underwent kidney biopsy (Karpinski values are reported in table 1).

Induction therapy was with aTG in DCD KTx and ECD DBD KTx and with anti-interleukin-2 receptor monoclonal antibodies in SCD DBD KTx. Maintenance immunosuppression consisted in steroid, tacrolimus and mycophenolic acid.

KTx outcomes were reported in table 1 with no differences in both groups between creatinine (p0.3) and eGFR (p0.25).

We analyzed KDPI and KDRI values from DBD and DCD KTx and we stratified them as reported in table 2.

We found 7 DGF in DBD KTx (85% with KDPI >85% and KDRI >1.5) and only 1 DGF in DCD KTx with KDPI>85% and KDRI > 1.5.

We did not find a statistical correlation between KDPI- KDRI and eGFR in both DBD KTx (2 patients died and 3 patients were lost at follow up) (r -0.32, p 0.13; r -0.26, p 0.22) and DCD KTx (r -0.59, p 0.15; r -0.47, p 0.28). (Figure 1)

	DBD DONOR	DCD DONOR	DBD RECIPIENT	DCD RECIPIENT
CAUSE OF DEATH				
Head Trauma	4	1		
Ischemic Stroke	3	1		
Cerebral Hemorrhage	17	2		
Post anoxic encephalopathy	4	3		
MEAN AGE at Tx (year)	59.8 ± 23.12	58.7 ±7.2	58.6 ± 16.6	57.4 ± 4.2
WAITING LIST (Month)			29,7±30,1	22,45±41,23
KARPINSKI (Mean)				
Double: Right Kidney	3,8±0,9	4,6±0,5		
Double: Left Kidney	4,4 ± 1,1	5±1		
Single	2,1±0,7	1,6±0,5		
MEAN COLD ISCHEMIA TIME (hh:mm)				
Double: Right Kidney			13:00 ± 02:47	12:30 ± 00:44
Double: Left Kidney			13:30 ± 02:56	13:51 ± 01:06
Single			12:32 ± 03:29	09:46 ± 02:40
HLA MISMATCH			4±0.78	4.1±0.98
KTx OUTCOMES				
Mean Creatinine (mg/dl)			1.54±0.79	1.43±0.31
Mean eGFR CKD EPI (ml/min)			62.7±25.3	54.71±14.66
DGF n (%)			7(25%)	1 (14,3)
PNF (n)			0	0
PATIENT LOST AT FOLLOW UP (n)			3	0
DEATH (n)			2	0

Table 1 Population characteristics. DBD: Deceased after Brain Death; DCD: Deceased after Circulatory Death; eGFR (estimated Glomerular Filtration Rate, CKD-EPI formula); DGF: Delayed Graft Function; KTx: Kidney Transplantation; PNF: Primary Non Function

Figure:

We performed a ROC curve Analysis to investigate the role of KDPI – KDRI and the risk of DGF. We found no statistical correlation in DCD KTx, considering the small sample size (p 0.61) but we found a significant statistical value in DBD KTx (p 0.03 – p 0.02 with a AUC of 0.77-0.78).

Survival analysis did not show statistical difference between DBD and DCD (p 0.72), no graft loss in the first year, although two DBD (92.8%) recipients died (1circulatory arrest,1 sepsis), no one died in DCD group.

Conclusion:

cDCD is a valid resource for KTx, with similar outcomes to DBD. This remarks the importance of a multidisciplinary team and a correct selection of donors. We did not find a correlation between KDPI-KDRI and KTX function after one year of follow up in our population for either group.

P1689 **COMPARISON OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS(NSAIDS) AND/OR PAINKILLERS USE BY KIDNEY (KTRS) AND HEART TRANSPLANT RECIPIENTS (HTRS).**

Anna Jędrzejczak[1], Wioletta Szczurek[2], Michał Zakliczyński[3], Bartosz Foroncewicz[1], Rafał Staros[1], Leszek Pączek[1], Krzysztof Mucha[1]

[1]Medical University of Warsaw, Department of Immunology, Transplantology and Internal Medicine, Warsaw, Poland, [2]Medical University of Silesia, 3rd Department of Cardiology, School of Medicine with the Division of Dentistry in Zabrze, Katowice, Poland and [3]Medical University of Silesia, Department of Cardiosurgery, Transplantation, Vascular and Endovascular Surgery, Zabrze, Poland

Background and Aims: Solid organ transplantation (SOT) has become the therapy of choice for the treatment of end-stage organ failure. The non-steroidal anti-inflammatory drugs (NSAIDs) and over-the- counter (OTC) painkillers are ofenly used. In a group of SOT recipients, co-morbidities and immunosuppression interactions significantly increase the risk of side effects. The aim of the study was to analyze the frequency and reasons of the NSAIDs and/or painkillers use by renal (RTRs) and heart transplant recipients (HTRs).

Method: This cross-sectional study was perfomed in randomly selected 388 RTRs and 286 HTRs aged from 18 to 82 years. The original annonymus questionnaire consisting of 32 questions related to health status and NSAIDs and/or analgesics use was applied. Questionnaire was distributed in paper-form and completed with the participation of medical worker either in transplant cardiosurgical or renal transplantation center. "R" v. 3.6.1. was used for statistical analysis and p-value <0.05 was considered significant.

Results: 674 patients were surveyed. All patients: 34,3% (n=231) women and 65,7% (n=443) men in the mean age of 62.27 years completed the questionnaire. 70% (n=451) of respondents declared using NSAIDs and/or analgesics. Furthermore, 87% of participants declared using OTC painkillers. The most frequent causes for using analgesics are listed in Table 1.

68,5% of our SOT recipients declared that they were informed by their doctor about consequences of other drugs used with immunosuppression. 69,9% of HTRs comparing to 54,3% of RTRs ask their doctor before taking analgesics. Nevertheless, the survey also showed that every third patient (31,5%) was not sufficiently informed. Acetaminophen was the first-choice drug taken by 67,6% of patients (Fig. 1). Only 20% of patients declared not using NSAIDs and/or analgesics at all.

Conclusion: The result of our study indicates high frequency of NSAID and painkillers usage by RTRs and HTRs. Considering potentially harmful influence on transplanted organs, the costs of transplantation and post-trasplant care, the awareness of drug-related side effects or interactions and patients compliance need to be highlighted.

Table 1. The most frequent causes for using alagesics.

headache	49,57%
backache	26,81%
bone and joint pain	19,79%
cold	8,30%
menstrual cramps	6,60%
legs pain	3,62%

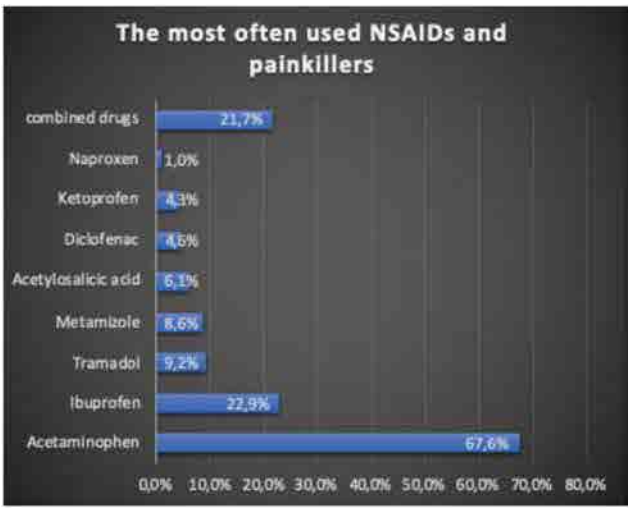


Figure 1. The most often used NSAIDs' and painkillers.

P1690 **EXPERIENCE WITH EXPANDED CRITERIA DONORS: 10-YEAR SINGLE CENTER ANALYSIS**

Karol Graňák[1], Vnuäã¡k Matej[1], Petra Skálová[1], Juraj Miklušica[1], L'udovít Laca[1], Ivana Dedinska[1]

[1]*University hospital Martin and Jessenius Faculty of Medicine Comenius University, Surgery department and Transplant Center, Martin, Slovakia*

Background and Aims:

Kidneys from expanded criteria donors with diagnosis of brain death have become a part of the organ transplant program, which have thus increased the number of transplants.

Method:

In this retrospective analysis, we identified the expanded criteria donors in a group of 156 kidney donors at our center. Basic parameters of the donors before kidney recovery were collected. Graft function, graft survival, and patient survival at 1, 3, and 5 years posttransplant were compared in expanded criteria versus standard criteria donors.

Results:

Expanded criteria donors were significantly older than standard criteria donors (P < .001), had higher body mass index (P = .006), and had more frequent arterial hypertension (P < .001) and diabetes mellitus (P = .004) in their histories. When we considered the estimated glomerular filtration rate, graft function in the first 6 months after transplant was significantly worse in kidneys from expanded criteria donors (P = .011). In addition, recipients of grafts from expanded criteria donors had significantly worse survival in the first year posttransplant (P = .023); however, no differences in graft survival were observed.

Conclusion:

From the long-term aspect, graft function and graft and patient survival in cases of kidneys from expanded criteria donors were comparable to results with kidneys from standard criteria donors. Expanded use of organs available for transplant is important due to the constantly increasing demands versus limited offers of organs.

Table 1. Characteristics of Expanded Criteria Donors and Standard Criteria Donors

	SCD (n = 107)	ECD (n = 50)	*P* Value
Average age, years	40 ± 13	60 ± 5.3	< .001
Male patients, %	71	64.4	.423
Body mass index, kg/m²	24.5 ± 2.8	26.1 ± 4	.006
Abuse of alcohol in history, %	25.2	28.9	.637
Cause of death by head trauma, %	57.9	20	< .001
Cause of death by hemorrhagic ABA, %	24.3	75.6	< .001
Cause of death by ischemic ABA, %	15	4.4	.066
Cause of death by brain tumor, %	2.8	0	.259
History of arterial hypertension, %	20.6	64.4	< .001
History of diabetes mellitus, %	2.2	20.6	.004
Creatinine before organ recovery, µmol/L	93.2 ± 26.4	88.8 ± 23.8	.336
eGFR before organ recovery, mL/s	1.41 ± 0.65	1.23 ± 0.33	.080
Best adjusted glomerular filtration, mL/s	1.89 ± 0.88	2.06 ± 2.96	.589
Sodium before organ recovery, mmol/L	142 ± 10	142 ± 8.3	1.00
Potassium before organ recovery, mmol/L	4.1 ± 0.5	4.1 ± 0.4	1.00
Chloride before organ recovery, mmol/L	112 ± 10	111 ± 8.6	.559
QP before collection, g/collection	0.436 ± 0.426	0.634 ± 1.153	.124

Abbreviations: ABA, arterial brain accident; ECD, expanded criteria donor; eGFR, estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology Collaboration formula; QP, quantitative proteinuria; SCD, standard criteria donor

Table 2. Characteristics of Recipients of Kidneys from Expanded Versus Standard Criteria Donors

	SCD (n = 107)	ECD (n = 50)	*P* Value
Age at time of transplant, years	46.9 ± 11.5	51.3 ± 10.4	.020
Male patient, %	57.4	82	.002
Cold ischemia duration, min	687.2 ± 336.5	666.5 ± 253	.694
No induction, %	13.8	28.3	.027
Induction of basiliximab/daclizumab, %	77.7	47.8	< .001
Induction with ATG, %	8.6	23.9	.007
Tacrolimus, %	79.2	84.8	.410
Cyclosporine, %	20.8	15.2	.410
Revision due to bleeding, %	6.2	6	.960
Lymphocele, %	5.4	0	.095
Ureter stricture, %	5.4	2	.324
Primary function of graft, %	82.9	72	.104
Delayed graft function, %	10.9	14	.565
Acute rejection within 12 mo posttransplant	20.2	18	.740
Acute rejection > 12 mo posttransplant	27.1	38	.155
Day 7 creatinine, µmol/L	218 ± 185	287 ± 238	.041
Month 1 creatinine, µmol/L	143 ± 42.9	163 ± 44.2	.006
Month 3 creatinine, µmol/L	148 ± 39.9	172 ± 44.9	< .001
Month 6 creatinine, µmol/L	142.9 ± 45.5	163 ± 44.9	.009
Year 1 creatinine, µmol/L	133.6 ± 40.6	161 ± 62.4	< .001
Year 3 creatinine, µmol/L	130.7 ± 37.4	149 ± 41	.005
Year 5 creatinine, µmol/L	127.6 ± 28.4	146 ± 41.8	< .001
Month 1 eGFR, mL/s	0.74 ± 0.19	0.67 ± 0.18	.026
Month 3 eGFR, mL/s	0.71 ± 0.18	0.63 ± 0.17	.007
Month 6 eGFR, mL/s	0.74 ± 0.20	0.69 ± 0.21	.011
Year 1 eGFR, mL/s	0.80 ± 0.21	0.71 ± 0.21	.141
Year 3 eGFR, mL/s	0.80 ± 0.17	0.75 ± 0.21	.108
Year 5 eGFR, mL/s	0.80 ± 0.19	0.78 ± 0.22	.547

Abbreviations: ATG, antithymocyte globulin; ECD, expanded criteria donor; eGFR, estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology Collaboration formula; SCD, standard criteria donor

Figure:

P1691 **URINARY CXCL10 AT SIX AND TWELVE MONTH PREDICTS SUBCLINICAL ANTIBODY MEDIATED REJECTION AT 1 YEAR**

Alvaro Arnau[1], Adalberto Benito Hernandez[2], M Angeles Ramos Barron[2], José Luis Pérez Canga[2], Covadonga Lopez del Moral Cuesta[2], Marcos López-Hoyos[3], Rosalía Valero San Cecilio[2], Juan Carlos Ruiz San Millán[2], Emilio Rodrigo[2]

[1]Hospital Universitario Donostia, Nephrology, Donostia, Spain, [2]Hospital Marqués de Valdecilla-IDIVAL, University of Cantabria, Nephrology, SANTANDER, Spain and [3]Hospital Marqués de Valdecilla-IDIVAL, University of Cantabria, Immunology, SANTANDER, Spain

Background and Aims: Despite the improvement in renal transplant results, the rate of graft loss from the first year has improved poorly, antibody-mediated rejection (AbMR) being the first cause of renal graft loss. Renal transplantation is usually monitored by measuring creatinine, proteinuria, immunosuppressive blood levels and, recently, donor specific antibodies and polyomavirus load. However, currently the only way to detect the alloimmune graft damage is to perform a surveillance o by indication renal biopsy. Non-invasive monitoring of the alloimmune response could contribute to improving renal transplant results. Previous studies have shown that urinary CXCL10 relates to both clinical and subclinical allograft rejection and graft loss. Our aim was to analyze the relationship between urinary CXCL10 and the biopsy findings of 1-year surveillance biopsies.

Method: From Dec/2013 to Nov/2017 90 surveillance biopsies were performed in our center at 1 year after kidney transplantation. Urine were prospectively collected at 6 and 12 month and urine samples were frozen at -70°. CXCL10 was measured by using human CXCL10/IP-10 DuoSet ELISA kits (R&D Systems) according to the protocols recommended by the company. Biopsies were classified according to Banff criteria.

Results: Median values of CXCL10 were 51.2 pg/ml (IQR 38.5 – 98.9 pg/ml) at 6 month and 62.8 pg/ml (IQR 42.7 – 99.4 pg/ml) at 12 month after transplantation. Both values were statistically related ($r = 0.400$, $p = 0.012$), and there were no significant statistical differences between both (Wilcoxon's test $p = 0.063$). CXCL10 did not relate to serum creatinine, glomerular filtration rate, albuminuria, tacrolimus blood levels or prednisone dose at 1 year. Some 16.7% allograft biopsies showed subclinical cellular rejection, 26.7% showed antibody mediated rejection and 20.0% transplant glomerulopathy. Patients with antibody mediated rejection (AbMR) had higher levels of 1-year urinary CXCL10 [55.4 pg/ml (IQR 39.3) vs. 97.4 pg/ml (IQR 103.9), $p = 0.021$], lower GFR [68.0 ml/min/1.73m^2 (IQR 33.5) vs. 43.5 ml/min/1.73m^2 (IQR 22.8), $p < 0.001$] and similar albuminuria ($p = 0.079$). According to ROC curve, 1-year urinary CXCL10 could discriminate patients with subclinical AbMR (AUC-ROC 0.660, 95%CI 0.511-0.809, $p = 0.021$). After adjusting by GFR and albuminuria, 1-year urinary CXCL10 in a logarithmic scale was able to predict subclinical AbMR (OR 2.254, 95%CI 1.012-5.021, $p = 0.047$) by logistic regression analysis. Similarly, patients with subclinical AbMR at 1 year had higher levels of 6-month urinary CXCL10 [45.9 pg/ml (IQR 41.4) vs. 102.3 pg/ml (IQR 1935), $p = 0.026$]. Moreover, 6-month urinary CXCL10 could discriminate those patients who were going to show subclinical AbMR at 1-year (see figure; AUC-ROC 0.731, 95%CI 0.545-0.916, $p = 0.027$). After logistic regression, each tertil of 6-month urinary CXCL10 increased the risk of suffering subclinical AbMR more than thrice (OR 3.346, 95%CI 1.184-9.456, $p = 0.023$).

Conclusion: Both 6- and 12-month urinary CXCL10 relate to the diagnosis of subclinical AbMR by 1-year surveillance biopsies independently of other variables such as renal function and albuminuria. Of interest, by a non-invasive monitoring of urinary CXCL10 as early as at 6 months we can predict some subclinical histologic findings at 1 year, such as AbMR, that can have a strong impact on the transplant outcome.

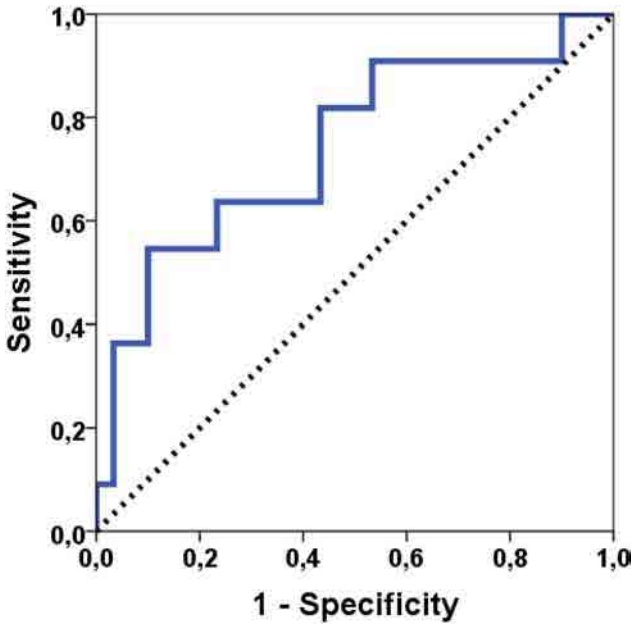


Figure:

P1692 **CANCER-RELATED EPIDEMIOLOGY AND OUTCOMES IN KIDNEY ALLOGRAFT RECIPIENTS FROM TWO TRANSPLANT CENTRES IN ITALY**

Letizia Zeni[1,2], Pietro Manuel Ferraro[2,3], Giuseppina D'Ettorre[4], Simona Simone[4], Loreto Gesualdo[4], Franco Citterio[3,5], Giuseppe Grandaliano[2,3]

[1]Università degli Studi della Campania "Luigi Vanvitelli", Caserta, Italy, [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Nefrologia, Roma, Italy, [3]Università Cattolica del Sacro Cuore, Roma, Italy, [4]Università degli Studi di Bari "Aldo Moro", Dipartimento Emergenza e Trapianti di Organi, Bari, Italy and [5]Fondazione Policlinico Universitario A. Gemelli IRCCS, U.O.C. Trapianti di Rene, Roma, Italy

Background and Aims: One of the major immunosuppression-related complications of kidney transplant (KT) is the increased risk of cancer development. KT patients have at least a twofold higher risk of developing or dying from cancer than the general population. Indeed, malignancy is currently the second most common cause of death after cardiovascular disease in these patients. After the substantial rise in post-transplant graft survival in the last decades, the present study aims to evaluate the post–KT cancer incidence, the mortality risk and associated risk factors in two transplant centres over a long period of time.

Method: A retrospective cohort study used clinical and epidemiological information among KT patients transplanted between 1993 and 2017 in two renal transplant centres in Italy and diagnosed with *de novo* cancers (DNC). Data on vital status and graft loss were available for most subjects and assessed in December 2019. Survival analyses were performed using parametric survival models assuming a Weibull distribution of the baseline hazard; these models were used to test the association between predictors measured at baseline and a) time from KT to development of DNC, and b) time from development of DNC to death, loss to follow-up or administrative censoring, whichever occurred first. Hazard ratios (HR) and 95% confidence intervals (CI) were obtained. Kaplan–Meier curves were generated. A p-value < 0.05 was considered as statistically significant. Data were analyzed using Stata.

Results: In the present study, 201 DNCs were diagnosed in subjects who underwent KT between 1993 and 2017. Median follow-up after kidney transplantation was 12.1 years (IQR: 7.0–17.5). The proportion of subjects who received allograft from deceased donor was 89%, 61% had 4 or more mismatches, 68% were male. At the time of KT, the average age was 52.4±12.3 years and renal replacement therapy (RRT) vintage was 39 months (IQR: 22–69). The incidence rate of DNC for the whole cohort was 145 per 1,000 person-years, with a median time to cancer from KT of 5.5 years (IQR: 2.8–10.5) [Figure 1]. Skin cancers accounted for most cases (59%), followed by solid tumors (30%), post-transplant lymphoproliferative disorders (6%), Kaposi's sarcoma (3%) and other malignancies (2%). In the multivariable model, increasing age was significantly associated with time to development of DNC (HR for 1 year 1.03, 95% CI 1.01, 1.04; p = 0.001). Induction therapy with a combination of rabbit antithymocyte globulin and basiliximab resulted to be a risk factor for time to DNC (HR compared with none 3.16, 95% CI 2.04, 4.91; $p < 0.001$). None of the following pre- and peri-transplant predictors was significantly associated with time to DNC: RRT vintage and technique, episodes of acute rejection, chronic kidney disease etiology, presence of delayed graft function, type of donor (deceased or living), number of mismatches. The incidence rate of death for the whole cohort was 47 per 1,000 person-years [Figure 2]. According to type of cancer, death incidence rate was 73, 56, 34 per 1,000 person-years for solid tumors, non-solid and non-skin tumors (i.e PTLD, Kaposi and other tumors) and skin cancer, respectively. In multivariable analysis, age at time of cancer (HR for 1 year 1.04, 95% CI 1.00, 1.07; p = 0.037) and previous acute rejection (HR 2.51, 95% CI 1.23, 5.11; p = 0.011) were significantly associated with time to death.

Conclusion: In a large sample of KT recipients with DNC, age and type of induction therapy were significantly associated with time to development of cancer. Age and previous acute rejection were significant predictors of death after DNC. Epidemiological studies could help in risk estimation of graft and patient survival after cancer development and guide in post KT clinical care.

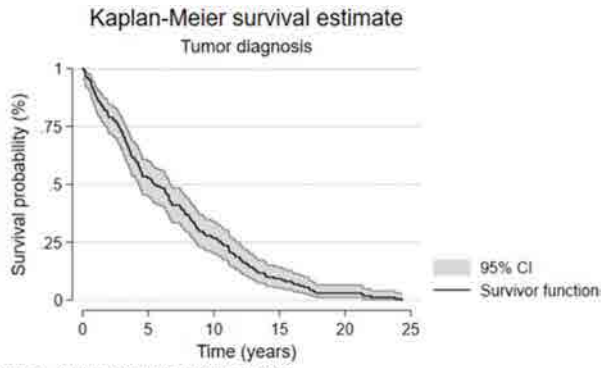


Figure 1. Kaplan–Meier plot of time to DNC

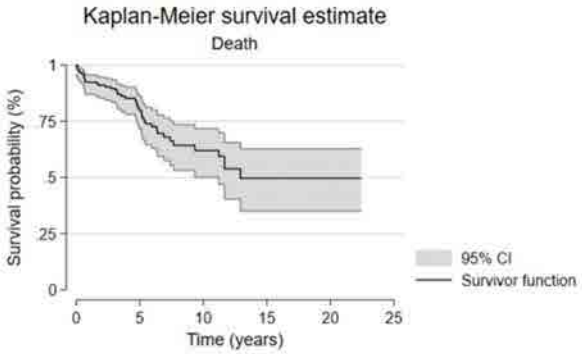


Figure 2. Kaplan–Meier plot of time to death

Figure:

P1693 LONG-TERM OUTCOME OF KIDNEY TRANSPLANTATION IN PLASMA CELLS DYSCRASIAS

Fulvia Zappulo[1], Gabriele Donati[1], Giorgia Comai[1], Claudia Bini[1], Andrea Angeletti[1], Anna Scrivo[1], Elena Zamagni[2], Michele Cavo[2], Gaetano La Manna[1]

[1]Nephrology, Dialysis and Renal Transplant Unit, S. Orsola Hospital, University of Bologna, Department of Experimental Diagnostic and Specialty Medicine (DIMES), Bologna, Italy and [2]Institute of Hematology and Medical Oncology, Seràgnoli, University of Bologna, Bologna, Italy

Background and Aims: Survival of patients with Multiple Myeloma (MM), Light Chain Amyloidosis (LCA) and Monoclonal Gammopathies of renal significance (MGRS) on chronic renal replacement therapy (RRT) is poor. The gold standand treatment of plasma cell dyscrasias (PCD) is high-dose chemotherapy followed by Autologous Stem Cell Transplantation (ASCT) which can induce complete remission and longer survival than chemotherapy alone. Kidney transplantation (KT) after ASCT could represent an option for patients with PCD and End Stage Renal Disease (ESRD). There is no evidence about the time of follow up required from MM remission and KT.

Method: We present a case series of 5 patients who underwent KT after ASCT and remission of MM among 2,500 transplant recipients followed at the Nephrology Dialysis and Renal Transplantation Unit of S.Orsola University Hospital from 1967 untill now. As in case of recovery from solid cancers, the feasibility of KT after MM was considered when no signs of relapse were assessed. In our cohort 3 patients were affected by Light Chain Deposition Disease (LCDD), 1 patient presented Myeloma Cast Nephropathy (MCN) and one patient Light Chain Amyloidosis (LCA). They all required RRT and underwent KT after ASCT.

Results: Time between ASCT and KT ranged from 3 and 11 years and clinical outcome was very different. The mean follow up period ranged from 2 to 4 years. In the first case (LCDD) KT was performed 11 years after ASCT, the graft failure occurred 6 years later because of chronic allograft nephropathy requiring RRT. In the second case (LCDD) patient received KT 3 years after ASCT. He developed Bence-Jones proteinuria requiring specific therapy with Dexametasone and Bortezomib determining progressive graft failure. In the third case (LCDD) KT was performed 4 years after ASCT and the 4 year follow up is negative for relapse of MM or ESRD. The fourth patient presented MCN and received KT 8 years after ASCT. MCN relapsed 6 years later; it caused ESRD requiring RRT. In the last patient (LCA) KT was performed 4 years after ASCT. No recurrence occurred in a 2-year follow up.

Conclusion: MM is the most frequent malignancy in dialytic population; the need for KT in MM remains high. ASCT improves the quality of life and offers higher survival in patients with myeloma/MGRS/amyloidosis-related ESRD. Therefore the combination of chemotherapy/ASCT and KT is pivotal to pursue renal restoring. Since high risk of recurrence larger study are required to clarify the better follow up period after MM remission and KT.

Patient	Age (years)	Sex	Nephropathy	Monoclonal Component	Therapy	Time from ASTC to KT	Follow-up	Out-come
1	54	F	LCDD	IgG/K	Dexamethasone + Etoposide +VAD	11 years	6 years	Chronic allograft nephropathyESRD
2	58	M	LCDD	IgG/K	Dexamethasone+Cyclophosphamide	3 years	8 years	Recurrence of BJ proteinuria
3	54	F	LCDD	IgG/ λ	Dexamethasone + Bortezomib	4 years	4 years	No recurrenceGraft working
4	58	M	MCN	IgA/K	Dexamethasone + Cyclophosphamide	8 years	6 years	Recurrence of MM –ESRD
5	59	F	LCA	IgA/λ	Dexamethasone+ cyclophosphamide	4 years	2 years	No recurrenceGraft working

P1694 PROGNOSTIC VALUE OF BODY COMPOSITION ON GRAFT FUNCTIONING IN KIDNEY TRANSPLANT PATIENTS

Zorica Dimitrijevic[1,2], Branka Mitic[1,2], Goran Paunovic[1], Karolina Paunovic[1], Danijela Tasic[1], Tamara Vrecic[1], Mina Cvetkovic[1], Andriana Jovanovic[1], Nina Jancic[1]

[1]*Clinical Centre of Niš, Niš, Serbia and* [2]*Медицински факултет Универзитета у Нишу*

Background and Aims: Post-transplant weight gain and particularly visceral fat gain has been linked to the development of metabolic disorders and cardiovascular disease. Moreover, the effect of obesity on graft function after kidney transplantation has recently become a subject of interest. The aim of our study was to investigate the association of body mass index (BMI), body fat percentage (BF%) and waist-to-hip ratio (WHR) with the kidney function in kidney transplant patients.

Method: We conducted a cross-sectional study that enrolled 80 kidney transplant patients aged 23–75 years (mean age 46.7 ± 11.5 years, 60% males). Anthropometric measurements of weight, height, waist, and hip circumferences in addition to skinfold thickness were obtained. BH% was calculated using a 4-site skinfold thickness method calculated through the Jackson-Pollock equation with a Harpenden caliper, utilizing a BF% cutoff of 35% for women and 25% for men to define obesity.

Results: The calculated BMI in our study group was 32.7±8.7 kg/m^2, a mean BF% of 29.9±8.5% and a mean WHR of 0.9±0.1 Statistically significant difference in GFR, BMI, WHR and BF% were observed between males and females (r=0.455, p=0.02; r=0.412, p=0.016; r=0.437, p=0.022; r=0.348, p=0.011), respectively. After adjustment for age, gender, donor group, donor age and years of dialysis before transplantation, higher levels of all obesity measures were related to lower eGFR: BMI per 1 SD (β coefficient −3.883, 95% confidence interval [CI] −5,422 to −3,132), WHR (β coefficient −4.443, 95% CI −6.201 to −3.772), and BF% (β coefficient −3.722, 95% CI −4.332 to −3.461). The combination of higher BF% (BF% >33 kg/m^2) and central obesity (WHR >0.85 for women, >0.90 for men) was associated with the lowest eGFR compared with that in lean subjects.

Conclusion: The combination of high BF% and WHR may be an important risk factor for lower GFR in a kidney transplant recipient.

P1695 **OUTCOMES OF KIDNEY TRANSPLANTATION IN RECIPIENTS WITH MENTAL RETARDATION**

DAMLA ORS SENDOGAN[1], SIYAR ERDOGMUS[1], Gizem Kumru Şahin[1], SAHIN EYUPOGLU[1], Rezzan Eren Sadioğlu[1], ACAR TUZUNER[2], Kenan Keven[1], SULE SENGUL[1]

[1]Ankara University Faculty of Medicine, Neprology, Ankara, Turkey and [2]Ankara University Faculty of Medicine, Surgery, Ankara, Turkey

Background and Aims: Mental retardation in patients with chronic kidney disease is a relative contraindication for kidney transplantation. Currently, in the literature there are limited outcome data in renal transplant recipients with mental retardation and approaches to decision of transplantation changes in different centers. The aim of this study is to evaluate the results of kidney transplantation recipients with mental retardation in our center.

Method: In this study, we examined retrospectively 8 kidney transplant recipients with mental retardation in Renal Transplantation Unit of Ankara University School of Medicine between 2006-2018 years.

Results: The cause of mental retardation in these patients were; genetic syndromes in three patients, meningoencephalitis in one patient, prematurity in one patient, and chromosomal abnormality in one patient. In two patients, the cause of mental retardation is unknown. All patients had good social support for drug compliance and follow-up.

The causes of end-stage renal failure were; cystic kidney disease in three patients, hypertensive nephropathy in one patient and vesicoureteral reflux in one patient. In three patients, the etiology of kidney disease is unknown. At the time of pretransplantation period evaluation, six candidates were receiving hemodialysis and two candidates were receiving peritoneal dialysis respectively. Mean dialysis duration before transplantation was 50.7±22.8 months (min 4-max 180). Cadaveric kidney transplantation was performed in three of eight patients (deceased donor kidney allocated to patient with medical urgency in the event of potential imminent loss of dialysis access in one patient and in normal conditions in two patients) and living kidney transplantation was performed in five patients. The mean follow-up period after transplantation was 54.1±48.0 months. Three patients had early posttransplant complications; including urinary tract infection in three patients, deep vein trombosis in one patient and cardiopulmoner arrest with septic shock secondary to femoral graft infection and parailiac abscess in one patient (Table). No patients underwent graft biopsy and no patients experienced acute rejection episode. At the end of the follow-up time, graft and patient survival were 100%.

Conclusion: Mental retardation is not a contraindication for kidney transplantation in candidates without the history of noncompliance with proper social support.

Table. De mographic Characteristics and Outcomes Data of Patients After Kidney Transplantation:

Patient No	Age of tx (year)/ sex	Cause of MR	Pretx Dialysis Mode / Duration (mo)	Type of Tx / Duration of follow-up (mo)	Initial IS	Posttx Complications	AR
1.	19, F	Genetic syndrome (Senior-Löken Syndrome)	HD/11	Living/156	CS+AZT+TAC	None	None
2.	40, M	Unknown	HD/13	Living/52	CS+MMF+TAC	None	None
3.	21, M	Genetic syndrome (Retinitis pigmentosa)	HD/60	Living/95	CS+MMF+TAC	DVT	None
4.	23, F	Unknown	PD/13	Living/37	CS+MMF+TAC	UTI	None
5.	36, M	Down syndrome	HD/10	Living/36	CS+MMF+TAC	UTI	None
6.	49, F	Meningoencephalitis	HD/168	Deceased /36	CS+MMF+TAC	Femoral graft infection, parailiac abscess, septic shock, cardiopulmoner arrest	None
7.	35, F	Prematurity	HD/11	Deceased /23	CS+MMF+TAC	None	None
8.	19, F	Genetic syndrome (Joubert syndrome)	PD/108	Deceased /11	CS+MMF+TAC	UTI	None

CS: corticosteroid, DVT: deep vein trombosis, HD: hemodialysis, İS: immunsupression, MMF: mycophenolate mofetil, MR: mental retardation, PD: peritoneal dialysis, TAC: tacrolimus, UTİ: urinary tract infections, VUR: vesicoureteral reflux

P1696 VASCULAR CALCIFICATION IN RENAL TRANSPLANTED PATIENTS

Ana Carina Ferreira[1,2], Marco Mendes[1,2], Cecília Silva[1], Patrícia Cotovio[1], Inês Aires[1,2], David Navarro[1], Fernando Correia Caeiro Pereira[1,2], Rúben Ramos[3], Rute Salvador[4], Bruna Correia[4], Guadalupe Cabral[4], Fernando Nolasco[1,2], Manuel Anibal A. Ferreira[1,2]

[1]Hospital Curry Cabral, Nephrology, Lisboa, Portugal, [2]Nova Medical School, ., Lisboa, Portugal, [3]Santa Marta Hospital, Cardiology, Lisboa, Portugal and [4]CEDOC, Tissue Repair and Inflammation Lab, Lisboa, Portugal

Background and Aims: Chronic kidney disease – mineral and bone disorder (CKD-MBD) is a well-known syndrome in end stage renal disease. Vascular calcifications are one of its components. Renal transplantation seemed to halt the progression of vascular calcifications.

The aim of this study was to analyse the progression of vascular calcifications in a cohort of renal transplanted patients, and the associations of those with the old and new bone-derived hormones.

Method: We performed a prospective cohort study of a consecutive sample of *de novo* single renal transplanted patients in our unit. All patients were submitted to a bone biopsy and laboratorial evaluation at baseline (time 0) including measurements of calcium (Ca), phosphorus (Pi), magnesium (Mg), vitamin D (vitD), calcitonin, parathyroid hormone (PTH), bone alkaline phosphatase (bAP) and total alkaline phosphatase (tAP), alpha-klotho, fibroblast grow-factor 23 (FGF23) and sclerostin. Patients were followed for 12 months, after which performed a second bone biopsy and laboratorial evaluation (time 1). At inclusion, demographic, clinical and transplant-related data were collected, X-ray of the pelvis and hands (Adragão score) and echocardiographic findings were recorded. At the end of the study, echocardiogram, X-ray of pelvis and hands, bone densitometry and non-contrast cardiac CT (Agatston score) were performed. Immunosuppression included induction therapy followed by tacrolimus, mycophenolate mofetil and prednisolone. Continuous variables are presented as medians and categorical variables as frequencies. Associations between variables were performed using Wilcoxon rank sum test and Spearman correlation test. STATA software was used and $p < 0.05$ was considered statistically significant.

Results: We recruited 85 patients from 1st October 2015 to 1st March 2018. Mean age 50.1 ± 12.7 years, 59 men (69.4%), 66 caucasian (77.6%), median BMI 25.1 ± 3.4. At the end of 12 months, 6 patients refuse to perform the 2nd evaluation, 5 had primary non-function of the kidney graft, 1 had no sample on bone biopsy in time 0 and 4 patients died. We performed a 2nd evaluation in 69 patients and included those in this study.

The median baseline and 12 months Adragão score had no differences [1 (0 – 2)]. The median coronary artery calcium score was 48.5 (0 – 535) and median percentile was 80 (0 – 92.5). Valvular calcifications were present in 15 and 16 patients at baseline and after 1 year respectively, with no statistical difference between the two time points.

Coronary artery calcium scores were correlated with age ($p<0.001$), two time points Adragão score ($p<0.001$), presence of valvular calcification in time 1 evaluation ($p=0.004$), baseline calcium ($p=0.02$), baseline and 1-year sclerostin ($p=0.01$; $p=0.04$). Coronary artery calcium scores were higher in patients with highest values of FGF23 at baseline ($p=0.04$). Using a pairwise correlation, vitamin D levels ($r=0.4$, $p=0.0004$), iPTH ($r=0.6$, $p<0.001$) and total cholesterol levels ($r=-0.3$, $p=0.01$) were correlated with the score. Coronary calcium Percentile (adjusted for age, gender and race) was correlated with Adragão score in the two time points ($p=0.0001$; $p=0.002$), with presence of valvular calcifications in time 1 evaluation ($p=0.02$), baseline and 1-year calcium serum levels ($p=0.004$; $p=0.02$) and baseline sclerostin ($p=0.01$).

Conclusion: In conclusion, vascular calcifications stabilize after renal transplant. Adragão score, that is a less expensive exam than cardiac CT, can assess vascular calcifications in renal transplanted patients. Only calcium and sclerostin correlated with both Agatston scores and coronary calcium percentiles.

P1697

MULTI- NATIONAL SURVEY AMONG NEPHROLOGISTS AND TRANSPLANT SURGEONS ABOUT THE SUITABILITY AND ACCEPTABILITY OF MARGINAL LIVE KIDNEY DONORS WITH OBESITY OR ABNORMAL BLOOD SUGAR PROFILE

Ziad Arabi[1], Mohammad Bukhari[2]

[1]Adult Transplant Nephrology, The Organ Transplant Center, King Abdulaziz Medical City, King Abdullah International Medical Research Center & King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia and [2]University of Taif, Department of Nephrology, Taif, Saudi Arabia

Background and Aims: There are no clear guidelines about the suitability and acceptance of living- kidney donors with obesity or abnormal blood sugar profile.

Method: To form a consensus about the acceptance of these donors, a survey was distributed to nephrologists and transplant surgeons in different countries and through AST and ERA-EDTA.

Results: Of a total of (n=122) respondents from 22 countries: 80% (N= 96) were nephrologists and 20% (N=23) were transplant surgeons. The majority were heavily involved in pre-transplant evaluations of donors and recipients and have > 6 years in practice. 75% of the respondents will accept obese donors (BMI 30-35) if donors show some weight loss before donation or at least show commitment to lose weight in the future. However, the presence of a strong family history of diabetes (DM) in obese donors (even with normal fasting blood sugar (FBS) and hemoglobin A1C [Hgb A1C]) mandates weight lose preferably to BMI of 30 (n=46, 38%) or at least to lose some weight before being considered for donation (n=30, 25%). On the other hand, morbidly obese donors (BMI 36-40) with normal FBS, Hgb A1C and negative family history of DM thought to need to decrease their weight to BMI 30 (47% of the respondents) or at least lose some weight before being considered for donation (n=30, 25%). However, 22% of the respondents would decline these donors due to the risk of relapse of obesity. If an obese donor started to have impaired fasting blood sugar (IFG), the majority (47%) will decline him/her because of the higher risk to develop DM. (33%) will delay the donation till BMI reaches below 30 and IFG is resolved as a result of weight reduction. Most of the respondents (52%) will not rely solely on isolated mildly elevated Hgb A1C (e.g. Hgb A1C = 5.7- 6) or isolated (IFG) as the critical indicator to decline a young donor with normal weight and normal FBS. Instead 2hrs- glucose tolerance test will be indicated. The presence of even mild and controlled diabetes in a middle age (e.g. 55 years old donor) thought to be a contraindication for kidney donation in 62% of the respondents. However, such donors might be allowed to donate if no alternative donor is available after clearly explaining the risks (23%). In regard to resolved DM after bariatric surgery and weight loss, 43% of the respondents said they will consider them for donation if two years passed after bariatric surgery without obesity relapse (43%). Up to one forth may consider these donors earlier (once BMI is below 30). Despite the surgical difficulties related to obesity in kidney donors, transplant surgeons seem more likely than nephrologists to accept obese donors (P= 0.046), morbidly obese (P=NS).

Conclusion: Living kidney donors with isolated obesity, (IFG), mildly abnormal HgbA1C or history of bariatric surgery are still considered for kidney donation by many centers. However, donors with more than one abnormality especially at young age are not considered for donation.

Figure:

P1698

MULTI- NATIONAL SURVEY AMONG NEPHROLOGISTS AND TRANSPLANT SURGEONS ABOUT THE SUITABILITY AND ACCEPTANCE OF MARGINAL LIVE KIDNEY DONORS WITH MILD HYPERTENSION

Ziad Arabi[1], El Waleed El Hassan[2], Abdulrahman Altheaby[3], Abdullah Hamad[4], Kaysi Saleh[5]

[1]King Abdulaziz Medical City, King Abdullah International Medical Research Center & King Saud Bin Abdulaziz University for Health Sciences, Adult Transplant Nephrology, Organ Transplant Center, Riyadh, Saudi Arabia, [2]King Abdulaziz Medical City, Department of Nephrology, Riaydh, United States of America, [3]King Abdulaziz Medical City, King Abdullah International Medical Research Center & King Saud Bin Abdulaziz University for Health Sciences, Adult Transplant Nephrology, Organ Transplant Center, Riaydh, Saudi Arabia, [4]The Regional Medical Center, Orangeburg, SC,, United States of America and [5]CHU Clermont-Ferrand,, Saint Pryv/ Saint Mesmin, France

Background and Aims: There is variability among transplant centers in the acceptance of living donor candidates with well-controlled hypertension. Increased gestational hypertension and preeclampsia are more common in donors than in the general population especially if the donor is hypertensive at baseline. The purpose of this survey is to form a consensus about the evaluation of marginal live kidney donors (women and men) with hypertension.

Method: This is a cross-sectional survey of nephrologists and transplant surgeons about Suitability and Acceptance of The Marginal live Kidney Donors. The survey was sent to nephrologists in different countries and it was also distributed through AST & ERA-EDTA.

Results: A total of 122 practitioners from 22 countries responded to the survey. Of those, (N=96, 80.2%) were nephrologists and (n=23 19.83%) were transplant surgeons. The majority (45%) of the respondents were from USA. Most of the respondents (N=85, 69.7%) would allow a multiparous female (MPW) with mild and controlled hypertension (on a single blood pressure medication) who is not planning to have more children to donate. The rest would either advise against donation unless there is no alternative donor (n=23, 18.85%), or decline it altogether (n=14, 11.5%). In contrast, more respondents would reject a primiparous donor woman (PPW) with the same clinical scenario who considers having children (n=51, 42.2%, P=0.00001), or accept it only if there is no alternative donor (n=46, 38.0%, P=0.0009). Furthermore, most would not allow donation of a 20 years old male (M) with an apparent white coat hypertension if his 24-hour ambulatory blood pressure monitoring shows non-dipping nocturnal pattern (n=67, 54.9%), or only accept it if there is no alternative donor (n=36, 29.5%). When comparing the rejection rate among the three donors: 11% for MPW, 41% for PPW and 54% for M. (P = 0.0001 for MPW vs PPW; P=0.00001 for MPW vs M; P=0.04 for PPW vs M).

Conclusion: Most of the nephrologists and transplant surgeons will clear mulptiparous women with mild and controlled hypertension for kidney donation as long as there no further plans for pregnancy. However, the majority of respondents will not clear a hypertensive primiparous due to the increased risk of gestational hypertension and pre-eclampsia after kidney donation. Most would be also reluctant to accept very young male donors if they show indicators of higher risk of developing hypertension in future.

Figure:

P1699 **EFFECT OF UREMIA IN THE POSTOPERATIVE OF PREEMPTIVE LIVING-DONOR KIDNEY TRANSPLANT PATIENTS**

Alã-cia Molina Andã°jar[1], Elena Cuadrado[1], David Cucchiari[1], Erika De Sousa[1], Federico Oppenheimer[1], Fritz Diekmann[1], Ignacio Revuelta[1]

[1]*Hospital Clínic de Barcelona, Barcelona, Spain*

Background and Aims: Getting a preemptive kidney transplant has many benefits but no studies have assessed the potential deleterious effect of uremia on peritransplant complications. Uremic toxins interact negatively with biologic functions and may contribute to infections and bleeding or thormbosis.

Method: we evaluated 255 living-donor kidney transplant recipients (117 preemptive and 138 non-preemptive) from January 2006 to December 2015. Patients iniciated immunosuppression treatment 3 days prior to transplant. Exclusion criteria included: history of solid organ transplant, chronic immunosuppression treatment at the time of transplant (including prednisone), peritransplant rituximab/eculizumab treatment and HIV infection. An analysis of baseline characteristics and the incidence of symptomatic infection, bleeding or thrombosis during first week was performed in both groups. To analyze bleeding, the need of transfusion, drop of hematocrit in 72h and need of bladder washout was assessed.

Results: baseline characteristics are descrived in table 1. Non preemptive patients were older (50 vs 46 years) and had a higher prevalence of Diabetes Mellitus and dialypemia (22 vs 11% and 43 vs 30% respectively), without differences in the immunosupression scheme. The median eGFR in preemptive group at transplant was 12 ml/min. A more anemic profile was detected in the preemptive group with median hemoglobin of 116 vs 127 g/L in the non-preemptive group with no-differences in albumin levels. There were a total of 38 symptomatic infections (22 in the preemptive and 16 in the non-preemptive group), without statistical differences in the incidence between the groups (OR 1,75 CI 0,879-3,5, P =0,107). Hematocrit drop was greater in the non-preemptive group (8 vs 6 points in the first 72h p = 0.004) but thrombosis was more common in the preemptive group (5 vs 1, OR 6,116 CI 0,704-53,1, p = 0.062).

Conclusion: Uremia in preemptive living kidney transplant recipients does not seem to have influence on the incidence of infections in the first week after transplantation. The bleeding profile in the non-preemptive group in contrast to the prothrombotic profile in preemptive recipients needs further investigation in future studies that assess parameters of platelet and coagulation function as well as endothelial activation.

	Preemptive (n=117)	Non-preemptive (n=138)	P value
Sex (%males)	67 (57,3)	87 (63)	0,37
Age (SD)	45,7 (14)	49,7 (14,4)	**0,027**
Days from 1st visit to transplant (IQR)	133 (88-201)	160 (76-296)	0,891
eGFR -6m (IQR)ml/min	15 (13-19,7)		
eGFR -3m (IQR)ml/min	14 (12-18)		
GFR at transplant (IQR)ml/min	12 (10-15)		
Albumin (IQR) g/L	42 (39-44)	41 (38-44)	0,276
DM (%yes)	13 (11,1)	31 (22)	**0,017**
HTA (%yes)	91 (77,8)	118 (85)	0,11
Dyslipemia (%yes)	35 (29,9)	60 (43)	**0,026**
Cause of nephropathy	36 (30,8) Glomerulonephritis 25 (21,4) Polycystic kidney disease 19 (16,2) unknown	33 (23,9) Glomerylonephritis 25 (18,1) unknown 21 (15,2) Diabetes	0,151
Anticoagulantion or antiplatelet treatment (%yes)	2 (1,7) Anticoagulant 9 (7,7) AAS 2 (1,7) Clopidogrel	1 (1) Anticoagulant 28 (20) AAS 7 (5) Clopidogrel	0,467 **0,004** 0,184
Tacrolimus levels at transplant (IQR)	8,6 (5,6-11,9)	9,5 (6,2-13,9)	0,081
Induction therapy (%)	63 (53,8) basiliximab 31 (26,5) thymoglobulin 21 (17,9) no induction 2 (1,7) other	72 (52,2) basiliximab 37 (26,8) thymoglobulin 27 (19,6) no induction 2 (1,7) other	0.978
Immunosupression scheme (%)	89 (76) CNI + MPA 24 (20,5) CNI + iMTOR 4 (3,4) other	110 (79,7) CNI + MPA 28 (20,3) CNI + iMTOR	0.833
Blood test (IQR)	Hemoglobin: 116 (106-126) g/L Hematocrit: 36 (33,5-39)L/L Platelets: 200000 (165500-259000)/L Prothrombin time: 93 (84-100)%	Hemoglobin: 127 (115-140) g/L Hematocrit: 39 (35-43)L/L Platelets: 202500 (169000-246000)/L Prothrombin time: 92 (85.7-99.9)%	**<0.001** **<0.001** 0.772 0.662
Days in Renal Replacement therapy (IQR)		436 (154-1004)	

Figure

P1700

CYTOMEGALOVIRUS DISEASE IN RENAL TRANSPLANTED PATIENTS: DETERMINING FACTORS AND ITS RELATION WITH GRAFT OUTCOME AND PATIENTS SURVIVAL

Carlo Maria Alfieri[1,2], Paolo Molinari[1], Maria Teresa Gandolfo[1], Maria Rosaria Campise[1], Donata Cresseri[1], Valentina Binda[1], Piergiorgio Messa[1,2]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Nephrology, dialysis and renal transplantation, Milano, Italy and [2]University of Milan, Department of Clinical Sciences and Community Health, Milano, Italy

Background : CMV disease (CMVd) is a frequent complication in renal transplanted patients (RTxp), especially during the first year of transplantation (RTx). CMVd impacts on long term graft and patients outcomes is still debated. Our observational retrospective study aims to evaluate: 1) the prevalence of CMVd during the first year of RTx; 2) the factors related to CMVd; 3) the relationship between CMVd and early and long term graft and patients survival.

Method In 505 RTxp (age: 50[41;58]yrs – 292 males), up to the 616 transplanted in our unit between 2004 and 2016, clinical, blood and urinary parameters were recorded after 1 (T1) and 12 (T12) months of RTx. eGFR was estimated by MDRD formula. Donor (D) and Recipient (R) CMV serology was tested at the moment of RTx. CMV IgG-D+/IgG-R- RTxp (12%) and high risk patients (second or more RTx, ATG induction therapy), received prophylaxis therapy until the 3rd month of RTx. CMVd, was defined by the presence either of CMVr (CMV replication without clinical signs of CMV disease) or CMVs (CMV replication with signs of disease and/or need of antiviral therapy/reduction of immunosuppressive therapy). Median follow up (FU) was 8[5-11]yrs. The following outcomes were investigated: 1) graft: reduction of eGFR >20% between T1 and T12; reduction of eGFR >50% between T1 and end of FU (eGFRr>50%); graft loss (GL); eGFRr>50% + GL.; 2) RTxp survival at the end of FU.

Results Ninty percent of RTxp had a kidney from a deceased D; 73% and 21% received haemodialysis (HD+) and peritoneal dialysis before RTx. Dialysis vintage was 50[33-75] months. In 12% of RTxp, induction therapy included ATG. Cumulative steroids dose was 880[840-105]mg and 2272[2598-3223]mg at T1 and T12 respectively. During the first year of RTx, 45% of patients had CMVd (CMVd+). CMVd+ were older than CMV free RTxp (CMVd-). Female gender, HD+ and CMV IgG-D+/IgG-R- were more prevalent in CMVd+. In addition, at T1, CMVd+ had lower albumin, haemoglobin and higher PTH, uric acid and reactive C protein levels than CMVd- and, both at T1 and T12, received higher steroid dose. In multivariate analysis, albumin-T1 was the most significant modifiable factor in determining CMVd+ (p=0.009 OR 0.50 – IC 0.29-0.84). Albumin-T1 maintained its significance also after the addiction of CMV serology IgG-D+/IgG-R- to the model (albumin T1: p=0.008 OR 0.48 – IC 0.29-0.84; CMV serology IgG-D+/IgG-R-: p=0.01 OR 2.16 – IC 1,18 -3,95). Among CMVd, 19% and 25% had respectively CMVr and CMVs. CMVs were characterized by lower dialysis vintage and higher prevalence of CMV IgG-D+/IgG-R- than CMVr. GL and death were observed in 11% and 8% of RTxp respectively. In univariate and survival analyses, CMVd, CMVr and CMVs didn't show any impact on the graft and patients outcomes examined.

Conclusion Our retrospective study confirms the high prevalence of CMVd during the first year of RTx, and identifies albumin at T1 as the most impacting parameter in influence CMVd insurgence. This might reflect the importance of the pre-RTx status in CMVd development after RTx. Nevertheless, CMVd seems not impact significantly on early and long term outcomes, experienced however in a small part of the cohort studied. Future studies, possibly prospective and including higher number of patients might better elucidate this issue.

P1701 **ANTIBODY MEDIATED REJECTION: CLINICAL PHENOTYPE MATTERS**

Carla Burballa Tarrega[1,2], Laura Llinás[2], Anna Buxeda[1,2], Carlos Arias Cabrales[1,2], María José Pérez Sáez[1,2], M. Dolores Redondo Pachón[1,2], Marisa Mir Fontana[1,2], Anna Faura[1], Marta Crespo Barrio[1,2], Julio Pascual Santos[1,2]

[1]Hospital del Mar. Barcelona, Nephrology Department, Barcelona, Spain and [2]IMIM – Institute Hospital del Mar for Medical Research. Barcelona, Nephrology Department, Barcelona, Spain

Background and Aims: Protocol biopsies following kidney transplantation (KT) allow the histological diagnosis of antibody-mediated rejection (ABMR) with stable renal function (RF). Controversy arises when considering isolated proteinuria as a clinical biomarker. Currently, there is no effective treatment for ABMR and transplant units may decide on treatment independently of the clinical expression.

Method: KT recipients (1987-2017) with post-KT biopsies (2008-2018) showing *ABMR* graft *lesions* (category 2-Banff 2015) >1year post-KT were included. Cases were grouped into phenotypes of ABMR according to the clinical picture at biopsy : 1) acute RF impairment (↑creatinine >15% three weeks before biopsy) with/without proteinuria and with/without DSA detection. 2) sub-acute RF impairment (↑creatinine >15% six months before biopsy) with/without proteinuria and with/without DSA detection, 3) performed for DSA detection with stable RF and no proteinuria or 4) protocol biopsy, with stable RF, no proteinuria or DSA detection. We considered an additional category: 5) isolated proteinuria (↑>500 mg or x2 six months before biopsy). Categories 1), 2) and 5) were considered clinical ABMR. Categories 3) and 4) were considered subclinical ABMR. We aimed to evaluate graft outcomes in the different ABMR phenotypes.

Results: In a cohort of 105 KT recipients with histologic lesions of ABMR, biopsies corresponded to phenotypes 1) in 35 (33%), 2) 10 (9,5%), 3) 21 (20,3%), 4) 14 (13,4%) and 5) in 25 23,8%). No differences between clinical and subclinical ABMR were found in baseline characteristics except for donors 'age, who were older within the clinical group (51.8±18.8 vs. 43.88 ±16.1; p=0.04). At time of biopsy, subclinical had better RF than clinical ABMR (creatinine 1.3±0.4 mg/dl vs. 2.2±1.1 mg/dl; p=0.02) and less proteinuria (161 mg/g [IQR 93-269] vs 939 mg/g [IQR 412-2000]; p=0.001)

Graft survival was worse in those patients with acute and sub-acute RF impairment, followed by those with isolated proteinuria (Figure 1). In comparison to subclinical ABMR, those with RF impairment and isolated proteinuria had an increased risk of graft lost; HR 9.4 (95% IC 2.2-40.7, p=0.002) and 4.8 (95% IC 1.01-23.2, P=0.05) respectively. DSA detection in these groups did not impact graft survival. Specific treatment was not different among groups, except for steroid pulses, which were more frequently applied in cases of ABMR with clinical manifestation.

Conclusion: The clinical phenotypes of ABMR influence long-term graft survival independently from treatment. Understanding graft evolution according to clinical phenotype at the time of histologic diagnosis should guide the therapeutic strategy, to balance risk-benefit ratio.

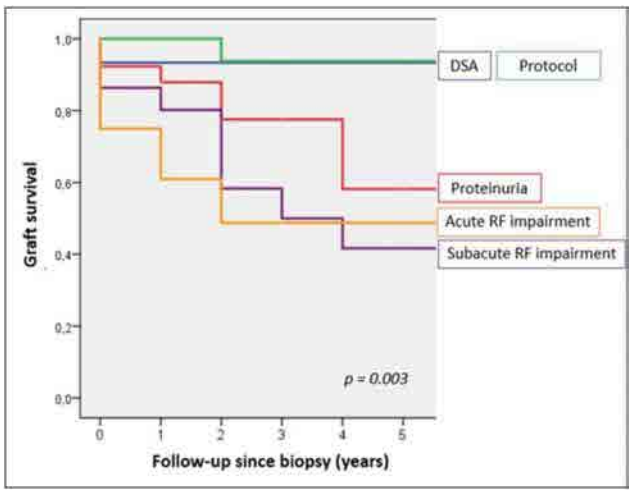


Figure:

P1702 **THROMBOTIC MICROANGIOPATHY IN KIDNEY TRANSPLANT RECIPIENTS**

Vojtěch Petr[1], Petra Hrubá[2], Roman Šafránek[3], Jarmila Dedochova[4], Karel Krejčí[5], Sona Stepankova[6], Jana Machová[7], Janka Slatinska[1], Marek Kollár[8], Eva Honsova[8], Sylvie Dusilova Sulkova[3], Ondrej Viklicky[1,2]

[1]Institute of Clinical and Experimental Medicine, Transplantcentre, Department of Nephrology, Prague, Czech Republic, [2]Institute of Clinical and Experimental Medicine, Transplant Laboratory, Prague, Czech Republic, [3]Fakultní nemocnice Hradec Králové, Hemodialysis Department, Hradec Kralove, Czech Republic, [4]University Hospital in Ostrava, Department of Medicine, Ostrava-Poruba, Czech Republic, [5]University Hospital Olomouc, 3rd Department of Medicine, Olomouc, Czech Republic, [6]Center of Cardiovascular and Transplant Surgery, Brno, Czech Republic, [7]University Hospital in Pilsen, Department of Medicine, Plzen, Czech Republic and [8]Institute of Clinical and Experimental Medicine, Clinical and Transplant Pathology Centre, Prague, Czech Republic

Background and Aims: Thrombotic microangiopathy (TMA) pathogenesis in kidney transplantation is poorly understood. The aim of this study was to evaluate donor and recipients risk factors for posttransplant TMA.

Method: In this retrospective multicenter national study, we identified both the case and 3M protocol kidney graft biopsies in 5258 recipients with TMA (n=57, 1.1 %) in 1994-2019. To further evaluate the effect of donor kidney on TMA development, the outcomes of the pair kidney grafts from the identical donors (n=43, 6 living donor, 1 pair kidney discarded, 6 insufficient data) as control group was analyzed.

Results: TMA occurred in 57 patients at 8th (median) post-operative day. Interestingly, neither histological nor laboratory signs of TMA were present in controls but in one case where TMA was evident in both recipients and in donor zero-hour biopsy. TMA associated with acute antibody mediated rejection was found in 11 cases (19%). Basic demographics between TMA and control group were similar, however longer cold ischemia time ($p < 0,05$, Figure 1) and more frequent delayed graft function ($p < 0,05$) were observed in TMA group. Patients with TMA experienced lower death-censored 5-year graft survival (56 vs. 84 %) in comparison with control group ($p < 0,05$, HR 2,904 (95% CI 1,411; 6,127), Figure 2).

Conclusion: TMA significantly affects the long-term kidney graft survival. Longer cold ischemia time was identified as the only risk factor and thus recipients genetic background is highly suspected in its pathogenesis.

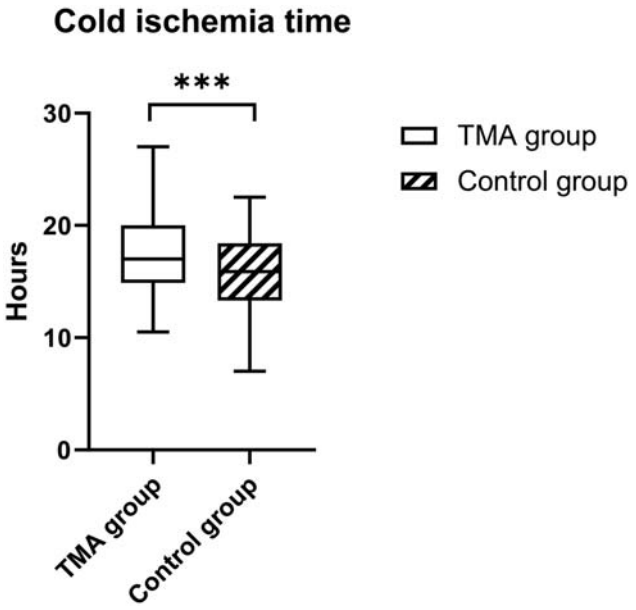


Figure 1 (Cold ischemia time)

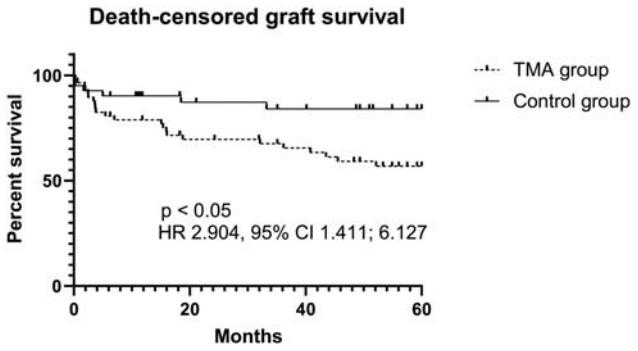


Figure 2 (Death-censored graft survival)

P1703 **RESULTS OF RENAL TRANSPLANTATION IN PATIENTS WITH RHEUMATIC DISEASES**

Mariya Likhavets[1], Konstantin Chyzh[2], Aleh Kalachyk[3], Nikolay Soroka[2]

[1]GU "Minsk Scientific-Practical Center of Surgery, Transplantation and Hematology", Rheumatological, Minsk, Belarus, [2]Belarusian State Medical University, The Chair of Internal Diseases 2d, Minsk, Belarus and [3]GU "Minsk Scientific-Practical Center of Surgery, Transplantation and Hematology", Nephrology and dialysis, Minsk, Belarus

Background and Aims: Rheumatic diseases often involve the kidneys and it might lead to chronic kidney disease (CKD). In its final stage it must be treated with renal replacement methods such as dialysis (hemodialysis or peritoneal dialysis) or renal transplantation. Kidney transplantation is the preferred and most cost-effective treatment for the end-stage renal disease, it offers a better quality of life than dialysis. The most common types of renal pathology in rheumatic diseases include glomerular (systemic lupus erythematosus), vascular (ANCA-associated vasculitides) and tubulointerstitial (goat) diseases. According to a research conducted in 2010 at the Minsk Rheumatological Department, 25% of patients had clinical or laboratory features of CKD. The aims were to reveal the most frequent rheumatic diseases affecting the kidneys and evaluate the post-transplant period in these patients.

Method: 94 medical case were studied retrospectively. All these patients had the end-stage renal disease with GFR of <15 ml/min/1.73m2 and underwent renal transplantation between January 2011 and September 2019.

Results: A retrospective study of 94 kidney transplant patients was conducted on renal transplantation centers in Belarus. Among the patients that underwent renal transplantation from January 2011 till September 2019, the percentage of recipients with rheumatic diseases was 3.64%. The majority of the recipients (52 %) were females. The mean age was 44.36 years (range, 16-78 years). Of the sample, 90% of kidney allografts were received from brain-dead donors, whereas only 10% of recipients got a new kidney from living-donors. Systemic lupus erythematosus was the most common causative disease in patients with rheumatic diseases (31 cases, 33%) followed by goat (28 cases, 30%) and secondary amyloidosis (17 cases, 18%) that complicated the course of rheumatoid arthritis and seronegative spondylarthritis. The remaining part of patients suffered from ANCA-associated vasculitides (10 cases, 10.6%), anti-glomerular basement membrane disease (6 cases, 6.4%), and single cases were represented by progressive systemic sclerosis and antiphospholipid syndrome (2%). In the post-transplant period, the most common complications were arterial hypertension (38%), anemia (20%), infectious diseases (27%), among them the most frequent were urinary tract infection (20%) and cytomegalovirus infection (7%). The 1-year allograft survival rate was 86%, the 5-year rate was about 82%. The main reasons for failed outcomes were acute renal allograft rejection, postoperative complications and infection. The patient survival rate after 1 and 5 years after transplantation was 93% and 86%, respectively. Infectious diseases (44%) such as nosocomial pneumonia, sepsis and cardiovascular disease (33%) are still the two most important reasons of death.

Conclusion: 1. The most common rheumatic diseases causing the end-stage renal disease are systemic lupus erythematosus (33%), goat (30%), rheumatoid arthritis, and seronegative spondylarthritis that lead to secondary amyloidosis (18%). 2. The 1-year allograft survival rate was 86%, the 5-year rate was about 82%, the patient survival rate after 1 and 5 years after transplantation was 93% and 86%, respectively. 3. The survival of patients with rheumatic diseases who underwent renal transplantation is comparable to patient survival after transplantation with another kidney pathology. 4. The main causes of death following renal transplantation are infectious and cardiovascular complications. Acute renal allograft rejection, postoperative complications, and infection are the main reasons of allograft failure.

P1704

POST-TRANSPLANTATION LYPMHOPROLIFERATIVE DISORDER (PTLD) RISK AND PROGNOSTIC FACTORS IN KIDNEY AND LIVER TRANSPLANT RECIPIENTS

Rafal Staros[1], Bartosz Foroncewicz[1], Krzysztof Zieniewicz[2], Maciej Kosieradzki[3], Sławomir Nazarewski[4], Bogna Ziarkiewicz-Wróblewska[5], Raszeja-Wyszomirska Joanna[6], Anna Jędrzejczak[1], Leszek Pączek[1], Krzysztof Mucha[1]

[1]Medical University of Warsaw, Department of Immunology, Transplantology and Internal Diseases, Warsaw, Poland, [2]Medical University of Warsaw, Department of General, Transplant and Liver Surgery, Warsaw, Poland, [3]Medical University of Warsaw, Department of General and Transplantation Surgery, Warsaw, Poland, [4]Medical University of Warsaw, Department of General, Vascular and Transplant Surgery,, Warsaw, Poland, [5]Medical University of Warsaw, Department of Pathology, Center for Biostructure Research, Warsaw, Poland and [6]Medical University of Warsaw, Department of Hepatology and Internal Medicine, Warszawa, Poland

Background and Aims: Post-transplantation lymphoprolipherative disorder [PTLD] is a serious, potentially fatal complication of transplantation [Tx], pathogenesis of which remains to be fully understood. Due to the intrinsic difficulty of assembling a large cohort of rare disease patients, most research papers have investigated PTLD in the general graft recipient population. They report however, that the relative risk of disease development significantly varies in relation to the type of transplanted organ, with multiorgan and intestinal graft recipients possessing the highest risk (RR=239.5), liver (RR=29.9) and the lowest for kidney transplant recipients (RR=12.6).

The aim of this study was to investigate the factors contributing to the development, course, treatment and outcomes of PTLD and compare their impact on the populations of liver [LTR] and kidney [KTR] transplant recipients.

Method: In this retrospective cohort study we have included all KTRs and LTRs diagnosed with PTLD at our centres between 2002 and 2017. The following data were collected from the patients' medical records: immunosuppression (IS), viral infections, PTLD type, treatment and outcomes. Mann-Whitney U-test was used to assess the differences in group composition, and the Log-rank test was used to compare Kaplan-Meier curves. Statistical analysis was performed in R version 3.2.3., p-values below .05 were considered statistically significant.

Results: We have identified 23 LTR and 16 KTR who matched our inclusion criteria. The mean age was 40.69 years. 61.5% of the patients were male, 38.5% female. Analysis of Kaplan-Meier curves revealed that PTLD occurred earlier in: LTRs ($p<.001$); patients above the median age of 45 years at Tx ($p=.002$); patients whose IS regimens at the time of PTLD diagnosis contained tacrolimus [TAC] ($p<.001$) or did not contain cyclosporin [CsA]. Among KTRs PTLD was diagnosed earlier in males ($p<0.05$), patients over 45 years at Tx ($p<0.05$), and those receiving TAC-containing IS regimens at PTLD diagnosis ($p<0.05$). These factors were not statistically significant for LTRs, among whom PTLD development was affected by the presence of MMF in IS regimens at diagnosis ($p<0.05$). Survival time was longer for patients receiving MMF-containing IS regimens ($p<0.05$). LTRs were more likely than KTRs to achieve complete remission in response to treatment ($p<0.05$).

Conclusion: Our results indicate, that in comparable KTR and LTR populations, the course of PLTD and response to treatment vary significantly. Factors such as patients' age at transplantation, sex, type of maintenance IS have a different impact depending on graft type. In our opinion these findings, when applied to further research, could enhance our ability to identify patients at risk and potentially lead to the formation of more personalised guidelines to the diagnosis and treatment of PTLD.

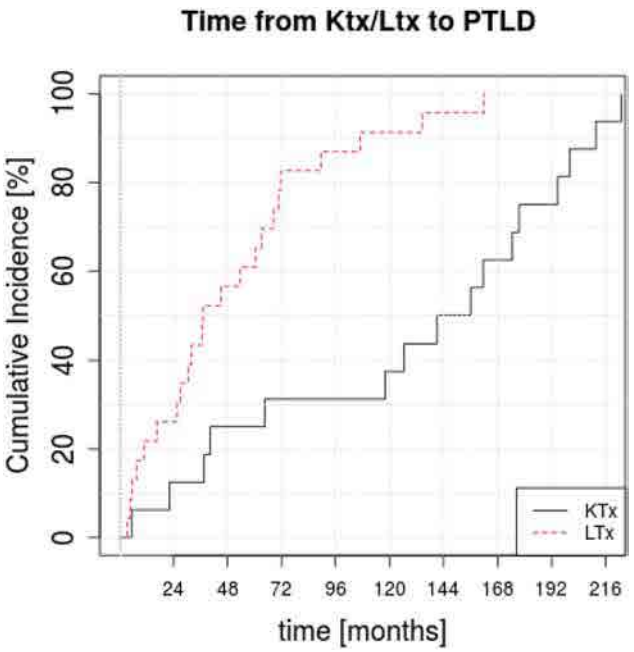


Fig. 1 LTRs (red curve) develop PTLD significantly earlier after transplantation compared to KTRs (black curve). $p<.001$

P1705

ARE DIRECT-ACTING ANTI-VIRAL DRUGS ACCUSED OF INCREASED INCIDENCE OF HEPATOCELLULAR CARCINOMA IN ENDEMIC AREA: A PILOT STUDY

Ahmed Elmowafy[1], Mohamed Abbas[1], Rasha T Abouelkheir[2], Ayman Refaie[1], Lionel Rostaing[3,4], Mohammed Bakr[1]

[1]Urology & Nephrology center Mansoura university, Nephrology, Mansoura, Egypt, [2]Urology & Nephrology center Mansoura university, Radiology, Mansoura, Egypt, [3]Chu Grenoble Alpes, Nephrology, Hemodialysis, Apheresis, and Kidney Transplantation, La Tronche, France and [4]Université Grenoble Alpes, Grenoble, France

Background and Aims: Great progression in treating hepatitis C infection has been made with the new Interferon-free regimens. Reports about developing hepatocellular carcinoma after DAAs have been spotlighted. Kidney transplantation and hemodialysis are considered risk factors for developing malignancies. Here we are evaluating the prevalence of HCC after DAAs treatment in high risk population.

Method: This cross-sectional study was held in Urology and Nephrology Center, Mansoura University, Egypt including. Total number of 165 patients received DAAs included in this study in 2 phases. The first phase included 50 patients (12 hemodialysis and 38 kidney transplant recipients). All patients completed DAAs course as treatment for hepatitis C infection (HCV) 24 months ago. Alfa feto protein and liver ultrasound (Use of both modalities combined yielded sensitivity (99.2%) and specificity (68.3%)) was used to screening of HCC for all patients. Triphasic CT liver with 86% to 94% sensitivity was done for all hemodialysis patients and KTRs with suspicious lesions or high alfa-feto protein.

Results: Our patients mean age was 52.32±3.2 years with male predominance. Mean Hemodialysis duration was 48.21±12.3 months and mean kidney transplantation duration was 36.21±6.7 months. Baseline laboratory investigations: ALT: 39.17±16.3 iu/l, Albumin: 3.6±1.32 g/dl, Bilirubin: 0.54±0.21, Hemoglobin: 10.57±1.9 g/dl, AFP: 5.3±2.4 ng/ml. Baseline liver US: normal (49%), enlarged (42%) and cirrhotic (9%) (No focal lesions). Fibro scan: F0 (26%), F1 (31%), F2 (32%) and F3 (11%). None of them experienced hepatic encephalopathy attacks or bleeding varices. All hemodialysis patients received Ombitasvir/Paritaprevir/Ritonavir (OMV/PTV/RTV) regimen (3 months). Only 2 KTRs received OMV/PTV/RTV regimen (3 months), the remaining 36 KTRs received Sofosbuvir/Daclatasvir regimen (6 months). Only 1 case reported relapse within 3 month after completing treatment. The rest achieved 12-week and 24-week SVR successfully. After 2 years from completing treatment, there was significant improvement in ALT levels. Four KTRs passed to graft failure due to accelerated immunologic response (rejection episodes) and 7 KTRs showed rise of serum creatinine (biopsy-proven rejection). Mean AFP rose up to 7.6±2.4 ng/ml with no statistical difference. Three hemodialysis patients and 4 KTRs showed rise in alfa-feto protein above normal values (10ng/dl). Four out of them exceeded 500ng/ml (1 HD and 3 KTRs). Abdominal US revealed: no change (39 patients), enlargement (6 patients) and cirrhosis (5 patients). Suspicious mass was found in 11 patients. Triphasic CT then was done for all hemodialysis patients and 9 KTRs. Regarding hemodialysis, 1 patient was diagnosed as HCC based on increased enhancement by Triphasic CT and alfa-fetoprotein was >500 ng/ml. Regarding KTRs, HCC was diagnosed in 2 patients and liver metastasis secondary to lymphoma was diagnosed in 1 case. The other patients with suspicious lesions (5 patients) showed uniform enhancement by Triphasic CT suggesting benign lesions. So, we have 3 (6%) out of 50 patients has been diagnosed as HCC after DAAs. By retrieval of their data, HCV duration was over 10 years and the liver was cirrhotic or enlarged with cirrhotic changes by ultrasound. Baseline ALT was slightly high without significant improvement after treatment. Also, baseline alfa-feto protein was high. The 3 patients were F2 or F3.

Conclusion: Hepatocellular carcinoma incidence after Direct-acting anti-virals is related mostly to the poor condition of the patients at baseline not to the drug itself and HCC in such cases could be considered as a part of disease progression not a drug complication.

P1706

THE GRAFT SURVIVAL OF KIDNEY TRANSPLANTATION ACCORDING TO ETHNICITY IN KIDNEY TRANSPLANT RECIPIENTS

Yeonsoon Jung[1], Jisu Kim[1], Haesu Jeon[1], Ye Na Kim[1], Ho Sik Shin[1], Hark Rim[1]

[1]*Gospel Hospital, Internal Medicine, Busan, Korea, Rep. of South*

Background: African American kidney transplant recipients experience disproportionately high rates of graft loss. The aim of this analysis was to use a UNOS data set that contains detailed baseline and longitudinal clinical data to establish and quantify the impact of the current overall graft loss definition on suppressing the true disparity magnitude in US AA kidney transplant outcomes.

Methods: Longitudinal cohort study of kidney transplant recipients using a data set created by United Network for Organ Sharing (UNOS), including 266,128 (African American 70,215, Non-African American 195,913) transplant patient between 1987 and December 2016. Multivariable analysis was conducted using 2-stage joint modeling of random and fixed effects of longitudinal data (linear mixed model) with time to event outcomes (Cox regression).

Results: 195,913 non-African American (AA) (73.6%) were compared with 70,215 AA (26.4%) recipients. 10-year-graft survival of AA in all era is lower than that of non-AA (31% in deceased kidney transplants (DKT) AA recipient and 42% in living kidney transplantation (LKT) non-AA recipient). 10-year-patient survival of AA with functioning graft in all era is similar that of non-AA. Multivariate Cox regression of factors associated with patient survival with functioning graft are acute rejection within 6 months, DM, hypertension and etc. Pre-transplant recipient BMI in AA show the trend as a protective factor in patient survival with functioning graft although not significantly in statistics

Conclusions: African American kidney transplant recipients experience a substantial disparity in graft loss, but not patient death with functioning graft.

P1707 SIMULTANEOUS HEART-KIDNEY TRANSPLANT: OUR 10 YEARS' EXPERIENCE

Clara Pardinhas[1], Rita Leal[1], Catarina Romãozinho[1], Lidia Santos[1], Arnaldo Figueiredo[2], Pedro Antunes[3], Manuel Batista[3], Rui Alves[1]

[1]Coimbra University and Hospital Center, Nephrology, Coimbra, Portugal, [2]Coimbra University and Hospital Center, Urology, Coimbra, Portugal and [3]Coimbra University and Hospital Center, Cardiothoracic Surgery, Coimbra, Portugal

Background and Aims: The number of patients listed and receiving simultaneous heart-kidney transplantation (SHKT) has significantly increased in the last decade. This is likely due to the increased knowledge that SHKT is associated with a significant survival benefit in patients with heart failure with chronic kidney disease (CKD), compared to isolated heart transplant and sequential heart and kidney transplantation. Recent analysis of large data bases has shown a survival benefit in SHKT even in older patients and beyond dialysis dependent patients. However, this benefit is only proven for irreversible CKD which is often difficult to prove in patients with severe heart failure.

Our center has the largest experience in SHKT in Portugal, and our aim is to report our experience with a total of 8 recipients and their outcomes after 10 years of follow up.

Method: We performed a retrospective analysis of all the patients submitted to SHKT in Coimbra University Hospital Center from 1 January 2009 to 31 December 2019. Data was collected using the clinical and laboratorial registries from our database. Follow up at December 2019 varied between 6 months to 10 years (median 5,5 years).

Results: A total of 8 patients received SHKT between 1 January 2009 and 31 December 2019. Only one patient was female and the mean age at transplant was 58.88 ± 9.7 years. The etiology of heart failure was dilated cardiomyopathy (N=4, 50%), severe valvular disease (N=2, 25%), ischemic cardiomyopathy (N=1, 12,5%) and one patient had familiar amyloidosis (N=1, 12,5%). Regarding CKD, the majority of the patients had type 2 cardiorenal syndrome (N=5, 62,5%), one patient had calcineurin toxicity due to previous liver transplantation, one patient had autosomal dominant polycystic disease, and in one patient the etiology remained unknown. Half of the patients were on chronic hemodialysis program for more than 3 months, and the remaining were preemptive. Regarding post-transplant results, average hospitalization was 19 days. Seven patients (87,5%) had immediate cardiac graft function (mean LVEF 70 ± 5.8% and mean PSAP 22.25 ± 5.6 mmHg). One patient had acute cardiac and subsequent renal graft dysfunction and died during hospitalization. Regarding renal graft outcomes, besides the patient that died, another patient had primary renal graft dysfunction due to renal artery thrombosis and one patient presented late graft function. The remaining five patients had immediate graft function and presented normal kidney graft function at follow up. Regarding complications, neoplasia was reported in two patients (one with sarcoma and the other with prostatic cancer), and there were twenty-five episodes of infection, present in all patients. Mortality at follow up was 37% (N=3). One of these, described above, died during hospitalization twenty-two days after transplant, and the other two died 4 and 5 years later due to a cardiovascular event and sarcoma, respectively. At follow up in 2019 five patients present stable kidney graft, good cardiac function and no recent complications.

Conclusion: In selected patients with co-existing heart and kidney failure, combined heart and kidney transplantation might be the best approach and appears to be associated with better graft and patient survival. Despite having a small number of cases, our center has the biggest experience in SHKT in Portugal and our results are very satisfying. A multidisciplinary approach between Nephrology, Cardiology and Cardiothoracic Surgery is fundamental and in the next decades it is expected an increase in SHKT number.

P1708 **EFFECT OF PREGNANCY ON KIDNEY TRANSPLANT RECIPIENTS: A PROPENSITY SCORE-MATCHED STUDY.**

Toyofumi Abe[1], Taniguchi Ayumu[1], Kawamura Masataka[1], Kato Taigo[1], Tomoko Namba-Hamano[2], Imamura Ryoichi[1], Nonomura Norio[1]

[1]Osaka University Graduate School of Medicine, Department of Urology, Suita, Japan and [2]Osaka University Graduate School of Medicine, Department of Nephrology, Suita, Japan

Background and Aims: This study aimed to evaluate whether the experience of pregnancy and delivery would be associated with poor maternal outcome among kidney transplant recipients.

Method: A total of 401 female transplant recipients from the Osaka University Transplantation Group Database were included in this study. 73 women who underwent renal transplantation between 1970 and 2017 and became pregnant and delivered at Osaka University Kidney Transplant Group Hospitals. Multivariable logistic regression analysis was used to assess the impact of pregnancy and delivery on renal transplant recipient outcome after one-to-one propensity score (PS) matching for 12 variables including serum creatinine at one year post-transplant between the parous group and the nulliparous group. The outcomes were kidney graft survival and patient survival.

Results: In all patients before PS matching, 75 (18.7%) of the 401 patients died and 137 (34.2%) of the 401 patients lost their kidney grafts during the follow-up period. In the multivariate analysis, pregnancy and delivery was not a significant risk factor for death (adjusted HR 0.662 [95%CI, 0.265-1.656], p-value 0.378) and for death-censored graft survival (adjusted HR 1.224 [95%CI, 0.683-2.196], p-value 0.497). In the PS matched population, 14 (17.5%) of the 80 patients died and 31 (38.8%) of the 80 patients lost their grafts. In the multivariate analysis, pregnancy and delivery was not a significant risk factor for death (adjusted HR 0.611 [95%CI, 0.180-2.072], p-value 0.430) and for death-censored graft survival (adjusted HR 1.308 [95%CI, 0.501-3.416], p-value 0.584).

Conclusion: Pregnancy and delivery after kidney transplantation was not associated with poor kidney transplant outcome in recipients with adequate and stable graft function.

P1709

THE ROLE OF CXCL9 AND CXCL13 IN PREDICTION OF POSTTRANSPLANT INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

Yangjuan Bai[1], Lin Yan[1], Yi Li[1], Yamei Li[1], Xianding Wang[2], Lanlan Wang[1], Yunying Shi[3]

[1]West China Hospital of Sichuan University, Laboratory Medicine, Chengdu, P.R. China, [2]West China Hospital of Sichuan University, Urology, Chengdu, P.R. China and [3]West China Hospital of Sichuan University, Nephrology, Chengdu, P.R. China

Background and Aims:

Chemokines are deeply involved in the process of inflammatory and immune responses. Interferon-γ-inducible chemokines C-X-C motif chemokine 9 and 10 (CXCL9 and CXCL10) are significantly associated with Th1 cells and monocytes and rise rapidly during early episode of renal allograft rejection and various infectious diseases. CXCL13 is one of the most potent B cells and T follicular helper (Tfh) cells chemoattractants when acts through its cognate receptor CXCR5. Recent work of CXCL13 indicated a critical immune regulatory role in both multiple infectious diseases and kidney transplantation. Additionally, C-C motif chemokine 2 (CCL2) is shown to be is critical for chronic kidney diseases. The aim of this study was to identify the predictive role of serum CXCL9, CXCL10, CXCL13 or CCL2 on kidney posttransplant infection.

Method:

95 kidney transplant recipients (KTRs) were enrolled in this study. 31 recipients experienced at least once infection episodes within the first posttransplant 12 months and 64 KTRs did not experience any infection episode during the follow-up period. Serum CXCL9, CXCL10, CXCL13 and CCL2 at the time points of pre-transplantation and post-transplant 30 days (POD 30) were analyzed with Bio-Plex® suspension array system.

Results:

It was found that serum level of POD 30 CXCL9 and POD 30 CXCL13 was associated with infection within one year after transplantation (P=0.021, P=0.002, respectively, shown in Figure 1). The serum level of CXCL9 and CXCL13 before surgery, the serum level of CCL2 and CXCL10 before and after surgery were not associated with infection within posttransplant one year (P>0.05, shown in Figure 1). The combination of POD 30 CXCL9 plus POD 30 CXCL13 provided the best results with AUC of 0.721 (95%CI, 0.591-0.852), sensitivity of 71.4% and specificity of 68.5% at the optimal cut-off value of 52.72 pg/ml (shown in Figure 2).

Conclusion:

Chemokines CXCL9 and CXCL13 as important chemokines could be used to predict the occurrence of infection within posttransplant one year in kidney transplant recipients.

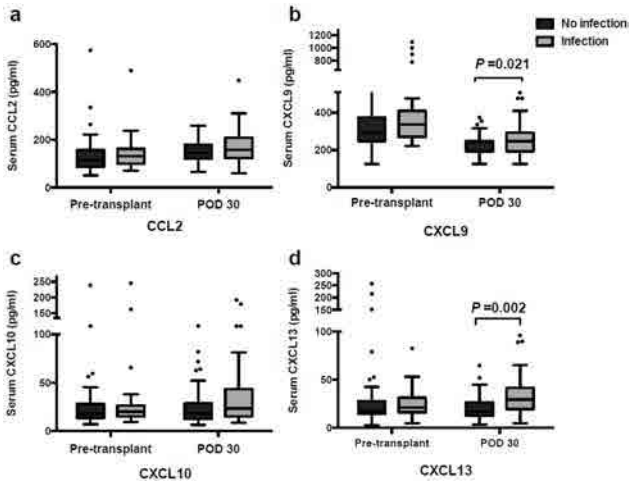


Figure 1

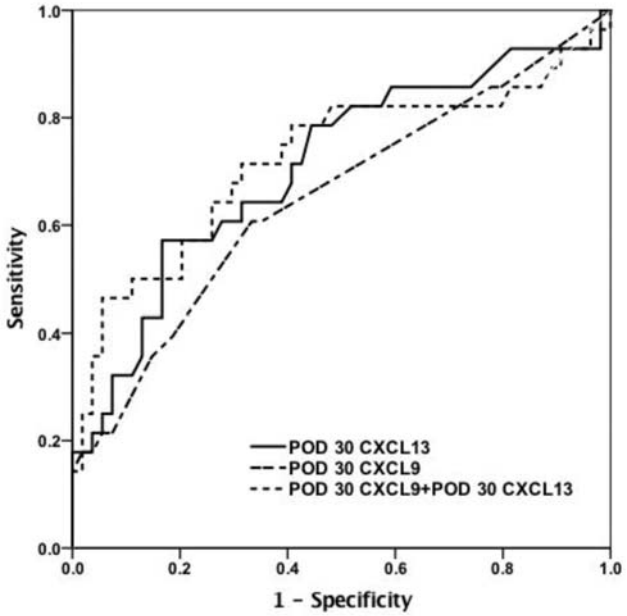


Figure 2

P1710

MULTI-NATIONAL SURVEY AMONG NEPHROLOGISTS AND TRANSPLANT SURGEONS ABOUT THE SUITABILITY AND ACCEPTANCE OF MARGINAL LIVE KIDNEY DONORS WITH SICKLE CELL TRAIT

Ziad Arabi[1], Atif Mateen[2], Abdulrahman Altheaby[1], Abdullah Hamad[3], Kaysi Saleh[4], El Waleed El Hassan[5]

[1]King Abdulaziz Medical City, King Abdullah International Medical Research Center & King Saud Bin Abdulaziz University for Health Sciences, Adult Transplant Nephrology, Organ Transplant Center, Riyadh, Saudi Arabia, [2]King Abdulaziz Medical City, Department of Nephrology, Riaydh, Saudi Arabia, [3]The Regional Medical Center, Orangeburg, SC,, United States of America, [4]CHU Clermont-Ferrand,, Saint Pryv/ Saint Mesmin, France and [5]The Regional Medical Center, Department of Nephrology, Riyadh, Saudi Arabia

Background and Aims: Due to organ shortage, many transplant centers may consider "marginal" kidney donors as those with sickle cell trait (SCT) for donation. Acceptance of kidney donors with SCT is in the grey zone, where there are no clear guidelines or consensus toward them. To form a consensus, we conducted a short survey about the suitability and acceptance of living kidney donors with SCT.

Method: This is a cross-sectional survey of nephrologists and transplant surgeons about Suitability and Acceptance of The Marginal Live Kidney Donors. The survey was sent to nephrologists in different countries and it was also distributed through AST& ERA-EDTA.

Results: Of a total of (n=122) respondents from 22 countries: 80.17% (N= 96) were nephrologists and 19.83% (N=23) were transplant surgeons. N= 88 of the respondents (72%) have more than 6 years in practice and they are heavily involved in pre- transplant evaluations of donors and recipients (68.5% of respondents perform donors' evaluation on weekly or monthly basis and 60 % perform recipient evaluation on weekly basis). The majority (45%) of the respondents were from USA. The completion rate of the survey was 99%. The presence of sickle cell trait was not considered as a contraindication to donor nephrectomy by the majority of respondents (57.38%). Of those (N= 34) 27.87 % of respondents consider them fit for donor nephrectomy after explanation of the risks involved while (N= 36) 29.51 consider them for donor nephrectomy only if there is no other suitable donor available. Out of the total respondents (N= 52) 42.62% considered the presence of sickle cell trait a contraindication to donor nephrectomy.

Conclusion: With lack of consensus and guidelines we found that a significant pool of the transplant physicians and surgeons will consider donors with sickle cell trait for kidney donation especially if there is no other acceptable donor.

Figure:

P1711 **RENAL RESISTIVE INDEX (RRI) OF KIDNEY ALLOGRAFT. OMEN OF THE OUTCOME OF TRANSPLANTION?**

Maria Smyrli[1], Glykeria Tsouka[1], Theodora Oikonomaki[2], Vasileios Vougas[3], Theofanis Apostolou[1], Christallenia Christodoulidou[1]

[1]General hospital of Euaggelismos, Nephrology Department "Antonios G Billis, Athens, Greece, [2]Protypo Nefrologiko Center of Athens, Dialysis Unit, Athens, Greece and [3]General hospital of Euaggelismos, 1st Surgical Clinic/Transplantion Unit, Athens, Greece

Background and Aims: Renal resistive index (RRI) of ultrasonography is a useful and potent tool for assessment and evaluation of renal hyperfiltration status of the transplanted patients. The aim of this study was to evaluate the association of RRI with renal function one year after transplant.

Method: We evaluated retrospectively 98 kidney allograft recipients. Data were collected from transplantations performed in our medical center between 01/2014 and 09/2018. Patients with acute loss of the renal function and renal survival less than a year were excluded from the study. We compared longitudinally the RRI at the first week after transplant and the third month, with glomerular filtration rate (eGFR, by CKD-EPI) at the end of the first year of transplantation. RRI was measured on the interlobular artery level, in each of the aforementioned time periods, and results were classified into 2 groups, RRI <0,8 or>0,8. In addition, age, gender and delayed graft function (DGF) were also determined in all patients.

Results: Sixty seven (67) of the recipients were males and 31 females with a mean age of 48±12years. The corresponding demographics for the donors were 46 males and 52 females with a mean age of 53 ±14. No correlations were found between RRI of the first week with gender and age, of both donors and recipients (p>0.05). Similarly, RRI of the first week was not correlated with DGF and one-year eGFR after transplant (p>0.05). On the contrary, RRI performed at the third month was strongly correlated to DGF and eGFR at the end of the first year. In other words, allograft recipients with a resistive index less than 0.80, had a higher eGFR and reduced frequency of DGF (p=0.01 and 0.03 respectively). Last but not least, higher recipient age and not gender was the main determinant of an increase of resistive index in the third month after transplant (P=0.02).

Conclusion: RRI offers interesting and helpful data on kidney allograft function. RRI of the third month less than 0.8 was related to better renal function at the end of the first year after transplant mainly and a lower incidence of DGF.

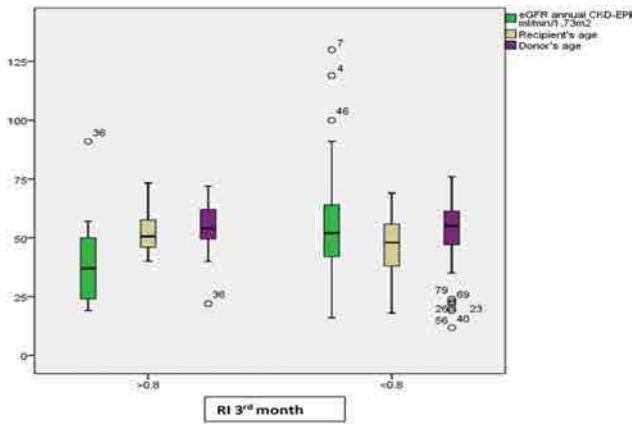


Figure:

P1712 **INFLUENCE OF DONOR AGE ON KIDNEY GRAFT SURVIVAL**

Carmen Grande Cabrerizo[1], Jorge Calvillo[2], Miguel Ángel Pérez valdivia[1], Marta Suñer Poblet[1], Alejandro Suarez Benjumea[1], Blanca Gasco Martos[1]

[1]Virgen del Rocio University Hospital, Nephrology, Seville, Spain and [2]Virgen del Rocio University Hospital, Bio-medical engineer, Seville, Spain

Background and Aims:

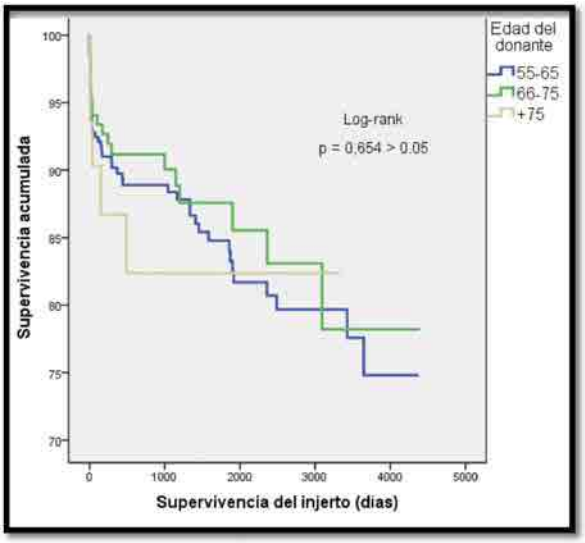
Kidney transplantation is the treatment of choice in patients with end stage kidney disease (ESKD). In recent years, donation activity and kidney transplant in Spain has suffered a significant increase, accompanied by a change in the profile of donors to cope with the waiting list. It has been produced a decrease in mortality due to traffic accidents, the main source of donation, in contrast, strokes are currently the main source. The donor is of older age and with greater morbidity, especially cardiovascular, which makes doubts about its functionality and Whether this is an adequate strategy to expand the donor pool. The objective To analyze if the survival of the graft is worse in donors of very advanced age with respect to other groups of expanded criteria deceased donors.

Method: A retrospective analysis was carried out with data from SICATA regarding kidney transplant from a deceased donor with age ≥55 years made between 1/1/06 -12/31/15 at the Virgen del Rocío University Hospital. The graft failure was defined as return to dialysis. 495 cases were obtained, which were divided by the age of the donor in three groups: between 55-65 (N = 310), between 66 -75 (N = 154) and> 75 (N = 31). These groups were compared in terms of graft survival (censored for death) using analysis of survival Kaplan-Meier log-rank. We also performed a multivariate analysis of risk-adjusted graft survival using the Cox proportional hazard technique with the relevant predictive factors and the age of the donor, as a categorical and continuous variable. Analysis with SPSS 24.0.

Results: The table shows the comparisons between the different population groups and in the Figure is shown the survival functions for each one. Taking into account those results, it cannot be concluded that the age of the donor in these different age groups has significant influence on graft survival with the data we handle.

The multivariate analysis concluded that, for this population group and the data handled, the variables that influence the failure of the graft are: the height of the donor, the sex of the recipient and the time in renal replacement therapy. In no case does the age of the donor influence the survival of the graft.

Conclusion: Kidney transplant improves survival and quality of life in comparison with dialysis long term. Our data did not show significant differences between the different groups of age, which indicates that the use of kidney grafts from elderly donors is acceptable and can greatly expand the donor group. The decision to use or not a kidney elderly donor should be based on the individual characteristics of the donor, as well as in other factors related to the standard clinical criteria for kidney transplant.



	Univariate analysis			Multivariate analysis		
	β	RR (IC del 95%)	p	β	RR (IC del 95%)	p
DONOR						
HEIGT	-0.044	0.957 (0.924-0.991)	0.015	-0.043	0.957 (0.923-0.993)	0.02
YEARS	0.055	1.056 (0.651-1.713)	0.824	-	-	-
DONATION TYPE	0.431	1.538 (0.589-4.021)	0.38	-	-	-
GENDER	0.545	1.725 (0.954-3.119)	0.071	-	-	-
HYPERTENSION	0.261	1.298 (0.722-2.332)	0.383	-	-	-
CREATININE	-0.049	0.953 (0.45-2.015)	0.89	-	-	-
WEIGHT	-0.012	0.988 (0.964-1.012)	0.314	-	-	-
DIABETES	-0.119	0.888 (0.349-2.259)	0.804	-	-	-
VHC	-3.019	0.049 (0.0 – 14486)	0.639	-	-	-
CAUSE OF DEATH	0.464	1.591 (0.764-3.314)	0.215	-	-	-
RECEPTOR						
GENDER	0.917	2.501 (1.368-4.57)	0.003	0.865	2.374 (1.29-4.367)	0.005
VHC RECEIVER	1.344	3.833 (1.372-10.71)	0.01	0.789	2.202 (0.739-6.562)	0.156
YEARS	0.004	1.004 (0.974-1.035)	0.781	-	-	-
HEIGT	-0.037	0.964 (0.916-1.014)	0.158	-	-	-
TIME IN SUBSTITUTE RENAL THERAPY	0.000035	1.0 (1.0-1.0)	0.012	0.000024	1.0 (1.0-1.0)	0.011
IHLA-DR INCOMPATIBILITES	0.38	1.462 (1.005-2.126)	0.047	0.309	1.362 (0.934-1.984)	0.108

Figure:

P1713

A CASE OF DEVASTATING BARIATRIC SURGERY-RELATED ACUTE OXALATE NEPHROPATHY FIRST DIAGNOSED AFTER KIDNEY TRANSPLANTATION

Francesca Santarsia[1], Ilaria Gandolfini[1], Marco Delsante[1], Alessandra Palmisano[1], Francesco Peyronel[1], Alice Sabatino[1], Giuseppe Regolisti[1], Enrico Fiaccadori[1], Umberto Maggiore[1]

[1]Parma University Hospital, Parma, Italy, Nephrology Unit; Department of Medicine and Surgery, Parma, Italy

Background and Aims: Despite the obvious efficacy in achieving weight loss, traditional malabsorptive procedures (intestinal by-pass) used for the treatment of obesity, may be associated with enteric oxaluria. Enteric oxaluria, by causing calcium-oxalate stones and nephrocalcinosis, represents an under-recognized cause of end-stage kidney disease in patients with history of intestinal by-pass. Herein, we describe a patient with a long-standing history of intestinal by-pass who developed a devastating acute oxalate nephropathy first diagnosed after kidney transplantation.

Method: A white female aged 50, who started hemodialysis one year earlier because of tubule-interstitial nephritis on a kidney biopsy, and who had history of recurrent kidney stones (calcium oxalate), underwent urgent deceased-donor kidney transplantation because of exhausted vascular access for hemodialysis (tunneled CVC right giugular vein as the last resort). She had received intestinal by-pass surgery 20 yrs earlier, and had a pacemaker implantation in the left sublavian vein for AV block two years earlier. She was highly sensitized because of blood transfusions at the time of surgery.

Results: After transplantation, graft function had immediate recovery, serum creatinine decreasing to 2.0mg/dL (117 mmol/L) on post-operative day (POD) 3. Shortly after, serum creatinine started rising until it reached 4.0mg/dL (354mmol/L) on POD 5. Three graft biopsies (performed on POD 6, 9 and 15 post-transplant) revealed acute oxalate nephropathy (**Figure1-2 :** large oxalate crystals on fresh unfixed core of kidney tissue analyzed under bright field microscope using polarized light) with no sign of rejection. Serial monitoring of Luminex SAB did not reveal circulating anti-HLA donor specific antibodies. Fundus examination revealed two tiny mono-lateral retinal oxalate deposits, whereas bone biopsy did not reveal oxalate accumulation. Plasma oxalate levels were 43 mmol/L on POD 10 were urinary oxalate excretion was 29mg /day on POD 14.

The patient slowly progressed to end-stage kidney disease 2-month post-transplantation despite daily high flux dialysis since POD 7, fat-free and oxalate-free diet, oral potassium and high dose pyridoxine supplements.

Conclusion: Patients on chronic dialysis with a previous history of bariatric surgery via intestinal by-pass may have oxalate nephropathy caused by enteric oxaluria as unknown primary renal disease. The disease may recur shortly after transplantation despite the adoption of prompt aggressive treatment for oxalate removal.

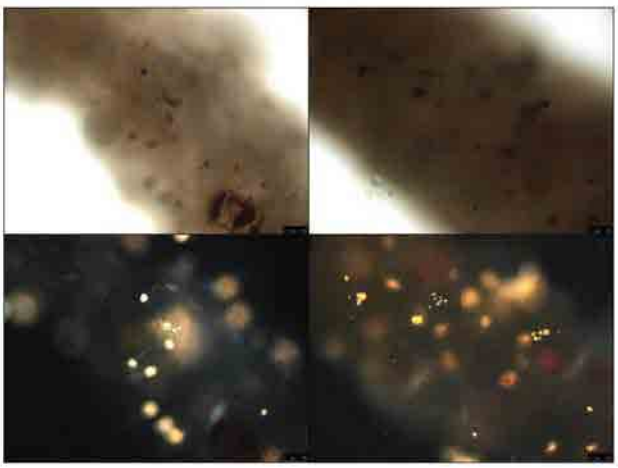


Figure 1: Biopsy POD 6 (intratubular and birefringent inclusions compatible with calcium oxalate crystals)

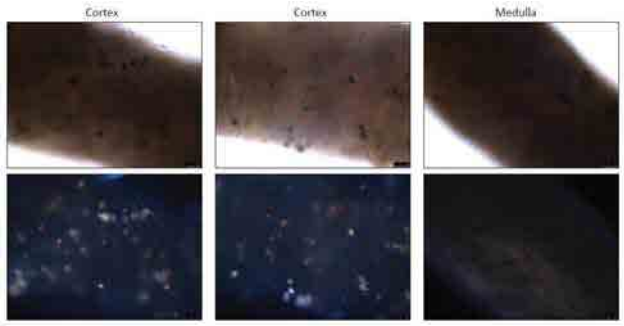


Fig 2: Biopsy POD15 (oxalate crystals confined to the cortex)

P1714 **INTRA-ABDOMINAL PRESSURE IS ASSOCIATED WITH HIGHER RENAL RESISTIVE INDEX AFTER RENAL TRANSPLANTATION**

Armando Coca[1], Pablo Gonzalez[1], Carlos Arias-Cabrales[2], Maria Jose Perez-Saez[2], Maria Jesus Rollan[1], Isabel Acosta-Ochoa[1], Elena Bustamante-Munguira[3], Alicia Mendiluce[1], Julio Pascual[2], Juan Bustamante-Munguira[4]

[1]Hospital Clinico Universitario, Nephrology, Valladolid, Spain, [2]Hospital del Mar, Nephrology, Barcelona, Spain, [3]Hospital Clinico Universitario, Intensive Care Medicine, Valladolid, Spain and [4]Hospital Clinico Universitario, Cardiac Surgery, Valladolid, Spain

Background and Aims: The renal arterial resistive index (RRI) reflects renal hemodynamics non-invasively using Doppler arterial waveforms. RRI is defined by factors such as age, sex, weight, height or mean arterial pressure. Intra-abdominal hypertension (IAH) is a common complication among post-surgical patients that can affect renal blood flow. We aimed to determine the relationship between intra-abdominal pressure (IAP) and RRI in a sample of incident kidney transplant patients (KTs).

Method: Single-center prospective cohort of deceased-donor KTs. Anesthesia, surgical technique and immunosuppression induction therapy was the same in all cases. IAP monitoring was performed according to WSACS guidelines using the urinary bladder technique (UnoMeter Abdo-Pressure kit). IAP values were registered every 8h during the first 72h after surgery or until reoperation. Mean IAP values during the first 24h (24h-IAP) were used in this analysis. Doppler ultrasonography was performed 24h after surgery. RRI was calculated using the following formula: (peak systolic velocity – end-diastolic velocity)/peak systolic velocity. The study was approved by the local ethics committee and written informed consent was obtained in all cases.

Results: 137 patients were enrolled. Table 1 summarizes relevant patient and hemodynamic variables. Stepwise multivariate linear regression analysis was used to examine independent predictors of RRI in this sample, including all variables in Table 1. Age (β=0.005, std.error=0.001, P<0.001), dialysis vintage (β=0.001, std.error<0.001, P=0.02) and 24h-IAP (β=0.005, std.error=0.003, P=0.041) were independent predictors of RRI.

Conclusion: Increased IAP in the first 24h after surgery is common in KTs and is correlated with higher RRI, which is associated with increased risk of graft loss and death.

	All	No IAH	IAH	P
N	137	61	76	
Age (years)	62 (52-69)	63 (51-73)	62 (53-69)	0,719
Male sex, n(%)	91 (66)	30 (49,2)	61 (80,3)	**<0,001**
Weight (kg)	71±13	64,9±11,5	75,5±12,7	**<0,001**
Height (cm)	165±9	162,9±9,1	167,3±8,5	**0,004**
Dialysis vintage (months)	19 (10-34)	15 (10-31)	23 (10-37)	0,248
HTN, n(%)	124 (91)	55 (90,2)	69 (90,8)	0,901
Diabetes, n(%)	23 (17)	11 (18)	12 (15,8	0,727
MAP (mmHg)	93 (90-98)	93 (90-98)	93 (90-98)	0,721
24h-IAP (mmHg)	12,4±3,5	9,3±1,7	14,9±2,4	**<0,001**
RRI	0,77 (0,7-0,83)	0,76 (0,7-0,82)	0,79 (0,73-0,88)	**0,031**

HTN, hypertension. IAH, intra-abdominal hypertension. IAP, intra-abdominal pressure. MAP, mean arterial pressure. RRI, renal resistive index.

P1715

CORRELATION OF DONATED KIDNEY MASS AND GRAFT FUNCTION IN RECIPIENTS OF LIVING DONOR KIDNEY TRANSPLANTATION

Filipa Silva[1], Nicole Pestana[2], Catarina Isabel Ribeiro[3], Diogo Carneiro[4], Mariana Madanelo[4], Joana Tavares[1], Sofia Pedroso[1], Manuela Almeida[1], Jorge Malheiro[1], Leonídio Dias[1], Miguel Silva Ramos[4], La Salete Martins[1], António Castro Henriques[1]

[1]Centro Hospitalar e Universitário do Porto, Nephrology and Kidney Transplantation, Porto, Portugal, [2]Hospital Dr. Nélio Mendonça, Nephrology, Funchal, Portugal, [3]Centro Hospitalar Vila Nova de Gaia e Espinho, Nephrology, Vila Nova de Gaia, Portugal and [4]Centro Hospitalar e Universitário do Porto, Urology, Porto, Portugal

Background and Aims: Kidney volume has been proven to be a surrogate marker of nephron mass and renal function in living donors. Although many studies correlate the kidney mass with renal donors' function after donation, few studies have compared the donated kidney mass with estimated glomerular filtration rate (eGFR) in the kidney's recipients.

The purpose of this study is to examine the relationship between donor kidney volume and post-transplantation graft function by using computerized tomography to obtain renal volumes.

Method: Clinical data off all donor and recipient pairs undergoing live donor kidney transplantation (KT) at our institution between January 2008 and December 2017 (n=195) were reviewed. The volume of the kidney selected for transplant was determined using volume calculating software and correlate to transplant recipient eGFR.

Results: All metrics of donor kidney volume (DKV): DKV alone, ADK adjusted for weight, body mass index (BMI) or body surface area (BSA), correlated significantly with eGFR (all with p<0,001) at 1 year after KT, with DKV/BSA having the highest correlation (r=0,431). Hence, recipients were divided into terciles according their DKV/BSA (cm^3/m^2): tercile 1 (DKV/BSA between 49,7-77,5, n=64), tercile 2 (78-95,2, n=63) and tercile 3 (95,4-176, n=63). eGFR differences between groups at each time point were all significant (P<0.05), except for the comparison between T1 and T2 at month 6 (figure 1)

Significant risk factors for eGFR<60 ml/min at 1-year were: acute rejection (AR) at 1-year (OR=4.116, P=0.018); calculated PRA>0% (OR=2.075, P=0.039); higher donor age (OR per unit=1.033, P=0.047); and peritoneal dialysis modality (in comparison with preemptive KT: OR=3.232, P=0.013). Higher (T3) DKV/BSA tercile (in comparison with T1: OR=0.306, P=0.004) was protective of this outcome.

Patients that experienced AR at 1-year had significantly lower DKV/BSA, particularly those with acute cellular rejection (ACR).

The median follow-up was 4,8 years (IQR: 3.2-7.5). The censored graft survival by DKV/BSA terciles at 10 years were 59,3% for group 1, 91.3% for group 2 and 91.1% for group 3 (figure 3).

Conclusion: Our study demonstrates that transplantation of donor-recipient pairs with lower DKV/BSA ratio were associated with significantly worse graft function and higher incidence of AR. This data suggests that a larger mass of nephrons remaining adjusted to recipient's weight seems to predict a better long-term eGFR. This method can be useful in order to identify patients at risk for a low eGFR after KT and, in cases of multiple potential donors, optimize donor selection.

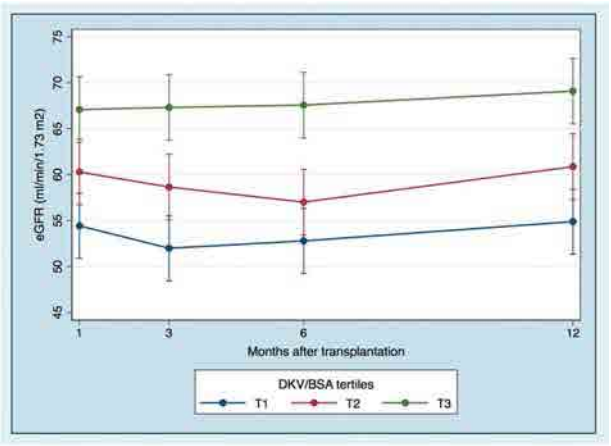


Figure:

P1716

MULTI-NATIONAL SURVEY AMONG NEPHROLOGISTS & TRANSPLANT SURGEONS ABOUT THE SUITABILITY & ACCEPTANCE OF MARGINAL LIVE KIDNEY DONORS REGARDING AGE DISCREPANCY

Ziad Arabi[1], Kaysi Saleh[2], Abdullah Hamad[3], Mohammad Bukhari[4], Atif Mateen[5], El Waleed El Hassan[6], Abdulrahman Altheaby[7]

[1]King Abdulaziz Medical City, King Abdullah International Medical Research Center & King Saud Bin Abdulaziz University for Health Sciences, Adult Transplant Nephrology, Organ Transplant Center, Riyadh, Saudi Arabia, [2]CHU Clermont-Ferrand,, Department of Nephrology, Saint Pryv/ Saint Mesmin, France, [3]The Regional Medical Center, Orangeburg, SC,, United States of America, [4]University of Taif, Taif, Saudi Arabia, [5]King Abdulaziz Medical City, Department of Nephrology, Riyadh, Saudi Arabia, [6]King Abdulaziz Medical City, Department of Nephrology, Riaydh, Saudi Arabia and [7]King Abdulaziz Medical City, King Abdullah International Medical Research Center & King Saud Bin Abdulaziz University for Health Sciences, Department of Nephrology, Riyadh, Saudi Arabia

Background and Aims: Living donor kidney transplantation is the best option for patients on dialysis. There are no guidelines or generally accepted consensus about the acceptable kidney donor age and what is the acceptable donor-recipient age discrepancy.

Method: This is a cross sectional survey of nephrologists and transplant surgeons about acceptable age of living kidney donors. The survey was sent to participants in different countries and through AST and ERA/EDTA.

Results: 122 respondents from 22 countries answered 4 questions related to donor age. Most respondents (N=86, 70%) would allow an 18-years old man to donate to his older sibling. However, this percentage would fall to (N=69, 57%) if the donor was an 18-years old woman (P=0.02), reflecting the impact of childbearing period as a major criterion in considering kidney donation. On the opposite side, up to 20% of respondents will decline a very young donor regardless of the gender of the donor. The acceptance rate of a very young donor drops to only 37% if the recipient is 75-year-old (versus 70% in case of younger recipient, P = 0.004). In case of old donor($>$ 65 years old) old to an 18 year old recipient with expected prolonged waiting time for deceased donor, (N= 80, 65%) will advise to find an alternative donor but will allow the donation if no alternative donor is available.

Conclusion: The majority of the nephrologists and transplant surgeons will allow a very young donor to donate to a sibling especially if the donor is a male. However up to 20% will decline this donation regardless of the gender of the donor.

The transplant community is divided about allowing a very young donor to donate to a very old recipient. However, the majority will accept $>$ 65 years old donor to donate to an 18 years old recipient with expected prolonged waiting time for deceased donor.

Figure:

P1717 **OUTCOMES OF INCREASED INTRA-ABDOMINAL PRESSURE AFTER KIDNEY TRANSPLANTATION**

Armando Coca[1], Carlos Arias-Cabrales[2], Maria José Pérez-Sáez[2], Pablo Gonzalez[1], Isabel Acosta-Ochoa[1], Elena Bustamante-Munguira[3], Maria Jesus Rollan[1], Alicia Mendiluce[1], Julio Pascual[2], Juan Bustamante-Munguira[4]

[1]Hospital Clinico Universitario, Nephrology, Valladolid, Spain, [2]Hospital del Mar, Nephrology, Barcelona, Spain, [3]Hospital Clinico Universitario, Intensive Care Medicine, Valladolid, Spain and [4]Hospital Clinico Universitario, Cardiac Surgery, Valladolid, Spain

Background and Aims: Increased intra-abdominal pressure (IAP) is commonly found among post-surgical patients and can induce organ dysfunction. However, its prevalence and impact after kidney transplantation have not been adequately described. We aimed to study the prevalence of increased IAP after kidney transplantation and its consequences on transplant outcomes.

Method: IAP was prospectively measured in 121 kidney transplant recipients every 8h during the first 72h after surgery using the urinary bladder technique (UnoMeter Abdo-Pressure kit). Mean IAP values during the first 24h (24h-IAP) were used in this analysis. Grading of intra-abdominal hypertension was defined according to WSACS guidelines. Patients were followed for at least 12 months or until graft failure or death. The study was approved by the local ethics committee and informed consent was obtained in all cases.

Results: 24h-IAP was 12.6±3.5 mmHg. 84.2% of subjects presented with intra-abdominal hypertension during the first 72h after kidney transplantation. Body mass index (OR: 1.35, 95% CI 1.12-1.63; P=0.002), male sex (OR: 3.34, 95% CI 1.1-10.3; P=0.032) and hemodialysis as renal replacement therapy before transplantation (OR: 4.35, 95% CI 1.32-14.4; P=0.016) were independent determinants of intra-abdominal hypertension. IAP was an independent risk factor for delayed graft function (*model adjusted for recipient age, sex, history of previous kidney transplants, recipient comorbidities, donor terminal serum creatinine and comorbidities, number of HLA mismatches >4, cold ischemia time and donation after cardiac death status), graft failure and death (**model adjusted for all variables included in the previous model plus delayed graft failure) (Figure).

Conclusion: Increased IAP was highly common after transplant surgery and was associated with higher rates of delayed graft function, graft failure and death. Routine IAP monitoring should be considered after transplantation to facilitate early identification of complications and initiation of the appropriate treatment to stop its effects.

	No IAH	Grade I IAH	Grade II IAH	Grade III IAH	p-value
N	21	68	27	5	
Age, years	61 (46-68)	62 (52-71)	58 (52-68)	68 (50-73)	0.3
Male sex, n (%)	8 (38.1)	46 (67.6)	22 (81.5)	5 (100)	0.005
Dialysis vintage, months	21 (11-47.5)	18.5 (10-32.8)	29 (11-54)	30 (22-53.5)	0.367
BMI, kg/m2	22.9±3.8	25.8±3.5	27.3±3.2	28.9±5.9	<0.001
PKD, n (%)	3 (14.3)	15 (22.1)	4 (14.8)	1 (20)	0.795
PD as RRT, n (%)	13 (61.9)	28 (41.2)	9 (33.3)	0 (0)	0.048
First renal transplant, n (%)	16 (76.2)	62 (91.2)	22 (81.5)	3 (60)	0.108
Hypertension, n (%)	17 (81)	62 (91.2)	24 (88.9)	5 (100)	0.498
Diabetes, n (%)	2 (9.5)	14 (20.6)	5 (18.5)	2 (40)	0.428
Age (donor), years	54 (35.5-62)	66 (54-72)	58 (49-72)	69 (50-78)	0.046
Male sex (donor), n (%)	15 (71.4)	42 (61.8)	18 (66.7)	4 (80)	0.748
SCr (donor), mg/dl	0.75 (0.64-0.89)	0.79 (0.68-0.93)	0.76 (0.68-1)	0.93 (0.71-1.02)	0.751
DCD, n (%)	1 (4.8)	1 (1.5)	2 (7.4)	0 (0)	0.485
CIT, hours	14 (12-19)	16 (13-18)	16 (13-19)	18 (15-23)	0.622
HLA mismatches, number	4 (4-6)	4 (4-5)	4 (4-5)	3 (2-5)	0.338
	OR	**95% Con˚dence Interval**		**p-value**	
		Lower	**Upper**		
Delayed graft function; 24h-IAP	1.214	1.072	1.375	0.002	
Graft failure or recipient death**	**OR**	**95% Con˚dence Interval**		**p-value**	
		Lower	**Upper**		
At discharge; 24h-IAP	1.363	1.065	1.745	0.014	
At 6 months; 24h-IAP	1.199	1.017	1.415	0.031	
At 12 months; 24h-IAP	1.244	1.045	1.481	0.014	

BMI, body mass index. CIT, cold ischemia time. DCD, donation after cardiac death. HLA, human leukocyte antigen. IAH, intra-abdominal hypertension. IAP, intra-abdominal pressure. OR, odds ratio. PD, peritoneal dialysis. PKD, polycystic kidney disease. RRT, renal replacement therapy. SCr, serum creatinine.

P1718

COMPARISON OF MEASURED GLOMERULAR FILTRATION RATE USING 24-HOUR URINE CREATININE CLEARANCE WITH 51-CHROMIUM EDTA IN A MALAYSIAN COHORT OF LIVING KIDNEY DONOR CANDIDATES

Chee Keong Thye[1], Yee Wan Lee[1], Maisarah Jalalonmuhali[1], Soo Kun Lim[1], Kok Peng Ng[1]

[1]*University of Malaya, Faculty of Medicine, Kuala Lumpur, Malaysia*

Background and Aims: All living kidney donors undergo assessment of renal function by evaluation of Glomerular Filtration Rate (GFR). ^{51}Cr-EDTA is one of the most widely used marker for measuring GFR but it is hampered by cost and laboriousness as well as not being widely available in Malaysia. Measuring 24-hour urine for creatinine clearance (Ccr) is a common alternative when exogenous filtration markers are not available. Ccr suffers from over/underestimation of measured GFR (mGFR) due to errors in urine collection and tubular secretion of creatinine. This is a study to compare the correlation of Ccr against ^{51}Cr-EDTA in measuring GFR among the living donors in Malaysian population.

Method: This is a cross-sectional, single-centre study of a cohort of living kidney donor candidates from January 2007 to March 2019. All candidates who had mGFR done with both ^{51}Cr-EDTA and Ccr in University Malaya Medical Centre were enrolled. Special consideration was taken to account for adequate urine sampling for Ccr. Clinical data was analysed for correlation, bias, precision and accuracy between Ccr and ^{51}Cr-EDTA.

Results: A total of 83 living kidney donors with a mean age of 45.60 ± 11.06 years and body mass index (BMI) of 24.36 ± 4.03 were enrolled. Female comprised 74.7% of the donors while Chinese, Malay and Indian accounted for 67.5%, 20.5% and 7.2% of the donors respectively. The study group had a mean serum creatinine of 63.37 ± 16.00 umol/L with a urine volume of 2.03 ± 0.81 L (range 0.70 – 3.82). mGFR from ^{51}Cr-EDTA was 125.56 ± 27.64 ml/min/1.73m^2 (range 77.0 – 194.3) whereas calculated Ccr was 136.05 ± 36.15 ml/min/1.73m^2 (range 75.32 – 280.06). The correlation coefficient between Ccr and ^{51}Cr-EDTA is moderate ($r = 0.43$) ($p < 0.01$). Mean absolute bias between Ccr and ^{51}Cr-EDTA was 10.59 ± 37.99 ml/min/1.73m^2 ($p < 0.05$). The accuracy of Ccr within 30% of ^{51}Cr-EDTA was 77.11%.

Conclusion: Our study showed that Ccr significantly overestimates mGFR compared to ^{51}Cr-EDTA. However, there is a significantly moderate positive correlation between Ccr and ^{51}Cr-EDTA. Thus, in the absence of ^{51}Cr-EDTA, Ccr is a clinically acceptable alternative if utilized with care and understanding its limitations.

Table 1: Baseline Characteristics

Characteristic (*n* = 83)	Mean ± SD or *n* (%)
Sex	Female 62 (74.7%)
Age (years)	45.60 ± 11.06
Race	Chinese 56 (67.5%)
	Malay 17 (20.5%)
	Indian 6 (7.2%)
	Others 4 (4.8%)
BMI (kg/m^2)	24.36 ± 4.03
BSA (m^2)	1.64 ± 0.18
Plasma creatinine (umol/l)	63.37 ± 16.00
mGFR by ^{51}Cr-EDTA (ml/min/1.73 m^2)	125.56 ± 27.64
mGFR by Ccr (ml/min/1.73 m^2)	136.05 ± 36.15

Table 2: Analysis of Ccr in comparison to ^{51}Cr-EDTA

mGFR (ml/min/1.73 m2)	Correlation coefficient (r)	Mean difference (bias)	SD of mean bias (precision)	Accuracy within 30% (%)
^{51}Cr-EDTA				
Ccr	0.43	10.59	37.99	77.11

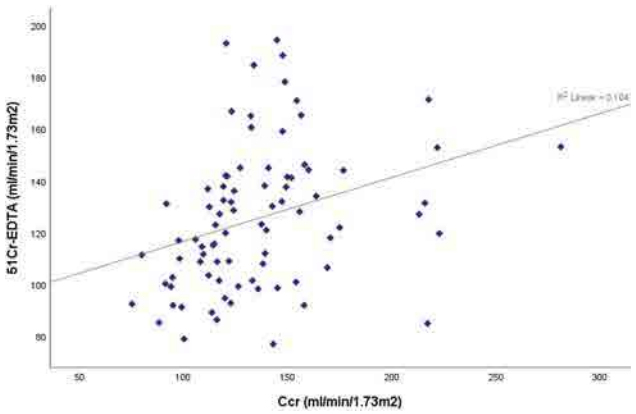


Fig. 1 Relationship between ^{51}Cr-EDTA and Ccr. The correlation coefficient is 0.43

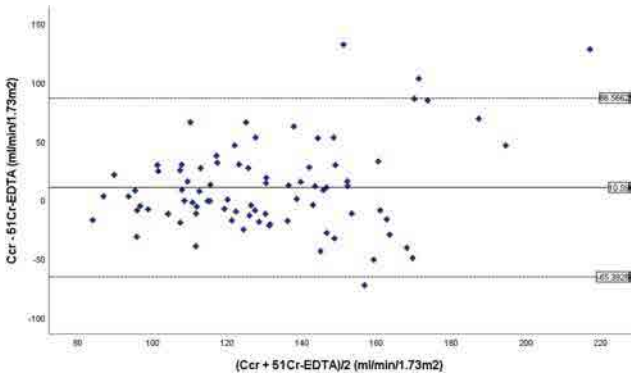


Figure 2: Bland and Altman plot whereby the differences between Ccr and ^{51}Cr-EDTA are plotted against the mean of the Ccr and ^{51}Cr-EDTA. The solid line represents the mean difference (bias) while the dotted lines indicate ±2 SD.

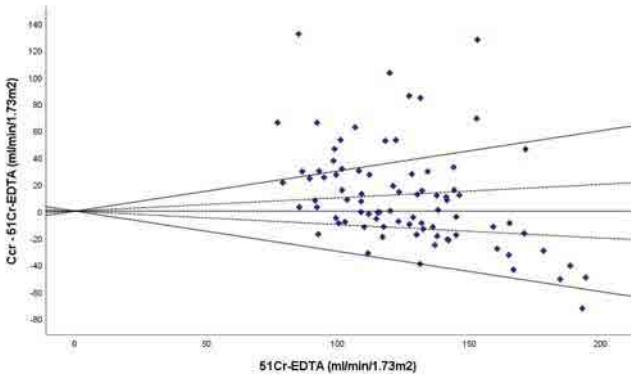


Figure 3: Modified Bland-Altman plot whereby the differences between Ccr and ^{51}Cr-EDTA are plotted against 51Cr-EDTA (reference method) to visualize bias and accuracy. The proportion of errors in the index measurements that did not exceed 30% (P30) limits (solid lines) and 10% (P10) limits (dashed lines) are shown. This is an alternative approach when one of the methods is considered more accurate.

P1719

GASTRODUODENAL LESIONS AND HELICOBACTER PYLORI INFECTION IN ASYMPTOMATIC RENAL TRANSPLANT CANDIDATES

Abbasali Zeraati[1], Ladan Goshayeshi[2], Zahra Kazemi[2], Ali akbar Hekmat[3], Tina Zeraati[4], Dorsa Zeraati[5]

[1]Renal transplantation Complications Research Center, Imam Reza Hospital, Mashhad University of Medical Sciences, internal Medicine, Mashhad, Iran, [2]Mashhad university of medical science, internal medicine, Mashhad, Iran, [3]Mashhad University Of Medical Science, Internal Medicine, Mashhad, Iran, [4]Renal transplantation Complications Research Center, internal medicine, Mashhhad, Iran and [5]Mashhad Azad university of medical science, Internal Medicine, Mashhad, Iran

Background and Aims: Patients suffering from end stage renal disease usually cope with many problems due to their lengthy illness and its complications. Renal transplantation is the most effective therapeutic strategy in these patients. One of the post transplantation complications is gastrointestinal bleeding due to peptic ulcers and other upper gastrointestinal diseases which can affect the morbidity and mortality of these patients. The present research aims to shed lights on prevalence of gastrointestinal lesions and Helicobacter pylori infection using upper endoscopy in asymptomatic candidates for renal transplantation.

Method: The present cross-sectional research was performed on renal transplant candidates suffering chronic renal failure referred to Montaserie organ transplantation center in the time period of January 2016, to January 2018. Eighty five ESRD patients, 45 male and 40 female, mean age 39.09 ± 11.09 years, enrolled in the study. Hypertension and diabetes were the most common causes of kidney failure in the patients. In the present research about 90.6% of patients had been on chronic dialysis,. Mean duration of vintage time on dialysis was 20.46 ±16.12 months, and hemodialysis (87%) was the most common dialysis method. Including criteria were patients candidature for renal transplant and consent for involvement in the research. Excluding criteria were patients with apparent dyspeptic symptoms, patients with known upper gastrointestinal diseases, and patients who have been using PPIs (proton pump inhibitors), NSAIDs(non-steroid anti-inflammatory drug), H2 blockers or antibiotics over the past two weeks preceding the enrollment in study . Patients who met criteria underwent endoscopy and were classified according to endoscopic findings, Helicobacter pylori infection and pathologic findings. Chi-square statistics was used for evaluating the correlation between categorical endoscopic or pathologic findings with categorical demographic and dialysis characteristics parameters. The Statistical Package for the Social Sciences software (SPSS version 20.0, SPSS Inc., Chicago, IL, USA) was used for data analyses. A $P < 0.05$ was considered significant.

Results: Sixty two patients (72%) had significant endoscopic findings; erosive gastroduodenitis (32.5%) was the most common findings. There was not a significant correlation between endoscopic findings and: age (p = 0.5), cause of renal failure (p-value = 0.9), dialysis type (p-value = 0.08), gender (p-value = 0.9), infection with H. Pylori (p-value = 0.2) and mean duration of vintage dialysis time (p = 0.4).All the patients with significant endoscopic findings, had also significant abnormal pathologic findings on endoscopic obtained biopsied samples. Helicobacter pylori infection was seen in, 36 patient(42%)s. Significant association between H. Pylori infection and abnormal pathology was found (p=0.04) .

Conclusion: Asymptomatic gastrointestinal lesions and Helicobacter pylori infection are prevalent in renal transplant candidates, so routine upper endoscopy in these patients is strongly recommended.

P1720 POSTTRANSPLANT TUBERCULOSIS IN LIVE DONOR RENAL TRANSPLANTATION : A SINGLE-CENTER EXPERIENCE

Ahmed Mohamed Naguib Attiya[1], Mohamed Hamed abbas[1], Ahmed Mansour Hassan Abdel-Rahman[1], Ayman Refaie[1]

[1]*urology and nephrology center. Mansoura University., nephrology, Mansoura, Egypt*

Background and Aims:

Tuberculosis (TB) is one of the not uncommon serious bacterial infections which affect renal transplant recipients notably in endemic areas. Posttransplant TB occurs peculiarly due to reactivation of latent infection in the recipient or acquiring de novo infection after transplantation or rarely as donor transmitted infection. The aim of this study is to investigate the impact of TB disease and treatment drugs on renal graft and assess the risk factors for graft dysfunction during and after course of treatment.

Method:

This retrospective single-center study investigated 3000 patients who underwent live donor renal allograft transplantation in our center between the years 1988-2019. TB diagnosis was confirmed in 44 patients. All proven-TB patients were evaluated regarding pretransplant demographic and immunological data. Posttransplant evaluation included kidney function tests, immunosuppressive therapy regimens, incidence of rejection episodes and anti-rejection therapies before, during and after TB.

Results:

Patients were predominantly young (32±9.8 years), male (60%), There was no significant difference regarding other pretransplant demographic and immunological data. Regarding induction therapy, 13 patients received induction therapy; 7 patients received ATG, 6 patients received basiliximab and 31 patients did not receive induction therapy with no significant difference (p=0.07). Concerning maintenance immunosuppressive agents, no significant difference was found regarding different protocols of immunosuppression (p=0.11); however, regarding total dose of the steroid in 1st three months post-transplant, there was significant difference (p=0.017). As regards to rejection episodes, 16 patients were not exposed to rejection episodes before TB, 27 patients developed cellular rejection and only 1 patient developed humoral rejection with no statistical difference (p=0.18). In reference to management of rejection episodes, 25 patients received pulse steroid, 2 patients received pulse steroid and ATG, 1 patient received pulse steroid and plasma exchange (p=0.28) prior to infection with TB with no significant difference. A significant increase was noticed in serum Cr during TB disease and treatment:1.5 mg/dL at baseline (Crbase), 1.8 mg/dL at diagnosis (*P*=0.43 vs. Crbase), and 2.0 mg/dL during the peak (*P*=0.03 vs. Crbase).

Conclusion:

Posttransplant TB drastically affects kidney function and graft outcome. Cumulative steroid dose in the first 3 months may be considered a risk factor for TB.

P1721 PERI-OPERATIVE HYPERKALAEMIA IN DECEASED-DONOR KIDNEY TRANSPLANT RECIPIENTS

Toby Humphrey[1,2,3], Nicholas Torpey[2], Thomas Hiemstra[1,2,3]

[1]Department of Medicine, University of Cambridge, [2]Department of Nephrology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom and [3]Cambridge Clinical Trials Unit, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

Background: Hyperkalaemia is a common and life-threatening medical emergency present in up to 10% of acute hospital admissions. End-stage Kidney Disease (ESKD) patients undergoing transplantation are at increased risk of hyperkalaemia and although the prevalence of hyperkalaemia in ESKD is well described, few studies have assessed the incidence and treatment of hyperkalaemia in kidney transplant recipients. Here, we describe the results from a retrospective review of peri-operative hyperkalaemia in incident deceased-donor kidney transplant recipients.

Methods: We conducted a retrospective electronic health record review of 172 consecutive deceased-donor kidney recipients at Addenbrooke's Hospital, Cambridge between November 2018 and November 2019. Patients receiving simultaneous pancreas/kidney transplants, simultaneous liver/kidney or multi-visceral transplants were excluded as were living-donor kidney recipients. Variables abstracted included demographics, the type of organ received, pre-transplant renal replacement modality, treatments received for hyperkalaemia, serum potassium values and admission and discharge dates.

Data were summarised as frequency (%), mean ± standard deviation (SD) or median with interquartile range (IQR) as appropriate. Categorical variables were compared by Chi-squared test and continuous variables by Student's *t*-test or Mann–Whitney *U*-test based on their distribution.

Results: 172 patients received a deceased-donor kidney during the study period and the median age of all recipients was 56 (IQR 46-64.5) years. 110 (64%) patients received a DCD (donation after circulatory death) kidney with the remaining 62 (36%) receiving DBD (donation after brainstem death) kidneys. 110 (64%) of recipients received haemodialysis prior to transplant. Mean serum potassium prior to transplant was 4.22±0.61 mmol/L and immediately post-operatively was 4.69±0.61 mmol/L.

85 (49%) recipients required emergency treatment for hyperkalaemia post-operatively. The median serum potassium prior to treatment was 5.98mmol/L (IQR 5.7-6.2) with median time to treatment of 6.8 hours (IQR 2.4-9.6) after kidney reperfusion. Of these patients 64% underwent emergency haemodialysis as the first line treatment for hyperkalaemia, whilst 24 of the 31 patients treated with insulin/dextrose for hyperkalaemia went on to receive haemodialysis for hyperkalaemia. Median length of stay was longer in those receiving treatment for hyperkalaemia (9 days (7-13) vs 7 days (6-10), p=0.005). Additional data is described in the figure below.

Conclusion: Hyperkalaemia amongst kidney transplant recipients is common, particularly in the peri-operative period. Current management strategies contribute to morbidity, with haemodialysis in the first week also independently associated with increased healthcare costs per patient in the first year following transplantation. New oral potassium binders may offer an alternative or adjunct to current management but there is a lack of data for their use in transplant patients. Clinical trials in the transplant peri-operative setting are warranted.

	Treated for hyperkalaemia	Not treated for hyperkalaemia	Statistical Significance
Number of recipients (%)	85 (49.4)	87 (50.6)	
Median age (IQR)	55 (44-64)	57 (50-65)	p=0.37
Type of organ			p=0.05
DBD	25	37	
DCD	60	50	
Pre-Transplant RRT modality			p=0.09
HD	61	49	
PD	13	17	
Pre-dialysis	11	21	
Serum potassium			
Mean pre-op serum potassium (+/- SD)	4.42 (+/- 0.55)	4.01 (+/- 0.60)	p<0.001
Mean post-op serum potassium (+/- SD)	4.96 (+/- 0.50)	4.42 (+/- 0.59)	p<0.001

Figure:

P1722

HIGH INTENSITY INTERVAL TRAINING AND MODERATE INTENSITY CONTINUOUS TRAINING IN RENAL TRANSPLANT RECIPIENTS: THE PACE-KD STUDY

Roseanne E Billany[1,2], Alice Smith[2,3], Ganisha Hutchinson[4], Daniel Nixon[2,3], Nicolette Bishop[1]

[1]Loughborough University, School of Sport, Exercise and Health Sciences, United Kingdom, [2]University Hospitals of Leicester NHS Trust, John Walls Renal Unit, United Kingdom, [3]University of Leicester, Department of Health Sciences, United Kingdom and [4]University of Leicester, Department of Respiratory Sciences, United Kingdom

Background and Aims: Cardiovascular disease (CVD) is a major cause of morbidity and mortality in renal transplant recipients (RTRs). General CVD risk scores underestimate the risk in RTRs who also exhibit elevated inflammation and impaired immune function. Exercise has a positive impact on these unique factors and there is growing consensus on the need for formal and specific exercise guidelines in RTRs. Despite this, there is limited rigorous research in this population, particularly surrounding novel high intensity interval training (HIIT) versus moderate intensity continuous training (MICT).

Method: 24 RTRs (male 17; eGFR 55 ml/min/1.73 m^2 [26-90]; age 48 years [27-76]) were randomised to: HIITA (n=8; 4, 2 and 1 min intervals; 80-90% of watts at peak oxygen uptake (VO_2 peak)), HIITB (n=8, 4 × 4 min intervals; 80-90% VO_2 peak) or MICT (n=8, ~35.5 min; 50-60% VO_2 peak) for 24 supervised sessions on a stationary bike (approx. 3x/week over 8 weeks). Assessments of cardiorespiratory fitness, body composition (weight and body fat %), and physical function (sit-to-stand 60 (STS60), gait speed, and calf strength) were conducted pre and post-intervention. Data were analysed using ANCOVA and paired samples t-tests.

Results: Twenty participants completed the intervention, 8 of whom reached the required intensity (HIITA 0/6 [0%], HIITB 3/8 [38%], MICT 5/6 [83%]). Although participants completed 92% (average) of the 24 sessions, there were 105 cancelled/rearranged sessions (illness 68, other commitments 33, investigator illness 4) and an average duration of 10 weeks to complete the intervention. There were significant post-training improvements in VO_2 peak (ml/kg/min)(See Table 1: HIITA, p=0.007; HIITB, p=0.025; MICT, p=0.012) and in peak power output ($watt_{peak}$)(HIITA, p=0.001; HIITB, p=0.005; MICT, p=0.002) for all groups. There was a significant post-training reduction in systolic and diastolic blood pressure (SBP and DBP, respectively) in MICT ($p<0.001$) and a significant reduction in DBP in HIITB ($p<0.001$). There were no significant changes in body composition. Gait speed improved in MICT (p=0043) and STS60 performance improved in HIITA (p=0.012). After controlling for baseline values, there were no significant between group differences for any post-training variables.

Conclusion: Enhanced cardiorespiratory fitness has been widely reported to correlate with a reduced risk of CVD and mortality. These early feasibility results, whilst acknowledging some baseline variations, show promising effects of both HIIT and MICT on the cardiorespiratory fitness of RTRs. Results also show promising reductions in blood pressure, a leading risk factor for CVD. Although fewer RTRs met the required intensity for the HIIT protocols than MICT, there were no serious adverse events or detrimental results reported. There were a large number of sessions cancelled due to illness; potentially attributable to immunosuppressive agents. We would recommend further large-scale trials of different HIIT protocols potentially with shorter intervals and less intense recovery periods in order to facilitate the achievement of the required intensity. Overall, these results further support the call for specific exercise guidance in this population in order to supplement current post-transplantation clinical advice.

Table 1. Change in cardiorespiratory fitness, body composition, and physical function over 8-week intervention

Variable	HIIT A	HIIT B	MICT
$VO_{2\ peak}$ (L/min)			
Baseline	1.55 ± 0.30	2.09 ± 0.86	2.25 ± 0.63
Change	0.17 (0.07 - 0.27)	0.22 (0.08 - 0.36)	0.28 (0.12 - 0.44)
P†	0.007	0.008	0.009
$VO_{2\ peak}$ (ml/kg/min)			
Baseline	24.23 ± 4.90	24.65 ± 7.67	29.33 ± 9.03
Change	2.78 (0.74 - 4.81)	2.83 (0.48 - 5.18)	3.72 (1.34 - 6.10)
P†	0.017	0.025	0.012
Peak power output (Wpeak)			
Baseline	119 ± 22	148 ± 67	176 ± 34
Change	22 (14 - 29)	32 (13 - 51)	30 (17 - 43)
P†	0.001	0.005	0.002
Weight (kg)			
Baseline	64.53 ± 11.19	84.05 ± 23.97	79.63 ± 9.50
Change	-0.83 (-0.7-0.53)	0.18 (-1.81 - 2.16)	-0.17 (-1.63 - 1.61)
P†	0.741	0.841	0.980
Body Fat (%)			
Baseline	27.65 ± 7.55	31.10 ± 10.46	21.43 ± 5.77
Change	0.73 (-1.05-2.52)	-0.66 (-6.16 - 4.83)	-0.41 (-2.64 - 1.80)
P†	0.340	0.784	0.650
Sit-to-stand 60			
Baseline	34 ± 9	35 ± 9	28 ± 8
Change	10 (3 - 16)	4 (-1 - 8)	2 (-3 - 6)
P†	0.012	0.096	0.340
Gait Speed (m/s)			
Baseline	1.16 ± 0.06	1.22 ± 0.07	1.15 ± 0.09
Change	0.04 (-0.03 - 0.12)	0.05 (-0.06 - 0.15)	0.72 (-0.14 - 0.16)
P†	0.081	0.341	0.043
Calf Strength (kg)			
Baseline	44.52 ± 16.67	58.20 ± 43.14	57.54 ± 17.18
Change	8.45 (0.09 - 16.80)	15.69 (-0.98 - 32.35)	7.70 (-19.69 - 35.09)
P†	0.048	0.061	0.479
Systolic blood pressure (mmHg)			
Baseline	124 ± 11	135 ± 17	137 ± 15
Change	-2 (-20 - -3)	-9 (-20 - -3)	-9 (-11 - -7)
P†	0.761	0.055	0.000
Diastolic blood pressure (mmHg)			
Baseline	83 ± 6	81 ± 7	91 ± 10
Change	-3 (-11 - 5)	-7 (-15 - 0)	-7 (-9 - -5)
P†	0.389	0.000	0.000

† = within-group difference (pre-post)

Figure:

P1723

CLINICAL AND LABORATORY CHARACTERISTICS OF RENAL TRANSPLANT PATIENTS WITH AA AMYLOIDOSIS IN A TERTIARY CENTER IN TURKEY

Ece Bilgic[1], Rezzan Eren Sadioğlu[2], Şahin Eyüpoğlu[2], Akın fırat Kocaay[3], ACAR TUZUNER[3], Şule Şengül[2], Kenan Keven[2]

[1]Ankara University School of Medicine, Department of Internal Medicine, Ankara, Turkey, [2]Ankara University School of Medicine, Department of Nephrology, Ankara, Turkey and [3]Ankara University School of Medicine, Department of General Surgery, Ankara, Turkey

Background and Aims: Despite improved therapeutic regimens, AA amyloidosis is still associated with higher risk of mortality after renal transplantation (RT). Moreover the clinical, laboratory characteristics and prognostic factors remain poorly understood. We aimed to identify predictive parameters of prognosis, investigate the etiology, clinical and laboratory features of renal transplant patients with biopsy proven AA amyloidosis.

Method: We conducted a retrospective study using twenty-eight renal transplant patients with AA amyloidosis and twenty-eight renal transplant control patients without amyloidosis matched for age and time after transplantation that were regularly followed in University of Ankara School of Medicine Nephrology Department between October 2018-October 2019. Causes of AA amyloidosis, treatment (colchicine and/ or anti-interleukin (IL) 1 treatment) and number of Familial Mediterranean Fever (FMF) attacks in the last year in case of FMF, biochemical values such as mean CRP, hemoglobin, serum albumin, proteinuria, glomerular filtration rate (GFR), serum creatinine levels were compared between groups.

Results: In amyloidosis and non-amyloiodosis group, the mean age was 44±13 and 44±12 years; 57% and 54% were males, mean time after transplantation was 95±64 and 93±12 month, respectively. FMF was found as the most common cause of AA amyloidosis (86%). All FMF patients received colchicine and eight (33%) FMF patients with AA amyloidosis with insufficient response to colchicine were treated with anti-IL-1 agents. The mean colchicine dose was 0,92±0,34 mg/day. The mean GFR were 63±24 ml/dk/1,73 m^2 in amyloidosis and 71±19 ml/dk/1,73 m^2 in non amyloidosis group, (p=0.195). The most important finding of present study was significantly higher CRP levels in patients with AA amyloidosis compared to non-amyloidosis group (15,12±15,16 mg/L vs 6,59±8,20 mg/L, p=0,011, respectively).

Conclusion: In this study, we found higher CRP levels in renal transplant patients with AA amyloidosis which indicates persistent ongoing chronic inflammation among these patients.

	Amyloidosis Group (n=28)	Non-amyloidosis Group (n=28)	P Value
Age (mean±SD), years	43,71±12,94	43,89±12,42	,876
Male sex, %	57,1	53,6	,788
Time after transplantation (mean±SD), months	95,07±64,06	92,82±12,42	,781
GFR (mean±SD), ml/dk/1,73 m^2	63,38±24,32	70,65±19,44	,195
Serum Albumin (mean±SD), mg/dL	4,09±0,44	4,16±0,29	,896
CRP (mean±SD), mg/L	15,12±15,16	6,59±8,20	**,011**
Hemoglobin (mean±SD), mg/L	12,70±2,94	13,26±1,58	,617

Figure: Clinical and Laboratory Characteristics of Patient Groups

P1724 RISK FACTORS FOR BK VIRUS INFECTION AFTER KIDNEY TRANSPLANTATION IN THE CONTEMPORARY ERA: A SINGLE-CENTRE OBSERVATIONAL STUDY

Nuvreen Phagura[1], Karanjeet Thandi[1], Felicity Evison[2], Suzy Gallier[2], Adnan Sharif[3,4]

[1]College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom, [2]Department of Health Informatics, University Hospitals Birmingham, Birmingham, United Kingdom, [3]Department of Nephrology and Transplantation, University Hospitals Birmingham, Birmingham, United Kingdom and [4]Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom

Background and Aims: BK infection remains a risk factor for kidney transplant dysfunction and allograft loss. While many risk factors are reported in the literature, many are from historical cohorts and have never been validated in the contemporary era. The aim of this study was to explore risk factors for BK virus infection in the contemporary era of kidney transplantation and immunosuppression using a well-phenotyped clinical cohort.

Method: In this single-centre observational study, data was extracted from hospital informatics systems for all kidney allograft recipients transplanted between January 1st 2007 and June 30th 2018. BK virus was checked in the context of any transplant dysfunction (indication-based) aligned with UK guidance. Positive BK virus results were defined as >200 copies/ml. Clinical outcomes extracted from electronic hospital records were linked with national datasets. Univariate analysis was undertaken to investigate the association between donor-, recipient- and transplant-related variables and risk for BK virus reactivation. Any variable with a p-value <0.15 in univariate

Results: Data was analysed for 1,770 kidney transplant recipients with median follow up 5.3 years (IQR 2.7 to 8.7 years). BK virus was associated with (versus without); male sex (8.3% versus 5.3% respectively, p=0.010), ABO-incompatible transplantation (12.7% versus 5.9% respectively, p=0.021) and delayed graft function (9.0% versus 6.3% respectively, p=0.032). In a multivariate analysis, including all variables in univariate analysis with p-value <0.15, the only independent variables associated with BK infection were recipient male sex (OR 2.051 [95% CI 1.196-3.519], p=0.009 and ABO-incompatible transplantation (OR 4.087 {95% CI 1.847-9.042], p=0.001). From an outcome perspective, recipients with BK viraemia had worse graft function at 1-, 3- and 5-year post kidney transplantation but no increased risk for death-censored graft loss.

Conclusion: In the contemporary era, only recipient male sex and ABO-incompatible kidney transplantation are independently associated with risk for BK infection. Study limitations include lack of data regarding novel risk factors (e.g. BK virus serostatus). Association does not imply causality and we suggest further work is warranted to validate contemporary risk factors for BK infection in different kidney transplant population cohorts.

P1725

USAGE AND OUTCOMES FOR EXPANDED CRITERIA DONOR KIDNEY TRANSPLANTATION IN THE KOREA CHARACTERIZED BY KIDNEY DONOR PROFILE INDEX, SINGLE CENTER STUDY

Jun Young Lee[1], Miryung Kim[1], You Jin Kim[1], Hanwul Shin[1], Byoung Geun Han[1]

[1]*Yonsei University Wonju College of Medicine, Nephrology, Wonju, Korea, Rep. of South*

Background and Aims: The demand for Kidney transplantation (KT) is increasing and the number of patients who are waiting for KT is steadily increasing. Therefore, there is an increasing prevalence of KT done by cadaver donor especially, expanded criteria donor. We used Kidney Donor Profile Index (KDPI) to predict the renal prognosis of expanded criteria donor (ECD) KT recipient.

Method: We investigated patients undergo KT by ECD from March 2013 to June 2018 respectively. Through the donor's last creatinine level, KDPI score, and Kidney Donor Risk Index (KDRI) score the renal survival rate was compared with ROC curve analysis.

Results: The mean age of a total 59 ECD KT recipient is 53.85 ± 9.9 years old. Mean follow up duration after KT was 35.0 ± 18.5 months. 10 patients had KDPI score above 85 (KDPI ≥ 85). Five cases undergo dialysis after KT. Nine cases expired during follow up (four sepsis, three sudden cardiac arrest, one hyperkalemia). Glomerular filtration rate one year after KT was significantly associated with KDPI ($r=-0.772$, $p<0.001$). The area under curve (AUC) of KDPI was 0.700 (95% CI 0.494-0.906) and cut off point was 75.5. All renal survival patients had KDPI score below 75.5

Conclusion: Our results show that KDPI could be used as an indicator for predicting the prognosis of the Korean ECD KT.

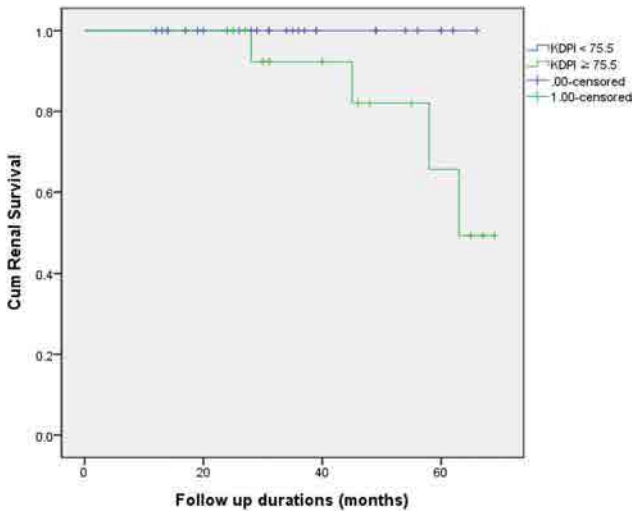


Figure: Cumulative renal survival period according to KDPI level

P1726 C3 GLOMERULOPATHY RECURRENCE AFTER KIDNEY TRANSPLANT: A SYSTEMATIC REVIEW

Oumayma Taroua[1,2], Yassir Selouani[3]

[1]Al-Zahrawi International University of Health Sciences, Nephrology, Rabat, Morocco, [2]Hôpital Cheikh Zayd, Nephrology, Rabat, Morocco and [3]Faculty Of Medicine And Pharmacy Of Rabat, Rabat, Morocco

Background and Aims: C3 glomerulopathy (C3G) is a recently defined entity, characterized by the dysregulation of the complement pathway, leading to deposition of C3 complement in the glomeruli, with no immunoglobulins, leading to glomerular inflammation. C3G encompasses 2 disorders: C3 glomerulonephritis (C3GN) and Dense Deposit Disease (DDD), distinguished by their morphological pattern. Although multiple pharmacological treatments exist to control the progression of the disease, for patients reaching End-Stage Kidney Disease, kidney transplantation remains the last resort. While it is known that membranoproliferative glomerulopathies carry a risk of recurrence after transplant, no large-scale meta-analysis was done after 2015 to assess if the precise recurrence risk and remission duration for C3 glomerulopathies.

The goal of this work is to determine if there is currently enough literature specific for C3G to conduct such a meta-analysis.

Method: Our research protocol was guided by the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P), and the Joanna Briggs Institute Critical Appraisal Tools. A search was conducted in PubMed, Web of Science and Scopus databases, using a specific search string, at the conclusion of which, 185 papers were found. The identified papers were subsequently screened by the 2 authors independently using precise inclusion and exclusion criteria. The screening resulted in the final inclusion of 7 papers, on which a qualitative synthesis was performed. The information extracted was organized on basis of demographics, time of transplantation, disease recurrence and disease-free period post-transplantation.

Results: Among the 7 papers selected, 2 were case series and 5 were case reports. In total, 23 patients were reported as having recurrence of C3G. For the patients whose age at diagnosis was known, it ranged between 9 and 51 years of age. Among the 23 patients, 16 of them were male, while 7 of them were females. The C3G subtype was determined for 21 patients, with 7 being classified as having DDD, and 14 having C3GN. The age of transplant was reported for 20 patients, ranging from 11 to 70 years old. The disease-free period between the kidney transplant and the recurrence of the disease ranged from 14 days to 101 months, with 1 case series paper only reported the median time to recurrence in months (14[0-80] for C3GN patients and 15[2-32] for DDD patients). The same paper reported the post-transplant recurrence rate among transplanted patients, determined as 10 to 12 for C3GN patients and 6 to 7 for DDD patients.

Conclusion: While C3G, with its 2 subtypes, have been well defined entities for 5 years, our review reveals that very little research about the post-transplant evolution and recurrence of these disease has been done. While extensive research can be found on the recurrence risks of Membranoproliferative Glomerulonephritis, we believe that with the new classification, more data on the new subtypes is necessary to guide the decision-making of clinicians for these patients.

P1727 **DECEASED DONOR KIDNEY CHARACTERISTICS AND IMPACT ON 10-YEAR GRAFT SURVIVAL - A LONG-TERM OBSERVATIONAL STUDY**

Chee Yong Ng[1], Wenxiang Yeon[1], Terence Kee[2], Yun Ting Yap[3], Chang yin Chionh[1]

[1]Changi General Hospital, Renal Medicine, Singapore, Singapore, [2]Singapore General Hospital, Renal Medicine, Singapore, Singapore and [3]Nanyang Technological University, Lee Kong Chian School of Medicine, Singapore, Singapore

Background and Aims: The long waiting list for deceased donor kidney transplantation has prompted the use of Expanded Criteria Donors (ECD) though it is possibly associated with worse graft function and outcomes than Standard Criteria Donors (SCD). Our centre had also implemented a protocol kidney biopsy at implantation from 2005 to 2009.

The aim of this study was to evaluate the impact of donor factors and donor kidney histology on 10-year graft outcomes.

Method: A retrospective analysis was performed on 108 kidney transplant recipients who underwent a protocol biopsy at implantation from November 2005 to November 2009. The biopsy sample was evaluated for glomerulosclerosis, tubular atrophy, interstitial fibrosis and arteriolar narrowing and scored according to Remuzzi et al., N Engl J Med. 2006;354(4):343 (Remuzzi score). Donor factors evaluated were donor age, hypertension, diabetes mellitus, and terminal serum creatinine. The 10-year graft survival and estimated glomerular filtration rate (eGFR) was the main outcome of interest.

Results: The deceased donors included 58% males, 85% Chinese, with a median age of 49 (IQR 12) years. There were 13% diabetics, 51% hypertensive donors and the median terminal creatinine was 95 umol/L. The recipients were 51% male, 79% Chinese, with a median age of 47 (IQR 11) years at transplant. The time interval to transplant was 9.2 (IQR 3.0) years and the overall 10-year graft survival was 67.6%.

Remuzzi score of $\leq$3 was associated with better 10-year graft survival compared with Remuzzi score of >3 (76.6% versus 45.2%, P =0.02). 10-year graft survival for SCD and ECD was not statistically different (71.6% versus 58.8%, P=0.187).

A multivariate analysis was performed which included donor status (ECD vs SCD), Remuzzi score (>3 vs $\leq$3), donor age ($\geq$60 or <60 years), donor hypertension, donor diabetes mellitus and terminal serum creatinine ($\geq$133 umol/L versus <133 umol/L). Only Remuzzi score correlated with a better 10-year graft survival rate (P=0.020). All other factors did not correlate with 10-year graft survival.

Amongst the 73 ten-year graft survivors, the median eGFR at year 10 was 47.5 (IQR 20.3) ml/min if the Remuzzi Score was $\leq$3 while the eGFR was 39.7 (IQR 33.0) ml/min if Remuzzi score was >3. However, this difference was not statistically significant (P=0.570).

The 10-year eGFR was 45.8 (IQR 22.2) for SCD kidney recipients vs 49.5 (IQR 25.6) for ECD kidney recipients. Paradoxically, the median eGFR was higher with the ECD cohort but this was not statistically significant (P=0.443).

Conclusion: An implantation Remuzzi score of more than 3 is associated with poorer long-term graft survival as compared to other donor factors evaluated on 10-year graft survival or eGFR. Where possible, assessment of the kidney histology should be included as part of the kidney selection and allocation process in order to determine long term outcomes.

Table 1: Baseline recipient and donor characteristics

Recipient characteristics	
Age at transplant, years (IQR)	47 (10.25)
Gender, n (%)	
Female	53 (49)
Male	55 (51)
Race, n (%)	
Chinese	85 (79)
Indian	5 (4)
Malay	17 (16)
Others	1 (1)
Donor characteristics	
Age, years (IQR)	Median: 49 (12)
Diabetes, n (%)	14 (13)
Hypertension, n (%)	55 (51)
Terminal serum creatinine, umol/L (IQR)	95 (55)

Table 2: 10-year graft survival rate stratified by donor and histological factors

	n (%)	P
Donor Status		
Standard Criteria Donors	53 (71.6%)	0.187
Expanded Criteria Donors	20 (58.8%)	
Remuzzi scores		
$\leq$ 3	59 (76.6%)	0.02
>3	14 (45.2%)	
Terminal creatinine, umol/L		
< 133	58 (66.7%)	0.676
$\geq$133	15 (71.4%)	
Diabetes mellitus		
Yes	7 (50.0%)	0.132
No	66 (70.2%)	
Hypertension		
Yes	33 (60.0%)	0.086
No	40 (75.5%)	

P1728 **FUROSEMIDE STRESS TEST PREDICTS DISCHARGE SERUM CREATININE AFTER KIDNEY TRANSPLANTATION**

Armando Coca[1], Guadalupe Tabernero[2], Carlos Arias-Cabrales[3], Jimmy Reinaldo Sanchez Gil[1], Jose Antonio Menacho Miguel[2], Maria José Pérez-Sáez[3], Alicia Mendiluce[1], Jesus Martin Centellas[2], Julio Pascual[3]

[1]Hospital Clinico Universitario, Nephrology, Valladolid, Spain, [2]Hospital Universitario de Salamanca, Nephrology, Salamanca, Spain and [3]Hospital del Mar, Nephrology, Barcelona, Spain

Background and Aims: Acute tubular necrosis is a common complication after kidney transplantation and is closely related to delayed graft function (DGF) and slower graft function recovery after surgery. The furosemide stress test (FST) uses a standardized dose of furosemide to evaluate the integrity of the renal tubule and determine which patients have developed severe tubular damage. We aimed to apply the FST to a sample of incident deceased-donor kidney transplant recipients and describe its association with DGF and serum creatinine (SCr) at discharge.

Method: Single-center prospective observational study of deceased-donor kidney transplant recipients. The FST, a standardized bolus dose of furosemide (1.5 mg/kg) was administered between the 3rd and 5th day after surgery. Patients were excluded if, during that time period, they presented evidence of active bleeding, obstructive uropathy or volume depletion. Urine output (UO) 60 and 120 min after FST was registered. To reduce the risk of hypovolemia, each ml of UO produced for six hours after FST was replaced with 1 ml of normal saline.

Results: 25 patients were included in the study. Mean 2h FST UO was 1012±570 ml. Demographic and clinical data are summarized in Table 1. Subjects that suffered DGF had a significantly lower 2h FST UO (534 vs 1164 ml; P=0.015). In adjusted linear regression analysis only a 2h FST UO<1000 ml (β=0.906; 95%CI: 0.04-1.772; P=0.041) and DGF (β=1.592; 95%CI: 0.488-2.696; P=0.008) were independent predictors of SCr at discharge (model adjusted for recipient age, cold ischemia time, number of HLA mismatches, donor SCr and donor hypertension).

Conclusion: Recipients with a 2h FST UO <1000 ml suffered DGF more frequently. FST and DGF were independent predictors of SCr at discharge. A standardized FST could help clinicians distinguish patients with more severe tubular dysfunction and higher risk of DGF.

	2h FST UO <1000 ml	2h FST UO ≥1000 ml	P value
N	12	13	
Age, years	61±10	58±11	0.461
Male sex, n (%)	9 (75)	8 (61.5)	0.471
Dialysis vintage, months	29 (10-42)	33 (11-70)	0.406
PD as RRT, n (%)	4 (33.3)	5 (38.5)	0.79
First KT, n (%)	11 (91.7)	10 (76.9)	0.315
HTN, n (%)	11 (91.7)	12 (92.3)	0.953
Diabetes, n (%)	2 (16.7)	2 (15.4)	0.93
Age (D), years	59±11	57±13	0.72
Male sex (D), n (%)	9 (75)	10 (76.9)	0.91
Surgery duration, min	200±69	197±52	0.9
CIT, hours	16±4	15±3	0.511
HLA mismatches, number	5±1	4±1	0.221
2h FST UO, ml	546±317	1443±371	<0.001
DGF, n (%)	5 (41.7)	1 (7.7)	0.047
Scr at discharge, mg/dl	2.65 (1.77-3.76)	1.54 (1.4-2.3)	0.006

P1729

HEMODYNAMIC AND AUTONOMIC PERFORMANCE IN CHRONIC DIALYSIS AND RENAL TRANSPLANT PATIENTS. IS THERE AN IMPROVEMENT?

Leonel Brukman[1], Gustavo Laham[1], Carlos Castelaro[1], Jihan Sleiman[1], Gervasio Soler Pujol[1], Maria Elena Biaiñ[1], Maximo Schiavone[2], Carlos Diaz[1]

[1]CEMIC, Internal Medicine, Nephrology Section, Buenos Aires, Argentina and [2]Charité Universitätsmedizin, Internal Medicine and Cardiology Service, Berlin, Germany

Background and Aims: Chronic kidney disease (CKD) is a major public health problem, with high prevalence worldwide. It's associated with high morbidity and mortality, especially in the advanced stage when substitution therapies are needed. It's well established that Ps with end-stage kidney disease have increased mortality due to an elevated incidence of cardiovascular diseases (CVD). The best treatment for this population it's definitely the kidney transplant (KT), mostly because it improves the quality of life and reduces global and CV mortality compared with Ps treated with chronic dialysis (Dx). There is not a convincing explanation about the physiological mechanisms involved in this improvement. Impedance cardiography (IC) it's a well established, validated method to asses hemodynamics parameters.

Study and describe the differences between hemodynamic and autonomic profiles between KT and Dx Ps using IC.

Method: We studied 331 Ps as part of a cardiovascular evaluation program in Ps with ESKD which is being carried out in our institution (CEMIC, Buenos Aires). Of these, 190 were on Dx and 141 on KT. Non-invasive hemodynamic assessment was performed using IC (Z Logic- Exxer SA) in supine and standing position, taking into account the following variables: heart rate (HR), thoracic fluid content (TFC), stroke volume (SV), systemic vascular resistance index (SVRI), arterial compliance index (ACI), and pre-ejection period (PEP). Ps in the Dx group were studied on the interdialytic day. We evaluated the autonomic profile by studying the variability of HR (Kubios Finland) for three minutes, with measurements of the spectral components, high frequency (HF), low frequency (LF), total power (totpowar) and the ratio LF/HF. We compared absolute supine variables and then the differences between supine and standing positions. Exclusions criteria: less than six months of KT or Dx; incomplete basic hemodynamic study or lack of data; amputation; previous KT.

Results: We included 107 Ps of Dx and 118 of KT. No significant differences were detected in terms of age, sex, diabetes, and antihypertensive treatment. Ps on Dx had more prevalence of hypertension and CVD. Those in KT group had a median time of 72,5 months of transplantation and 46 months of prior dialysis time, with a media of eGFR (CKD-Epi) of 56 ml/min/1,72 m2. Ps on Dx had a median of 22 months on substitution treatment. The hemodynamic evaluation showed that KT Ps had lower HR (p=o,oo1), higher ACI (p=0,002) and PEP (p=0,05), and a tendency of higher SV (p=0,07). The autonomic evaluation showed no significant differences between the two groups, though the totpowar had a tendency to be higher in the KT group with a median of 367(200-625) compared with 248 (103-465) in the Dx group (p=0,07). The changes in the variables during the standing position evidenced that Ps on Dx had a lower elevation of HR (p=0,04) and SVRI ($p<0,001$). We assessed the prevalence of orthostatic hypotension defined as a reduction of the SBP in 20 mmHg and/or the DBP in 10 mmHg after standing up. The Dx group had a prevalence of 30% and the KT group of 20%, but the difference was not significant.

Conclusion: Ps with KT seems to have a better hemodynamic profile than those on Dx, mainly, a better vascular response with a more physiological- compensatory elevation of HR and VSRI when they stand up. Although the autonomic activity showed no significant statistical difference, the total power, an expression of the whole autonomic activity, showed us a clear tendency in favor of KT, which needs to be confirmed with a larger size sample.

P1730 KIDNEY PAIRED DONATION IN SLOVAKIA - TOWARDS TO THE NATIONALLY COORDINATED PROGRAMME

Tatiana Baltesova[1], Luboslav Bena[2], Eva Lacková[3], Ivana Dedinska[4], Magdalena Krátka[5], Daniel Kuba[6] , Zuzana Zilinska[7]

[1]Unversity Hospital L.Pasteur Kosice, Transplantation dpt., Kosice, Slovakia, [2]Unversity Hospital L.Pasteur Kosice, Transplantation Dpt, Kosice, Slovakia, [3]FN F.D.Roosevelta, Transplantcenter, Banská Bystrica, Slovakia, [4]UN Martin, Transplantcenter, Martin, Slovakia, [5]Národná Transplantačná Organizácia, Directory, Bratislava, Slovakia and [7]Nemocnica akademika Ladislava Dérera, Urologická klinika s centrom pre transplantácie obličiek, Bratislava, Slovakia

Background and Aims: AB0 and HLA incompatibility between donor and recipient is one of the possible reasons of the low rate of living kidney donation in Slovakia.

Method: We present a retrospective analysis of living donor kidney transplantations (LDKT) in Slovakia including kidney paired donations.

Results: During the period from 2015 to 2019 there were 823 kidney transplantations, 81 (9,8%) were from living donors. Kidney paired donations are performed since 2005. Altogether 8 two-way paired exchanges were done in 3 transplant centers. The first exchange between two centers was carried out in 2015. A majority of the involved pairs (81%) were married couples, one exchange was initiated by compatible pair. Surgical procedures were simultaneous, cold ischemia times were comparable to other LDKT (median 162 vs 182 minutes). Two recipients had early acute rejection, 3-year graft survival is 100%. There were no serious complications in donors. The participation in EU project ENCKEP (European Network for Collaboration on Kidney Exchange Programmes) has led to the creation of national registry of incompatible pairs in 2018 and the standardization of medical and legal processes of paired exchanges.

Conclusion: Above reported experience is adequate prerequisite for the launch of nationally coordinated programme and international cooperation.

P1731 ABO INCOMPATIBLE DONOR KIDNEY TRANSPLANTATION IN PORTUGAL

Natalia Silva[1], Catarina Isabel Ribeiro[2], Jorge Malheiro[3], Manuela Almeida[3], Sofia Pedroso[3], La Salete Martins[3], Leonídio Dias[3], António Castro Henriques[3], António Cabrita[3]

[1]Centro Hospitalar De Trás-Os-Montes E Alto Douro, E.P.E., Nephrology, Vila Real, Portugal, [2]Centro Hospitalar Vila Nova de Gaia / Espinho - Unit 1, Vila Nova de Gaia, Portugal and [3]Hospital Geral de Santo António, Porto, Portugal

Background and Aims: ABO incompatiblitity was considered a barrier to kidney transplant. However, the shortage of available organs for transplantation and the excellent long term results further establish ABO-incompatible (ABOi) as a safe and effective therapeutic strategy.

The aim of the present study was to evaluate the outcomes of ABOi transplantation in terms of graft survival and function, rejection episodes and infections complications.

Method: The authors present a single center retrospective observational study, that include the analyse of 12 patients who underwent ABOi kidney transplantation between November 2014 and July 2019. All patients received Rituximab (375mg/m^2) pre-operation and started Tacrolimus, Mycophenolate Mofetil and Prednisolone one week before surgery. Plasmapheresis was done to remove anti-A or B antibodies until their titles were $<$1:8 during the first post-operative week and $<$1:16 at the second.

Results: : A total of 12 patients were included in the study, 75,0% male with 43 years (IQR 31-50) The most common blood group mismatch was A to O (n=4; 33%). In the first year, 2 of patients (17%) developed acute rejection. The follow-up time was 17 months (IQR 7-36). Five patients (42%) developed infectious complications. None patients developed cytomegalovirus or BK polyomavirus infections. At the end graft and patient survival were 100%.

Conclusion: ABOi kidney transplantation has become a routine procedure. By this approach, about 30% of living donors who were refused in the past can now donate their kidneys and thereby significantly expand the living donor pool. Immunosuppressive protocol of this Center can be considered safe.

P1732 RECURRENCE OF GLOMERULONEPHRITIS POST TRANSPLANT

Umesh Lingaraj[1], Ricken Mehta[2,2], Shivaprasad SM[2], Kishan A[2], Leelavathi V[2], Sreedhara C[2], MYTHRI V[2]

[1]Institute of Nephro Urology, nephrology, Bengaluru, India and [2]Institute of Nephro Urology, Bengaluru, India

Background and Aims: Glomerulonephritis (GN) is a major cause of end stage renal disease (ESRD)[1].

It represents the primary cause of end stage renal disease (ESRD) for 25% of the dialysis population[1] and 45% of the transplant population.

For patients with GN requiring renal replacement therapy, kidney transplantation is associated with superior outcomes compared with dialysis[2].

The possibility of recurrence of the original disease after transplantation was described in a seminal paper more than 40 years ago, and it is now clear that all forms of GN may recur after kidney transplantation.[3]

To study the recurrence of glomerulonephritis post-transplant in a tertiary care centre.

Method: 120 renal transplant recipients were analyzed from September 2015 to August 2019 at the Institute of Nephro-Urology, Bangalore.

It was a retrospective analysis of data

Results: 120 adult patients underwent kidney transplantation, out of these 70 had GN as primary cause of kidney disease.

85.8% were males, 14.2 % females.

58.9 % were biopsy proven GN, remaining 41.1 % diagnosed based on history and clinical presentation.

All but one patient had their first transplant.

Out of these kidney transplant recipients 08 (11.4%) had recurrence of GN. From these 4/08 was recurrent IgA N, 2/08 were PGNMID, 1/08 MGN, 1/08 aHUS. Graft loss due to recurrent GN was seen in 1/08 patients (12.5%).

Conclusion: Our study showed that 11.4 % of kidney transplant recipients with GN as their cause of ESRD had recurrent GN post kidney transplantation. IgAN was the most type of GN that recurred most frequently followed by PGNMID. Recurrence of GN was in par with other studies and did not affect graft survival

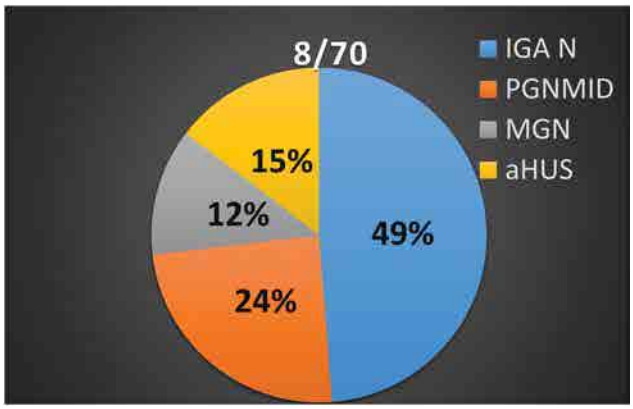


Figure:

P1733 MINERAL BONE DISEASE (MBD) IS THE POST KIDNEY TRANSPLANTATION POPULATION

Louise Ryan[1], Eva Ruane[1], Alan Watson[1], John Holian[1], Aisling O'Riordan[1]
[1]St Vincent's University Hospital, Nephrology, Dublin, Ireland

Background and Aims:

Patients with ESRD have a 4-fold higher risk of fracture compared to the general population. ([1]) Transplant bone disease is a combination of mineral bone disease sustained pre transplantation and damage incurred post transplantation, risk factors for which include immunosuppression and immobility in the early post transplantation period. Given the high morbidity, mortality and financial burden associated with fractures, the management and prevent of osteoporosis is fundamental. ([2]) We aimed to compare the management of MBD in our patient cohort to international nephrology and rheumatology guidelines. ([1, 3])

Method:

A retrospective review of all patients post kidney transplantation attending our department was carried out. Information pertaining to patient demographics, renal history, osteoporosis investigation and management was collected. The results were analysed with Microsoft Excel.

Results:

154 patient records (92 male, 62 female) were reviewed. Mean age was 52 years (range 19-80). Mean eGFR was 54ml/min (range 9-90). 82% of patients were taking corticosteroids, the mean dose was 5mg. 9% were taking corticosteroids pre-transplantation. 11 patients (7%) had a history of parathyroidectomy. 19% of patients had a history of a fracture. 26% of patients had a DEXA scan performed which demonstrated 50% had osteopenia and 29% had osteoporosis. The mean fracture risk assessment tool (FRAX) score (risk of having an osteoporosis-related fracture in the next 10 years) for a major osteoporotic fracture was 10.2% (range 2.1-34%) and for a hip fracture was 3.1% (range 0.2-18). Based on these scores 19% and 26% of patients respectively met the criteria for treatment. Overall, 58% of patients were on treatment for either osteoporosis prevention or management or for mineral bone disease. 74% of patients with osteopenia were on treatment (32% calcium supplementation, 5% alfacalcidol, and 63% cholecalciferol). 82% of patients with osteoporosis were on treatment (45% cinacalcet, 36% cholecalciferol, 18% bisphosphonate and 9% denosumab). 27% of patients with osteoporosis were managed in keeping the guidelines.

Conclusion:

Our cohort have significant risk factors for osteoporosis including maintenance corticosteroid treatment and previous fractures. There is a high prevalence of osteoporosis in our cohort compared to that reported internationally ([4]) and they had a high predicted rate of future fractures. Increased screening with targeted treatment is required to reduce the risk of fractures in our post renal transplant patients.

RENAL TRANSPLANTATION. TREATMENT AND IMMUNOSUPPRESSION

P1735 **USING PRONASE PRE-TREATMENT CDC-CROSSMATCH TO STUDY THE RITUXIMAB KINETICS IN KIDNEY TRANSPLANT CANDIDATES AND RECIPIENTS**

Ilaria Gandolfini[1,1], Paola Zanelli[2], Alessandra Palmisano[1], Giuseppe Daniele Benigno[1], Enrico Fiaccadori[1], Umberto Maggiore[2]

[1]University Hospital of Parma, Nephrology, Parma, Italy and [2]University Hospital of Parma, Immunogenetics, Parma, Italy

Background and Aims:

Rituximab (RTX) is a monoclonal antibody that targets CD20 on B cells. It is often used in the desensitization before ABO- and HLA-incompatible kidney transplant (KT) and in the treatment of antibody-mediated rejection (ABMR), glomerulonephritis and post-transplant lymphoproliferative disorders (PTLDs) in KT recipients, however in most of these conditions the kinetics of the drug has not been widely investigated. Because of its intrinsic B cytotoxic property, its use can interfere with immunogenetic techniques such as B-cell complement mediated cytotoxic crossmatch (CDCXM). Low dose pronase pretreatment has been proposed to reverse this interference, cleaving the CD20 rituximab target from these cells. We wanted therefore to test the kinetics of rituximab in the serum of kidney transplant candidates or recipients using CDCXM with or without pronase pretreatment.

Method:

We conducted a retrospective monocentric study on all KT candidates and recipients that underwent RTX therapy at the Parma Kidney Transplant Nephrology Unit (Parma, Italy) with serial biobanked frozen sera stored at the Immunogenetic Unit of Parma (Parma, Italy). B-cell CDCXM was performed in the presence or absence of low-dose (0.5 mg/mL) B-cells pretreatment. The difference between 2 intervals was analysed by Mann-Whitney test, groups analysis was analysed by Kruskal-Wallis test. The difference in the presence of absence of pronase pretreatment was analyzed by Wilcoxon test for paired data.

Results:

We included 31 patients, 58% were male, the average age was 46+/- 13. The majority (74%) of the patients received a living donor KT and the most common indication for RTX was the desensitization for ABO- (58%) or HLA-(13%) incompatible living donor KT. Other indications were the treatment of glomerulonephritis (13%), ABMR (10%) or PTLD (6%). One patient received 2 doses of 1 g, the rest of the patients received 375 mg/m2 once (84%) or twice (16%). In 48% of the patients RTX therapy was followed by isolated plasmapheresis (PEX) or in combination with immunoadsorption (IA)(32%). In most of the patients B-cell CXCXM turned negative at 6 months after RTX treatment ($p<0.001$)(Figure 1), however this cytotoxicity was more persistent (up to 12 months) in patients who did not underwent PEX+/-IA after RTX (Figure 2). The B-cell pretreatment with pronase was able to turn negative this reaction ($p=0.002$) in these patients.

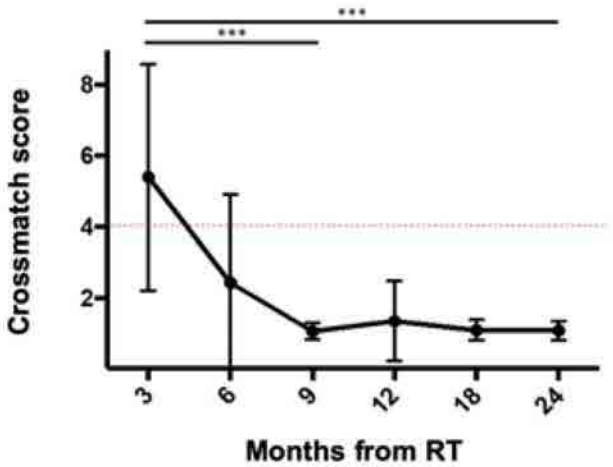


Figure 1. B-cell CDCXM score after RTX in all patients.

The scores represent the mortality rate. The red line is the positive cutoff value. Score: 1 = 0-10%; 2 = 10-20%; 4 = 20-50%; 6 = 50-80%; 8 = 80-100%;

*** $p<0.0001$.

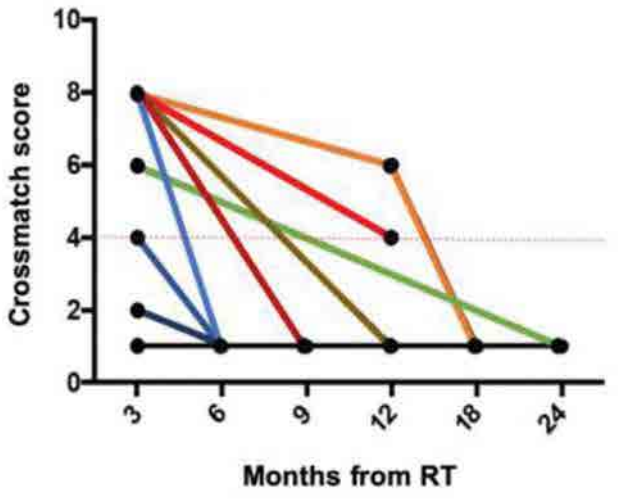


Figure 2. B-cell CDCXM score after RTX in patients free from EPX or IA treatment after RTX.

The scores represent the mortality rate. The red line is the positive cutoff value. Score: 1 = 0-10%; 2 = 10-20%; 4 = 20-50%; 6 = 50-80%; 8 = 80-100%;

Conclusions:

The data of our study seem to suggest a persistence of RTX in the sera of KT patients among the 4 months of onlabel treatments, especially in the absence of PEX or IA treatment following RTX.

Moreover the use of B-cell CDCXM in the the presence or absence of pronase could be used to monitor circulating levels of RTX in different diseases.

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P1736 FIRST PROSPECTIVE CLINICAL STUDY OF A SINGLE-USE STERILE CYSTOSCOPE DESIGNED FOR DOUBLE J (DJ) STENT REMOVAL IN AN ITALIAN TRANSPLANT CENTER

Antonio AMATO[1]

[1]*Civico Di Cristina Benfratelli Azienda Di Rilievo Nazionale ad Alta Specializzazione, Nephrology, Palermo, Italy*

Background and Aims: A DJ is routinely placed during kidney transplantation then post-operatively removed, usually within the first month after transplantation.

The removal is mainly performed in urology unit, through reusable rigid scope in an operating theatre with anesthesiologist assistance. Such removal procedure requires a complex environment with reprocessing, periodic maintenance and repairs of scopes, leading to delays and postponed stent removals.

Hematuria, pain or dysuria due to the local trauma, and urinary infection are the most common complications of the DJ removal procedure.

To overcome these issues, we introduced in April 2018 in our unit the single use sterile cystoscope ready to use with integrated grasper designed for DJ removals.

Method: We hereby report our experience with single-use flexible cystoscope (Isiris® – Coloplast).

We prospectively collected data of any DJ stent removal operation from April 2018 to December 2019 (92 procedures). Urine culture at the removal day and usually 1 week after, at the first outpatient control was performed. All complications (related or not to the procedure) were recorded.

All removals were performed in our unit by the nephrologist.

87 patients were treated, from which 82 as outpatients, and 5 as in-patients.

Results: 86 out of 87 patients stent removals were effectively done with Isiris®.

In a single case, we could not remove the stent with the single-use instrument and resorted to traditional rigid cystoscopy under general anaesthesia. This happened with the sixth patient of our series and we think that this failure happened in the learning curve phase.

In 4 cases stent removal wasn't possible at first attempt due to likely interference of the internal stitches of the anastomosis: our policy is NOT to force stent removal if any resistance is felt to light pulling. Indeed, in all 4 cases a second procedure performed one month later was completely successful with smooth withdrawal of the device.

In one case, a removal procedure was not possible because of urethral stricture and stent removal was postponed after its treatment.

Taking into account these five patients the success rate of using Isiris® is 98.9% during this period.

No patient was admitted for complications related to the removal procedure, namely for symptomatic urinary tract infection requiring antibiotics.

Two patients were admitted for obstructive nephropathy (namely ureteral stenosis) which became evident after stent removal.

16 patients had an asymptomatic positive urine culture for a multi-resistant microbe before the stent removal and maintained positivity after the procedure.

11 patients were negative on the day of the stent removal and resulted positive in the control done at the first control. Again, none developed symptoms, and none required treatment.

9 patients were positive before stent removal and were negative on the first control.

The rest of the patients were negative both at baseline and thereafter.

Conclusion: Due to the simplicity of the procedure by the single use solution (with 98.9% removal success, no operating theatre, no anaesthesiologist) and the fact that it is entirely managed by the transplantation clinic staff, the timing of the stent removal always respected physician's indication, with no procedure delayed for organizational reasons. Knowing the infection risk associated with longest ureteral stent dwell durations, and the vulnerability of these immunosuppressed patients, it is important to remove the DJ as safely as possible and in defined time. In our study, no patient had to be admitted for urinary tract infection after the procedure nor developed symptomatic urinary tract infection to be treated with antibiotics.

P1737 MICROBIOLOGICAL DIAGNOSIS OF DIARRHEA IN RENAL TRANSPLANT PATIENT BY MULTIPLEX PCR

Vaibhav Tiwari[1], Anurag Gupta[1], Yogeshman Anand[1], Vinant Bhargava[1], Manish Malik[1], Ashwani Gupta[1], A K Bhalla[1], Devinder Singh Rana[1]

[1]*Sir Ganga Ram Hospital, New Delhi, India*

Background and Aims: Acute gastroenteritis is an unwelcome and harmful yet unavoidable complication in the renal transplant patient. Infections, especially atypical organisms like Norovirus, *Cryptosporidium*, along with typical microorganisms like *E. coli* and *Giardia*, form the significant players in the pathogenesis of diarrhea. Standard methods of staining and culture have reduced sensitivity as well as require considerable time for the reports. Stool Polymerase Chain Reaction (PCR)is a quick, sensitive, and hassle-free method that diagnoses more than 20 organisms within 1 hour. This study aims to determine the infective etiology of acute gastroenteritis in the transplant population as well to compare the yield of stool PCR with conservative methods.

Method: We retrospectively analyzed all renal transplant patients admitted between 2015 to 2018 with complaints of diarrhea (>3 stools/day with loose consistency). The sample was tested for conventional microbiological methods, including a stool routine for microscopy and culture. A stool sample was also sent for Multiplex PCR, which was analyzed by Bio Fire FilmArray GI Panel, which identifies 22 enteropathogens. Endoscopic procedures were also undertaken in suspected cases for CMV colitis and pseudomembranous colitis.

Results: 110 diarrheal events (admission for diarrhea) were recorded in 82 patients, with 181 organisms isolated in all samples. 16 events did not reveal any organisms in stool PCR. 85% sample yielded a positive result. The conventional method yielded a positive result in only 32.3% as compared to stool PCR. Co-infections were common, as 71.2% of events were associated with 2 or more organisms. Conventional methods failed to diagnose any co-infections. Norovirus G1/G2(20%) was the most common organism isolated from the stool, followed by *Giardia* (17%) and *Enteropathogenic E. coli* (16%). *Giardia Lamblia* with Norovirus G1/G2 was the most common co-infection in 19% of patients.

Conclusion: Stool PCR significantly improves the diagnostic yield in diagnosing enteric pathogens. Stool PCR is especially sensitive in detecting multiple organisms where conventional microbiological methods were completely unsuccessful. Norovirus is the most common enteropathogen, which is not picked by the conventional method. *Giardia* with Norovirus was the most common co-infection among post-transplant patients.

Frequency of Organisms	No. of Positive cases	%
Norovirus GI/GII	37	20%
Giardia lamblia	30	17%
Enteropathogenic E.Coli	29	16%
Cryptosporidium	21	12%
Shigella/Enteroinvasive E.Coli	20	11%
Enteroaggregative E.Coli	17	9%
Enterotoxigenic E.Coli	12	7%
Campylobacter	7	4%
Clostridium defficile (toxin A/B)	3	2%
Vibrio cholerae	3	2%
Plesiomonas shigelloides	1	1%
Sapovirus (I, II, IV, and V)	1	1%
TOTAL	181	100%

Figure 1: frequency of organisms diagnosed by Stool Polymerase Chain Reaction in transplant patients presenting with acute gastroenteritis

Figure 1: frequency of organisms diagnosed by Stool Polymerase Chain Reaction in transplant patients presenting with acute gastroenteritis

P1738

COULD ADDING BORTEZOMIB HAVE BENEFIT FOR ANTIBODY MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION?

Nooshin Dalili[1], Mohsen Nafar[1]

[1]*Department of Nephrology, Labbafinejad Medical Center, CKDRC, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Background and Aims: Antibody Mediated Rejection (ABMR) is a severe complication that frequently occurs after kidney transplantation. The present RCT designed to evaluate the role of adding Bortezomib to standard regimen with plasma exchange, intravenous immunoglobulin and Rituximab in treatment of AMR after kidney transplantation.

Method: 26 kidney transplant recipients (KTRs) with a biopsy proven diagnosis of AMR and positive DSA in a randomized clinical trial were compared: Thirteen KTRs treated with plasmapheresis, intravenous immunoglobulin and rituximab (PE-IVIG-RTX) plus bortezomib versus 13 patients treated with standard of care regimen without bortezomib. We evaluated graft survival and DSA titer with MFI during a year after biopsy proven diagnosis.

Results: Statistical difference in graft survival between the two groups was noted: three out of 13 patients in the PE-IVIG-RTX group (23%) and 1/13 in the bortezomib group (7.5%) experienced loss of allograft function at a median time after diagnosis of 6 month and 12 month, respectively. DSA MFI titers 12 month after AMR diagnosis showed significant reducing slope in Bortezomib group. Regarding pathological changes micro vascular inflammation (glomerulitis + peritubular capillaritis score) reduced after PE-IVIG- RTX plus bortezomib in 7 out of 13 patients whom underwent protocol biopsies after treatment (53%) (Median score 3 in pre- treatment biopsy vs. 1 in post-treatment biopsy; $P = 0.036$).

Conclusion: Although DSA titer may not differ at 6 months after treatment of AMR between those who received standard regimen and those treated with adding Bortezomib, but at the end of one year patients treated with standard regimen plus Bortezomib reached lower MFI DSA titer. Adding Bortezomib to PE-IVIG- RTX for the treatment of AMR after kidney transplantation may enable clinicians to fight the DSA better and change the future of next generation of highly sensitized kidney transplant candidates.

P1739

IMMUNOSUPPRESSION WITH CALCINEURIN INHIBITOR AFTER RENAL TRANSPLANT FAILURE PREVENTS ALLOSENSITIZATION

Covadonga López del Moral Cuesta[1], Sandra Guiral[2], Marina De Cos Gomez[1], David Gómez Pereda[1], Emilio Rodrigo[1], Rosalía Valero San Cecilio[1], José Iñigo Romón Alonso[3], David San Segundo Arribas[2], Marcos López-Hoyos[2], Juan Carlos Ruiz San Millán[1]

[1]University Hospital Marques de Valdecilla, Nephrology, Santander, Cantabria, Spain, [2]University Hospital Marques de Valdecilla, Immunology, Santander, Cantabria, Spain and [3]University Hospital Marques de Valdecilla, Hematology, Santander, Cantabria, Spain

Background and Aims: Retransplantation is an important option to consider in patients who return to dialysis after graft failure since it reduces mortality. HLA allosensitization hinders retransplantation, and immunosuppression withdrawal after graft failure seems to favor sensitization. There are no established protocols on the immunosuppressive treatment that should be maintained after transplant failure in order to reduce the development of anti-HLA antibodies. The aim of the study is to evaluate the effect of immunosuppression withdrawal on the development of anti-HLA antibodies after graft loss.

Method: A retrospective analysis including 77 patients who lost their first renal graft between 1/1/2006-12/31/2015 was performed. 22 patients with preemptive second kidney transplant were included. Maintenance immunosuppression was collected in months 1, 3 and 6 after graft failure. Patients were divided into two groups according to the presence or not of calcineurin inhibitor (CNI) as maintenance treatment. Two sera were analyzed per patient, one immediately prior to graft loss and another one after graft failure (Luminex®, Single Antigen). In patients in whom transplantectomy was performed, the selected serum after transplant failure was already after graft nephrectomy. PRA was calculated (cPRA) in each serum and the development of de novo donor-specific antibodies (dnDSA) was evaluated.

Results: Selected sera were extracted 1.0 month before graft failure (interquartile range 0.3-2.0) and 7.6 months after transplant failure (interquartile range 6.0-12.2). By multivariate logistic regression analysis, graft nephrectomy was an independent risk factor for cPRA>75% after transplant failure (OR 4.9, CI 95% 1.0-22.2, p=0.038). Similarly, the absence of CNI at 6 months after graft failure was significantly related to cPRA>75% in the multivariate analysis (OR 4.8, CI 95% 1.5-15.0, p=0.006). It was possible to analyze dnDSA formation in 73 patients. The absence of CNI at 6 months after graft loss was an independent risk factor for dnDSA development (OR 23.2, CI 95% 5.3-100.6, p <0.001). There were no differences in the management of other immunosuppressive drugs.

Conclusion: The absence of maintenance treatment with CNI at the sixth month after graft loss is a risk factor for sensitization. Therefore, immunosuppressive maintenance treatment based on CNI after transplant failure should be considered, since it seems to prevent HLA allosensitization.

P1740

KINETICS OF B-CELL SUBSETS RECONSTITUTION FOLLOWING RITUXIMAB TREATMENT IN ABO-INCOMPATIBLE KIDNEY TRANSPLANT RECIPIENTS

Yamei Li[1], Yunying Shi[2], Tao Lin[3], Xianding Wang[3], Lin Yan[1], Yi Li[1], Yangjuan Bai[1], Cuili Yang[1], Zhengli Wan[1], Lanlan Wang[1]

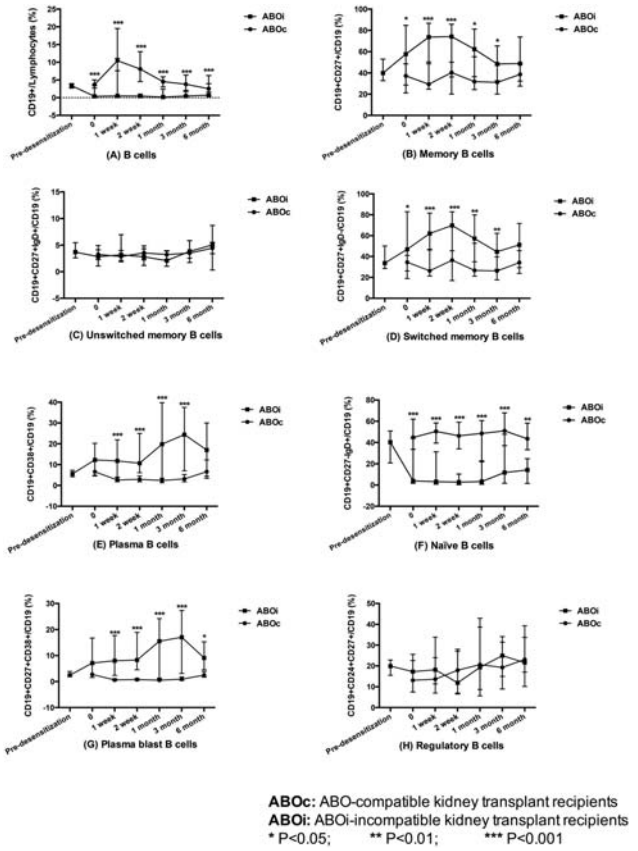
[1]West China Hospital of Sichuan University, Department of Laboratory Medicine, Chengdu, P.R. China, [2]West China Hospital of Sichuan University, Department of Nephrology, Chengdu, P.R. China and [3]West China Hospital of Sichuan University, Department of Urology/Institute of Urology, Chengdu, P.R. China

Background and Aims: With the application of B-cell-depleting agent rituximab, plasmapheresis and powerful immunosuppression, ABO-incompatible kidney transplant recipients (ABOi-KT) have successfully overcome the ABO antibody barrier. As an important immune cell population, B cells are not only involved in antibody-mediated rejection, but also have been reported to have different immunoregulatory effects due to the existence of distinct B cell subsets. Therefore, comprehensively understanding the reconstitution of B-cell subsets in ABOi-KTRs is crucial to know the immune status that may be related to the subsequent complications.

Method: Fresh whole blood were collected from 22 ABOi-KTRs and 22 ABO-compatible recipients (ABOc-KTRs) at 0, 1week, 2 weeks ,1month, 3months, and 6 months post-transplantation between October 2018 and May 2019. In addition, pre-desensitization samples were also collected from ABOi-KTRs. B cell subsets including total, naïve, memory, plasma, plasma blast and regulatory B cells were determined by flow cytometry.

Results: The percentages of B cells in ABOi group remained extremely low and significantly lower than ABOc group through the first 6 months after rituximab treatment (**Fig. A**). Similar trends were observed in total memory and switched memory B cells whose frequencies increased within first 2 weeks, then decreased thereafter. Meanwhile, the significant differences between ABOi and ABOc groups disappeared at 6 months (**Fig. B-D**). In addition, plasma and plasma blast B cells increased 2 weeks after transplantation and were significantly higher in ABOi group compared to ABOc group (**Fig. E, G**), while Naïve B cells started to elevate 1 month after transplantation in ABOi-KTRs and significantly higher proportions were found in ABOc group through the entire 6 months (**Fig. F**). No obvious difference was observed between ABOi and ABOc groups regarding unswitched memory and regulatory B cell percentages (**Fig. C, H**).

Conclusion: Our preliminary results indicated that B-cell depletion therapy applied in ABOi-KTRs not only significantly reduced the number of B cells, but also changed the composition of B cell subsets in the remaining B cell population. Whether such alteration would be clinical significance requires further follow-up.



ABOc: ABO-compatible kidney transplant recipients
ABOi: ABOi-incompatible kidney transplant recipients
* P<0.05; ** P<0.01; *** P<0.001

Figure:

P1741 **TACROLIMUS FAST METABOLIZERS SHOW A HIGHER PROGRESSION OF INTERTITIAL FIBROSIS AND TUBULAR ATROPHY DURING THE FIRST YEAR AFTER RENAL TRASPLANTATION**

Betty Chamoun Huacon[1], Irina Torres[1], Alejandra Gabaldon[2], Néstor Toapanta[1], Joana Sellares[1], Manel Perello[1], Francesc Moreso[1], Daniel Seron Micas[1]

[1]Hospital Universitari Vall d'Hebron, Neprhology, Barcelona, Spain and [2]Hospital Universitari Vall d'Hebron, Pathology

Background and Aims: Fast tacrolimus metabolizers (expressed as the blood concentration/ dose ratio; C / D; ng / mL * mg) showed poorer renal function at 2 years, a higher incidence of nephrotoxicity and BK polyomavirus infection. Greater variability of tacrolimus trough levels (CV) from six to twelve months is associated with the appearance of HLA antibodies, interstitial fibrosis / tubular atrophy (IFTA) progression and allograft loss. We evaluate the relationship between C / D, CV and IFTA progression.

Method: We evaluated a cohort of 87 low immunological risk renal transplants treated with prolonged-release tacrolimus, mycophenolate mofetil and steroids. We analyzed paired protocol biopsies at 4 and 18 months. Biopsies were evaluated according to the Banff classification and the progression of IFTA was defined as the difference of ci + ct score> 0 between 18 and 4 months. The C / D ratio was calculated as the average of the value recorded at 3, 6 and 12 months of follow-up. The tacrolimus CV between 6 and 12 months was calculated using all the available determinations.

Results: IFTA progression was observed in 36 cases (41%). In the univariate analysis, it was found that the progression of IFTA was associated with the ci + ct score at 4 months (0.92 ± 0.94 for progressors vs. 1.89 ± 1.26 not progressors, $p = 0.0003$), and with the average of the C / D ratio (1.70 ± 0.73 for progressors vs. 2.28 ± 1.25 not progressors; $p = 0.0144$, table 1). An independent association between the C/D ratio and the progression of IFTA was observed in the multivariate analysis (OR: 0.42; 95% CI: 0.22-0.82, $p = 0.027$).

Conclusion: The results of our work suggest that fast tacrolimus metabolizers (lower C / D ratio) are more susceptible to the nephrotoxic effect of tacrolimus.

Table 1. Characteristics of renal transplant recipients in the group without progression of fibrosis and with progression.

	Without progression (n=51)	With Progression (n = 36)	p-value
Recepient			
Age of recepient (years)	54 ±13	50 ± 14	ns
Gender recepient (Male/Female)	38/13	29/7	ns
Repeat trasplant (No/Yes)	46/5	31/5	ns
Donor			
Age of donor (years)	54 ± 16	50 ± 13	ns
Donor type (Deceased/Living)	43/8	30/6	ns
Cold ischemia time (h)	14 ±7	14 ± 8	ns
Trasplant			
HLA mismatch DR	1,0 ± 0,7	0,9 ± 0,7	ns
Induction theraphy (Basiliximab/ ATG)	29/22	22/13	ns
Delayed graft function (No/Yes)	49/2	33/3	ns
Acute rejetion (No/Yes)	47/4	35/1	ns
Renal function, tacrolimus and select histologic (first biopsy)			
Serum creatinine (mg/dl)			
Proteinuria (mg/g)	1,29 ± 0,35	1,35 ± 0,28	ns
Tacrolimus	0,26 ± 0,15	0,27 ± 0,19	ns
i + t	9,78 ± 2,69	9,43 ± 1,95	ns
IFTA (ci + ct)	0,55 ± 1,08	0,30 ±0,78	ns
	1,89 ± 1,26	0,92 ± 0,94	0,0002
Renal function, tacrolimus and select histologic (second biopsy)			
Serum creatinine (mg/dl)			
Proteinuria (mg/g)	1,24 ± 0,30	1,30 ± 0,28	ns
Tacrolimus	0,31 ± 0,33	0,32 ± 0,41	ns
i + t	8,20 ± 1,89	9,04 ± 2,78	ns
IFTA (ci + ct)	0,50 ± 0,99	0,46 ± 0,91	ns
	1,59 ± 1,27	2,72 ± 1,52	0,0003
CV_TAC 6-12 m	21,34 ± 17,61	18,16 ± 6,68	ns
Mean C/D_ TAC 3-12 m	2,28 ± 1,25	1,70 ± 0,73	0,0144

ATG: anti-thymocyte globulina, IFTA: intertitial fibrosis/tubular atrophy, CV: coefficient of variation, C/D: concentration dose ratio.

P1742

POTENTIAL TREATMENT METHOD OF RECURRENT URINARY TRACT INFECTION IN POSTMENOPAUSAL KIDNEY TRANSPLANT RECIPIENTS: THE RESULTS OF PILOT STUDY

Anna Dolgolikova[1], Maryna Huberskaya[2], Denis Efimov[2], Denis Sadouski[2], Pavel Viarshynin[2], Aleh Kalachyk[2]

[1]Belarussian Medical Academy of Postgraduate Education, Minsk, Belarus and [2]Minsk Scientific and Practical Center for Surgery, Transplantation and Hematology, State Institution, Minsk, Belarus

Background and Aims: Infectious complications remain a major cause of morbidity and mortality among transplant recipients. Urinary tract infection (UTI), especially recurrent UTI, is a common problem, with the prevalence up to 75% among kidney transplant (KTx) recipients. Older age, female gender and delayed graft function are among the independent risk factors for recurrent UTIs in renal transplant recipients*. Postmenopausal women with recurrent UTI after KTx especially caused by bacteria with multidrug antibiotic resistance (MDR) form a large and growing up group of patients with almost unachievable remission. The aim of the study was to assess the efficiency of different treatment schemes of recurrent UTI in postmenopausal female transplant recipients.

**prospective study presented at the 50th Interscience Conference on Antimicrobial Agents and Chemotherapy*

Method: The randomized prospective pilot study was conducted to assess the efficiency of 3 different therapy schemes, study period: 2017-2019. Recurrent UTIs were defined as ≥2 UTIs in 6 months or ≥3 UTIs in 12 months. A UTI was diagnosed based upon the presence of pyuria defined as >5 WBCs/high-power field and a urine culture of >100,000 colonies/mL. All consecutive female patients with postmenopausal history who presented to the transplant clinic for follow-up over the study period of six months were prospectively randomized into 3 groups. The primary outcome was occurrence of UTI at 6 months.

Results: Escherichia coli was the responsible pathogen for recurrent UTI in 55% of cases. Other causative organisms include Klebsiella pneumoniae (35%) as well as Enterobacter spp (10%). The rate of resistance to all tested antibiotics was the highest in Klebsiella pneumoniae. The first episode of UTI occurred at 16 (8,5;42) week after KTx.

The total number of UTI episodes (per year) after treatment varies from 7 [5;8] in the 1st Group to 0 [0;0] at the 3rd Group (p<0,001), in which 13 out of 15 patients achieved long-term remission during the observation period. Clinical data on the 1st check-up after treatment course and about UTI episodes are given bellow.

Conclusion: Frequent antibiotic usage often causes MDR as well as result in intestinal dysbacteriosis. Immunosuppression state, frequent antibiotic usage, intestinal disbiosis and also vaginal Ph decline form pathogenic vicious circle. Complex usage of fosfomycin that remains active against a considerable proportion of MDR gram-negative bacteria with bacteriophages, estrogen treatment and long-term probiotic supplement may reduce the UTI frequency in postmenopausal women after KTx.

Table 1. Patient's groups according to the ongoing therapy

Group / Patients number	Group 1 N=15	Group 2 N=15	Group 3 N=15
Therapy	Antibiotics according to urine culturefollowed by low dose of antimicrobial agents 21 days.	3-6 doses of fosfomycin q 48 hrs+ polyvalent bacteriophage 20 ml twice daily for 10-14 days followed by low dose of antimicrobial agents for 21 days.	3-6 doses of fosfomycin q 48 hrs+polyvalent bacteriophage 20 ml twice daily for 10-14 days+ estrogen treatment delivered vaginally + 2 caps long term two-component product**

***two-component product containing 2x10[9] live probiotic lactobacilli - L. acidophilus, L. rhamnosus, L. casei and cranberry extract, standardized for proanthocyanidin - 72 mg in each capsule.*

Table 2. Selected demographic and clinical data of patients depending on the treatment group

	1st Group	2nd Group	3rd Group	p
Age (Me [25%;75%])	59,4 [50;67]	55,4 [49;61]	54,6 [48;60]	NS
UTI episodes per year (Me 25%;75%])	7 [5;8]	2 [1;4]	0 [0;0]	p<0,001 between group 3 vs. group 1 and 2
Relapse rate, %	100% (15/15)	93% (14/15)	13% (2/15)	p<0,001 between group 3 vs. group 1 and 2
CRP, mg/l (Me [25%;75%])	13 [4;15]	7,2 [2,8;7,5]	4,6 [0,7;7,1]	NS
Leukocyturia, / per power field (Me [25%;75%])	35 [20;100]	42 [12;100]	5 [0;5]	p<0,001 between group 3 vs. group 1 and 2
GFR, ml/min (Me [25%;75%])	55 [45;69]	47 [32;60]	61 [54;76]	NS

P1743 **IMPORTANCE OF KIDNEY ALLOGRAFT REJECTİON IN BK VIRUS NEPHROPATHY**

Erol Demir[1], Kamil Kayaş[1], Cansu Erel[1], Bilge Caparali[1], Tuba Elif Ozler[2], Ahmet Burak Dirim[1], Nezahat Muge Catikkas[1], Nurana Guller[1], Seda Safak[1], Ali Riza Ucar[1], Ozgur Akin Oto[1], Halil Yazici[1], Yasar Kerem Caliskan[1], Sebahat Usta Akgul[3], Sonay Temurhan[3], Yasemin Ozluk[4], Isin Kilicaslan[4], Alaattin Yildiz[1], Aydin Turkmen[1], Mehmet Sukru Sever[1]

[1]Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Nephrology, Istanbul, Turkey, [2]Haseki Education Research Hospital, Department of Internal Medicine, Division of Nephrology, Istanbul, Turkey, [3]Istanbul University, Istanbul Faculty of Medicine, Department of Medical Biology, Istanbul, Turkey and [4]Istanbul University, Istanbul Faculty of Medicine, Department of Pathology, Istanbul, Turkey

Background and Aims: Allograft rejection following BK virus nephropathy (BKVN) is an important cause of allograft loss in kidney transplant recipients. However, the effect of rejection type on allograft survival in patients with BKVN has not been described previously. This study aimed to investigate the relationship between allograft rejection type and graft survival in patients with BKVN.

Method: We retrospectively analyzed the data of 159 kidney transplant recipients diagnosed BKVN and followed-up in our center between January 2009 and December 2019. BKVN was diagnosed by persistent viremia of more than 10000 copies/mL for four weeks or allograft biopsy. Vascular, obstructive or other non-parenchymal etiologies for allograft dysfunction were excluded. All patients were investigated for the presence of anti-HLA antibody at 6 and 12 months after BKVN diagnosis. Luminex solid-phase assay was used to investigate Class I and Class II PRA and MFI values greater than 1000 were accepted as positive. Allograft biopsy was performed in patients with progressive graft dysfunction or the presence of donor-specific antibodies (DSA) and analyzed according to the Banff Classification. The primary outcomes were defined as allograft loss or the allograft dysfunction which defined as was doubling serum creatinine levels.

Results: Patients were followed-up median 70 (IQR 13-198) months after kidney transplantation. Demographic data and clinical characteristics are provided in the table. 28 kidney transplant recipients suffered from allograft rejection after BKVN. Median rejection time to rejection after BKVN was 9 (IQR 5-164) months. 3 patients (18,8%) in the AMR group and 1 patient (8,3%) in the TCMR group experienced graft loss during follow-up. The mean serum creatinine levels at the last clinical visit were significantly higher in the AMR group compared to the TCMR group (1,9±0,8 vs 1,3±1,2 mg/dl; p=0,002). In multivariate analysis, AMR was an independent risk factor for allograft dysfunction (HR, 1,735; 95% CI 1,060 to 2,839; p=0,028).

Conclusion: The occurrence of AMR after BKVN is an important indicator of allograft dysfunction compared to TCMR. DSA screening should be routinely used in this group for early diagnosis and treatment of AMR.

Table: Demographic data and clinical characteristics of the patients

	All patients (n=159)	Patients with TCMR (n=12)	Patients with AMR (n=16)	p
Age, median (IQR) year	45 (22-63)	49 (34-60)	42 (22-60)	NS
Sex, n (%)				
Female	62 (38,9%)	2 (16,7%)	5 (31,3%)	
Male	97 (61,1%)	10 (83,3%)	11 (68,7%)	NS
Type of DSA in pre-tx, n				
Class I	0	0	0	
Class II	1	0	1	NS
Class I and II	0	0	0	
Cause of ESRD (n, %)				
Hypertension	22 (13,8%)	0	3 (18,75%)	
Diabetes Mellitus	8 (5%)	1 (8,3%)	0	
Chronic Glomerulonephritis	31 (19,6%)	4 (25%)	3 (18,75%)	NS
Polycystic Kidney Disease	22 (13,8%)	0	3 (18,75%)	
Other	8 (5%)	0	2 (12,5%)	
Unknown	68 (%42,8)	7 (58,3%)	5 (31,3%)	
Organ source (n, %)				
Deceased donor	84 (52,9%)	10 (83,3%)	9 (56,2%)	
Living donor	75 (47,1)	2 (16,7%)	7 (43,8%)	NS
HLA mismatch, mean±SD	1,5±1,6	1,3±1,3	1,4±1,8	NS
Serum creatinine at BKVN diagnosis median (IQR) mg/dl	1,2 (0,4-2,2)	1,3 (1,2-1,6)	1,45 (1,2-1,6)	NS
Induction Regimen				
Basiliximab	9 (56,7%)	1 (8,3%)	3 (18,8%)	
ATG	68 (42,8%)	4 (33,3%)	6 (37,5%)	NS
Basiliximab and ATG	21 (13,2%)	0	4 (25%)	
Maintenance immunosuppression at BKVN diagnosis (n, %)				
Tacrolimus				
Mycofenolate Derivates	98 (61,6%)	9 (75%)	11 (68,8%)	NS
Steroid	87 (54,7%)	10 (83,3%)	15 (93,7%)	
	91 (57,2%)	10 (83,3%)	16 (100%)	
Time to onset of BKVN, median (IQR) months	10 (1-172)	10 (4-35)	6 (1-169)	NS
Type of de novo DSA after BKVN (n, %)				
Class I				
Class II	6 (3,7%)	0	3 (18,8%)	<0,001
Class I and II	16 (10%)	1 (8,3%)	7 (38,9%)	<0,001
	5 (3,1%)	0	4 (25%)	<0,001

Abbreviations; TCMR; T cell mediated rejection, tx; transplant, AMR; Antibody-mediated rejection, BKVN; Bk virus nephropathy, ESRD; End-stage renal disease, DSA; Donor-specific antibodies.

P1744

EFFECT OF TREATMENT WITH ALLOPURINOL ON BLOOD PRESSURE, CREATININ CLEARENCE AND PROTEINURIA IN ADULT RENAL ALLOGRAFT RECIPIENTS: A RANDOMIZED CONTROLLED TRIAL.

Mukaddes Cingöz[1], Orhan Özdemir[2], Özlem Usalan[2], Celalettin Usalan[2]

[1]Gaziantep University school of medicine, internal medicine, gaziantep, Turkey and
[2]Gaziantep University School of Medicine, Nephrology, Gaziantep, Turkey

Background and Aims: Hyperuricemia has been associated with the development of hypertension, cardiovascular, and renal disease. However, there is no data about the effect of lowering uric acid level on hypertension, renal function, and proteinuria in renal transplant patients. We therefore conducted a prospective study to investigate the benefits of allopurinol treatment in renal transplant patients and to investigate indirectly its effect on graft survival.

Method: A total of 105 Renal transplant recipients(RTRs) were included in this study. Patients were randomized to receive either placebo (n=51) or 300 mg/day allopurinol (n=54). We have examined uric acide, urinary albümin/Cr ratio, eGFR, CRP and blood pressure before and 24 weeks later after treatment in both group.

Results: In the allopurinol group, the mean serum uric acid levels, eGFR, creatinine urinary albümin/Cr ratio significantly improved($P < 0.001$). However, blood pressure, CRP not statistically significant ($P > 0.05$). No correlation was observed between changes in uric acide and changes in CRP, or blood pressure in the allopurinol group. No significant changes were observed in the control group ($P > 0.05$). Multivariable regression analysis showed that uric acide was positively correlated with UACR (r= 0,473, $\beta = 0.021$, $P = 0.002$) and negatively correlated with eGFR (r= -0554 $\beta = 0.016$, $P = 0.001$) in RTRs.

Conclusion: We bring indirect evidence that hyperuricemia increases urinary albümin/Cr ratio, and decreases eGFR. Hence, management of hyperuricemia may prevent the progression of renal disease, even in patients with normal renal function, suggesting that early treatment with allopurinol should be an important part of the management of renal transplant recipients. Long-term follow-up studies are warranted to identify the benefits of uric acid management on renal function and proteinuria.

P1745

EFFECTS OF DESENSITIZATION THERAPY ON LYMPH NODES AND PERIPHERAL BLOOD TFH AND TFR CELLS IN ABO-INCOMPATIBLE KIDNEY TRANSPLANT RECIPIENTS

Yunying Shi[1], Yamei Li[2], Tao Lin[3], Xianding Wang[3], Lin Yan[2], Yi Li[2], Yangjuan Bai[2], Cuili Yang[2], Zhengli Wan[2], Lanlan Wang[2]

[1]West China Hospital of Sichuan University, Department of Nephrology, Chengdu, P.R. China, [2]West China Hospital of Sichuan University, Department of Laboratory Medicine, Chengdu, P.R. China and [3]West China Hospital of Sichuan University, Department of Urology/Institute of Urology, Chengdu, P.R. China

Background and Aims: Desensitization therapy has enabled successful transplantation of renal allografts across the ABO blood group barrier, which significantly expands the living donor pool. Whether the B cell depletion induced by rituximab would affect the proportions of peripheral blood (PB) and lymph nodes (LN) T follicular helper (Tfh) and T follicular regulatory (Tfr) cells, whose survival depends on B cells, in ABO-incompatible kidney transplant recipients (ABOi-KTRs) is unknown.

Method: PB and LN samples were simultaneously collected on the day of transplantation from 14 ABOi-KTRs and 12 ABO-compatible KTRs (ABOc-KTRs) between January to October 2019. Additional PB from ABOi-KTRs was obtained before desensitization treatment (Rituximab+plasmapheresis+ immunosuppression). All recipients were undergone living donor transplantation. The frequency of B, Tfh (CD4+CXCR5+Foxp3-) and Tfr (CD4+CXCR5+Foxp3+) cells and the expression the PD-1, ICOS on Tfh and Tfr cells were quantified by flow cytometry.

Results: After desensitization treatment, significantly lower proportions of PB and LN B cells were observed in ABOi-KTRs (ABOi-a) when compared to ABOc and ABOi-b (ABOi-KTRs before desensitization) groups (**Fig. A**). Circulating Tfr cells decreased significantly after desensitization therapy, while no difference was found in LN Tfr cells (**Fig. F**). In addition, ABOi-a group showed higher expression of PD-1 on Tfr cell within PB, but lower within LN when compared to ABOi-b and ABOc groups, respectively (**Fig. G**). For Tfh proportion and its expression of PD-1 and ICOS within PB and LN, no significant difference was observed among groups (**Fig. B-D**). Significantly lower ratio of Tfr to Tfh was observed after ABO desensitization (**Fig. E**).

Conclusion: Our results indicated that ABO desensitization had significant suppression effects on B cells both within the PB and LN of ABOi-KTRs. In addition, the desensitization treatment mainly affected circulating Tfr cells, instead of Tfh cells, which shifted the balance between Tfr and Tfh cells towards Tfr cells in PB. Whereas, this treatment showed no influence on Tfh and Tfr populations within LN in ABOi-KTRs.

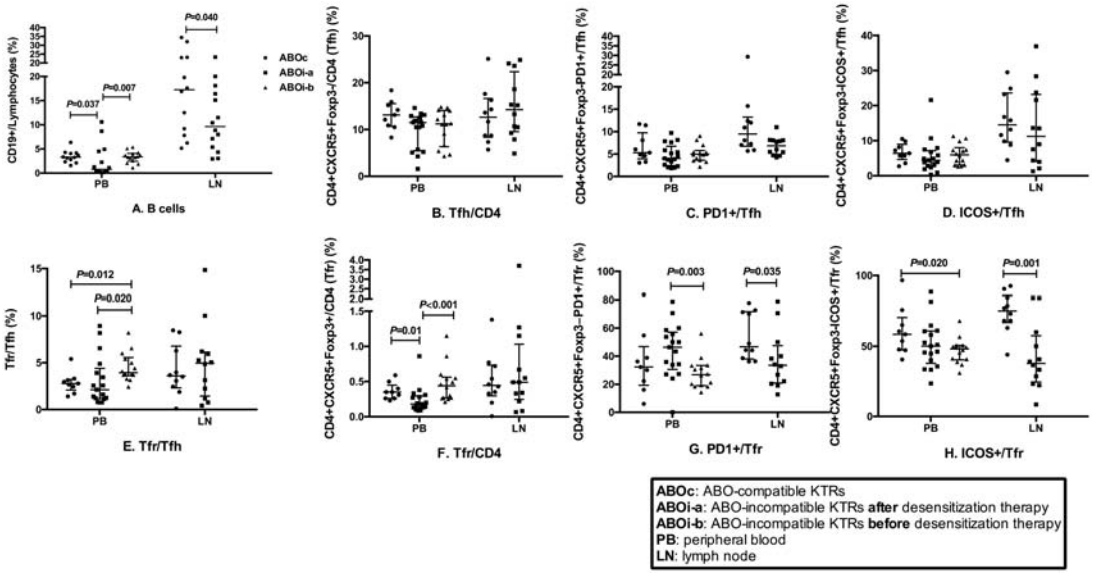


Figure:

P1746 **EFFICACY OF EXTRACORPOREAL PHOTOPHERESIS FOR THE TREATMENT OF RENAL CHRONIC ANTIBODY MEDIATED REJECTION: A PILOT STUDY**

Eleonora Francesca Pattonieri[1], Marilena Gregorini[1,2], Gianlcuca Viarengo[3], Claudia Del Fante[3], Cesare Perotti[3], Maria Antonietta Grignano[1], Vincenzo Sepe[1], Carmelo Libetta[1,2], Massimo Abelli[4], Elena Ticozzelli[4], Teresa RAmpino[1]

[1] Fondazione IRCCS Policlinico San Matteo, Unit of Nephrology, Dialysis and Transplantation, pavia, Italy, [2]University of Pavia, Internal Medicine Department,, Pavia, Italy, [3]Fondazione IRCCS Policlinico San Matteo, Immunohaematology and Transfusion Service, Apheresis and Cell Therapy Unit, pavia, Italy and [4]Fondazione IRCCS Policlinico San Matteo, Unit of General Surgery, pavia, Italy

Background and Aims: Chronic antibody-mediated rejection (cABMR) is the main cause of kidney allograft failure. Currently there is no effective treatment. Extracorporeal photopheresis (ECP) is an immunomodulating therapy that acts increasing regulatory T cells and reducing effector T cells. ECP has been used with success to treat heart and lung rejection, acute and chronic Graft versus Host Disease and few cases of acute antibody mediated kidney rejection.

The aim of this study was to describe the preliminary experience of ECP use to treat kidney cABMR.

Method: This is an ongoing prospective observational study approved by the ethical committee of our institution. The study started in 2017 on kidney transplant recipients (KTR) with cABMR diagnosis bioptically proved. All patients received ECP in addition to the standard treatment. ECP schedule is reported in Figure 1. Serum and urine samples were collected at the beginning of the study and every 6 months during the follow up period. Analyzed variables were: glomerular filtration rate (GFR), urine albumin-creatinine ratio (UACR), Donor Specific Antibodies (DSA) measeured as Mean Intensity Fluorescence (MIF) by Luminex. Collected clinical data included: death, hospital admission number, cancer diagnosis, infections. Quality of life (QoL) scale was also recorded.

Results: We enrolled 6 KTR equally distributed in gender (3 M, 3 F) and aged 49.16 ± 7.15 years (mean ± ds) .

Median follow up time was 12 months (min 12 – max 36).

All KTR had both class I and class II DSA with MFI > 5000 (min 5000 – max 36780).

In all patients no GFR deterioration was observed during follow up. UACR improved in 3 KTR while remained stable in the other 3 patients. No deaths or infections or cancer diagnosis or hospital admissions occurred. QoL ameliorated in all KTR.

DSA MIF decreased in all KTR and in 3 of them became even negative after 12 months of treatment.

Conclusion: ECP is a safe and effective treatment to slow down the deterioration of kidney function in cABMR patients. Further studies are necessary to identify the responder patients and to better tailor the treatment schedule.



Figure 1 Extracorporeal photopheresis schedule

P1747

GLOBAL MIRNOME PROFILE REVEALS INVOLMENT OF MITOGEN ACTIVATED PROTEIN KINASE (MAPK) PATHWAY IN PATIENTS WITH ANTIBODY MEDIATED REJECTION (CABMR) OF RENAL TRANSPLANT

Narayan Prasad[1], Sushma Singh[1], Mantabya Singh[1], Vikas Agarwal[2], HARSHIT SINGH[2]

[1]SGPGIMS, Nephrology, lucknow, India and [2]SGPGIMS, Clinical Immunology, lucknow, India

Background and Aims: MicroRNAs (miRNAs) are non-coding RNA that play pivotal role in modulating expression of multiple target genes at post-transcriptional level and have potential to modulate physiological & pathological processes thus can be used as potential therapeutic targets. The impact of miRNA regulations have been shown in various kidney disorders but its involvement in allograft function and immunity has not been investigated thoroughly thus we studied the miRNAs expression involved in CABMR.

The impact of miRNA regulation involved in allograft function and immunity has not been investigated thoroughly thus we studied the miRNAs expression involved in CABMR.

Method: Patients with CABMR (Banff's classification- 2017) were included. 25 blood donors (M=18) with a mean age of 52.4Y were served as controls. Samples were processed for RNA isolation. RNA integrity was checked by running over 1% agarose gel and quantity and qualities were checked using nanodrop with 260/230 and 260/280 $\geq$ 1.8. Massive parallel sequencing was performed by HiSeq 3000 sequencing system (Illumina Inc.,USA). The data obtained from the sequencing run were processed and filtered using the miRNA analysis app (Illumina Inc., USA) and analysis were performed using the BaseSpace Sequence Hub genomics computing environment (Illumina Inc., USA). Dysregulated miRNAs were detected by quantitative miRNA stem loop RT-PCR technology (TaqMan MicroRNA Assays, Applied Biosystems, CA) as per manufactures protocol. Expression was measured by calculating fold change. Targets of dysregulated miRNAs were predicted by computational analysis using bioinformatics tools like miRTarBase and Target Scan Human as well as using databases. Pathway analysis of predicted targets were performed using DIANA - mirPath online analysis tool and Kyoto Encyclopedia Genes and Genomes (KEGG) database**.** Evaluation of MAPK signaling pathway was done by Immuno histochemistry (IHC).

Results: Total 46 patients (Male=40 with mean age of 46.82 Y) were enrolled for the study with post- transplant duration of 33.72 months. The demographic details with mean values were: S Creatinine = 1.68 mg/dl, BUN = 28.26 mg/dl, Tac level = 5.98 ng/ml, S Uric Acid = 6.95 mg/dl, S Albumin = 3.46 g/dl, Na+/K+ = 128.9/4.16 mmol/L, S Phosphorus = 3.18 mg/dl, S Alkaline phosphate = 83.22 u/L. Induction regimen (Basiliximab=40, ATG= 6) Baseline Immunosuppression MMF+Pred (Tacrolimus/Cyclosporin) = 43/3. C4d were positive in 23 and DSA+ in 3 patients.

Comparative miRnome analysis revealed that a total of 123 miRNAs showed differential level of expression in CABMR patients (n=3) as compared to the control (n=1) out of which 93 were upregulated while 40 were downregulated. Conserved level of differential expression shows upregulation of miR-9 ($p \leq 0.0001$), miR-21 (p=0.0024), miR-29a (p=0.0001), miR-126 (p=0.0076), miR-210 (p=0.0001) and miR-223 (p=0.0006) while hsa-miR-221 was downregulated.

Pathway analysis shows involvement of MAPK signaling pathways, Transforming growth factor-β (TGF-β) superfamily signaling pathways, Wnt signaling pathways, ErbB signaling pathways. IHC of MAPK signaling shows significantly positive cytoplasmic tubular intensity as well as inflammatory cells intensity.

Conclusion: Altered miRNA expression profiling was found in CABMR compared to healthy controls. MAPK signaling pathways is involved in the pathogenesis of CABMR MicroRNAs are crucial regulators of cell function. They are easy to detect and represent potentially good targets for novel therapies.

P1748

PARATHYROIDECTOMY REMAINS EFFECTIVE FOR TREATING TERTIARY HYPERPARATHYROIDISM: LONG-TERM RESULTS OF A RANDOMIZED STUDY

Ana Coloma Lopez[1], Pablo Moreno[2], Jose-Vicente Torregrosa[3], Nuria Montero[1], Anna Manonelles[1], Edoardo Melilli[1], Josep Cruzado[1]

[1]Hospital Universitari de Bellvitge, Nephrology, Hospitalet de LLobregat, Spain, [2]Hospital Universitari de Bellvitge, Surgery, Hospitalet de LLobregat, Spain and [3]Hospital Clinic, Nephrology, Barcelona, Spain

Background and Aims: Tertiary hyperparathyroidism is a common cause of hypercalcemia after kidney transplant (KT) and has been associated with renal dysfunction, loss bone mineral density and increased risk of fracture, vascular calcification, and increased risk of cardiovascular events. Long clinical management remains controversial. The aim of this study is to evaluate the long-term effectiveness and safety of parathyroidectomy versus cinacalcet in patients with persistent hyperparathyroidism.

Method: A 12-month prospective, multicenter, randomized study demonstrated than subtotal parathyroidectomy is more effective than cinacalcet for controlling hypercalcemia. Now, we evaluate in the same cohort of patients if this effect is maintained after 5 years of follow-up. Laboratory assessment included serum calcium, serum phosphate, intact parathyroid hormone (iPTH), calcidiol levels, estimated glomerular filtration rate and proteinuria at 2, 3, 4 and 5 year follow-up. Therapeutic details about the use of vitamin D, calcium supplementation and phosphate binders were compiled. Fragility fractures were also collected.

Results: In total, 24 patients had data available at 5 years, 13 in the cinacalcet group and 11 in the parathyroidectomy group. At 5 years, six of 13 patients in the cinacalcet group and ten of 11 patients in the parathyroidectomy group (p=0.015) showed normocalcemia (Figure 1). Subtotal parathyroidectomy retained a greater reduction of iPTH compared with cinacalcet group (Figure 2). No differences were observed in kidney function and incidence of fragility fractures between both groups. In relation of treatment, 8 of 13 patients in cinacalcet group maintained treatment with cinacalcet after 5 years follow-up.

Conclusion: Subtotal parathyroidectomy is more effective in long term to maintain normal serum calcium and iPTH compared with cinacalcet in kidney transplant patients with tertiary hyperparathyroidism.

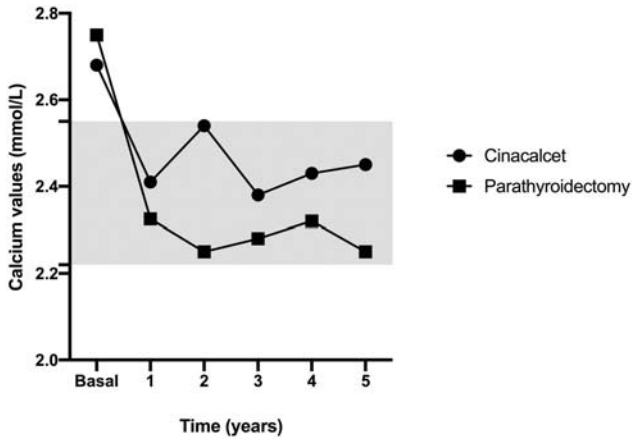


Figure 1:

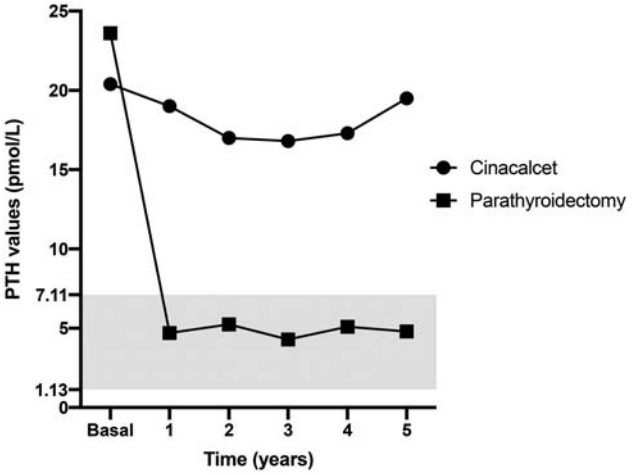


Figure 2

P1749 DECEASED DONOR KIDNEY TRANSPLANTATION IN AHUS: A PROPHYLAXIS-FREE APPROACH EXPERIENCE.

Anna Manonelles[1], Alexandre Favà[1], Nuria Montero[1], Edoardo Melilli[1], Oriol Bestard[1], Josep Cruzado[1]

[1]*Hospital Universitari de Bellvitge, NEphrology and Transplant Unit, Barcelona, Spain*

Background and Aims: Atypical hemolytic uremic syndrome (aHUS) has been associated with high risk for recurrence after kidney transplantation. In 2017, a consensus report on aHUS was published by KDIGO working group whereby eculizumab prophylaxis approach was recommended in renal transplantation. Here we report a series of 5 cases of successful deceased donor kidney transplantation in aHUS affected recipients following a preemptive approach free of Eculizumab treatment.

Method: Five patients with history of end stage kidney disease due to aHUS were eligible for kidney transplantation. All of them had a functional and genetic complement pathway evaluation, showing pathologic mutations to CFI, MCP, CFH and CFB respectively.

All of them received a cadaveric donor after a selection of optimal donors with minimal delayed graft function risk and low immunological risk. They accomplished a therapeutic strategy of plasmapheresis prior and in 3 cases 5 days after transplantation. After that, an intensive follow-up was performed with hemolyitic parameters monitoring (blood cell count and extension, LDH, haptoglobin, C3 and C4) regularly.

The immediate clinical course was uneventful, without hemodialysis requirements nor biochemical microangiophatic anemia signs.

One patient received iMTOR maintenance treatment, three patients received a CNI-based therapy with tacrolimus, mycophenolate and steroids, and one patient was treated with belatacept, mycophenolate and steroids.

Results: Patients presented an uneventful immediate transplant follow-up, with early graft function recovery and without surgical nor infectious complications.

4 patients completed long follow-up without complications (6 months to 12 years respectively). The patient with belatacept treatment (CFI mutation and MCP risk polymorphism) presented acute aHUS recurrence at 90 days after transplantation, with hypertension, hemolytic anemia, plaquetopenia and acute kidney injury (serum creatinine raised from 115µmol/L to 190µmol/L), but thanks to an early diagnose received immediate treatment with Eculizumab with complete resolution of the event, and with a current optimal outcome of 9 years follow up with normal GFR without proteinuria.

Conclusion: It has recently been described the potential benefits from living kidney donors and low tacrolimus use to minimize recurrence rates in aSHU, thereby averting endothelial injury. However, deceased donor transplantation is a beneficial option to patients affected of aHUS CKD without living donors.

According to our experience, preemptive plasma therapy could be effective in the prevention of immediate disease recurrence in patients with high risk mutations with deceased kidney donors.

Precocious diagnose of recurrence is mandatory and a rapid establishment of treatment with eculizumab brings optimal outcomes.

A preemptive approach is safe when intensive clinical and analytical controls are performed, and represent a better cost-effective strategy.

More evidence to define risk groups and tailor individualized treatments represent a future prospect in these patients.

AGE	GENDER	AFFECTED GENE	sC3	INDUCTION THERAPY	MAINTAINANCE THERAPY	RECURRENCE	GFR (CKD-EPI)	FOLLOW-UP TIME (Years)
36	M	MUT CFIMUT MCPPR CFHPR MCP	N	PlasmarATG	SRLMPAPDN	N	57	12
36	M	MUT CFIPR MCP	Low	PFrATG	BELAMPAPDN	Y	90	8
42	F	MUT CFBPR MCP	Low	PFrATG	TACMPAPDN	N	39	6
57	F	MUT CFI	N (low CFI)	PFrATG	TACMPAPDN	N	77	2
46	F	MUT MCP	N	rATG	TACMPAPDN	N	69	0.5

P1750

IMMUNE-ADSORPTION COLUMNS IN ABOI INCOMPATIBLE RENAL TRANSPLANTATION: EXPERIENCE FROM DEVELOPING WORLD

Sourabh Sharma[1], Debabrata Mukherjee[2]

[1]Gaur Hospital, Sriganganagar, Nephrology, India and [2]Army Hospital R&R, Nephrology, Delhi, India

Background and Aims:

We present our experience of ABO-incompatible renal transplant using immunoadsorption (IA) columns. We have compared efficacy of two commercially available columns

Method:

This single-center prospective study was conducted at Army Hospital Research and Referral, Delhi. All consecutive ABO-incompatible renal transplants from January 2014 to February 2018 were analyzed. Of 30 patients who underwent transplantations, 28 underwent antibody depletion with immunoadsorption columns. Of them, 14 cases were in the "Glycosorb group," while 14 in the "Adsopak group."

Results:

The donors in the Adsopak group were older than those in the Glycosorb group ($p < 0.05$). Both groups had spousal donors in majority. The cutoff for the antibody titer was 1:8. Themedian titer in the Adsopak group was 128 (range, 1:4 to 1:2048), while that in the Glycosorb group was 24 (range, 1:8 to 1:128). All patients in the Glycosorb group had baseline titers 1:128, while 13 patients in the Adsopak group had baseline titers 1:512. Nil titer was achievable with Glycosorb®(50%,7/14) but notwith Adsopak®($P< 0.001$). The Glycosorb group was advantageous in terms of graft failure because no rejection was noticed in these patients in their follow-up period. Three patients in the Adsopak group developed rejection (two had mixed rejection, and one had antibody-mediated rejection). Four patients died of sepsis (three in the Glycosorb and one in the Adsopak group). Lower baseline serum creatinine level was achieved in the Glycosorb group.

Conclusion:

Results of ABO-incompatible renal transplantation were satisfactory, and the use of immunoadsorption columns could effectively deplete antibody titers. Glycosorb columns were more efficient than Adsopak columns. Graft survival was better with Glycosorb. Post-transplant infections were a major cause of mortality.

P1751

THE GUANYLATE CYCLASE C AGONIST LINACLOTIDE LIMITS PROGRESSION TO RENAL FIBROSIS AND IMPROVE RENAL FUNCTION IN MOUSE MODEL OF CHRONIC KIDNEY DISEASE AFTER ISCHEMIA-REPERFUSION INJURY

Yuki Nakayama[1], Naohito Isoyama[1], Kimihiko Nakamura[1], Toshiya Hiroyoshi[1], Kouki Fujikawa[1], Hideyasu Matsuyama[1]

[1]*Yamaguchi university, urology, Ube, Yamguchi, Japan*

Background and Aims: Renal ischemia-reperfusion injury (IRI) is a clinically significant condition that leads to acute kidney injury (AKI). AKI is followed by tissue repair characterized by collagen deposition and fibrosis which ultimately results in progression to chronic kidney disease (CKD). Especially in renal transplantation, the degree of IRI has directly led to poor long-term graft survival. Trimethylamine-N-oxide (TMAO), a hepatic metabolic product of trimethylamine generated from dietary phosphatidylcholine, has been linked with progression of CKD. Linaclotide, a guanylate cyclase C agonist, has been reported decrease the plasma levels of TMAO. We investigated whether the reduction of TMAO by linaclotide protect renal function after IRI using an experimental mouse model.

Method: Linaclotide (100μg/kg) was administered for 2weeks before IRI and continued for 2weeks after IRI. After 2weeks since IRI, the renal function was evaluated by serum creatinine level and removed kidneys sections were performed Azan stain to evaluate the level of fibrosis.

Results: The administration of linaclotide before IRI significantly improved renal function. (Fig.1) Histological examination of kidneys showed linaclotide limits to expand fibrosis area after I/R injury. (Fig.2)

Conclusion: The reduction of TMAO by linaclotide before renal IRI could prevent renal fibrosis and improve renal function. Linaclotide may be useful for the patient expected to suffer renal IRI for example renal transplantation and partial nephrectomy.

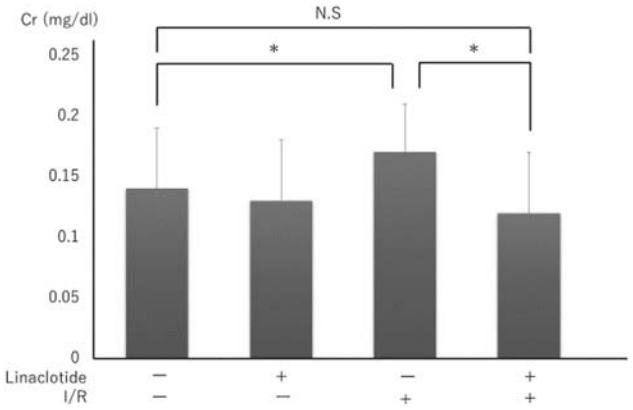


Figure:

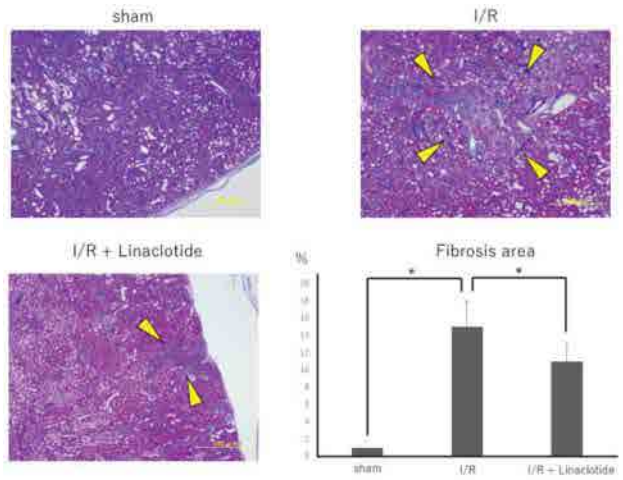


Fig1

Fig2

P1752

THE ROLE OF MTOR INHIBITORS ON CARDIOVASCULAR AGING IN RENAL TRANSPLANT PATIENTS WITH CHRONIC GRAFT DYSFUNCTION

Barbara Infante[1], Giuseppe Castellano[1], Concetta Prisciandaro[1], Adelaide Dilorenzo[1], Francesco Bellanti[1], Nicola Coviello[1], Paola Pontrelli[2], Federica Rascio[1], ROSSANA FRANZIN[2], Loreto Gesualdo[2], Gaetano Serviddio[1], Giuseppe Grandaliano[3], Giovanni Stallone[1]

[1]Università degli studi di Foggia, nephrology, Foggia, Italy, [2]Azienda Ospedaliero Universitaria Consorziale Policlinico, Bari, Italy and [3]Agostino Gemelli University Polyclinic, Roma, Italy

Background and Aims: Chronic Kidney Disease (CKD) is strongly associated with increased circulatory complications that can lead to accelerated cardiovascular aging. During CKD, persistent oxidative stress triggered by mitochondrial dysfunction can affect Klotho protein levels together with circulating FGF23. mTOR pathway is involved in pro-survival mechanism and can be differently modulated by several available therapeutics, therefore exerting central function in senescence, autophagy and cellular regeneration. The aim of this study was to evaluate the beneficial effect of mTOR inhibition on cardiovascular aging in transplanted patient with Chronic Allograft Dysfunction.

Method: In this study, 250 transplanted patients with calcineurin inhibitory (CNI) therapy and graft survival higher than 6 months and lower than 60 months were enrolled.

The patients were then divided in three groups: (MMF group) patients undergoing CNI therapy with CS (Ciclosporin) and MMF, (mTOR Inhibitors group) patients undergoing CNI, CS and mTOR Inhibitors therapy and (MMF to mTOR Inhibitors group) with patients shifting from MMF to mTOR Inhibitors therapy. Renal function, FGF-23, Klotho, PTH, 1-25OH-Vitamina D, arterial stiffness by Pulse Wave Velocity (PWV), left ventricular hypertrophy expressed by the MSV and endothelial function by Flow Mediated Dilation (FMD) were measured. PBMC were isolated by gradient centrifugation.

Results: Between the MMF group and the mTOR Inhibitors groups we did not find significant differences in renal function, PTH, 1-25OH-Vitamina D, PRA, DSA, PWV, FM e DFE. However, FGF23, Klotho, phosphate levels were significantly changed. (FGF-23 pg/ml; p=0,00001; Klotho p=0,01; fosfaturia p=0,03; MMF group vs mTOR Inhibitors group)

Interestingly, mTOR Inhibitors group patients showed a higher O2 consumption level associated to increased mitochondrial respiratory function. Pentraxin 3 (PTX-3) and p21 as inflammaging and senescence biomarkers were also detected to be significantly increased in MMF group compared to mTOR Inhibitors group (p=0,002).

Conclusion: In conclusion these data suggest that the use of mTOR Inhibitors in transplanted patients could prevent the occurrence of circulating complication and reduce the cardiovascular aging risk.

P1753 EFFECTIVENESS AND TOLERABILITY OF 500 MG-I.V. FERRIC CARBOXYMALTOSE FOR THE TREATMENT OF IRON DEFICIENCY IN PATIENTS WITH KIDNEY TRANSPLANT.

Giorgio Soragna[1], Amelia Rodofili[1], Alberto Tricerri[1], Ada Ramondetti[1], Gianfranca Gerbino[1], Corrado Vitale[1]

[1]*AO Ordine Mauriziano di Torino, Nephrology Unit, Torino, Italy*

Background and Aims: Post transplantation anaemia (PTA) is a common finding in kidney transplant patients, with reported prevalence ranging from 25 to 40%, and it is associated with adverse outcomes for the kidney allograft and the recipient. The pathogenesis of PTA is multifactorial, including iron deficiency, reduced graft function, untoward effects of drugs (immunosuppressants, ACE-I and ARB), folic acid and vitamin B12 deficiency, inflammatory states.

Ferric carboxymaltose (FCM) reportedly improved haemoglobin (Hb) levels and replenished depleted iron stores in various populations of patients with iron-deficiency anaemia, but there are few data about its use in PTA.

In this study we evaluated the effectiveness and tolerability of high intravenous doses of FCM (500 mg) for the treatment of iron deficiency and anaemia in patients with kidney transplant.

Method: Absolute iron deficiency was considered as transferrin saturation (TSAT) less than 20% with ferritin levels below 100 μg/L. Anaemia was defined as Hb<13 g/dL in males and Hb<12 g/dL in females.

Out of 101 patients with kidney transplant, 56 presented with absolute iron deficiency (59±13 years old, M/F=0.95, 8±4.6 years of transplantation; serum creatinine 1.45±0.64 mg/dL): of these, 40 patients had anaemia (7 were also taking ESAs) and 16 had normal Hb levels.

The 16 patients with absolute iron deficiency and normal Hb were not prescribed iron supplements, fearing of causing erythrocytosis, whereas 36 of 40 patients with anaemia and iron deficiency were given FCM 500 mg, as i.v. infusion for 30 minutes.

Hb, ferritin and TSAT were assayed either before and 45-60 days after FCM supplementation, which was repeated if Hb levels were less than 0.5 g/dL below the normal value. Data were reported as mean±SD.

Results: Among the 56 patients with absolute iron deficiency, there were not any significant differences in serum levels of folic acid and vitamin B12 between those with and without anaemia (p=ns).

After the first dose of FCM, in 36 patients with iron deficiency and anaemia, ferritin levels increased from 55±69 ng/mL to 111±107 ng/mL (p<0.01), TSAT increased from 12.2±5.9% to 20.4±10.3% (p<0.01) and Hb increased from 10.9±0.9 g/dL to 12.3±1.3 g/dL (p<0.01). Furthermore, 24/36 patients (67%) no longer had absolute iron deficiency and 19/36 (53%) were not anaemic anymore.

Out of the 17 patients still showing anaemia after the first FCM dose, 10 had Hb levels less than 0.5 g/dL below the normal value and were given a second dose of FCM. In this subset, Hb level increased on average from 11.4±0.5 g/dL to 12±0.9 g/dL (p<0.01) and became normal in 3 patients.

After the FCM course, in 2 out of 7 patients ESAs were discontinued, whereas in 3 patients their doses were reduced and in 2 patients remained unchanged.

Only one patient had an adverse effect during FCM infusion, namely, a transient skin flushing on her face during the second dose, which immediately remitted when the infusion was interrupted.

Conclusion: In patients with PTA and absolute iron deficiency, single or repeated doses of 500 mg of i.v. FCM were effective in improving Hb levels, well tolerated and reduced the need for ESAs.

Of 56 patients with kidney transplant and absolute iron deficiency, 16 (28%) had normal Hb levels. We did not treat such subjects, fearing of causing erythrocytosis. However, given that iron deficiency may affect negatively both heart and muscle metabolism, what is the best management of iron deficiency in transplanted patients without anaemia is still an open question.

P1754 **ASSOCIATION OF GUT MICROBIAL FERMENTATION WITH DIARRHEA IN KIDNEY TRANSPLANT RECIPIENTS**

Fernanda Guedes Rodrigues[1,2], Johann Casper Swarte[2,3], Rianne M. Douwes[2], Tim J. Knobbe[2], Ita Pfeferman Heilberg[1,4], Stephan Bakker[2], Martin De Borst[2]

[1]Federal University of São Paulo Unifesp, Nutrition Program, São Paulo, Brazil, [2]University of Groningen, Department of Nephrology, Groningen, Netherlands, [3]University of Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands and [4]Federal University of São Paulo Unifesp, Nephrology Division, São Paulo, Brazil

Background and Aims: Diarrhea is a common complaint by kidney transplantation recipients (KTR). Metabolic abnormalities and immunosuppressive drugs may cause alterations in the gut microbiome possibly leading to diarrhea. A hydrogen (H_2) breath test, reflecting nutrient fermentation, can detect changes in the composition of gut microbiota. In the present study, we studied the association of exhaled H_2 with diarrhea in KTR, and investigated its determinants.

Method: All data were collected from the TransplantLines Biobank Cohort Study (NCT03272841). Living kidney donors were used as healthy controls. Breath H_2 concentrations were analysed using solid state-sensor gas-chromatography. The stool water content was measured by faecal dry matter analysis and diarrhea was classified as >80% of water content in stools. Age, sex, body mass index (BMI), diabetes mellitus, eGFR and immunosuppressive medication were tested as potential determinants for H_2 using linear multivariable regression.

Results: We included 424 KTR (mean age 55.4 ± 13.2 years, 39,1% female, transplant vintage 5.5 ± 9.5 years) and 164 healthy controls in this study. Immunosuppressive drugs included tacrolimus (78.5%), mycophenolate mofetil (MMF, 73.3%), cyclosporine (9.0%), and everolimus (2.4%) in various combinations. The median concentration of H_2 in exhaled breath was significantly higher among KTR versus healthy controls (11.0 ppm [5.0 - 25.0] vs 9.0 ppm [4.0-22.5] p=0.005). The exhaled H_2 was correlated with stool water content (r=0.24, p=0.04), as shown in figure 1. Serum tacrolimus trough levels were associated with exhaled H_2 (standardized β=0.14, p=0.01), independent of age, sex, BMI, diabetes mellitus, eGFR and other immunosuppressive medication. In contrast, MMF trough levels were not independently associated with H_2 (standardized β=0.07, p=0.21).

Conclusion: Exhaled H_2, a marker of gut fermentation, is higher in KTR compared to healthy controls, and is associated with stool water content. Present results suggest that altered gut microbial fermentation contributes to the occurrence of diarrhea in KTR. Tacrolimus trough level was an independent determinant of H_2. These data encourage further studies to validate the association of immunosuppressive drugs, gut microbiota and post-transplant diarrhea.

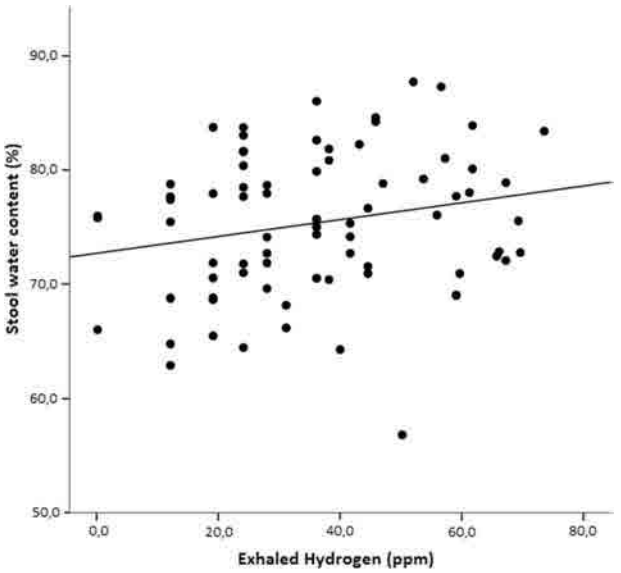


Figure:

Figure 1. Correlation between exhaled H_2 (ppm) and water content in stool (%) among KTR (r=0.24, p=0.04).

P1755 **EFFICACY AND SAFETY ECULIZUMAB FOR THE TREATMENT OF ANTIBODY MEDIATED REJECTION FOLLOWING RENAL TRANSPLANTATION**

Hark Rim[1], Jisu Kim[1], Haesu Jeon[1], Ye Na Kim[1], Ho Sik Shin[1], Yeonsoon Jung[1]

[1]*Gospel Hospital, Internal Medicine, Busan, Korea, Rep. of South*

Background and Aims: : We evaluated the efficacy and safety of eculizumab in comparison with plasmapheresis (PP) and intravenous immunoglobulin (IVIG) therapy in renal transplant recipients diagnosed with antibody-mediated rejection (AMR).

Methods: This was a multi-center, open-label, prospective, randomized analysis. The patients were randomized as to therapy type (eculizumab infusions or standard of care, SOC: PP/IVIG). The patients (eculizumab arm: 7 patients, SOC arm: 4 patient) were evaluated for the continuing presence of donor-specific antibodies (DSAs) and C4d (staining on biopsy), as well as histological evidence, using repeat renal biopsies after treatment.

Results: The allograft biopsies revealed that eculizumab did not prevent the progression to transplant glomerulopathy. Only 2 patients in the SOC arm experienced rejection reversal, and no graft losses occurred in either group. Following AMR treatment, the DSA titers generally decreased compared to titers taken at the time of AMR diagnosis. There were no serious adverse effects in the eculizumab arm.

Conclusion: Eculizumab alone is not sufficient to treat AMR and does not prevent acute AMR from progressing to chronic AMR or to transplant glomerulopathy. However, it should be considered as a potential alternative therapy because it may be associated with decreased DSA levels.

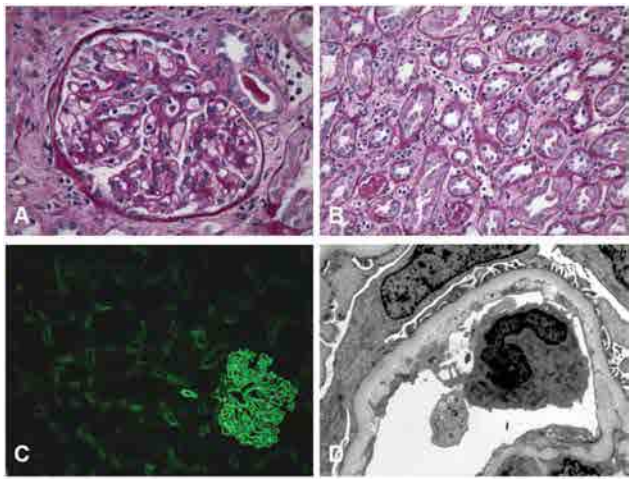


Figure 1. Allograft initial biopsy for case 8

A. Glomerulus shows capillary loops contain circulating mononuclear inflammatory cells and the mesangium is mildly expanded by ECM and increased numbers of mesangial cells corresponding to g1-2 Banff criteria. (periodicacid–Schiff, 400×)

B. Peritubular capillaries are infiltrated by mononuclear inflammatory cells corresponding to ptc2 Banff criteria (periodic acid–Schiff, 400×).

C. The C4d staining in immunofluorescence microscopy is diffusely positive along the peritubular capillaries corresponding to C4d3 Banff criteria (400×).

D. Electron microscopy shows mild segmental effacement of glomerular visceral epithelial foot processes and adherent mononucelar cell inside capillary (15,000×)

P1756

ANTI-ABO ANTIBODY- VERSUS ANTI-HLA ANTIBODY-INDUCED ANTIBODY MEDIATED REJECTION IN ABO-INCOMPATIBLE KIDNEY TRANSPLANT PATIENTS: RELATIVE INCIDENCE AND PHENOTYPE DIFFERENCE.

Jinmin Kong[1], Hyukyong Kwon[1], Sung Son[1], EUN Whang[2]

[1]Hanseo Hospital, Nephrology, Busan, Korea, Rep. of South and [2]Hanseo Hospital, Laboratory Medicine, Busan, Korea, Rep. of South

Background and Aims: Antibody-mediated rejection(AMR) in ABO incompatible(ABOi) kidney transplant(KT) patients can either be due to donor-specific anti-HLA antibody(DSA) or anti-blood group antibody. The relative frequency and possible phenotype difference of these two types of AMR in ABOi KT patients have not been reported.

Method: Of 111 ABOi KT patients between 2007 and 2019 in our center, 15(13.5%) patients developed acute AMR diagnosed by indication biopsy. Since there is no histologic distinction between DSA- and anti-ABO-induced AMR, we assumed the causative antibody in each case based on anti-ABO level and DSA, measured in serum collected at the time of AMR.

Results: Of these 15 cases of acute AMR, 5 were attributable to anti-ABO(ABO-AMR) since anti-ABO titer was higher ($\geq$16) and DSA was undetectable at the time of rejection. Five cases were attributable to DSA(DSA-AMR) since DSA was detectable and anti-ABO was lower during rejection. Another 3 cases with lower anti-ABO titer and undetectable DSA were also assumed to be DSA-induced, since this low level of anti-ABO is unlikely to cause rejection and DSA can be undetectable in DSA-induced AMR by adsorption of Ab on graft, as frequently seen in ABO-compatible patients Two cases with both higher anti-ABO titer and detectable DSA was regarded as undetermined. The onset of acute AMR was within 2 weeks in all cases(median 7.0 days) and comparable between DSA- and ABO-AMR. Initial anti-ABO titer was also not statistically different; median(range) 256(64-4096) in ABO-AMR and 64(16-256) in DSA-AMR. All the 5 patients with ABO-AMR had negative PRA before KT, whereas 5 of 8 patients with DSA-AMR had positive PRA before KT, and two DSA-AMR patients had preformed DSA before KT. There was no difference in peak creatinine and response to treatment. All the AMR were recovered by treatment and no graft was lost to rejection. No patient with ABO-AMR developed chronic AMR whereas one of DSA-AMR patients developed chronic AMR.

Conclusion: In summary, among 15 cases of acute AMR, 5 were ABO-AMR, 8 were DSA-AMR and 2 were undetermined. There was no difference in clinical feature between DSA- and ABO-AMR. No patient with ABO-AMR developed chronic AMR.

P1757

RITUXIMAB FOR RECURRENCE OF PRIMARY FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFTER KIDNEY TRANSPLANTATION: RESULTS OF A NATIONWIDE STUDY

Camille Lanaret[1], Dany Anglicheau[2], Audard Vincent[3], Celine Lambert[4], Lionel Couzi[5], Matthias Buchler[6], Sophie Ohlmann[7], Dominique Bertrand[8], Rérolle Jean-Philippe[9], Antoine Thierry[10], Nicolas Maillard[11], Betoul Schvartz[12], Leonard Golbin[13], Vincent Pernin[14], Didier Ducloux[15], Nicolas Bouvier[16], Coralie Poulain[17], Anne Elisabeth Heng[1], Clarisse Greze[18], Paolo Malvezzi[19], Frank Martinez[20], Nassim Kamar[21], Cyril Garrouste[1]

[1]CHU Montpied, Nephrology, CLERMONT FERRAND, France, [2]CHU Necker, Nephrology, PARIS, France, [3]CHU Henri Mondor, Nephrology, CRETEIL, France, [4]CHU Montpied, Biostatistics Unit, CLERMONT FERRAND, France, [5]CHU Bordeaux, Nephrology, BORDEAUX, France, [6]CHU Tours, Nephrology, TOURS, France, [7]CHU Strasbourg, Nephrology, Strasbourg, France, [8]CHU Rouen, Nephrology, Rouen, France, [9]CHU Limoges, Nephrology, Limoges, France, [10]CHU Poitiers, Nephrology, Poitiers, France, [11]CHU Saint Etienne, Saint Etienne, France, [12]CHU Reims, Nephrology, Reims, France, [13]CHU Rennes, Nephrology, Rennes, France, [14]CHU Montpellier, Nephrology, Montpellier, France, [15]CHU Besançon, Nephrology, Besançon, France, [16]CHU Caen, Nephrology, Caen, France, [17]CHU Amiens, Nephrology, Amiens, France, [18]CHU Bichat, Nephrology, Paris, France, [19]CHU Grenobles, Nephrology, Grenobles, France, [20]CHU Necker, Nephrology, Paris, France and [21]CHU Toulouse, Nephrology, Toulouse, France

Background and Aims: The indication of rituximab (RTX) in the treatment of primary focal segmental glomerulosclerosis (FSGS) recurrence after kidney transplantation (KT) remains controversial. The objective of our study was to evaluate the benefit and tolerability of adding RTX to the standard of care (SOC) comprising plasmapheresis (PP), corticosteroids, and high-dose anticalcineurins for the treatment of FSGS recurrence after KT.

Method: This retrospective, multicenter study reports on 148 patients, transplanted between 31 December 2004 and 31 December 2018, aged 39.9 $\pm$ 13.4 years, who developed FSGS recurrence at 7 [3–23] days. In all 109 patients received a SOC (Group 1). RTX was introduced in this group after more than 28 days of SOC for failure or for therapeutic intensification ($n = 19$, Group 1a), or for early discontinuation of PP ($n = 12$, Group 1b); 39 patients received RTX associated at the outset with SOC (Group 2).

Results: We observed 46.6% complete remission (CR) and 33.1% partial remission (PR). Ten-year graft survival was 65.6% [51.4–76.6] and 13.4% [3.4–30.0] in responders and non-responders respectively. There was no difference in CR + PR rate between G1 (82.5%) and G2 (71.8%), $p = 0.08$, confirmed by propensity score +4.3% (95% CI [−9.0%-17.5%], $p = 0.53$). Following addition of RTX (Group 1a), we observed a CR rate of 26.3% and a PR rate of 31.6%. Patients with and without RTX experienced similar rejection rates (18.6% and 28.2%, $p = 0.17$) and infection rates (71.4% and 79.5%, $p = 0.40$). In multivariate analysis, the infections were associted with hypogammaglobulinemia <5g/l (OR = 8.04, 95% CI [1.65,39.25], $p = 0.01$).

Conclusion: Rituximab could be used in cases of SOC failure or in remission patients for early weaning of plasmapheresis, without increasing infectious risk.

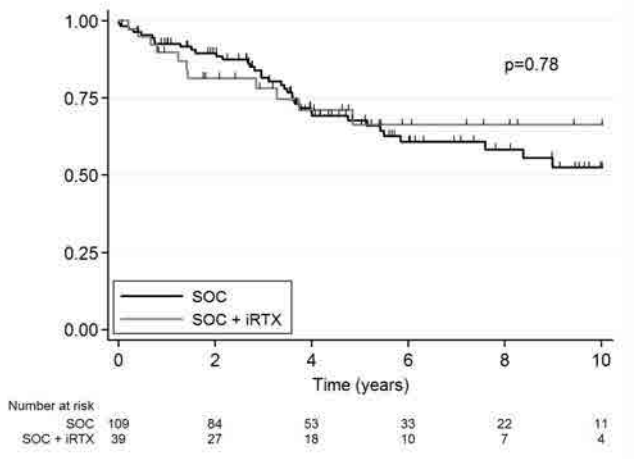


Figure1: Allograft survival rate after SOC (black line) or immediate rituximab in addition to SOC (grey line) for recurrence of FSGS.

Abbreviations: iRTX, immediate Rituximab ; SOC standard of care

P1758 **TOCILIZUMAB TREATMENT IN DSA POSITIVE ANTIBODY MEDIATED REJECTION AMONG KIDNEY TRANSPLANT RECIPIENTS**

Orsolya Cseprekal[1], Adrienn Marton[1], Sara Molnar[1], Attila Patonai[1], Attila Fintha[2], Tamás Micsik[2], Szilárd Török[1], Zsolt Mathe[1], Laszlo Wagner[1], Laszlo Kobori[1], Adam Remport[1]

[1]Semmelweis University, Department of Transplantation and Surgery, Budapest, Hungary and [2]Semmelweis University, Ist. Department of Pathology, Budapest, Hungary

Background and Aims: Pretransplant or de novo donor specific antibodies (DSA) may lead to active or chronic active antibody mediated rejection (a and cABMR) as leading cause of graft loss after kidney transplantation. There is no treatment protocol approved for ABMR. Anti Il-6 tocilizumab (TCZ), inhibitor of DSA production, is a potential approach to stabilize kidney allograft function, however, evidence based results are not available.

In our retrospective case series analysis, we assessed the changes in DSA and eGFR during and at the end of treatment with TCZ.

Method: In our single center case series analysis, 10 kidney transplant patients with biopsy proven ABMR (aABMR 6, cABMR 4, age 43±10.5ys, 6 males, time since transplantation 18(2-119)months, 7 first transplant, serum creatinine 224±80 umol/L at baseline) were studied between January 2017 – June 2019. Total plasma exchange (PE) (5x) was followed by TCZ (8 mg/kg, 1x monthly for 6 months) in case of a and cABMR. Intravenous immunoglobulin (IVIG, 1gr/kg) was added in case of aABMR. Routine laboratory parameters and DSA were reported retrospectively.

Results: 6 aABMR patients completed the treatment protocol. Class I DSA decreased significantly (MFI 4457(635-14084) vs. 877(595-5678); p=0.007), but Class II DSA remained the same during the treatment (MFI 4725 (586-17615) vs. 8097 (671-14636) p=NS). eGFR of aABMR patients and 1 cABMR patient were stabilized. 3 cABMR patients returned to dialysis. Reversible elevation of liver transaminases were detected in three patients. There was no any serious adverse event recorded.

Conclusion: The opportunely timed TCZ seems to be effective in reducing Class I DSA and stabilize graft function in patients with aABMR. Further studies are needed to prove the long-term efficacy and the exact role of TCZ in cABMR among kidney transplant patients.

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NEPHROTOXICITY OF CALCINEURIN INHIBITORS AS A RISK FACTOR FOR BK VIRUS REPLICATION AFTER KIDNEY TRANSPLANTATION

Karel Krejčí[1], Tomáš Tichý[2], Jana Bednaříková[3], Margita Bartková[4], Kamil Žamboch[1], Jiří Orság[1], František Mrázek[5], Josef Zadražil[1]

[1]University Hospital and Faculty of Medicine UP Olomouc, 3rd Department of Internal Medicine - Nephrology, Rheumatology and Endocrinology, Olomouc, Czech Republic, [2]University Hospital and Faculty of Medicine UP Olomouc, Department of Clinical and Molecular Pathology, Olomouc, Czech Republic, [3]University Hospital and Faculty of Medicine UP Olomouc, Department of Clinical Biochemistry, Olomouc, Czech Republic, [4]University Hospital and Faculty of Medicine UP Olomouc, Department of Microbiology, Olomouc, Czech Republic and [5]University Hospital and Faculty of Medicine UP Olomouc, Department of Immunology, Olomouc, Czech Republic

Background and Aims: BK virus nephropathy (BKVN) represents a serious complication of kidney transplantation and is responsible for significant percentage of transplanted kidneys prematurely terminating their function. Its occurrence is considered a complication of immunosuppressive therapy and is closely related to its intensity. The aim of our prospective study was to evaluate the incidence of subclinical and clinically manifest nephrotoxicity of calcineurin inhibitors (CI) in repeated protocol kidney graft biopsies as a manifestation of excessive immunosuppression and to evaluate its relationship to the PCR confirmed active BKV replication and bioptically proven BKVN during the first year after transplantation.

Method: In a group of 161 newly transplanted patients we prospectively evaluated 457 consecutive protocol renal biopsies performed within the first year after transplantation. Using the CI nephrotoxicity score, the incidence of nephrotoxicity was monitored. Findings were correlated with laboratory (PCR) and histological evidence of active BK virus (BKV) replication and BKVN.

Results: When compared to the normal histology, nephrotoxicity was associated with more frequent significant BKV viraemia and viruria ($P = 0.02$ and $P = 0.01$, respectively) and more common occurrence of BKVN. The persistence of toxicity in the subsequent biopsy proved to be a negative risk factor of significant BKV viraemia and viruria ($P = 0.03$ and $P = 0.01$, respectively), independently of the initial BKV status of the monitored groups. Toxicity could also be used as a predictor of significant viraemia and viruria ($P = 0.02$ and $P = 0.01$, respectively) even in the absence of viral replication at the time of initial biopsy.

Conclusion: Early histological detection of CI nephrotoxicity followed by pre-emptive CI dose reduction might prevent significant BKV reactivation in the risky first post-transplant year. The evaluation whether a regression of histological signs of nephrotoxicity after a CI dose reduction leads to a reduction in BKV replication, and whether a more frequent occurrence of rejection does not complicate further posttransplant course, will be the subject of our further investigation.

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P1760 EXTRACORPOREAL PHOTOPHERESIS AND KIDNEY ALLOGRAFT REJECTION

Saulo Jesús Fernández Granados[1], Ernesto Fernández Tagarro[1], Ana Ramirez Puga[1], Rita Guerra Rodriguez[1], Selene Gonzalez Nuez[1], Noa Diaz Novo[1], Cesar García Cantón[1]

[1]*Hospital Universitario Insular de Gran Canaria, Nephrology, Las Palmas de Gran Canaria, Spain*

Background and Aims: Extracorporeal photopheresis (ECP) is an apheresis modality that in the field of solid organ transplantation (SOT) has an indication in the treatment or prophylaxis of pulmonary, cardiac or hepatic graft rejection. The usefulness of ECP in renal transplantation (RTx) remains contradictory because of the few studies that evaluate the effectiveness and safety of this technique.

Method: Case series study of kidney transplant patients with histological diagnosis of rejection who have been treated with ECP during the 2013-2018 period (n = 8 patients). The technical characteristics of the ECP sessions (n = 89) were studied, including tolerance and complications in each of them.

Results: Demographic and clinical characteristics are shown in **Table 1**. The indication of FEC was the contraindication to conventional treatment (n = 4), mainly due to concomitant infection (50%), or refractoriness (n = 4) to the treatment prescribed in each case and it is specified in **Table 1**. The initial schedule was 2 consecutive weekly sessions for 5 weeks, with additional sessions depending on the evolution at the end of the first batch. The scheduled sessions could be completed in most patients (n = 5). The 3 reasons for discontinuation were the lack of response to treatment, hospital admission and thrombosis of the arteriovenous fistula (AVF). The improvement of graft function in terms of creatinine reduction at the end of therapy occurred among patients presenting with acute cellular rejection (ACR) (n = 4) and it remained 3 months after the end of the treatment. The only late ACR (> 3 months post-transplant) could not complete the initial programming. No graft with humoral component showed improvement in renal function. Graft loss and dialysis restart occurred in a patient with chronic active antibody-mediated rejection (cAMR). The other patient with cAMR is in a pre-dialysis situation. A total of 89 procedures were studied, all performed with the THERAKOS® CELLEX® Photopheresis System, with the administration of the methoxsalen solution (UVADEX®) and photoactivation with ultraviolet A light. Vascular access per session was the AVF (76%) or the central vascular catheter (CVC) (24%), under no circumstances was peripheral access used. Each procedure lasted on average 112.72 +/- 13.85 minutes (range, 86-145). The volume of treatment ("buffy coat") was 189.11 +/- 28.67 mL per session, and the total volume of fluids administered (NaCl and anticoagulation) was 559.40 +/- 41.17 mL. The complications observed during the sessions were fever (n = 2), thrombosis of the AVF (n = 1), coagulation of the extracorporeal system (n = 1) and anemization (n = 1). Interprocedure there was a case of urinary infection that conditioned hospital admission and discontinuation of therapy. One patient died of cardiovascular cause with a functioning graft 4 years after therapy.

Conclusion: The utility of the ECP seems to be in cases of cell rejection, probably related to the triggering of an immunomodulatory response of lymphocytes. It can be considered a well-tolerated and safe treatment. Special care should be taken with patients who require water restriction (infusion of 560 mL on average per session). We need more studies with a greater number of patients and a control group to be able to confirm the effectiveness and safety of PEC in RTx and to be considered a useful therapeutic tool as in other SOT.

Patient	1	2	3	4	5	6	7	8
Age (years)	61	24	47	49	56	68	45	61
Gender	M	M	W	M	M	M	W	M
Renal disease	PKD	GNP	IKD	Unknown	Unknown	DKD	IKD	DKD
Previous transplant	0	0	0	0	0	0	2	0
Type of donation	DBD	DBD	DBD	DBD	DBD	DBD	DCD	DBD
Immunosuppression*	FK	FK	FK	FK	imTOR	FK	FK	FK
Type of Rejection**	ACR IIA	ACR IIA and cAMR	ACR III and cAMR	Borderline	ACR IIA y AMR	ACR IIA	ACR IA	ACR IIA
Period***	Early	Late	Late	Early	Late	Early	Late	Early
Number of session	14	19	8	13	13	12	5	5
Complete programming	Yes	Yes	No	Yes	Yes	Yes	No	No
Reduction of Cr_s	Yes	No	No	Yes	No	Yes	No	Yes
Current situation, functional renal grafts?	Exitus	No	Pre-dialysis	Yes	Yes	Yes	Yes	Yes

Figure:

P1761 **SIDE EFFECTS OF MTOR INHIBITORS DEPEND ON THE BASELINE METABOLIC STATUS OF KIDNEY TRANSPLANT RECIPIENTS**

David Cucchiari[1], Alicia Molina-Andujar[1], Enrique Montagud-Marrahi[1], Jordi Rovira[1], Fritz Diekmann[1]

[1]*Hospital Clínic, Renal Transplant Unit, Barcelona, Spain*

Background and Aims: Biologically, the cellular activity of the mTOR complexes depends on the balance between the catabolic and the anabolic inputs. Hence, we hypothesized that the metabolic side effects of mTOR inhibitors (mTORi) in kidney transplantation depend on the baseline metabolic status of the patient.

Method: The analysis included all the patients that have been transplanted in our Center between June 2013 to December 2016, completed one year of follow-up and did not change medication during the first year after kidney transplantation (per-protocol population, n=298). Outcomes chosen include de novo diabetes, 1-year difference from baseline in glycated hemoglobin (HbA1c), triglycerides and total cholesterol. Kidney transplant recipients were treated either with an mTORi (either Sirolimus or Everolimus, n=134) or Mycophenolic Acid (MPA, n=164). Both drugs were always accompanied by tacrolimus and steroids. Patients were stratified according to the treatment received (mTORi versus MPA) and the baseline metabolic status (diabetes mellitus type 2 and obesity). Differences among groups were analyzed with exact Fisher test and ANOVA test with LSD post-hoc analysis.

Results: We observed a strong difference for 1-year change in HbA1c depending on the baseline metabolic status of the patients ($P<0.001$ between groups, Figure 1a). The worst results were observed for patients with baseline diabetes. Among these, obese patients treated with mTORi had the higher increase in HbA1c ($3.04 \pm 1.18\%$ from baseline, $P<0.01$ with all groups at post-hoc analysis). De-novo diabetes was more frequent in patients taking mTORi (23.4 vs. 13.1%), albeit not significantly ($P=0.100$) and without differences taking into account obesity as a covariate. Triglycerides increased substantially in patients without baseline diabetes and treated with mTORi ($P<0.05$). Surprisingly, in diabetic patients no differences were observed in triglycerides between mTORi and MPA groups (Figure 1b). There were no differences in the increase in total cholesterol among groups ($P=0.155$) (Figure 1c).

Conclusion: We observed that the 1-year increase in HbA1c and triglycerides attributable to mTORi after kidney transplantation depends on the baseline metabolic status of the patients. We propose that the metabolic side effects of mTORi depend on the balance between anabolic and catabolic inputs of every kidney transplant recipient.

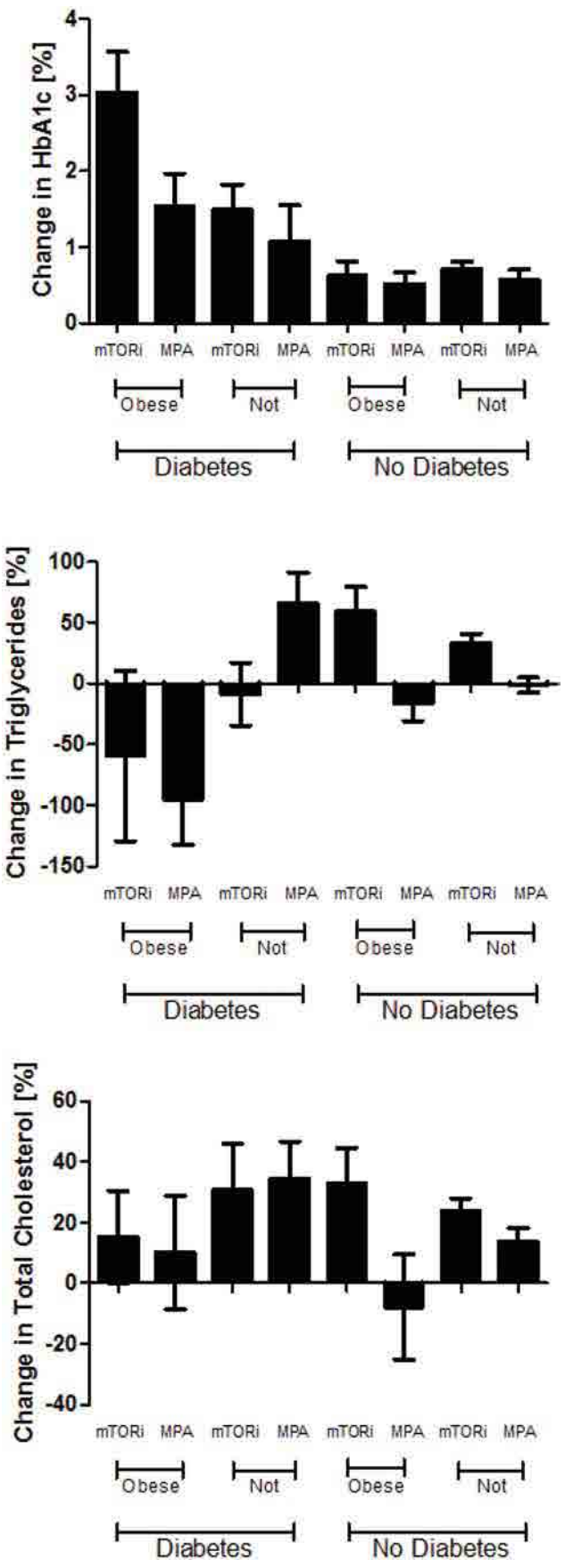


Figure: (below)

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THE EFFECT OF IMMUNOSUPPRESSIVE THERAPY ON THE CLINICAL FOLLOW-UP OF BK VIRUS IN KIDNEY TRANSPLANT RECIPIENTS

Gulay Yilmaz[1], Volkan Polatkan[2], Ebru Ozdemir[2], Turker Erturk[4,5], Emel Tatli[6], Ibrahim Berber[7], Ulkem Cakir[8]

[1]Acıbadem International Hospital, Nephrology, İstanbul, Turkey, [2]Acıbadem International Hospital, Organ transplantation, Istanbul, Turkey, [4]Acıbadem International Hospital, Organ transplantation, İstanbul, Turkey, [5]Acibadem University, istanbul, Turkey, [6]Acıbadem International Hospital, istanbul, Turkey, [7]Acibadem University, Acibadem International Hospital, Organ transplantation, istanbul, Turkey and [8]Acibadem University, Acibadem İnternational Hospital, Nephrology, istanbul, Turkey

Background and Aims: BK virus nephropathy occurs in up to 10% of kidney transplant recipients and can result in graft loss. The reactivation of BK virus is largely asymptomatic, and routine surveillance especially in the first 12-24 months after transplant is necessary for early recognition and intervention. Reduced immunosuppression and antiviral treatment in the early stages may be effective in stopping BK virus replication. This study is designed to investigate the effect of management in immunosuppressive therapy on BK virus titers and graft functions in our kidney transplant group.

Method: A total of 370 kidney transplant recipients between the ages of 18-69 years and receiving a triple immunosuppressive therapy (Tacrolimus+Mycophenoloic Acid+Prednisolone) were included in the study. Demographic characteristics, BK virus titers, serum creatinine and immunosuppressive drug (Tacrolimus, Everolimus) levels were measured at regular intervals in the first 24 months. Among these patients 43 of them were found to have BK virus positivity. At the time of the detection of BK virus positivity, patients were divided into three groups regarding the change in the immunosuppressive protocols: Group I: Tacrolimus + Everolimus + Prednisolone, Group II: Everolimus + Prednisolone, Group III: Tacrolimus + Prednisolone. BK virus titers and graft functions of all three groups were compared with each other. SPSS 15 for Windows was used for statistical analysis.

Results: The mean age of the patients was 45.3 years, and the mean duration of transplantation was 16.3 months at the time of the BK virus positivity. During the follow-up, mean Tacrolimus levels were found to be in their highest value (14.1 ng/mL) in the posttransplant three months while BK virus titer reached the highest value (1.1x106 copies/ml) in the posttransplant seven to nine months. Increased creatinine values two months after BK virus positivity were strongly correlated ($p = 0.02$, $p = 0.008$, $p = 0.05$, $p = 0.002$ at 6th, 9th, 12th and 24th months, respectively). A significant decrease in BK virus titers was observed in all three groups due to reductions in immunosuppressive treatment protocol ($p = 0.005$, $p = 0.003$, $p = 0.028$, in groups I, II, III respectively).

Conclusion: Our study favors the benefits of the prospective screening for BK virus to identify early viral replication, permit intervention, and prevent progression to nephropathy or allograft loss. The best studied treatment for BK viremia and nephropathy is careful reduction of immunosuppression

P1763

TUBERCULOSIS IN RENAL TRANSPLANT RECEPIENTS - DO RITUXIMAB AND OTHER IMMUNOSUPRESSION HAVE A ROLE?

Anupma Kaul[1], Dharmendra Bhaduria[1], Narayan Prasad[1], Amit Gupta[1]

[1]*Sanjay Gandhi Post Graduate Institute of Medical Sciences, Nephrology, Lucknow, India*

Background and Aims: Rituximab is an anti CD 20 agent used widely in renal transplant recipients. Its use is associated with various infections;however, its association with Tuberculosis (TB) is not well established and has not been studied in post renal transplantation patients.

Method: This is a single centre, retrospective analysis of 56 renal transplant recipients who received rituximab for various reasons and 287 post renal transplant patients who did not receive rituximab during the study period from January 2013 to June 2017. The association between use of rituximab and incidence of TB was studied. Other factors associated with tuberculosis were also investigated.

Results: Baseline characteristics were similar in both the groups. Mean time for occurrence of TB was 18.4 + 10.6 months after renal transplantation. Rituximab use was not significantly associated with tuberculosis or any other infection. Higher number of rejection episodes (60% vs 32.72%, p=0.029) was the only factor associated with greater incidence of TB. However, no specific type of rejection was associated with tuberculosis. Use of plasmapheresis in post transplant period for treatment of humoral rejections was associated with significantly higher incidence of TB (33.33% vs 13.41%, p=0.031), however when pre- transplant plasmapheresis was also considered, there was no significant difference. The choice of induction agent was not associated with higher incidence of TB.

Conclusion: Use of rituximab is not associated with higher incidence of TB when compared to other immunosuppressive agents. Routine screening and prophylaxis may not be advisable especially in a country like India with high prevalence of TB; as it will further delay transplantation and may adversely affect the outcome of the patients.

P1764 **EXPRESSION OF TOLL-LIKE RECEPTOR 4, BUT NOT THE TOLL-LIKE RECEPTOR 2, MAY BE USEFUL I ASSESING THE RISK OF RENAL TRANSPLANT DETERIORATION IN RECIPIENTS WHO HAVE RECOVERED FROM CYTOMEGALOVIRUS INFECTION.**

Sławomir Zmonarski[1,1], Mirosław Banasik[1], Tomasz Gołębiowski[1], Letachowicz Krzysztof[1], Joanna Zmonarska[2], Marta Myszka[1], Katarzyna Madziarska[1], Krajewska Magdalena[1]

[1]Wroclaw Medical University, Dept. of. Nephrology and Transplantation Medicine, Wroclaw, Poland and [2]Wroclaw Medical University, Faculty of Medicine, Wroclaw, Poland

Background and Aims: Data binding the expression of Toll-like (TLR) 4 receptor (TLR4ex), or TLR2 receptor (TLR2ex) and transplanted kidney (KT) function and symptomatic infections with CMV (CMV+) and are scarcely available.

Objective: To investigate the relationships between TLR4ex and TLR2ex, a relapse of CMV+ and transplant function.

Method: Materials and methods: TLR4ex and TLR2ex were measured in peripheral blood mononuclear cells of KT recipients.

We compared TLR4ex and TLR2ex among 25 CMV+ patients; 81 patients without CMV infection (CMVn). At the beginning (Day-0) TLR4ex, as well as concentrations of cyclosporin A (CyA) and tacrolimus (TAC) were determined.

Both CMV+ and CMVn patients were divided according to the respective median of TLR4ex into groups of low-TLR2/4 expression (L-TLR2/4ex) and high-TLR2/4 expression (H-TLR2/4ex). Glomerular filtration rate (EGFR) was assessed on Day-0 and after the follow-up (F-up). The magnitudes of EGFR change (ΔEGFR) were evaluated. Stable treatment along the F-up period (median 11.9 months) was applied.

Results: Results. In CMV+ TLR2ex of 64,3% and TLR4ex in 67% is below respective median. Past CMV strongly affected TLR2ex and moderately TLR4ex. On Day-0: in CMV+ we found no link of TLR2 ex and TLR4ex with EGFR; In CMV+ TLR2ex and TLR4ex were lower but Day-0 EGFR did not differ from H-TLR2 or H-TLR4ex. In CMVn: GFR-TLR4ex link was present with no similar in case of GFR-TLR2ex. In patients treated with tacrolimus CMV strongly affected TLR4ex, blurring CMV+/CMVn differences.

Post F-up: in CMV+ with L-TLR4ex EGFR declined, there was no change of EGFR in H-TLR4ex; L/H-TLR2ex showed no differences in EGFR. In CMVn with H-TLR4ex EGFR rose, there was no change in L-TLR4ex. In case of TLR2ex we showed no similar differences. Regression analysis points out the impact of CMV+ and TLR4ex on eGFR and ΔEGFR. No similar impact of CMV+ and TLR2ex on eEGFR and ΔEGFR was found.

Conclusion: Conclusion: In the group who had a symptomatic CMV + infection, low TLR4 expression increases the risk of worsening EGFR. In CMVn, high TLR4 expression increases the chance of EGFR improvement. Historic CMV + strongly affects TLR2ex. However, TLR2ex cannot be used as a factor in assessing the risk of EGFR deterioration.

P1765 **COMBINING THE BEST OF TWO OPTIONS: A SPLIT STRATEGY WITH PROPHYLAXIS OR PRE-EMPTIVE THERAPY TO PREVENT CYTOMEGALOVIRUS AFTER KIDNEY TRANSPLANTATION**

Rachel Hellemans[1], Veerle Wijtvliet[1], Kristof Bergs[2], Ester Philipse[1], Rowena Vleut[1], Annick Massart[1], Marie-Madeleine Couttenye[1], Veerle Mattheeussens[2], Daniel Abramowicz[1]

[1]University Hospital Antwerp, Nephrology, Edegem, Belgium and [2]University Hospital Antwerp, Microbiology, Edegem, Belgium

Background and Aims: Cytomegalovirus (CMV) remains an important challenge after kidney transplantation. Current Transplantation Society International Consensus Guidelines recommend antiviral prophylaxis or pre-emptive therapy for either high risk CMV-seronegative recipients of a CMV-seropositive donor (D+/R-) and moderate-risk CMV-seropositive recipients (R+). A split strategy according to CMV risk, however, is not specifically mentioned.

Method: We evaluated a split strategy to prevent cytomegalovirus infection after kidney transplantation. D+/R- patients received valganciclovir (VGC) prophylaxis during 200 days and R+ patients were treated pre-emptively according to CMV DNAemia.

Results: Between April 2014 and March 2018, 40 D+/R- and 92 R+ patients underwent kidney transplantation. Forty-six % received antithymocyte globuline (ATG) induction and 98 % were treated with calcineurin inhibitors, mycophenolic acid (MPA) and steroids. No D+/R- patient developed CMV disease during prophylaxis (median 200 days), 15 % developed late-onset disease. Fifty-three % developed neutropenia during prophylaxis, including 16/40 (40 %) grade 3 or 4 neutropenia requiring reduction/discontinuation of MPA (30 %) and/or VGC (30 %), and occasional need for granulocyte colony stimulating factors (5 %). In the R+ group, 40 % received antiviral therapy for a median duration of 21 days. Five percent developed CMV disease. Only 5 % developed neutropenia. D+/R+ status (hazard ratio (HR) 2.09, P 0.004) and ATG use (HR 2.81, $P < 0.0001$) were risk factors for CMV reactivation.

Conclusion: Prophylaxis leads to acceptable CMV control in high risk patients, but comes with a high risk of neutropenia. Pre-emptive therapy is effective and limits drug exposure in those at lower risk for CMV.

P1766 **EFFECT OF EVEROLIMUS AND REDUCED CALCINEURIN INHIBITORS ON BIOPSY PROVEN BK VIRUS ASSOCIATED NEPHROPATHY-**

Ziad Zaky[1]

[1]*Cleveland Clinic, Glickman Urological and Kidney Institute, Cleveland, United States of America*

Background and Aims: BK virus-associated nephropathy (BKVAN) is a clinically important entity that results in an allograft loss in kidney transplant recipients (KTRs). Mammalian target of rapamycin inhibitors (mTOR-i) have been proposed as possible immunosuppressive therapy in BK virus infection because of their antiviral capacity. However, the effect on biopsy (bx) proven BKVAN is still unclear.

Method: This a retrospective single center review of 27 (KTRs) on triple immunosuppression regimen (CNI/MMF/prednisone), who developed BK viremia and had bx proven BKVAN (n=13, 48%). Patients were converted to Everolimus, reduced/or no CNI and prednisone. We present the renal allograft function, BK viremia status and histological data after a mean follow up period of 28.4±17.9 months post-transplant.

Results: We reviewed 27 KTRs (17 males, 11 AA) transplanted between 2012 and 2019, who developed BK viremia, 23/27 patients (85%) underwent surveillance & for cause bx (n=55). All patients were switched to Everolimus, reduced CNI (one patient was on Cyclosporin) and prednisone regimen. Median time from transplant to BK viremia was 2.5 months (min 0.7-max 76.7). After a mean follow up period of 17.9±12 months post conversion, the mean serum creatinine remained relatively stable (1.54 mg/dl ±0.47; 1.79 mg/dl±0.82; P=0.17). The mean BK viral load was statistically significantly reduced (P=0.045), pre/post conversion median BK levels were (35900 (655-2.5 million copies) and 752 (0-92150) respectively), 13/27 (48%) patients had undetectable BK viral load. 13/27 (48%) had bx proven BKVAN, with 4/13 (31%) had no follow up bx, 4/13 (31%) had follow up bx proven resolved BKVAN and 5/13 (38%) had bx proven persistent BKVAN (figure 1). Post conversion 3/27 (11%) patients were treated for borderline acute cellular rejection with pulse steroids and had negative DSA.

Conclusion: Conversion to mTOR-i-based therapy could provide an added benefit in BK viremia as well as BKVAN and could be an effective strategy for the decrease of the viremia and increase of graft survival in selected patients. In the medium-term follow up, the BK viral load was statistically significantly lower even in bx proven persistent BKVAN, and almost half (4/9) of the bx proven BKVAN have resolved. The median time for conversion for patients with resolved BK nephropathy was 25 days (range 19-38) vs 263 days (range 17-931) in patients with persistent BK nephropathy (P<0.001), pointing to possible benefit of rapid conversion to mTOR-i based regimen in the setting of BK viremia.

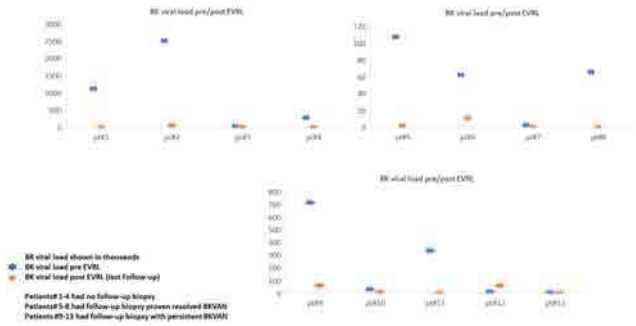


Figure:

P1767 ERALY VERSUS LATE GRAFT PYELONEPHRITIS- A RETROSPECTIVE ANALYSIS OF GRAFT AND PATIENT OUTCOME

Anupma Kaul[1], Thomas Mathews[1], Dharmendra Bhaduria[1], Narayan Prasad[1], Amit Gupta[1]

[1]*Sanjay Gandhi Post Graduate Institute of Medical Sciences, Nephrology, Lucknow, India*

Background and Aims: Acute graft pyelonephritis(AGPN) is thought to affect the graft and patient survival among the renal transplant recipients.Our objective was to compare these outcomes in those having early AGPN(<6 months from transplant) versus those having late AGPN(>6months from transpant)

Method: This retrospective study analysed 150 patients who had AGPN over a period of 8 years from 2005 to 2013.They were divided into early AGPN group and late AGPN group .Their baseline characteristics were compared.Predictors of graftloss and mortality were compared using logistic regression analysis.Graft survival and patient survival wereanalysed using Kaplan-Meyer survival plots

Results: A total of 150 patients with AGPN were analysed.Of these 55.3%(n=83) had early AGPN and 44.7%(n=67) had late AGPN.These two groups were comparable regarding baseline characteristics and immunosuppression.13.3%(n=11) patients in early AGPN group had CMV disease during follow up compared to 3%(n=2) in late AGPN group($p<0.05$).26.5%(n=22) in the early AGPN group had prolonged foley's catheterization(>5days) following transplant surgery compared to 7.5%(n=5) in late AGPN group($p<0.05$).38.6%(n=32) in the early AGPN group had prolonged DJ stent in-situ(>2weeks) following transplant surgery compared to 19.4%(n=13) in the late AGPN group($p<0.05$).Recurrent GPN was more common in the late AGPN group than the early AGPN group-35.8%(n=24) verus 18.1%(n=15).Predictors for graft loss was assessed in patients with AGPN and presence of renal abscess was predictive of graft loss in univariate analysis(HR-6.129 ,95 % CI 1.776-21.154,p-0.004).There were no significant predictors of mortality in univariateanalysis.KaplanMeiyer survival analysis showed decreased death censored graft survival in the early AGPN group(p-0.035).There was no significant difference in the patient survival among two groups.

Conclusion: Occurrence of early AGPN has significant impact on long term graft survival in renal transplant recipients with no significant effect on patient survival.This study underlines the paramount importance of prevention of UTIs in renal transplant recipients.

P1768 **EFFECTS OF HIGH INTENSITY INTERVAL TRAINING ON CIRCULATING LYMPHOCYTES, MONOCYTES AND CYTOKINES IN RENAL TRANSPLANT RECIPIENTS**

Ganisha Hutchinson[1], Roseanne E Billany[2], Nicolette Bishop[3], Andrea Cooper[1], Alice Smith[4]

[1]University of Leicester, Department of Respiratory Sciences, Leicester, United Kingdom, [2]University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom, [3]Loughborough University, School of Sport, Exercise and Health Sciences, Loughborough, United Kingdom and [4]University of Leicester, Department of Health Sciences, Leicester, United Kingdom

Background and Aims: High intensity interval training (HIIT) has been shown to improve traditional and non-traditional cardiovascular risk factors in the general population and in chronic diseases. However, intense exercise has the potential to suppress immune function and promote systemic inflammation. Renal transplant recipients (RTRs) are immunologically vulnerable and therefore thorough understanding of the effects of different exercise regimes is required to inform exercise advice and guidelines. The aim of this study was to explore the immune and inflammatory effects of HIIT in comparison to moderate intensity continuous training (MICT) in RTRs.

Method: Renal transplant recipients (n = 24, age (years) = 48 $\pm$ 13, BMI = 27.2 $\pm$ 5.6 kg.m^2, eGFR (mL·min· 1.73 m^2) = 58 $\pm$ 19) were randomised into one of three thrice-weekly 8 week exercise programmes: HIIT A (16 min interval training with 4, 2 and 1 min intervals at 80%–90% of peak oxygen uptake ($VO_{2\ peak}$), HIIT B (4 $\times$ 4 min interval training at 80%–90% VO_{2peak}) or MICT ($\sim$40 min cycling at 50%–60% VO_{2peak}). Peripheral blood mononuclear cells were isolated at baseline, mid-training, post-training and three months post-training and stained for lymphocyte and monocyte phenotypic and activation markers. Plasma cytokines (IL-6, IL-10 and TNF-α) were measured by affinity ELISA kits.

Results: Friedman's ANOVA was used to assess within-group differences and a Kruskal-Wallis H test was used to assess between-group differences; any significant findings were followed up using a post-*hoc* test. There were no differences in circulating lymphocyte or monocyte lineage markers within or between groups over time ($P >$ 0.05). Cytokines did not change in relation to exercise within or between groups over time ($P > 0.05$).

Conclusion: This is the first study to investigate the effects of HIIT on immune parameters and inflammation markers longitudinally in RTRs or other immunosuppressed populations. Our data do not indicate any evidence for adverse effects of HIIT on circulating lymphocytes, monocytes or cytokines and suggest that such exercise regimes may be immunologically safe for immunosuppressed patients. We recommend further investigations involving larger sample size to confirm our results.

P1769 **POST TRANSPLANT MALIGNANCY - OUR EXPERIENCE**

George Kurian[1], Gauri Shankar Jagadesh[1], Sandeep Sreedharan[1], Zachariah Paul[1], Anil Mathew[1], Rajesh Raj[1]

[1]*Amrita Institute of medical sciences, Nephrology, kochi, India*

Background and Aims: Cancer is now increasingly recognized as a major cause of death among patients especially after kidney transplantation. Malignancy represent a major burden in transplantation medicine. The Incidence is about 12 fold higher for PTLD and 3.5 fold higher for non-cutaneous malignancy compare to age-matched population. The increased risk is multifactorial and attributed to oncogenic viruses, immunosuppression and altered T cell immunity. In the era of longer graft survival and with the introduction of more potent immunosuppressive medication, malignancy represents a major burden. The incidence of malignancy after renal transplantation is 3 to 5 times higher. Incidence is higher in transplant patients even when compared to patients on hemodialysis.

Aim: We attempted to assess the incidence of post-transplant malignancies in patients who underwent renal transplantation at our centre, along with studying the presentation, type and other factors affecting their development.

Method: We analysed data retrospectively from 626patients who underwent renal transplantation atour centre from January 2003 to September 2018.Pre transplant history, post transplant course including duration on hemodialysis, immunosuppression details and duration till diagnosis of malignancies were collected. Details regarding type of malignancy, histopathology, staging and treatment given and outcome were collected.

Results: Number of transplant recipient-626. The total number of patients with malignancy is 12. Incidence of malignancy posttransplant is 1.9%.Male-7 and female-6.One patient was detected with 2 malignanciesduring her post transplant period. The types of malignancies encountered were

Patient no	Number of days on hemodialysis	Age at transplant	Type of malignancy	Malignancy interval
1	601	37	Squamous cell Ca tongue	90
2	250	20	Squamous cell Ca Tongue	4836
3	1826	42	Squamous cell Ca Tongue	1735
4	30	49	PTLD	3300
5	66	48	PTLD	700
6	1163	56	Adenocarcinoma pancreas	852
7	60	58	Squamous cell ca lung	2276
8	270	31	PTLD	1615
9	150	48	Adenocarcinoma of colon	2305
10	60	16	PTLD	260
11	350	45	PTLD	356
12	140	28	PTLD	398

None of these patients had any other risk factors for development of malignancies like exposure to radiation, smoking or family history of malignancies. None of the patients had any past history of malignancies. 3 (30%) out of 10 patients had under-gone deceased related donor transplantation, while the rest had live related renal transplant.

Patient No.	Malignancy	Creatinine at time of diagnosis of malignancy	Follow up Cr at 3 months	Long term
1	**Squamous cell tongue**	1.0	1.0	Expired
2	**Squamous cell tongue**	1.8	1.7	Expired
3	**Squamous cell tongue**	1.4	2.3	Expired
4	**Squamous cell Lung**	1.4	Expired	Expired
5	**AdenoCa pancreas**	0.9	1.1	Expired
6	**AdenoCa Colon**	1	0.9	Expired
7	**PTLD**	2	3.5	Expired
8	**PTLD**	4	ESRD	Expired
9	**PTLD**	1.2	1.4	Expired
10	**PTLD**	1.3	3	Alive (ON HD)
11	**PTLD**	1.4	1.3	Expired
12	**PTLD**	1.2	1.8	Expired

Conclusion: The incidence of malignancy – 1.9%.Probable reason for decreased incidence of malignancy is the decreased immunosuppression needed by South Asian people. The most common malignancy was solid organ tumour; tongue being the most common organ. Most common histological variant is squamous cell carcinoma.Non-Hodgkin is more common than Hodgkin. Incidence of malignancy is low. Decision regarding cancer screening should be made on individual basis.

P1770

HIGH PILL BURDEN INCREASES INTRAPATIENT TACROLIMUS TROUGH LEVELS VARIABILITY IN STABLE KIDNEY TRANSPLANT RECIPIENTS

Piotr Giza[1], Aureliusz Kolonko[1], Jerzy Chudek[2], Rafał Ficek[1], Tomasz Dwulit[1], Andrzej Jan Wiecek[1]

[1]Medical University of Silesia in Katowice, Nephrology, Transplantation and Internal Medicine, Katowice, Poland and [2]Medical University of Silesia in Katowice, Internal Medicine and Onkological Chemotherapy, Katowice, Poland

Background and Aims: High intrapatient variability (IPV) of tacrolimus trough levels is associated with poor long-term outcome after transplantation. Polypharmacy, related to the high co-morbidity, may affect the pharmacokinetics of tacrolimus in a substantial proportion of kidney transplant recipients (KTRs). We aimed to evaluate whether the number of regularly prescribed medications is associated with the tacrolimus IPV.

Method: We studied 152 tacrolimus-treated KTRs with mean post-transplant time 6.0±3.1 years, without dosing changes over the consecutive 2 years. The coefficient of variation (CV) as a measure IPV was calculated in each patient. Data concerning the type (generic name) and number of currently prescribed medications were collected. The participants were divided into 4 groups, based on the number of regularly prescribed drugs ($\leq$3; 4-6; 7-9; $\geq$10).

Results: The median daily pill burden was 6.2±2.5 (ranged 2 to 15). There was an increasing trend for median CV, proportional to the increasing number of medications [group 1: 0.11 (IQR 0.08-0.14); group 2: 0.14 (0.01-0.17); group 3: 0.17 (0.14-0.23); group 4: 0.17 (0.15-0.30); p value for trend = 0.001]. Stepwise backward multivariate regression analysis revealed that the number of medications [partial correlation coefficient ($r_{partial}$) = 0.503; p<0.001], age [$r_{partial}$ = -0.150; p=0.07] and eGFR [$r_{partial}$ = -0.140; p=0.09] independently influenced the tacrolimus IPV (R^2=0.30). Concomitant steroids or diuretics use increased IPV only in Advagraf-treated KTRs, whereas PPIs or statin use increased IPV in Prograf, but not Advagraf group.

Conclusion: : The number of medications is positively associated with tacrolimus IPV in stable KTRs. There were also tacrolimus formulation-dependent differences in the assumed influence of several concomitantly received classes of medications, including steroids, diuretics, PPIs and statins, on the tacrolimus IPV.

P1771 NOCARDIOSIS IN RENAL TRANSPLANT RECIPIENTS- TEN YEARS OF SINGLE CENTER EXPERIENCE

Ravi Kumar Singh[1], A K Bhalla[1], Anurag Gupta[1], Vinant Bhargava[1], Ashwani Gupta[1], Devinder Singh Rana[1]

[1]*Sir Ganga Ram Hospital, New Delhi, India*

Background and Aims: Nocardiosis is a localized or disseminated bacterial infection caused by aerobic Actinomyces that commonly affects immunocompromised hosts. This study aimed to retrospectively review the clinical course and outcome of nocardiosis in renal transplant recipients at our center

Method: Data was obtained from hospital records retrospectively. Sixteen cases of nocardiosis were identified in a series of more than 1800 consecutive renal transplants performed at Sir Ganga Ram Hospital in the last decade from the year 2010 to 2019.

Results: Thirteen out of Sixteen patients(81.25%) had developed nocardiosis within a 1-year post-renal transplant. The diabetic population constituted 31.3%. CMV disease was present in 25% of patients six months prior to the diagnosis of Nocardiosis.56.3% of patients were on Trimethoprim-sulfamethoxazole prophylaxis while they were diagnosed with nocardiosis. Pleuropulmonary nocardiosis was the most common form of infection(68.75%). Primary cutaneous nocardiosis was identified in one patient(6.25%). cerebral nocardiosis and disseminated nocardiosis was diagnosed in two patients each(12.5%).In the last 3 years with the introduction of MALDI-TOF led to the identification of the subspecies of Nocardia which was not possible earlier. In the last 3 years, 6 patients were diagnosed with nocardiosis, in which 4 were infected with Nocardia farcinica, one patient with Nocardia Asiatica and one with Nocardia cyrigeorgica. Nocardia farcinica was resistant to cotrimoxazole, which used to be first-line therapy against Nocardiosis before subspecies identification and sensitivity testing. With the help of proper identification of subspecies by MALDI-TOF and antibiotic susceptibility by E-testing, 5 out of 6 patients could be treated while earlier 6 out of 10 patients could be treated.

Conclusion: Nocardiosis is a rare, difficult-to-diagnose-and-treat infection following kidney transplantation. Trimethoprim-sulfamethoxazole prophylaxis was not effective in the prevention of disease. The Subspecies identification and modification of the plan of management according to antibiotic sensitivity results in improved outcomes.

P1772

CONVERSION TO BELATACEPT IMPROVES RENAL GRAFT FUNCTION OF PATIENTS WITH SEVERE HISTOLOGICAL AND FUNCTIONAL INVOLVEMENT. LONG-TERM UNICENTRIC EXPERIENCE

Maria Ovidia Lopez-Oliva[1], Laura Alvarez Garcia[1], Tamara Perez Robles[2], Marco Antonio Vaca Gallardo[1], Santacruz Juan[1], Elena Gonzalez Garcia[1], Rafael Selgas[1], Carlos Jimenez[1]

[1]Hospital Universitario La Paz, Nephrology, Spain and [2]Hospital Universitario La Paz, Pharmacy, Spain

Background and Aims: Belatacept selectively blocks the costimulation signal of T cells. Its use, both de novo and in conversion, is associated with a better renal graft function compared to the regimens that include a calcineurin inhibitor (CNI). We expose our experience with belatacept as a rescue therapy in patients who present moderate-severe dysfunction after renal transplantation and compare the evolution with those patients who received the contralateral kidney graft without change to belatacept.

Method: Adult kidney transplanted patients, with graft dysfunction and renal biopsy with CNI toxicity or chronic vascular lesions who are changed from CNI to belatacept were included. Efficacy (creatinine, proteinuria, TFGe, acute rejection tested by biopsy, anti HLA) and safety (adverse events, tumors or infections) variables were recorded before and after the change.

Results: 11 patients were included. The change to belatacept was made at a median of 13 months from the transplant (range 1-62 months) and the duration of the treatment ranged between 6 and 74 months. Renal function improved from a mean creatinine of 3.04±1.34 mg/dl before the change to 1.9±0.3 mg/dl at 6 and 12 months after conversion ($p = 0.016$), being the last average creatinine (December 2019) of 1.7±0.3 mg/dl.

Belatacept was withdrawn in one case, at one year, due to the development of specific donor antibodies without evidence of acute rejection. There were no cases of post-transplant lymphoproliferative syndrome. Two patients developed VBK replication controlled with immunosuppression modification and three patients developed CMV infection controlled with valganciclovir. There was no episode of acute rejection after conversion.

In 5 cases the contralateral kidney graft was not implanted, while in 6 cases it was implanted in another recipient who was not given belatacept and was taken on CNI therapy. The last average creatinine (December 2019) of patients without belatacept was 3.3±1.6 mg/dl vs. 1.6±0.2 mg/dl in patients with belatacept ($p = 0.03$).

Conclusion: The change to belatacept improves the renal function of all patients, even in those with severe histological and functional involvement. The improvement of renal function remains stable in the medium/long term and is significantly better than the renal function of patients with CNI.

P1773

BENEFITS OF CONTROL RENAL BIOPSIES IN THE ASSESSMENT OF ANTI-REJECTION THERAPY EFFICACY IN PATIENTS WITH HISTOLOGICAL LESIONS DIAGNOSED EITHER BY PROTOCOL OR BY "FOR CAUSE" BIOPSIES

Stefania Affatato[1], Silvio Sandrini[1], Simona Fisogni[2], Nicola Bossini[1], Francesca Valerio[1], Ezio Movilli[1], Camilla Maffei[1], Stefano Possenti[1], Francesco Scolari[1]

[1]ASST Civil Hospital of Brescia, Nephrology, Brescia, Italy and [2]ASST Civil Hospital of Brescia, Pathology, Brescia, Italy

Background and Aims: Efficacy of acute rejection (AR) therapy has always been evaluated based upon improvement of renal function. On the contrary, the degree of histological lesion (HL) regression has rarely been considered for this purpose.

The main goal of this study was to evaluate the percentage of failures in HLs regression after treatment aimed at both "subclinical" and "clinical" AR. Treatment efficacy was therefore evaluated with control renal biopsies (CBs) performed 30-60 days after anti-rejection therapy. In addition, the correlation between graft function and histological data was assessed. The results of treatment for "subclinical" and "clinical" AR were considered separately.

Method: Real-time ultrasound-guided CBs were performed in an outpatient setting using 16G tru-cut needles. The HLs considered were: interstitial inflammation (i), tubulitis (t), glomerulitis (g), arteritis (v), capillaritis (ptc). Each lesion was graded from 0 to 3 (sec Banff 2013-2017). For this study, only HLs with a score $\geq$2 were considered. Therapy failure was determined both by the percentage of patients (pts) with persistence of HLs and by the change of HLs score after treatment, in the control biopsies. Anti-rejection therapy varied according to AR type and severity. In patients failing AR therapy, serum creatinine was evaluated before and after the treatment.

Results: 111 BCs were performed after treatment either for subclinical (n = 47) or for clinical (n = 64) AR. Before therapy, HLs (with score $\geq$2) present in subclinical and clinical AR were: i: 23% and 52%; t: 30% and 30%; g: 34% and 41%; ptc: 11% and 28%; v: 15% and 19%.

After therapy, in the setting of subclinical AR, HLs were still present with a range between 29% (v) and 81% (g) with stable or improved histological score. In this scenario, renal function resulted stable and satisfactory (Tab 1).

In the case of clinical AR, the persistence of histological lesions ranged from 25% (v) to 92% (g), also with stable or improved histological scores. In this case, therapy was always followed by an improvement in renal function (Tab 2).

Conclusion: After AR therapy, only the morphological data obtained with histological analysis can disclose failures of anti-rejection therapy, both in presence of subclinical and clinical AR.

The high rate of treatment failure may explain the correlation between AR and worse graft survival.

Our results could lead us to consider the need for a more aggressive anti-rejection treatment.

Control renal biopsies after AR therapy should always be considered on clinical grounds.

Histological lesions (HLs) considered in the study	Pts with HLs score ≥ 2 at biopsy	Pts with persistance of HLs at control biopsy	Pts with persistance of HLs at control biopsy					
			Score of HLs (m±sd)			Serum Creatinine (mg/dL; m±sd)		
			pre therapy	post therapy	p	pre therapy	post therapy	p
Interstitial inflammation	11 (23%)	5 (45%)	2,1±0,3	1,4±0,5	0,003	1,6 ± 0,6	1,7 ± 0,6	0,762
Tubulitis	14 (30%)	11 (79%)	2,1±0,3	1,7±0,4	0,009	1,8 ± 0,7	1,8 ± 0,6	1
Glomerulitis	16 (34%)	13 (81%)	2,4±0,5	2,4±0,8	1	1,5±0,4	1,4±0,4	0,509
Capillaritis	5 (11%)	2 (40%)	2,0±0,0	2,0±1,4	1	1,7±0,3	1,3±0,0	0,125
Vasculitis	7 (15%)	2 (29%)	2,4±0,5	2,0±1,4	0,498	1,6±0,3	1,5±0,1	0,668

Table 1. Patients with persistence of HLs after subclinical AR treatment. Grading of histological lesions and renal function before and after therapy.

Histological lesions (HLs) considered in the study	Pts with HLs score ≥ 2 at biopsy	Pts with persistance of HLs at control biopsy	Pts with persistance of HLs at control biopsy					
			Score of HLs (m±sd)			Serum Creatinine (mg/dL; m±sd)		
			pre therapy	post therapy	p	pre therapy	post therapy	p
Interstitial inflammation	11 (23%)	5 (45%)	2,1±0,3	1,4±0,5	0,003	1,6 ± 0,6	1,7 ± 0,6	0,762
Tubulitis	14 (30%)	11 (79%)	2,1±0,3	1,7±0,4	0,009	1,8 ± 0,7	1,8 ± 0,6	1
Glomerulitis	16 (34%)	13 (81%)	2,4±0,5	2,4±0,8	1	1,5±0,4	1,4±0,4	0,509
Capillaritis	5 (11%)	2 (40%)	2,0±0,0	2,0±1,4	1	1,7±0,3	1,3±0,0	0,125
Vasculitis	7 (15%)	2 (29%)	2,4±0,5	2,0±1,4	0,498	1,6±0,3	1,5±0,1	0,668

Table 2. Patients with persistence of HLs after clinical AR treatment. Grading of histological lesions and renal function before and after therapy.

Figure:

P1774 **CONVERSION FROM TWICE-DAILY TACROLIMUS (TAC-IR) TO ONCE-DAILY EXTENDED RELEASE TACROLIMUS (LCPT) IN EVEROLIMUS TREATED STABLE KIDNEY TRANSPLANT RECIPIENTS**

Orsolya Cseprekal[1], Adrienn Marton[1], Szilárd Török[1], Attila Patonai[1], Katalin Földes[1], Laszlo Wagner[1], Miklos Zsolt Molnar[1,2,3], Zoltan Mathe[1], Laszlo Kobori[1], Adam Remport[1]

[1]Semmelweis University, Department of Transplantation and Surgery, Budapest, Hungary, [2]James D Eason Transplant Institute, Methodist University Hospital, Memphis, United States of America and [3]University of Tennessee Health Science Center, Department of Surgery, Memphis, United States of America

Background and Aims: Stable kidney transplant patients (KTX) treated according to TRANSFORM study protocol (TAC-IR + everolimus (EVR) + corticosteroid) were converted from twice daily TAC-IR to novel (MELT-dose) once-daily tacrolimus formulation (LCPT) on a 1:0.7 total daily dose (TDD) basis. Tolerability, safety, and trough level (Co) – TDD characteristics of the conversion (CV) was analyzed in a single center retrospective observational study.

Method: Between Sep. 2017 and Aug. 2018 38 KTX recipients were included. Pre- and post-CV TAC TDD, Co and TAC Co/D as well as EVR TDD and Co data were evaluated 4, 2 weeks before and 4 consecutive times after CV (94 (74-112 median IQR) post-transplant days). Pre- and post-CV eGFR, routine lab parameters and occurrence of adverse events were also investigated.

Results: In one patient 2 weeks after CV EVR was stopped due to infection, 37 KTX (males 22 (58%), age 54 (42-63) years) finished the entire observational period. According to CV protocol the median TDD of LCPT was lower than pre-CV TAC-IR at each visit: 4.5(3.5-7) mg/day pre-CV versus 3.5 (2.5-5), 3.6 (2.5-5), 3.5 (2.5-5) and 3.5 (2-5) ($p<0.001$) post-CV. Mean TAC Co decreased from pre-CV Co 7.8 (6.4-9.5) ng/ml to 6.7 (4.8, 8.6), 7.0 (5.2, 9.6), 6.5 (5.7, 8.4) and 7.2 (5.4, 8.7) ($p<0.001$). LCPT Co / TDD did not change: 1.6 (1.1-2.5) pre- and 2.1 (1.1- 2.9), 2.1 (1.1- 4.1), 1.6 (1.3- 3.5), 2.0 (1.4-4.1) ($p = 0.18$) post-CV. EVR Co /TDD (1.6 (1.3-2.1), 1.6 (1.3; 2.3), 1.6 (1.3-2.0), 1.6 (1.2-2.2)) remained similar to pre-CV: 1.6 (1.4- 2.4) ($p = 0.65$). There was no change in eGFR, hemoglobin levels and no drug related adverse event was observed during the study period.

Conclusion: Conversion from TAC-IR to LCPT in everolimus treated stable KTX recipients resulted in a significant post-CV decrease in TAC- Co, whilst Co/TDD remained unchanged. The conversion was safe and had no effect on EVR Co and TDD. Further investigations are needed to define optimal TAC-IR to LCPT conversion dose rate.

P1775

CMV VIREMIA IN KIDNEY TRANSPLANT RECIPIENTS RECEIVING BASILIXIMAB OR LOW DOSE ANTI THYMOCYTE GLOBULIN INDUCTION WITHOUT VALGANCICLOVIR PROPHYLAXIS- SINGLE CENTRE EXPERIENCE IN INDIA

Reetesh Sharma[1], Mayur Maksana[2], Naresh Trehan[2]

[1]Asian Institute of Medical Sciences, Nephrology and Kidney Transplant, Faridabad, India and [2]Medanta the Medicity, Cardiac surgery, Gurgaon, India

Background and Aims: CMV is a major cause of morbidity in transplant recipients and manifests as tissue invasive disease or CMV viral syndrome. Controversy exists regarding best method for CMV prevention. Therefore, we intended to evaluate incidence of CMV viremia and symptomatic CMV infection in adult KTR with basiliximab or antithymocyte globulin (ATG) induction without the use of valganciclovir prophylaxis. This study will help developing a protocol for management of CMV infection/disease in Indian patients since there is no such data amongst Indians.

Method: A prospective, open-label, single centre study. Patients were monitored for CMV DNA-PCR twice a week for month 1 post-transplant, once a week in month2, and then every 2 weeks in month 3, and then once a month from month 4 to 6.

Results: We included 17 patients with low-dose ATG induction (group1) and 20 patients with Basiliximab induction (group2). Mean recipient age was 42.9 and 45.9 yr in group 1 and 2 whereas mean donor age was 50.6 and 51.6 yr respectively. Male recipients were 76.4% (13/17) and 65% (13/20) in group 1 and 2 respectively; male donors were 11.7% (2/17) and 20% (4/20) respectively (not signficant). Average HLA mismatches were 3.4/6 and 3.7/6 (not significant). In group1 average transfusions per patient were 6units (vs 1.7units in group2) and 65% pts in group1 had >3 units transfusion ($p<0.05$). Mean follow-up was 12.7 and 20.7 months respectively.

Incidence of acute rejection was 5.8% (1/17) and 10% (2/20) in group 1 and 2 respectively. (not significant).

Incidence of CMV viremia requiring valganciclovir therapy was 11.6% (2/17) and 10% (2/20) in group 1 and 2 respectively. (not significant). No patient developed CMV disease.

Mean serum creatinine was 1.1 and 1.09 mg/dL at 1 month and 1.2 and 1.14 mg/dL at 3 months (not significant)

Conclusion: The incidence of CMV viremia is low and not significantly different in patients receiving basiliximab or low dose ATG induction in living donor kidney transplants on tacrolimus based immunosuppression. In our study patients in ATG group had significantly more transfusions vs basiliximab group and hence were more sensitised. Still the incidence of acute rejection remained low in both these groups (5.8% and 10%).

Hence universal prophylaxis with valganciclovir may not be required in all the patients with basiliximab and low dose ATG induction especially in developing countries where cost of therapy is borne by the patients.

P1776 HLA TYPING BY NGS ENHANCES MISMATCH DETECTION IN LIVING KIDNEY TRANSPLANTATION

Sarah Pehnke[1], Tom H. Lindner[1], Bernt Popp[2], Ilias Doxiadis[3], Ramona Landgraf[3], Claudia Lehmann[3], Jan Halbritter[1], Johannes Münch[1]

[1]University Hospital Leipzig, Division of Nephrology, Department of Internal Medicine, Leipzig, Germany, [2]University Hospital Leipzig, Institute of Human Genetics, Leipzig, Germany and [3]University Hospital Leipzig, Institute for Transfusion Medicine, Leipzig, Germany

Background and Aims: Antibody mediated rejection (ABMR) due to the development of donor specific HLA antibodies is the most common cause for graft loss in kidney transplant recipients. Therefore, a low count of HLA mismatches is favorable in the course of transplantation. Hitherto, several techniques for HLA typing have been adapted in parallel, e.g. serological or low-resolution PCR. In this single-center study, we aimed to perform "HLA re-typing" by next generation sequencing (NGS) in a living kidney transplant cohort (n=143), in order to identify HLA mismatches in donor/recipient pairs, that were missed by previous HLA typing methods.

Method: We isolated DNA of 102 donor/recipient pairs, that received a living kidney transplantation at the University Hospital Leipzig (Germany) between 1998 and 2018, and performed long range PCR of all known HLA loci. Using these NGS results, we compiled a genomic HLA mismatch formula. We evaluated, if genomic HLA typing identifies more HLA mismatches compared to the results of previous HLA typing methods, that were recorded in the *Eurotransplant* database for our donor/recipient pairs.

Results: By genomic HLA typing, we were able to identify HLA mismatches in 10.2 % of donor/recipient pairs, that have been missed by previous methods. In our cohort, we recognized most mismatches in the DRB1 locus, that were missed with other HLA typing techniques.

Conclusion: Our results suggest, that genomic HLA typing can be more precise in detecting HLA mismatches in donor recipient/pairs. Especially in the course of living kidney transplantation, a higher accuracy in HLA typing might enhance donor selection. Furthermore, accurate HLA typing can influence graft management in the course of ABMR, as it may improve the detection of donor specific HLA directed antibodies.

P1777

BIOMARKERS OF KIDNEY INJURY AS INDICATOR OF PRECLINICAL TRANSPLANT DYSFUNCTION IN PATIENTS WITH TYPE 1 DIABETES MELLITUS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION AND THEIR RELATIONSHIP WITH EARLY REPARATIVE PROCESSES OF NONMYELINATED FIBERS

Irina Larina[1], Anastasia Severina[1], Minara Shamhalova[1], Marina Shestakova[1], Larisa Nikankina[1], Ekaterina Artemova[1], Ilya Dmitriev[2], Aleksey Pinchuk[2], Michael Kaabak[3], Gulya Musaeva[4]

[1]Endocrinology Research Centre, Institute of diabetes, Moscow, Russia, [2]Scientific and Research Institute for Emergency Care named.after N.V. Sklifosovsky, Clinical Department of Kidney and Pancreas Transplantation, Moscow, Russia, [3]B.V. Petrovsky Russian Research Center of Surgery, Clinical Department of Kidney Transplantation, Moscow, Russia and [4]I.M. Sechenov First Moscow State Medical University, Moscow, Russia

Background and Aims: To evaluate the relationship of early kidney transplant dysfunction markers with complications of end-stage renal disease (ESRD) and corneal nerve structures in patients with type 1 diabetes mellitus (T1DM) and long-term history of diabetes, who reached stable euglycemia after simultaneous pancreas-kidney transplantation (SPKT).

Method: The study included 27 patients with T1DM duration for 21 [19; 28] years, diabetic nephropathy (DN) duration 7,0 [5,5; 13,5] years and duration of renal replacement therapy (dialysis) for 2 [1; 4] years after successful SPKT. The posttransplantation period at the time of inclusion was 61 [20; 90] months. Assessment included examination of level of the main kidney transplant dysfunction markers (KIM-1, NGAL, podocin), examination of state of corneal nerve structures according to corneal confocal microscopy (CCM) as indicator of early reparation processes, diabetes complications/ complications of ESRD with dynamic observation for 1 year. All patients received three-component immunosuppressive therapy.

Results: Despite of *reached stable euglycemia (HbA1c* 5.5 [5.1; 5.9] %, 5.5 [5.3; 5.7] % after 1 year of follow – up), the restoration of graft function to the rate of estimated glomerular filtration rate (eGFR) CKD-EPI stage C2, albuminuria stage A1, 41% of patients still needed antihypertensive therapy, 37% needed treatment with recombinant human erythropoietin and 30% - antiosteoporotic therapy. There were no statistically significant changes in NGAL, KIM-1, and podocin at baseline and after 1 year in assessment of early kidney transplant dysfunction markers. The results of the correlation analysis revealed associations of NGAL and indicators of CCM (CNFD & NGAL (R=0.61, p = 0.01), CNBD & NGAL (R=0.56, p=0.02), CNFL & NGAL (R=0.65, p=0.009) and vitamin D (R=-0.67, p = 0.008), correlation of KIM-1 with albumin-to-creatinine ratio (ACR) (R=0.43, p= 0.04), correlation of podocin with HbA1c (R=-0.46, p=0.03).

Conclusion: SPKT as the way to achieve euglycemia and compensation of uremia does not provide complete regress of DN and complications of ESRD. The revealed correlations of early, most sensitive kidney transplant dysfunction markers with degree of carbohydrate metabolism compensation, ACR and vitamin D level may reflect the persistence of microstructures damage with stable graft function and demonstrate need of multifactorial management in renal function preservation. At the same time, the statistically significant correlations of early kidney transplant dysfunction markers with the state of corneal nerve structures need more detailed investigation.

P1778 **PROFILE OF NON-BACTERIAL INFECTIONS SPECIFIC TO RENAL TRANSPLANT RECIPIENTS.**

Anurag Gupta[1], Rahul Kanjilal[1], Devinder Singh Rana[1], A K Bhalla[1], Ashwani Gupta[1], Manish Malik[1], Vinant Bhargava[1], Vaibhav Tiwari[1]

[1]*Sir Ganga Ram Hospital, New Delhi, India*

Background and Aims: Infections in renal transplant recipients are a major cause of morbidity and mortality. It is the one of the major cause of patient death with functioning graft. Hence this project was done to study the profile of non-bacterial infections specific to renal transplant recipients and to determine the risk factors associated with such infections.

Method: Renal-transplant recipients admitted to the department of nephrology with suspected infection were included in the study.

Results: : A total of 342 patients were included in the study. The mean age of the patients was 45.2 ± 13.3 years. 17.5% had ABO incompatible renal transplant. 91% (87% received leukocyte depleting and 4% received non-leukocyte depleting agents) had received induction as majority had three or more HLA mismatch (70%) and the most common donor was wife. 12.8% had history of graft rejection. A total of 147 infectious episodes were encountered in 121 patients. The incidence of non-bacterial infections was 35% (121/342). Viral infections (68/147 = 46%) and invasive fungal infections (44/147 = 30%) were the most common. Cytomegalovirus infection was the most common 35%. Other viral infections encountered were BK virus associated nephropathy (2.3%) and reactivation of Hepatitis B or C virus (2.6%). The most common site of invasive fungal infection were lower respiratory tract, urinary tract, CNS cryptococcosis, soft tissue infection or cellulitis and oesophageal candidiasis in 41%, 32%, 9%, 9% and 9% respectively. Aspergillus (61%) and Rhizopus (33%) was the most common organism causing fungal pneumonia. Four patients were diagnosed with Pneumocystis jirovecii pneumonia. Majority (60%) of the infections were detected after one year post-transplant. Risk factors found to have statistically significance were ABO incompatibility, diabetes mellitus (pre or post-transplant) and history of graft rejection. Nine patients (7%) died of non-bacterial infections specific to renal transplant recipients.

Conclusion: Non-bacterial infections are not uncommon in Indian scenario and the timeline of such infections has changed.

P1779

NOVEL ONCE-DAILY EXTENDED-RELEASE TACROLIMUS VERSUS TWICE -DAILY TACROLIMUS IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS DURING THE EARLY POSTTRANSPLANT PERIOD

Volkan Polatkan[1], Ebru Ozdemir[1], Turker Erturk[2], Emel Tatli[3], Ibrahim Berber[2], Ulkem Cakir[4], Gulay Yilmaz[3]

[1]Acıbadem International Hospital, Organ transplantation, İstanbul, Turkey, [2]Acibadem University, Acibadem İnternational Hospital, Organ transplantation, İstanbul, Turkey, [3]Acıbadem International Hospital, Nephrology, İstanbul, Turkey and [4]Acibadem University, Acibadem İnternational Hospital, Nephrology, İstanbul, Turkey

Background and Aims: Both under and over-dosing of tacrolimus may compromise clinical outcomes by exposing patients to either the risks of graft rejection or adverse events (AEs) associated with immunosuppressive therapy. This study is designed to compare the clinical follow-up of our kidney transplant recipients receiving once-daily, prolonged-release (PR-T; Advagraf) and twice-daily, immediate-release (IR-T; Prograf) tacrolimus in the early posttransplant period.

Method: This randomized study included 78 de novo, adult kidney transplant recipients to PR-T 0.15 mg/kg/day (Group I=39) and IR-T 0.15 mg/kg/day (Group II=39) for seven days in the posttransplant period. Demographic features and clinical parameters regarding levels of whole blood tacrolimus and serum creatinine were compared between the two groups. Presence of acute rejection and AEs were investigated. Dose adjustments were permitted to target a pre-defined therapeutic range based on measured trough blood concentrations in all patients. SPSS 15 for Windows was used for statistical analysis.

Results: None of the patients suffered from acute rejection and there were no AEs in the early posttransplant period. However, Group II patients were found to have higher whole blood tacrolimus levels on the posttransplant 1st, 4th and 7th days (*p=0.02*, *p=0.009* and *p=0.013* respectively). Also serum creatinine levels were significantly increased in Group II patients on the posttransplant 7th day (*p=0.02)*.

Conclusion: Prolonged release tacrolimus seems promising in preventing acute transplant rejection with adequate blood levels, as well as making it possible to avoid the interindividual variation in absorption and early calcineurin inhibitor toxicity.

P1780 RENAL ALLOGRAFT TUBERCULOSIS - A CASE SERIES

SREEJESH BALAKRISHNAN[1], ANJANEY YADUR[1], SAJITH NARAYANAN[1], FEROZ AZIZ[1], ISMAIL N.A.[1], BENIL HAFEEQ[2], RAGHURAMCHANDRA BHAT[1], SOORAJ SASIDHARAN[1], ABDUL GAFOOR[1], SHYSIL SHAFEEQ[1]

[1]ASTER MIMS, NEPHROLOGY, Kozhikode, India and [2]IQRAA INTERNATIONAL HOSPITAL, NEPHROLOGY, KOZHIKODE, India

Background and Aims: Renal transplant recipients are at increased risk of tuberculosis (TB) than the general population especially in endemic areas. Post-transplant tuberculosis poses challenges to the physician both for diagnosis and treatment. There are no solid data regarding occurrence of renal allograft tuberculosis in this population. Here we report a case series of renal allograft recipients with occurrence of renal allograft tuberculosis.

Method: We analyzed data of 610 patients who underwent renal transplantation in our center between 2006 to 2019. Clinical details were retrospectively analyzed from Hospital Information System (HIS).

Results: Out of 610 transplant recipients, four (0.65%) were found to have renal allograft TB. One of the donors had a history of pulmonary tuberculosis which was treated. Among the recipients, one had history of disseminated TB 2 years prior to transplantation. Only one patient received induction immunosuppression with lymphocyte depleting agent. All of them received triple immunosuppression with tacrolimus, mycophenolate and prednisolone. None of them received isoniazid/rifampicin prophylaxis. The shortest time interval to the occurrence of allograft tuberculosis was 2 months (donor had history of tuberculosis). The longest was 78 months. All patients presented with fever and allograft dysfunction. Three out of 4 patients had biopsy showing granulomatous interstitial nephritis with urine culture for Mycobacterium tuberculosis positive. One of them had PUJ obstruction due to tuberculosis for which Boari flap vesicocalicostomy was done. One patient had perigraft collection, drainage of which showed Acid Fast Bacilli (AFB) and culture positivity for mycobacterium tuberculosis. The immunosuppression was not reduced for any of them and all were treated with non Rifampicin containing anti-tuberculosis treatment (ATT) regime for 9 months to 1 year. All patients had good response and complete remission. There was no mortality related to allograft tuberculosis. All the patients had their renal function back to baseline at the end of treatment.

Conclusion: Graft tuberculosis may present as fever as allograft dysfunction. The treatment with Anti tuberculosis drugs is effective in achieving complete cure and restoring the graft function.

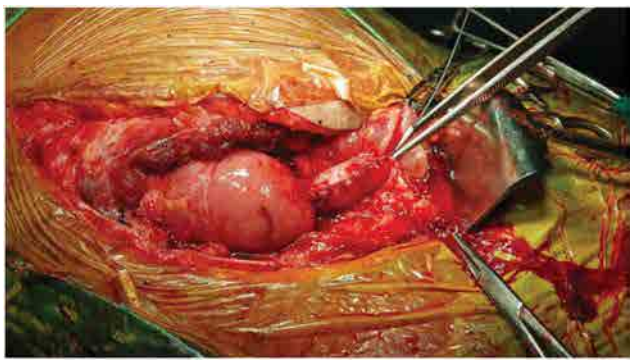


Figure:

Boari flap vesicocalicostomy.

P1781 CONVERSION TO SIROLIMUS IN ADVANCED STAGES OF CHRONIC ALLOGRAFT NEPHROPATHY. A RANDOMIZED CLINICAL TRIAL.

Ali Ghafari[1], Negar Ghafari[2]

[1]Tehran University of medical sciences, Internal medicine, Tehran, Iran and
[2]Semmelweis University, Pharmacy, Budapest, Hungary

Background and Aims:

Some studies have shown that proteinuria more than 800 mg per day and glomerular filtration rate (GFR) less than 40 ml/min are the most important relative contraindications for mTOR inhibitors prescription. There is no pathophysiologic reason to put aside mTOR inhibitors in more advanced stages of chronic allograft nephropathy(CAN). To clarify the safety of conversion to mTOR inhibitors in more advanced stages of CAN we conduct a randomized clinical trial

Method:

Among 1911 renal transplant recipients which was performed from May 1989 to May 2016, patients (pts) with CAN included to the study. CAN was defined by pathology results and rule out of other causes of renal dysfunction and GFR less than 60 ml/min. pts with recent acute rejection, chronic Ab mediated rejection, active viral infection, malignancy, advanced cardiac, liver and respiratory diseases, obstructive uropathy and non-adherence were excluded from the study. After exclusion there were 211 pts with CAN. Among CAN pts 112 pts have GFR less than 40 ml/min. These patients were assigned in two group randomly. Group 1 continued their immunosuppression which consists of mycophenolate mofetil/myfortic, Cyclosporin A /Tacrolimus and prednisolone. Group B which received Sirolimus 2 mg daily instead of CyclosporinA / tacrolimus. All pts followed for 18 months. allograft function and pts morbidity and mortality were monitored every two months. results were recorded in clinic sheets and were analyzed using SPss version 22

Results:

G1 consist of 53 and G2 59 pts. There were no differences in two group in respect to sex (M/F was 0.89 and 0.84 in G1 and G2 respectively), and age (mean age was 41 6 9.5 and 43 6 8.23 in G1 and G2 respectively). there were no differences in admission rate for medical reasons (0.43 and 0.39 admission per pts per year in G1 and G2 respectively p=0.23). There was no difference between two group in respect to cardiovascular events (0.23 and 0.27 events per pts per year in G1 and G2 respectively p=0.31). The average trough level of SRL was 8.38± 3.12 ng/mL at 18 months. At 18 months, the incidence of acute rejection was not higher in G2 (21% vs. 18.8 %, p = 0.21) and renal function was superior in patients converted to SRL (eGFR 32.3 vs. 23.4 mL/min/ 1.73 m2, p = 0.019) compared to those maintained on CsA/TAC. There were no significant differences in pts survival (one death in each group) Graft loss was higher in G1(5 versus 2 at 18 months p= 0.014). there were no significant differences in respect to liver, respiratory, GI, hematologic and infectious complications. pts in G2 group had lower BP and uric acid levels.

Conclusion:

Conversion to mTOR inhibitors in more advanced stages of CAN is safe and has beneficial effect on renal allograft function with no more side effect.

P1782

INFLUENCE OF IMMUNOSUPPRESSIVE REGIMEN ON OXYGENATION AND DIFFUSIVITY OF KIDNEY TRANSPLANTS - ANALYSIS OF FUNCTIONAL MRI DATA FROM THE RANDOMIZED ZEUS STUDY

Jasna Cotting[1], Ute Eisenberger[2,3], Peter Vermathen[1], Bruno Vogt[4,5], Laila-Yasmin Mani[4,5]

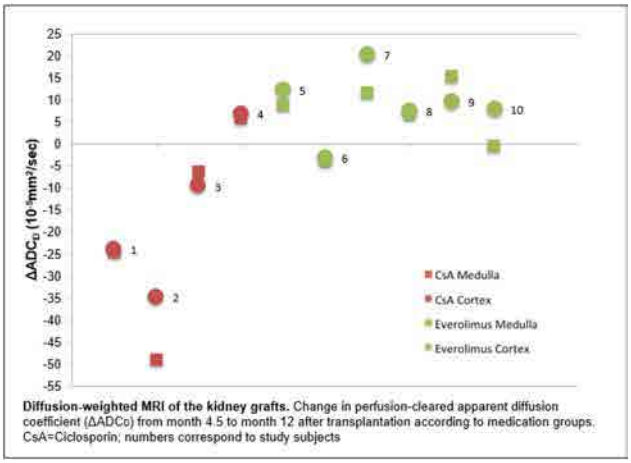
[1]University of Bern, Biomedical Research and Radiology, Switzerland, [2]University Hospital Essen, Department of Nephrology, Essen, Germany, [3]University of Duisburg-Essen, Germany, [4]University Hospital Bern, University Clinic for Nephrology and Hypertension, Bern, Switzerland and [5]University of Bern, Switzerland

Background and Aims: The ZEUS study was a multi-center open-label randomized controlled trial designed to investigate the effect of an early conversion from a calcineurin-inhibitor-based immunosuppression to a mammalian-target-of-rapamycin inhibitor-based regimen on graft function twelve months post-transplantation. Persistent improvement of renal function up to five years together with albeit higher rejection rates were found in the intervention group. In the context of an investigator-initiated local sub-study, functional magnetic resonance imaging (fMRI) was prospectively performed in a subset of the study population in order to non-invasively assess differences in renal graft oxygenation, diffusion and perfusion between groups and time-points using blood-oxygen level-dependent (BOLD)- and diffusion-weighted (DWI) MRI respectively.

Method: In the ZEUS trial, 300 de novo kidney graft recipients were randomized to continue ciclosporin (CsA) or be converted to everolimus (EVE) at 4.5 months post-transplant. Concomitant immunosuppression contained enteric-coated mycophenolic acid, steroids and basiliximab. From the 36 subjects included in the ZEUS study at our study center, sixteen were enrolled in the MRI sub-study. FMRI including BOLD-MRI and DWI was prospectively performed at month 4.5 and 12 post-transplantation on a 3 Tesla and 1.5 Tesla (n=3) MR scanner. Blinded image analysis was done by placing up to 24 regions of interest in cortex and medulla. BOLD-MRI yielded the relaxation rate R2*, a parameter indirectly proportional to tissue oxygen content, DWI yielded the perfusion-cleared apparent diffusion coefficient ADC_D, a marker of tissue diffusivity, and the perfusion fraction F_P, a marker of microperfusion. All data were analyzed using in-house custom-scripts written in IDL® and MATLAB®.

Results: After exclusion of subjects due to image quality, outlier values or missing data, BOLD data was analyzed in eight, DWI in ten subjects. Mean absolute values and standard deviations corresponded to published values. A clear cortico-medullary gradient was shown for R2* and F_P values, but not for ADC_D, corresponding to previous results. For all fMRI parameters, there was no change for the whole population from 4.5 to 12 months post-transplantation in cortex and medulla. FMRI parameters did not differ significantly between both medication groups at month 4.5. In BOLD, R2* values increased (decreased tissue oxygen) over time in the CsA-treated and decreased in the EVE-treated group in cortex and medulla. Similarly, R2* values at month 12 were higher in the CsA- vs. EVE-treated group; the low number of subjects having completed BOLD-MRI at month 12 precluded formal statistical testing. In DWI, ADC_D decreased in the CsA-group over time, whereas it increased in the EVE-group in cortex and medulla (p=0.046). Likewise, ADC_D at month 12 was lower by trend in the CsA- vs. EVE-treated group in both medulla and cortex. The change in ADC_D from month 4.5 to month 12 significantly differed in cortex (p=0.033) and medulla (p=0.019) between treatment groups. There was no significant difference for F_P between medication groups nor over time. Baseline renal function and blood pressure were comparable in both groups.

Conclusion: The R2* values obtained by BOLD point to reduced graft oxygenation on CsA and ameliorated graft oxygenation on EVE, possibly due to the known vasoconstrictor effect of calcineurin inhibitors. The observed decreased diffusivity by DWI on CsA might be due to increased tissue density in the context of beginning calcineurin inhibitor-induced interstitial fibrosis. There was no clear trend for microperfusion as assessed by F_P. Limitations of this study are the low number of subjects available for analysis. In conclusion, this prospective sub-study of the ZEUS trial suggests an impact of immunosuppressive regimen on fMRI parameters of the renal graft.



Diffusion-weighted MRI of the kidney grafts. Change in perfusion-cleared apparent diffusion coefficient (ΔADC$_D$) from month 4.5 to month 12 after transplantation according to medication groups. CsA=Ciclosporin; numbers correspond to study subjects

Figure:

P1783

ATG-F(GRAFALON) VS THYMOGLOBULIN(R ATG) AS AN INDUCTION AGENT IN LIVING DONOR RENAL TRANSPLANT - A RETROSPECTIVE SINGLE CENTER EXPERIENCE

Abhyudaysingh Rana[1], Pranaw Jha[1], Shyam Bansal[1], Amit Mahapatra[1], Ashish Nandwani[1], Manish Jain[1], Dinesh Kumar[1], Dinesh Bansal[1], Sidharth Sethi[1], Ashwini Gadde[1], Vijay Kher[1]

[1]Medanta-The Medicity, Department of Nephrology & Renal transplant, Gurugram, India

Background and Aims: The best modality of renal replacement therapy for patients with end stage renal disease is kidney transplantation. Induction agents play a crucial role in preventing acute rejection which also has bearing on long term graft outcomes. Lymphocyte depleting induction agents commonly used include r ATG (Thymoglobulin), ATG-F (Grafalon) & Alemtuzumab. In this study we compare Grafalon (ATG-F) with r ATG(Thymoglobulin) as induction agent for living donor renal transplant.

To study efficacy and safety of ATG-F (Grafalon) as induction agent in comparison to r ATG (Thymoglobulin) in living donor renal transplantation

Method: This was a single center retrospective study. All the patients who underwent living donor renal transplant at our centre since January 2017 with minimal follow up of 3 months were included. Retransplants & deceased donor transplants were excluded. ATG-F (Grafalon) was given at 6 mg /kg (2 divided doses) & r ATG (Thymoglobulin) at 3 mg/kg (2 divided doses) doses followed by triple immunosupression (Tacrolimus +MMF +Steroids) . Acute graft dysfunction was defined as a 25% increase in serum creatinine level from baseline. All acute rejection episodes were biopsy proven.

Results: During the study period 570 living donor renal transplants were done. Patients were followed up for median duration of 22 months (3-35 months). r ATG(Thymoglobulin) was given to 242 (42.4%) patients whereas 78 (13.6%) patients received ATG-F(Grafalon) as induction agent.

Mean recipient age was 43±12 years in ATG-F group vs 41±13 yrs in r ATG group (p=0.22) & mean donor age was 48±10 years(ATG-F) vs 47±11 yrs(r ATG) (p=0.48) . Recipients were predominantly male (92 % ,83% p =0.08) while donors were predominantly female (79% ,75% p=0.25) in both the groups.

Mean HLA mismatch was 4.1±1.2(ATG-F) vs 4.09±1.3(r ATG) p=0.95. The proportion of ABO and HLA incompatible transplants were comparable in both the groups. Incidence of BPAR was 11.5% vs 4.5 % in ATG-F vs Thymoglobulin group(p = 0.03)

Incidence of infection was comparable in both the groups (12.8% vs 14.46%, p=0.86). Two patients in Graflon group had BKV nephropathy while 2 patients in rATG had CMV infection. Mean serum creatinine level at follow up of 22 months (Median) was 1.26±0.35 mg/dl (ATG F) & 1.18±0.34 mg/dl (r ATG) (p =0.07) .Patient survival(p =1) & graft survival (p=0.24) were comparable in both the groups. One patient lost graft due to drug non compliance in grafalon group while there was no death censored graft loss in thymoglobulin group. There was no incidence of PTLD in either group and the incidence of NODAT was similar in both groups (5.1% vs 5.7% ,p =1)

Conclusion: -ATG-F (Grafalon- 6mg/kg dose) use as an induction agent was associated with significantly higher rate of biopsy proven acute rejection as compared to r ATG (Thymoglobulin-3mg/kg dose) with comparable short term graft survival, patient survival and infection rate.

P1784 **CARDIOVASCULAR RISK ASSESSMENT PRIOR TO KIDNEY TRANSPLANTATION**

Vnuää¡k Matej[1], Karol Graňák[1], Petra Skálová[1], Ivana Dedinska[1]
[1]University Hospital Martin, Surgery and Transplantation Centre, Martin, Slovakia

Background and Aims: Cardiovascular diseases (CVD) are the most frequent cause of death in dialysed patients. Patients in the risk group of CVD examined prior to kidney transplantation (KTx) are indicated for coronarography (SCG). The aim of our analysis was to identify risk factors (RF) for positive finding of patients undergoing SCG before KTx.

Method: Our analysis consisted of 55 dialysed patients (46 males, 9 females, P<0.0001), undergoing SCG before inclusion on waiting list (WL). We identified patient's information (age in the time of SCG, gender, ethiology of kidney failure, comorbidities - arterial hypertension, ischemic heart disease /IHD/, diabetes mellitus / DM/), biochemical parameters in the time of SCG (serum level of lipids, haemoglobin, calcium-phosphate metabolism). We divided patients, according to SCG results (negative finding; n=40 v.s positive finding; n=15).

Results: Patients without percutaneous coronary intervention (PCI) (negative finding) we confirmed significantly lower incidence of diabetic nephropathy (P=0.0484) IHD (P=0.0174) and coronary artery disease (P=0.0001). We confirmed, haemodynamically significant coronary stenosis correlate with the occurrence of stroke or transient ischemic attack in patient's history (P=0.0104). Consequently, we identified predictors for realization PCI (positive result): type 2 DM [OR 2,3492 (P=0.0472)], HDL ≤ 1,03 mmol/l [OR 4.3276 (P=0.0359)], total calcium level ≤ 2mmol/l [OR 2.4935 (P=0.0309)], phosphate level ≥ 1.45 mmol/l [OR 0.2034 (P=0.0351)]. In our analysis, patients non-listed on WL had significantly higher incidence of type 2 DM (P=0.0087), smoking (P=0.0079) and were treated more often with statins (P=0.0025).

Conclusion: In our analysis, patients with DM and poorly managed chronic kidney disease - mineral bone disease are the most at risk group in the group of patients with CVD with positive SCG finding. Patients with high cardiovascular risk, without DM or other RF can profit from non-invasive imaging methods following faster listing on WL.

PCI	Odds ratio	95 % CI	P value
Age in time of SCG ≥ 60 years	1,1244	0,3337 - 3,7879	0,8500
Gender (males)	2,0264	0,3056 - 13,4391	0,4644
BMI in time of SCG ≥ 30 kg/m^2	1,4966	0,3692 - 6,0661	0,5723
Smoking	2,5048	0,5049 - 12,4267	0,2612
Duration of haemodialysis ≥ 60 months	0,5870	0,1202 - 2,8675	0,5104
Diabetic nephropathy	5,2276	0,4684 - 58,3489	0,1790
Arterial hypertension in anamnesis	0,1277	0,0093 - 1,7490	0,1232
Diabetes mellitus in anamnesis	2,3492	1,0105 - 5,4615	**0,0472**
Stroke in anamnesis	0,3456	0,01684 - 7,0948	0,4908
Ischemic heart disease in anamnesis	13,5965	0,7529 - 24,5386	0,0771
Chronic heart failure in anamnesis	0,4968	0,02253 - 10,9519	0,6575
Peripheral artery disease in anamnesis	1,1234	0,1349 - 9,3582	0,9143
Cholesterol in time of SCG ≥ 5,17 mmol/l	2,6385	0,6589 - 10,5666	0,1705
HDL in time of SCG ≤ 1,03 mmol/l	4,3276	1,1009 - 17,0123	**0,0359**
LDL in time of SCG ≥ 3,3 mmol/l	2,2197	0,4771 - 10,3270	0,3094
TAG in time of SCG ≥ 1,7 mmol/l	1,1556	0,3499 - 3,8163	0,8125
Haemoglobin in time of SCG < 110 g/l	2,1725	0,5679 - 8,3114	0,2571
PTH in time of SCG > 300 ng/l	0,4130	0,1016 - 1,6785	0,2164
Ca in time of SCG ≤ 2 mmol/l	2,4935	1,0926 - 5,6905	**0,0309**
P in time of SCG ≥ 1,45 mmol/l	0,2034	0,0462 - 0,8946	**0,0351**
Ejection fraction of left ventricle < 50 %	0,8630	0,1645 - 4,5281	0,8617
IVS > 12 mm	1,4562	0,3653 - 5,8041	0,5942

PCI - percutaneous coronary intervention; SCG – selective coronarography; BMI – body mass index; HDL – high density lipoprotein; LDL - low density lipoprotein; TAG - triacylglycerides; PTH - parathormone; Ca - calcium; P - phosphate; IVS – intraventricular septum;

Tab 1 Logistic regression

Figure:

P1785

KIDNEY TRANSPLANTATION ACROSS VERY HIGH DONOR SPECIFIC ANTIBODIES(DSA) - A SINGLE CENTER EXPERIENCE OF A TERTIARY LEVEL HOSPITAL FROM INDIA

Jayanta Kumar Hota[1]

[1]*INDRAPRASTHA APOLLO HOSPITAL, NEPHROLOGY, NEW DELHI, India*

Background and Aims: Kidney Transplantation across very high donor specific antibodies (DSA) poses a significant challenge even today . With our current understanding and precise desensitization techniques, we are now able to do kidney transplantation across such high DSA . Here we are reporting ten such cases where baseline DSA were more than 10,000 mean fluroscent intensity (MFI) on Single Antigen Bead (SBA) Luminex.

Method: : It is a retrospective analiysis of ten kidney transplant patients from January 2017 to March 2019 . Patients with MFI more than 10,000 to class II HLA antigens at baseline with negative CDC and flow cytometry cross match were included in this study. All patients were treated with 1 dose of Rituximab (375mg/M? before plasma exchanges (PLEX) were started . Each session of PLEX was followed by 10 grams of intravenous human immunoglobulin (IVIg). Solid based SBA Luminex for both class I and II antigens was repeated after the third exchange and fifth exchange and seventh exchange depending on the level of MFI .

Results: Ten patients (seven males three females) of age 37± 7 years were included in this study . History of blood transfusion with 5±2 units was present in 7 patients . All females were multiparous (3±1children). Mean solid based SBA Luminex for class I HLA antigens was 12000 ± 1500 and for II HLA antigens with MFI 16500 ± 3500 (Chart 1). Mean number of PLEX needed was 5 ± 2 . All patients had solid based SBA MFI was 1500±300 and for class II antigens 2500 ± 1500 before transplantation(Chart 2).There was no incidence of acute antibody mediated rejection . Baseline serum creatinine at discharge was1.35±0.35mg%. There were 3 (30%) biopsy proven cases of acute cellular rejection . There was evidence of BK viremia in 3(30%) patients, CMV infection in 1 (10%) patient, Klebsiella pneumonia in 1(10%) patient and cryptosporium infection in 1 (10%) patient each . There was no mortality and mean serum creatinine at 6 months follow-up was 1.55±1.05mg%. All 3 patients of BK Viremia were treated with modification of immunosupression with substitution of leflunamide for mycophenolate and all are doing well with good graft function with a mean serum creatinine of 1.75±0.55mg% . Other infections were treated accordingly.

Conclusion: : Transplantation across very high donor specific antibodies is possible with excellent immediate and short term graft function with judicious de-sensitization techniques . There was increase in infection rate but none was life threatening and can be managed with proper care.

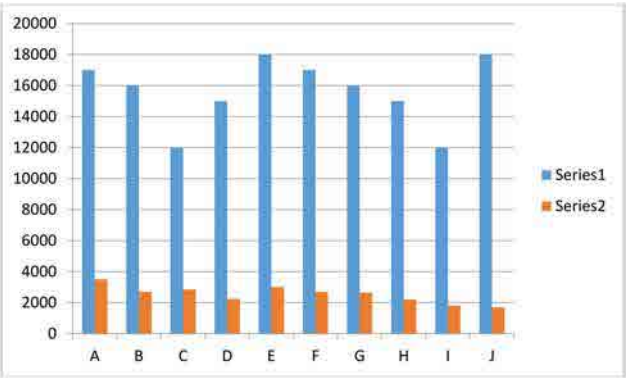


Chart 1 – MFI BEFORE AND AFTER DE-SENSITIZATION

P1786 THE HIGHWAY TO KIDNEY TRANSPLANTATION

Daènne Scheuter-van Oers[1], Ton Kooij van[2], Renske Schelfhout[3], René Dorpel van den[4]

[1]Maasstad Hospital, nephrology / dialysis, Rotterdam, Netherlands, [2]Maasstad Hospital, nephrology /dialysis, Rotterdam, Netherlands, [3]Maasstad Hospital, nephrology, Rotterdam, Netherlands and [4]Maasstad Hospital, dialysis / nephrology, Rotterdam, Netherlands

Background and Aims: Close cooperation between nephrologist, nurse coördinator and social workers in a large non academic hospital.

By timely starting the process of education and examinations we have increased the possibilities of pre-emptive transplantation

Method: When a patiënt needs to be informed about renal replacement therapy, the digital program is used by the nephrologist to inform all necessary disciplines involved. They each will make an appointment within the given time slot with te patient. **At first** the social worker start the education process, preferably, in the home situation. General information about the procedures and actions to be taken in the coming period, is given to the patient and his family/friends. They support patients in making difficult dicisions. **Secondly**, the nurse coordinator in the process, gives information about all options in renal transplantation and gives an explanation about the test procedures which are necessary to decide if patients are able te receive a kidney and donors are appropriate candidates. In case of availability of a potential donor, information is directly given about living donation and the procedure can directly be started. The nurse coordinator ensures that the patient and potential donor complete all required tests in the shortest time possible in their own hospital.

The close cooperation consists of daily deliberation between all disciplines and quickly changing the process of a patient or donor when needed. The progress is reported in the digital file and everyone involved will be informed.

Results: From 2013 until 2020

516 patients entered the program. 575 donors (for 348 recipients) entered the program. 191 couples have been approved ans presented for transplantation of which 87 couples have been transplanted, 61 couples have been put on hold because of a stabilised kidney function. 40 couples are still in the work up program.

44 recipients were not transplantable due to medical/psychological reasons.

The median work up time of the procedure of the recipients was 260 days from start of the process to transfer tot he transplant centre. (2017) Various patient/medical retarding factors are discribed.

The median work up time fort he donors was 191 days (2017) days from start of the process to transfer tot the transplant centre. Various donor/medical retarding factors are discribed.

Conclusion: Patients and family are well informed about the treatment options, with a special attention for kidney transplantation. The efficient work up program in the patients treating hospital, results in a significant improvement of the possibility of pre-emptive renal transplantation, or otherwise, patients are earlier registered on the waiting list.

P1787 DESENSITIZATION IN LIVE KIDNEY DONOR RECIPIENTS PROVIDES GOOD OUTCOME AT MID-TERM FOLLOW-UP

SUHEYLA APAYDIN[1], UMUT KASAPOGLU[1], FATIH GOKHAN AKBAY[2], Arzu Ozdemir Kayalar[1], AYSEGUL KUDU[3], Mehmet Dikec[1], GUNDEN DEGER[1], ZEKI TOPRAK[1], MAHMUT CARIN[4]

[1]University of Health Science, Bakirkoy Dr. Sadi Konuk SUAM, Nephrology, Istanbul, Turkey, [2]University of Health Science, Meslek Yuksek Okulu, Istanbul, Turkey, [3]Bingol Devlet Hastanesi, Nefroloji, Bingol, Turkey and [4]Istinye University, Doku Laboratuarı, Istanbul, Turkey

Background and Aims: The recipients who have antibodies againts to donors' HLA (Anti HLA- DSA) carrie a huge risk for allograf (AG) losing. In current study, it was retrospectively evaluated whether the live donor kidney recipients (LDKRs) under desensitization (DS) were exposed to more AG loss, lower AG survival and more complications.

Method: In 17 of 269 LDKRs had high anti-HLA DSA were found prior to kidney transplantation (KTX). DS was performed with plasmapheresis (PF) and rituximab (RTX) before KTX. In order to determine the risks of DS, LDKRs who had not PF for any reason, were admitted immediately before and after those with LDKRs under DS were used as controls (n: 31). Immucor™ luminex method was used for detecting the anti HLA DSA. DS was performed to the Rs who had more than 5000 MFI DSA against to at least one donor HLA locus with double check. Non-parametric Fisher's exact test was used for statistical analysis because of distribution of our patients was heterogeneous.

Results: In 15 Rs had DSA more than 2 HLA loci (MFI range: 5880-21712), remaining 2 Rs had one HLA locus DSA (9959-7762). Mean PF number was of 7 before TX, while 3 after TX. RTX was used in 9 Rs (53%) before TX. KTX performed when anti DSA MFI below 2000 under triple immunosuppression plus anti-thymocitic globulin (ATG) induction therapy. In 4 Rs (13%) had DSA below 5000 MFI among controls (Cs). More female Rs (88% vs. 19%, $p<001$) were in Rs under DS. ATG was used in 65 % of Cs. Comparison of the complications between Rs under DS and Cs, rate of rejection (35% vs. 19%, respectively, $p>0.05$), rate of indication biopsy (24 % vs 16 %, $p>0.05$), rate of CNI toxicity (5.5% vs. 6.5%, $p>0.05$) were indifferent. During whole follow-up period, creatinine levels and eGFR were compatible at both groups. Urinary infections were more frequent in Rs under DS (53% vs 6.5%, $p<0.001$) while the rate of viral infections were same. Also, late AG rejection were found in only 2 Rs under DS. Loss of AG and mortality were not seen in Rs under DS. Allograft survival for 3 years were found same (100% vs 91.2%, respectively) in groups.

Conclusion: Although our results belong to a single center and also a small group, desensitization before kidney transplantation for high risk kidney recipients are seem to be useful, effective and successful procedure.

P1788

FACTORS AFFECTING EGFR SLOPE IN KIDNEY TRANSPLANT RECIPIENTS DURING 48 MONTHS AFTER TRANSPLANTATION

Irena Rambabova Bushljetikj[1,1], Saso Dohcev[2], Maja Mojsova Mijovska[3], Sotir Stavridis[2], Oliver Stankov[2], Goce Spasovski[1]

[1]University Clinic of Nephrology, Skopje, Republic Of North Macedonia, [2]University Clinic of Urology, Skopje, Republic Of North Macedonia and [3]University Clinic of Anesthesiology and Reanimation, Skopje, Republic Of North Macedonia

Background and Aims: After the first year following kidney transplantation approximately 3-5% of grafts fail each consecutive year. Many factors have impact on the graft function and only a few may be modifiable. Monitoring of the graft function by serum creatinine concentrations and estimated glomerular filtration rate (eGFR) are recommended methods for evaluation. The aim of the study was to assess the decline of graft function defined by change in the annual eGFR slope and factors that might affect it.

Method: A total number of 55 adult patients with living donor kidney transplant (LDKT) were included in the study. The inclusion criteria were: first transplantation of one organ - kidney, use of living donor related or unrelated (emotionally related - spouses) donor. Clinical and biochemical variables, serum creatinine, BUN, protein status, 24 hours proteinuria and body weight were analyzed at 12, 24, 36 and 48 months after transplantation. The Nankivell equation for estimating glomerular filtration rate was used to calculate the slope of renal function over time (1 to 4 years post-transplantayion) by linear regression analysis.

Results: Out of 55 kidney transplant recipients 18 (33.3%) were female. The majority of transplants had good function ($eGFR_{Nankivell} \geq 60$ ml/min) at 1 year.

The average GFR at 12 months was 67.81±16.7 mL/min/1.73 m^2 with majority of patients at stage 2 of chronic kidney disease classification. Thirty eight patients had eGFR slope <5ml/min/year and 12 patients had a higher slope (>5ml/min/year).

Only 5 patients (∼ 9%) have graft failure during the period of follow up of 48 months. The average slope decline calculated with linear regression analysis was -3.42 ± 3.2 mL/min/year (range -12.38 – 3.29) (slope ± standard error). Proteinuria was predictive for worsening of the graft function. Rapid progressors have been associated with a higher proteinuria at 24 and 48 months: 0.35 ± 0.39 g/24h, median 0.24 (range 0.11 – 0.43 g/24h) and 0.49 ± 0.59 g/24h, median 0.31 (range 0.14 – 0.48 g/24h), (p=0.044 and p=0.021, respectively).

Younger patients have more rapid eGFR slope decline (slope (-7.81 ± 2.12 vs. -2.40 ± 1.3, mL/min/year, p=0,0001). The mean recipient age in the group with stabile eGFR slope was 37.59± 8.7, and in the group with rapid progression was 29.1 ± 8.6 years (p=0.0046).

Conclusion: Proteinuria after kidney transplantation has been identified as a risk factor associated with poor graft survival. Younger renal transplant recipients are associated with more rapid decline of the graft function that could be partially explained with their more potent immune response

P1789 DE NOVO INFLAMMATORY BOWEL DISEASE AFTER KIDNEY TRANSPLANTATION - REPORT OF THREE CASES

Katarina Obrencevic[1], Marijana Petroviä‡[1], Neven Vavic[1], Stanko Petrovic[2], Ivana Tufegdzic[3], Violeta Rabrenovic[1], Jelena Tadiä‡[1], Mirjana Mijuskovic[1]

[1]Military Medical Academy, Clinic of nephrology, Belgrade, Serbia, [2]Military Medical Academy, Clinic of gastroenterology, Belgrade, Serbia and [3]Military Medical Academy, Pathology and Forensic Medicine Institute, Belgrade, Serbia

Background and Aims: Inflammatory bowel disease (IBD) are not common after kidney transplantation. Development of IBD in the patient on immunosuppression is unexpected, because IBD is believed to be the result of inappropriate and ongoing activation of the mucosal immune system and immunosuppressive drugs are used in the treatment of IBD. The aim of our study was to evaluate the occurrence of de novo IBD, ulcerative colitis and Crohn's disease, in the patients who received kidney transplant in our hospital, the time after transplantation and the immunosuppression therapy when diagnosis was made.

Method: We used an electronic medical archival system to identify the patients with IBD. Between 1996 and 2018 a total of 462 kidney transplantations were done in Military Medical Academy. Analysis in this study included 400 patients who were regulary controlled in our hospital. Demographic data and clinical findings including age, sex, primary renal disease, type of kidney donor, and immunosuppressive therapy were evaluated. The time of the occurrance of the IBD after transplantation, the colonoscopy and pathologic findings were also noted.

Results: de novo IBD was observed in three patients 19, 11 and 7 years after kidney transplantation respectively. In all patients end-stage renal disease was due to chronic glomerulonephritis without histology verification. Family history was negative in all. They were male, age 40, 42 i 47 years respectively when diagnosis was made. Their immunosuppressive regimen included prednisone, mycophenolate mofetil (MMF) and tacrolimus with a trough level between 5 and 7 ng/ml. They all developed constitutional symptoms with significant weight loss and fever, abdominal pain and cramps, diarrhoea which was in one case bloody. Infectious and other etiology was excluded. Colonoscopy showed ulcerative colitis in two patients and Crohn's disease in one. The patients with ulcerative colitis responded on maintenance therapy combined with 5-aminosalicylic acid, but one of them had common flare-ups with mild clinical picture. The patient with Crohn's disease was successfully treated with azathioprine instead of MMF with high-dose steroids.

Conclusion: We concluded that new onset of IBD can develop after kidney transplantation despite use of immunosuppressive therapy. It should be considered in all transplanted patients who develop gastrointestinal complaints. The future studies could answer why the immunosuppressive therapy is not effective for IBD in these group of patients.

P1790

A TWO-CASE COMPARISON: PREEMPTIVE AND PROPHYLACTIC USE OF DIRECT ANTIVIRAL DRUGS IN TRANSPLANTATION OF HCV-INFECTETD KIDNEYS TO UNINFECTED PATIENTS

Florian Westphal[1], Stefan Reuter[1], Christian Wilms[2], Alexandros Rovas[1], Brockmann Jens[3], Morgül Haluk[3], Hermann Josef Pavenstädt[1], Vogel Thomas[3], Barbara Suwelack[1]

[1]Münster University Hospital, Department of Medicine D, Division of General Internal Medicine, Nephrology and Rheumatology, Münster, Germany, [2]Münster University Hospital, Department of Internal Medicine B, Gastroenterology and Hepatology, Münster, and [3]Münster University Hospital, Department of General, Visceral and Transplant Surgery, Münster,

Background and Aims:

The organ shortage especially in blood group 0 forces transplant professionals to discuss new approaches to expand the donor pool. Recently, the successful therapy of HCV with direct antiviral agents in kidney transplanted patients has made the transplantation of HCV-infected kidneys to uninfected patients possible. Furthermore, these organs promise an above-average organ function as HCV-infected donors are usually young and have fewer comorbidities. Since there is no standard procedure for the treatment of kidney recipients with HCV grafts, we compared a preemptive and a prophylactic approach using direct antiviral drugs after kidney transplantation of two patients.

Method:

We report the transplantation of two HCV-positive kidneys. One recipient was a 49-year-old female patient, who suffered from ESRD caused by an atypical hemolytic uremic syndrome. The other recipient had autosomal dominant polycystic kidney disease. Since the genotype of the HCV donor was unknown at the time of transplantation, we decided to use the pangenotypic, fixed-dose combinations Glecaprevir/Pibrentasvir and Sofosbuvir/Velpatasvir.

Results:

Both patients had blood group 0 and received an AB0-compatible kidney transplant. The initial immunosuppressive therapy consisted of prednisolone, mycophenolate sodium, and tacrolimus. Furthermore, an induction therapy with Basiliximab was given. The first patient received Glecaprevir/Pibrentasvir immediately post-surgery. Treatment was carried on for eight weeks as a prophylactic approach. Frequent HCV-PCRs showed negative results over six months. However, the patient developed anti-HCV antibodies within six days after transplantation. The graft started working on postoperative day four, and the serum creatinine decreased to 1.33 mg/dl on the discharge day and stabilized on this level during further follow-up. Following a preemptive approach, our second patient was treated with Sofosbuvir/Velpatasvir after detection of HCV RNA and rising levels of transaminases on post-transplant day 7. This patient also received Entecavir because of a previous HBV-infection of the donor (non-viremic on the day of transplantation). The graft started working on day two, and the serum creatinine decreased to 1.28 mg/dl on the discharge day and stabilized on this level. Further HCV-PCRs also showed negative results.

Conclusion:

We conclude that kidneys from HCV-viremic donors can be transplanted with precaution. Both therapeutic strategies showed equally good results and can easily be implemented into kidney transplantation. Especially, the combination of Glecaprevir/Pibrentasvir offers a safe HCV prophylaxis without the need of adaptions to the renal function or HCV genotype. In case of a permanent absence of a HCV infection, the preemptive approach offers a chance to avoid the HCV-therapy. On the other hand, causing an iatrogenic infection of HCV in a patient with immunosuppression brings up ethical issues due to the risk of HCV-related liver diseases. Therefore, we favor the prophylactic approach. Further studies are needed to identify the optimal time frame for direct antiviral agents in HCV (D+/R-) transplantations.

P1791 HLA DESENSITIZATION- INDIAN EXPERIENCE

Shyam Bansal[1], Ashwini Gade[2]

[1]Medanta -The Medicity, Gurugram, India and [2]Medanta -The Medicity, nephrology and kidney transplantation, Gurugram, India

Background and Aims:

There are many barriers to kidney transplant and one of them is presence of donor specific antibodies (DSAs) in the recipients. Presence of strong DSA is considered a relative contraindication for kidney transplantation, however, if DSAs are of weak to moderate then desensitization is attempted in many centres with good success rate. Desensitizing such patients can be an acceptable approach to increase the donor pool and facilitating transplants. This is a retrospective analysis of patients who underwent desensitization at our centre after availability of luminex single antigen (LSA) assay

Method:

Between April 2014 and December 2018, 825 patients underwent kidney transplantation at our centre. Patients who were CDC negative but positive FCXM were further analysed with LSA to know the presence and strength of DSAs. Our protocol for desensitization consisted of plasmapheresis (PP) 1.5 volume by double filtration on alternate day and low dose IV IG 100 mg/kg after each PP. Whenever MFI was $<$1000 and/or FCXM was negative, patient was taken for transplant with thymoglobulin induction of 1.5 mg/kg for 2-3 doses. All patients were maintained on triple immunosuppression consisting of tacrolimus, mycophenolate mofetil and corticosteroids. We did not routinely followed DSAs in these patients post-transplant if there was no clinical indication. All adverse events during follow up including new onset diabetes after transplant (NODAT), infections, acute rejections (AR), graft loss and death

Results:

Out of 825 patients, 15 underwent HLA incompatible transplants, of which, 8 were males. All patients were first transplant and 11/13 had history of some sensitizing events in the form of blood transfusion and/or pregnancy. The mean dialysis duration was 8.6 $\pm$14.6 months. FCXM was positive in all the patients with 5 patients had T cell flow positive, 8 had B cell flow positive and 2 had both T & B cell FCXM positivity. Most patients had weak to moderate positive flow cross match. On further evaluation by LSA, all these patients had DSAs, with 3/15 had MFI $<$1000, 6 had MFI between1000-2000, and remaining 6 had MFI $>$2000, out of which one patient had MFI of 7195 and six patients had multiple DSAs. These patients underwent desensitization with PP and IVIG and the end point of treatment was either MFI $<$ 1000 or FCXM negative. Post-transplant DSAs were done in patients with high MFI or clinically indicated. Two patients had increase in post-transplant DSA titres requiring post-transplant plasmapheresis. The mean follow up was 29$\pm$6 months.

On follow up, only 1 patient developed borderline cellular rejection one year after transplant, which responded with pulse steroids. Three patients had biopsy for asymptomatic rise in creatinine but it showed patchy ATN with no evidence of rejection.. One patient developed transient CMV viremia, one patient developed lymph node tuberculosis (TB) and two patients had UTI, all of them responded to treatment. There was no graft or patient loss till last follow up.

Conclusion:

This study shows that HLA desensitisation is feasible and successful in if patients are selected carefully and evaluate thoroughly. HLA incompatible transplant can provide a new lease of life to those patients who would otherwise not get a kidney due to lack of paired exchange and deceased donor program

P1792 **SUCCESSFUL TRANSPLANTATION OF STEM CELLS AND KIDNEY IN REFRACTORY LUPUS NEPHRITIS: REMOTE OUTCOMES**

Aleksandr Demin[1], Larisa Demina[2]

[1]Novosibirsk State Medical University, Internal Medicine and Nephrology, Novosibirsk, Russia and [2]Novosibirsk State Medical University, Nephrology and Hemodialysis, Novosibirsk, Russia

Background and Aims: Lupus nephritis is a common part of systemic lupus erythematosus (SLE), severe autoimmune disease that affects multiple organ systems and associated with pure prognosis. Patients with lupus nephritis who experience persisted disease activity despite conventional immunosuppression are at high risk of early death. Re-setting of the immune system and self-tolerance by high-dose immunosuppressive therapy with autologous stem cell transplantation (ASCT) is a new approach in the treatment of refractory SLE. Remote outcomes of this method and effectiveness relapse treatment are still unclear and were the aims of this study.

Method: We report a sick woman 39 years old, with refractory severe lupus nephritis. Standard therapy was ineffective, SLEDAI score remains 22 so patient was underwent high dose immunosuppressive therapy with ASCT and included in European Group for Blood and Marrow Transplantation European League against Rheumatism (EBMT/EULAR) registry on 53 pts who received ASCT for SLE between 1996 and 2005. Ethical approval was obtained for this study from Cambridge University Hospital Ethics Committee.

Results: The ASCT induced complete clinical and serological remission (SLEDAI score was 0) for 3 years. Than relapse with nephritic syndrome and anti-dsDNA positivity occurred and caused renal failure, creatinine clearance decreased to 21. Despite therapy including prednisolone, 45 mg daily, and mycophenolate mofetil, 2000 mg daily, disease activity persisted, creatinine clearance remained decreasing and 3 years later became 15 ml/min. During 1 year patient was on regular hemodialysis, then renal transplantation performed. Now, follow up is 15 years after ASCT and 8 years after kidney transplantation. Patient received a standard post-transplant immunosuppression with prednisolone, 5 mg daily, tacrolimus, 2.5 mg daily, and azathioprine, 100 mg daily, and her conditions remains stable, she has functioning renal allograft, SLEDAI score is 2 (anti-dsDNA positivity in low titer).

Conclusion: We present the successful remote outcomes of first case of immunoablation and double transplantation of autologous stem cells and allogeneic kidney in severe refractory to conventional immunosuppression SLE with lupus nephritis.

P1793 **MICROBIAL URETERAL STENT COLONIZATION IN KIDNEY TRANSPLANTATION: INCIDENCE AND IMPACT IN URINARY TRACT INFECTION AND RENAL FUNCTION**

Melissa Rau[1], Anna Carrera Salinas[2], Sara Marti[2], Maria Fiol[3], Begoña Etcheverry[3], Luis Riera[1], Carmen Ardanuy Tisaire[2], Edoardo Melilli[1]

[1]*Bellvitge University Hospital, Renal Transplant Unit, L'Hospitalet de Llobregat, Spain,* [2]*Bellvitge University Hospital, Microbiology Unit, L'Hospitalet de Llobregat, Spain and* [3]*Bellvitge University Hospital, Urology, L'Hospitalet de Llobregat, Spain*

Background and Aims:

Ureteral stent insertion is nowadays a common practice in kidney transplantation, leading to a dramatic reduction of surgical issues. On the other hands, urinary tract infections are the most common complication in the first months after transplant.

Main scope of our study was to analyze the incidence of stent colonization and its impact on the development of urinary tract infection (UTI) in the first six months after transplantation

Method:

Prospective observational study including 23 consecutively recruited patients at one single center. Patients with a previous history of surgical intervention on urinary tract before transplant were excluded. Pigtail stents were removed as for local protocol between 3 and 4 weeks after transplantation in aseptic condition and were cut in a half (proximal and distal) and analyzed separately. Stent colonization were detected by sonication method. Urine culture timing are depicted in Figure 1. In case of clinical symptoms, extra urine cultive were performed as for clinical practice. Patient were followed for 6 months, and results of stent colonization were blinded to clinicians.

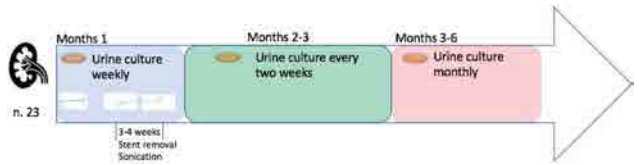


Figure 1. Study Design

Results:

Table 1 shows main characteristic of our cohort.

Table 1.

	n. 23
Age at transplant (mean±SD)	57 ± 10
Gender (Female/Male)	12/11
Delay in Stent Removal from Transplantation (Days Mean±SD)	24 ± 3
eGFR at 6 months (ml/min mean±SD)	54 ± 25
DGF (n/%)	7 (30)
Acute rejection (%)	2 (9)
UTI in the first six months (episodes)	
Asymptomatic Bacteriuria (n. episodes)	13
Cystitis (n. episodes)	3
Acute Pyelonephritis (n. episodes)	2

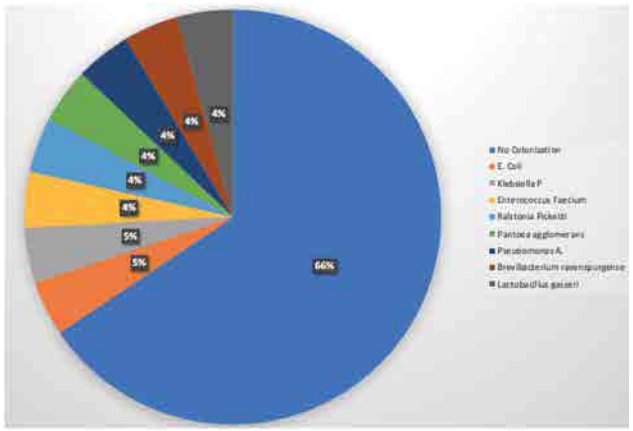


Figure 2. Type of Pathogens' colonization and distribution in the cohort of the study

Table 2.

	Stent sterile n. 15 (%)	Stent Colonization n. 8 (%)	p.
Time of stent removal from TR (Days Mean±SD)	24.5±3.7	23.8±3.6	0.4
eGFR at six months (ml/min mean±SD)	56±27	53±22	0.6
Acute Rejection n. (%)	3 (25)	0 (0)	0.26
DGF n. (%)	5 (33)	1 (14.3)	0.61
UTI	12 (80)	6 (75)	0.78
Asymptomatic Bacteriuria	8 (53)	5 (62)	
Cystitis	3 (20)	0 (0)	
Pyelonephritis	1 (6.7)	1 (12.5)	

Conclusion:

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CHANGES IN PHARMACOKINETIC PROFILE OF MYCOPHENOLATE MOFETIL AND TACROLIMUS IN THE TRANSPLANTED PATIENT AFTER BOWEL SURGERY: A PROSPECTIVE COHORT STUDY

Nuria Montero[1], Alexandre Favà[1], Anna Manonelles[1], José González Costello[3], Edoardo Melilli[1], Ana Coloma Lopez[1], Gil-Vernet Cebrian Salvador[1], Raul Rigo[4], Pere Fontova[1], Joan Torras[1], Josep Cruzado[1], Oriol Bestard[1], Núria Lloberas[1]

[1]Hospital Universitari de Bellvitge, Nephrology, L' Hospitalet de Llobregat, Spain, [3]Hospital Universitari de Bellvitge, Cardiology, L' Hospitalet de Llobregat, Spain and [4]Hospital Universitari de Bellvitge, Biochemistry, L' Hospitalet de Llobregat, Spain

Background and Aims:

Considering the particular pharmacokinetic (PK) profile of mycophenolate (MMF/MPS) with the important contribution of enterohepatic recirculation (EHC) and the potential alteration in tacrolimus (TAC) exposure, a PK study in solid-organ transplant patients who had undergone intestinal resection was carried out.

Method:

This is a prospective single-center study of MMF/MPS and TAC exposure changes after bowel resection and after reconstruction. Whole blood samples were collected at the following time points: 0, 0.5, 1, 1.5, 2, 4, 6, 8 and 12 hours post-dose. Areas under the curves (AUCs) were determined in both conditions: with ileostomy and after bowel reconstruction.

Results:

Six renal and two cardiac transplant recipients were included. Four subjects completed both pre- and post-reconstruction surgery procedures. Different intestinal anatomic resections were performed (Table 1). Patients with terminal ileostomy showed an under exposure to MMF/MPS. In three patients, initial MPA levels were on target, but they decreased >80% after 4 hours post-drug administration. After bowel reconstruction, the AUC increased maintaining MMF/MPA levels during 12h (Table 2). Before bowel reconstruction, TAC trough levels were within therapeutic target but, after reconstruction, AUCs normalized by dose were much higher than the expected.

Conclusion:

Transplant recipients with ileostomy showed infra-exposure to mycophenolate. After 4 hours post-dose, MMF/MPA was undetectable because of the absence of EHC, which was recovered after anatomical correction. TAC exposure was higher after bowel reconstruction suggesting changes in the absorption. The use of mTORi in such clinical situations would be an alternative.

Table 1. Characteristics of included patients and surgeries.

ID patient	Sex, age (years)	Diabetes mellitus /Hypertension (Y/N)	Type and date of transplant	Cause for surgery	Date of surgery and operative procedure
#1	Male, 41	N/N	Heart, 2016	Ischemic colitis and perforation	12/06/2016 Right hemicolectomy + terminal ileostomy
#2	Male, 72	Y/N	Renal, 1988	Sigmoid colon adenocarcinoma	04/08/2016 High (upper) anterior resection of rectum + terminal ileostomy
#3	Male, 45	N/Y	Renal, 2010	Ischemic colitis	16/12/2016 Small bowel resection + terminal ileostomy
#4	Male, 76	N/Y	Renal, 2017	Ulcerative colitis	24/06/2002 Total colectomy + terminal ileostomy
#5	Female, 73	N/Y	Renal, 2015	Ischemic colitis	25/01/2018 Right hemicolectomy + terminal ileostomy
#6	Male, 71	N/N	Renal, 2018	Colonic diverticulitis	07/06/2019 Sigmoidectomy + appendicectomy + terminal ileostomy
#7	Female, 61	N/N	Renal, 2019	Sigmoid colon adenocarcinoma	22/11/2006 Left hemicolectomy + terminal ileostomy
#8	Male, 53	N/Y	Renal, 2009	Crohn Disease	15/06/1997 Right hemicolectomy + terminal ileostomy

Table 2: Results of pharmacokinetic of tacrolimus and mycophenolate before and after

ID	After bowel resection				After intestinal reconstruction			
	MMF/MPS	AUC	TAC	AUC	MMF/MPS	AUC	TAC	AUC
	TDD	C0/Cmax	TDD	C0/Cmax	TDD	C0/Cmax	TDD	C0/Cmax
#1	MMF 2g	25.76 0.001/28.6	TAC-IR 6mg	ND	MMF 2g	39.01 1.32/24.7	TAC-IR 6mg	181.12 9.5/27.5
#2	MMF 2g	17.99 0.01/10.7	TAC-ER 5mg	88.63 3.5/15.5	MMF 1g	16.82 0.9/3.57	TAC-ER 4mg	131.49 7.2/15.3
#3	MPA 0.54g	0.59 0.01/0.01	TAC-IR 4mg	70.73 4.4/8	MPA 0.36g	3.32 0.4/0.6	TAC-ER 3mg	263.56 24.2/51
#4	MPA 2.16g	24.01 0.1/11.16	TAC-IR 3mg	66.35 7.9/16.1	ND	ND	ND	ND
#5	MMF 2g	32.77 2.4/11.6	TAC-IR 6mg	239.1 2.4/11.6	MMF 2g	32.77 2/12.4	TAC-IR 5mg	239.05 13/29.6
#6	MMF 2g	68.02 4.1/10.5	TAC-IR 3mg	7.99 0.11/3.28	ND	ND	ND	ND
#7	ND	ND	ND	ND	MPA 0.54	102.15 5.97/36.2	TAC-IR 5mg	107.2 7/20.2
#8	ND	ND	ND	ND	MPA 0.36	2.71 0.01/1	TAC-IR 2mg	170.43 11.6/17.2

*ER: extended release (advagraf®), IR: immediate release (prograf® or adoport®), ND: No data, MMF: Mycophenolate mofetil, MPS: Mycophenolate sodium, TAC: Tacrolimus, TDD: Total daily dose,
* UNITS: TAC AUC: ng.h/mL, MMF/MPA AUC: ug.h/mL, TAC Cmin: ng/mL, MMF/MPA Cmin: ug/mL

Figure:

P1795

ASSOCIATION BETWEEN T CELL INFILTRATION IN BIOPSY PROVEN ACUTE T CELL MEDIATED REJECTION AND RESPONSE TO THERAPY

Nooshin Dalili[1], Pedram Ahmadpoor[2], Behzad Einollahi[3], Hamed Azhdari Tehrani[2]

[1]Chronic Kidney Disease Research Center (CKDRC), Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran, Tehran, Iran, [2]Chronic Kidney Disease Research Center (CKDRC), Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran and [3]Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

Background and Aims: Renal transplantation is considered as the best replacement therapy for advanced ESRD patients. An allograft rejection happens as a result of post transplant immune reactions, which change the outcome of the organ transplantation. Today a major challenge in the field of transplantation is the identification of easy, reliable and non-invasive markers or methods that being able to predict the probability of organ rejection. One of the possible methods is looking for type of infiltrated cells in tissue obtaining by biopsy stained with specific cellular markers and assesses the infiltration of these cells in different types of rejection. Here the severity of CD3, CD20, Th17 and FOXP3 infiltration in patients with biopsy proven acute cellular rejection was evaluated based on IHC staining, whether these specific infiltrations can show an association with graft outcome or not.

Method: 50 patients with biopsy proven Acute T Cell Mediated Rejection (ATCMR) recruited. Previous clinical data and 1 year clinical follow up collected. The entire specimen assessed for infiltration of CD3, CD20, FOXP3 Tregs and Th17 with IHC. Patients divided into subgroups: stable graft function versus impaired graft function based on serum creatinine course in one year follow up after rejection therapy and appropriate response to treatment versus failure to response, based on allograft function throughout the course of admission.

Results: In impaired graft function arm, FOXP3 (7.88 vs. 8.02 with P-value 0.96) and Th17 cells were higher (5.01 vs. 10.2 with P-value 0.24) but with non-significant values. FOXP3/Th17 ratio was higher in stable group (1.4 vs. 1.12 with P-value 0.22). In failure to response to therapy group both FOXP3 (9.95 vs. 6.63 with P-value 0.1) and Th17 (11.3 vs. 8.3 with P-value 0.15) cells were higher. FOXP3/Th17 ratio was higher in proper response group (1.19 vs. 1.15 with P-value 0.8). No significant difference was obtained between CD3 and CD20 infiltration in these two groups.

Conclusion: Final results showed that Th17 has more important role in predicting the graft outcome and response to treatment and FOXP3 infiltration had a minor part. This may be in controversial with previous facts about the role of FOXP3 cells, which drive the allograft into stable condition.

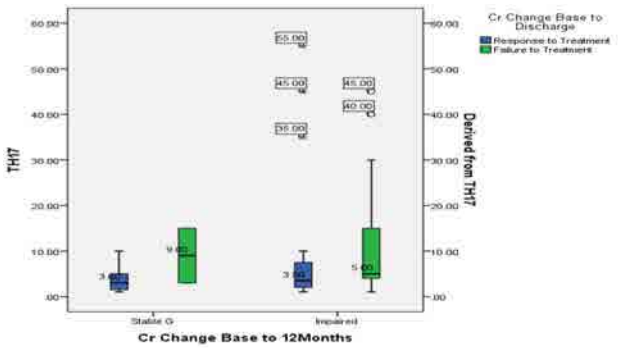


Figure 2. Th17 comparison in all groups. Mean value is higher in failure response to treatment in stable and impaired functions. Patients with stable and appropriate response had lowest values.

Figure:

P1796 FACTORS PREDICTING SUBCUTANEOUS INSULIN REQUIREMENT AFTER KIDNEY TRANSPLANT

Beena Bansal[1], Shyam Bansal[2]

[1]Door To Care, Endocrinology, GURGAON, India and [2]Medanta, the Medicity, Nephrology and kidney transplantation, Gurgaon, India

Background and Aims: Diabetes is the most common cause for end stage renal disease leading to kidney transplant. Post transplant glycemic management has significant impact on long term outcomes, but is challenging, especially while transitioning patients from intravenous to subcutaneous insulin dose. This study was therefore planned to assess factors which influence subcutaneous insulin dose after kidney transplant.

Method: Data was prospectively collected from 98 consecutive kidney transplant patients with type 2 diabetes at a tertiary care hospital in India, with regards to age, gender, height, weight, duration of diabetes, pre transplant insulin dose, pre transplant use of oral antidiabetics. First two days after transplant patients are nil by mouth and are on insulin infusion (column based method). On third day, patients are transitioned to multiple subcutaneous insulin. We assessed and recorded the subcutaneous insulin dose requirement by 4th and 5th day.

Results: Mean (SD) for patients' age was 52.28 (6.32) years, height 167.83 (5.64) cm, weight 70.55 (14.32) kg, body mass index 25.39 (4.72) kg/m2 and duration of diabetes 13.3 (7.02) years. All 98 transplant recipients were male. Mean insulin requirement before transplant was 15.37 (20.24) units/day. Mean post transplant intravenous insulin infusion rate for 4 hours before transitioning to subcutaneous insulin was 2.07 (0.987) units/hour. Mean subcutaneous insulin requirement after transplant was 73.18 (25.45) units/day or 1.12 (0.61) units/kgbw. Mean basal insulin dose was 25.32 (10.91) units. Mean bolus dose before breakfast was 10.75 (4.37) units, before lunch was 20.12 (7.4)) units, before evening snack was 6.65 (3.43) units and before dinner was 10.75 (4.11) units. In terms of proportion of total daily dose (TDD), mean basal insulin was 0.34 (0.08) of TDD, bolus dose before breakfast was 0.15 (0.03) of TDD, before lunch was 0.28 (0.05) of TDD, before evening snack was 0.09 (0.04) of TDD and before dinner was 0.15 (0.04) of TDD.

Subcutaneous insulin dose after transplant correlated with insulin dose of the recipient before transplant (Pearson's coefficient 0.43; p value 0.003) and weight of the patient (Pearson's coefficient 0.32; p value 0.001). It did not correlate with age of the recipient, duration of diabetes, intravenous insulin infusion rate or tac level.

On multivariate linear regression analysis to assess the factors predicting subcutaneous insulin dose after transplant, only pre-transplant insulin dose was significant (p value 0.046). Age of the recipient, duration of diabetes, weight of the patient, intravenous insulin infusion rate or preoperative use of oral anti diabetic were not significant

Conclusion: In kidney transplant patients with type 2 diabetes, only pre transplant insulin dose predicted the subcutaneous insulin dose post transplant.

P1797 ACUTE RENAL GRAFT FAILURE ASSOCIATED WITH AT1 RECEPTOR ANTIBODIES : 2 CASES IN SKMC

Nihal Bashir[1], Mohamed AlSeiari[1,1]

[1]*Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates*

Background and Aims: Some kidney transplantation recipients with negative donor specific antibodies can develop acute rejection episodes which are difficult to treat, associated with non-HLA antibodies like angiotensin 2 type 1 receptor antibodies (AT1R Ab). The mechanism of rejection by AT1R ab involves vascular injury. Our cases are unique as the first patient got mineralocorticoid deficiency like picture unexpectedly. For the second case, hyperacute rejection cause in the first allograft was not identified and but hyperacute rejection episodes involving antibodies against endothelial cells are reported in literature.

Method: 2 patients received renal transplantation from life related donors in out institute developed acute rejection episodes. As part of investigations, we did non -HLA antibodies testing which came positive .

Results: Case 1 30 years old male, with end stage renal disease on hemodialysis . The patient had a live related renal transplant with Mismatch 1-1-1 and negative DSA. Induction with Basiliximab was initiated but changed to ATG due to delayed graft function.

Kidney biopsy on day 6 post operatively showed diffuse moderate to severe acute tubular injury (up to necrosis) with glomerular intracapillary fibrin microthrombi, focal minimal peritubular capillaritis and mild glomerulitis and focal weak C4d positivity, highly suspicious for active antibody mediated rejection.

The patient was treated with pulse steroids, ATG total of 7.5mg/kg, 3 sessions of Plasma exchange and IVIG 2 g/kg and 2 doses of Rituximab for his hyperacute rejection. AT1R antibodies titer was 11U/ml. MICA was negative. Losartan was initiated as a maintenance therapy.

P1798

MYCOPHENOLIC ACID TROUGH CONCENTRATION AND DOSE ARE ASSOCIATED WITH HEMATOLOGIC ABNORMALITIES BUT NOT REJECTION IN KIDNEY TRANSPLANT RECIPIENTS

Hee-Yeon Jung[1], Sukyung Lee[2], Yena Jeon[3], Jeong-Hoon Lim[1], Ji-Young Choi[1], Jang-Hee Cho[1], Sun-Hee Park[1], Yong-Lim Kim[1], Chan Duck Kim[1]

[1]Kyungpook National University Hospital, Internal Medicine, Korea, Rep. of South, [2]Pohang St. Mary's Hospital, Internal Medicine, Korea, Rep. of South and [3]Kyungpook National University, Statistics, Korea, Rep. of South

Background and Aims: Little is known regarding the safe fixed dose of mycophenolic acid (MPA) for preventing biopsy-proven acute rejection (BPAR) in kidney transplant recipients (KTRs). We investigated the correlation of MPA trough concentration (MPA C_0) and dose with renal transplant outcomes and adverse events.

Method: This study included 79 consecutive KTRs who received MPA with tacrolimus (TAC) and corticosteroids. The MPA C_0 of all the enrolled KTRs was measured, which was determined monthly by using particle-enhanced turbidimetric inhibition immunoassay for 12 months, and clinical data were collected at each time point. The clinical endpoints included BPAR, any cytopenia, and BK or cytomegalovirus infections.

Results: No differences in MPA C_0 and dose were observed between KTRs with or without BPAR or viral infections under statistically comparable TAC concentrations. MPA C_0 was significantly higher in patients with leukopenia ($P = 0.021$) and anemia ($P = 0.002$) compared with those without cytopenia. The MPA dose was significantly higher in patients with thrombocytopenia ($P = 0.002$) compared with those without thrombocytopenia. MPA $C_0 \geq 3.5$ μg/mL was an independent risk factor for leukopenia (adjusted odds ratio [AOR] 3.80, 95% confidence interval [CI] 1.24–11.64, $P = 0.019$) and anemia (AOR 5.90, 95% CI 1.27–27.51, $P = 0.024$). An MPA dose greater than the mean value of 1188.8 mg/day was an independent risk factor for thrombocytopenia (AOR 3.83, 95% CI 1.15–12.78, $P = 0.029$). However, an MPA dose less than the mean value of 1137.3 mg/day did not increase the risk of BPAR.

Conclusion: Either a higher MPA C_0 or dose was associated with an increased risk of cytopenia, but neither a lower MPA C_0 nor dose was associated with BPAR within the first year of transplantation. Hence, a reduced MPA dose with TAC and corticosteroids might be safe in terms of reducing hematologic abnormalities without causing rejection.

PAEDIATRIC NEPHROLOGY

P1801 RISK FACTORS FOR URINARY TRACT INFECTION CAUSED BY EXTENDED-SPECTRUM BETA-LACTAMASE GRAM NEGATIVE BACTERIA IN INFANT

Juyoung Lee[1], Dong Hyun Kim[1], Ji Young Park[2], Hyunju Lee[2], Yo Han Ahn[3]

[1]Inha University Hospital, Department of Pediatrics, Incheon, Korea, Rep. of South, [2]Seoul National University Bundang Hospital, Department of Pediatrics, Seongnam, Korea, Rep. of South and [3]Seoul National University Children's Hospital, Department of Pediatrics, Seoul, Korea, Rep. of South

Background and Aims: Community-acquired extended-spectrum beta-lactamase (ESBL) producing bacterial infections are an evolving public health problem. Urinary tract infections (UTIs) due to ESBL-producing bacteria are increasing even in infants rarely exposed to antibiotic. We aimed to identify risk factors for UTI caused by ESBL-positive bacteria in infants.

Method: We retrospectively analyzed the medical records of hospitalized infants with first episode of UTI from March 2018 to August 2019. Data includes demographic characteristics, birth history, previous use of antibiotic, febrile event, urinalysis results, and urine isolated organisms and their ESBL status. Multivariate regression analysis was used to quantify independent risks associated with ESBL-positive UTI.

Results: UTIs were diagnosed in 266 patients at median age of 3.6 (interquartile range (IQR) 2.3-5.4) months. Sixty-two (30.4%) patients were diagnosed with UTI caused by ESBL-producing bacteria. When we divided patients according to ESBL status, there was no difference in gender, age, birth history, milk type, and use of postpartum care center. Maternal use of antibiotic during pregnancy and previous antibiotic exposure to patients were higher in ESBL-positive group than in ESBL-negative group (32.3% vs. 10.3%, $P<0.001$ and 22.6% vs. 12.3%, $P=0.044$, respectively). *Klebsiella* species was more frequently identified in ESBL-positive group than in ESBL-negative group (19.4% vs. 4.9%, $P=0.002$). In multivariate analysis, maternal use of antibiotic during pregnancy (odds ratio (OR), 3.817; 95% confidence interval (CI) 1.812-8.040, $P<0.001$), previous antibiotic exposure to patients (OR 2.418; 95% CI 1.071-5.461, $P=0.034$), and *Klebsiella* species as a causative organism (OR 6.222; 95% CI 2.396-16.158, $P<0.001$) were associated with ESBL positivity. In comparison of clinical courses of patients, ESBL-positive group showed severe leukocytosis (WBC 16,795 (IQR 12,210-20,270)/μL vs. WBC 14,620 (IQR 12,000-18,330)/μL, $P=0.04$), and stayed longer in hospital than ESBL-negative group (7.0 (IQR 5.5-8.5) days vs. 4.5 (IQR 3.7-5.1) days, $P<0.001$).

Conclusion: In this study, high rate of ESBL positivity was detected in infantile UTI. Antibiotics exposure on both patients and mothers was associated with UTI caused by ESBL producing bacteria. Identification of underlying risk factors could improve treatment and preventive strategies.

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P1802

EVALUATION OF THE GENETICAL FEATURES AFFECTING THE RENAL OUTCOMES IN CHILDREN WITH STEROID RESISTANT NEPHROTIC SYNDROME

Elif Comak[1], Aslı Toylu[2], Ugur Bilge[3], Gülsah Kaya Aksoy[1], Mustafa Koyun[1], Sema Akman[1]

[1]Akdeniz University Medical Faculty, Pediatric Nephrology, Antalya, Turkey, [2]Akdeniz University Medical Faculty, Medical Genetics, Antalya, Turkey and [3]Akdeniz University Medical Faculty, Biostatistics and Medical Informatics, Antalya, Turkey

Background and Aims: Nephrotic syndrome in childhood is characterized by proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Although most children respond to glucocorticoid therapy, approximately 10% of patients turn out to be steroid resistant (steroid-resistant nephrotic syndrome [SRNS]). Although several studies in children with SRNS have shown that mutations in genes encoding proteins in the podocyte skeleton may be responsible for the etiology in only one-third of cases, the genetic features related with renal prognosis and response to immunosuppressive agents are not fully recognized.

The aim of this study was to investigate the genomic alterations associated with renal prognosis and resistance to immunosuppression in children with SRNS.

Method: The children with SRNS were enrolled in this study. Custom gene panel was designed for next-generation sequencing analysis of more than 20 target genes (ABCB1, ABCC2, CTLA4, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, FOXP3, GSTP1, IMPDH1, IMPDH2, NOS3, NR3C1, SLCO1B1, SLCO1B3, TPMT, UGT1A9, UGT2B7) and 200 single nucleotide variants (SNVs) which were reported as implicated in renal prognosis of nephrotic syndrome. The target gene panel was enriched for drug metabolism regulating transporters and enzymes.

Results: A total of 25 children, 16 boys (64%), median age at last visit 17.5 years (13-18 years), median age at diagnosis 7.5 years (2-15), median follow-up 9.58±4.54 years, were included in the study. All patients were diagnosed focal segmental glomerulosclerosis on renal biopsy.

P1803 **EFFICACY, SAFETY AND IMPACT ON RENAL FUNCTIONALITY OF ACETAZOLAMIDE TREATMENT IN PATIENTS WITH PMM2-CDG (AZATAX CLINICAL TRIAL)**

Mercedes Serano Guimaré[1], Pedro Arango Sancho[1], Víctor López Baez[1], Elena Codina Sampera[1], Yolanda Calzada Baños[1], Ana Vinuesa Jaca[1], Lina Hernández Zúñiga[1], Álvaro Madrid Aris[2]

[1]Hospital Sant Joan de Déu, Nefrología Pediátrica, Esplugues de Lobregat, Spain and [2]Hospital Sant Joan de Déu, Nefrología Pediátrica, Esplugues de Lobregat,

Background and Aims: Deficit of phosphomanomutase-(PMM2-CDG) is the most frequent congenital N-glycosylation defect, producing cerebellar syndrome with intellectual deficit and "stroke-like" episodes. It has been associated with renal alterations such as proteinuria, diffuse cortical hyperechogenicity and malformations. We evaluated efficacy, safety and renal repercussion of acetazolamide as a new therapeutic tool.

Method: First clinical trial in phase II including PMM2-CDG patients (5-21-years). First phase: 6 months treatment group with acetazolamide. Second phase: 5 weeks randomized withdrawal in responders (acetazolamide vs placebo), assessing renal functionality and effects of this medication. Dosing acetazolamide by 8 to 30mg/kg/day in 2-3 doses. Controls were performed at 3, 6, 14, 25 and 30 weeks determining acid-base balance, ionogram, renal function (creatinine) and Pr/Cr, Ca/Cr index and B2-microglobulin in first morning urine. All patients underwent in a bone densitometry study and renal ultrasound.

Results: 24 patients were included (mean age 12.3 ± 4.5 years). Bicarbonate levels and plasma pH were significantly lower at week 25($p < 0.001$). 13 patient needs to reduce acetazolamide dose due to excessive metabolic acidosis or asthenia. They showed a decrease in sodium ($p=0.06$), potassium ($p<0.001$) and serum calcium($p=0.030$), although maintained in low normality limit with a decrease in protein loss($p=0.019$) and increase in calcium/creatinine index($p=0.025$) without B2-microglobulin alterations. The previously ultrasound renal described findings; the cortical hyperechogenicity was observed in 8.4% without renal dysfunction or associated nephrocalcinosis. One patient presented microlithiasis and another, symptomatic renal lithiasis. Densitometric study 69% of patients presented values in the range of osteopenia at the end of trial (-0.9 to -4.9SD, average of -2.36SD).

Conclusion: The efficacy of acetazolamide in the neurological symptoms of PMM2-CDG, due to an enzymatic stimulation mechanism mediated by acidosis, generates the possibility of chronic treatment with the drug in this group of patients, with possible renal adverse effects associated with long-term, overshadowing the skeletal and renal prognosis.

	At the beginning	**Week 30**
Proteinuria	No	No
Morphological alterations (polycystic disease. . .)	No	-
Renal dysfunction	No	No
Cortical hyperechogenicity	**8,4% (2/23)**	**8,4% (2/23)**
Nephrocalcinosis	No	No
Ultrasound microlithiasis	No	**4,2% (1/23)**
Asyntomatic renal lithiasis	No	**4,2% (1/23)**
Osteopenia	**36% (8/23)**	**69% (16/23)**
(densitometry)	**- 1,7 DS (Rank 0,7 a 2,4 DS)**	**- 2,36 DS (Rank -0,9 a-4,9 DS)**

P1804 **DIALYSIS AFTERKIDNEY GRAFT LOST: DATA OF THE ITALIAN REGISTRY OF PEDIATRIC DIALYSIS**

Edoardo La Porta[1,2], Ester Conversano[3], Daniela Zugna[4], Silvia Consolo[5], Raffaella Labbadia[6], Francesca Mattozzi[7], Mattia Parolin[8], Enrico Eugenio Verrina[1], Enrico Vidal[9]

[1]Istituto Giannina Gaslini, Dialysis Unit, Genova, Italy, [2]ICLAS - Istituto Clinico Ligure di Alta Specialità, Nephrocardiology, Rapallo, Italy, [3]Hospital Burlo Garofolo, Pediatric Clinic, Trieste, Italy, [4]University of Turin, Cancer-Epidemilogy Unit, Dept. Medical Sciences, Torino, Italy, [5]IRCCS Policlinico Milano, Pediatric Nephrology Unit, Milano, Italy, [6]Ospedale pediatrico Bambino Gesù, Pediatric Nephrology Unit, Roma, Italy, [7]Ospedale Regina Margherita, Pediatric Nephrology Unit, Torino, Italy, [8]Policlinico Universitario, Pediatric Nephrology Unit, Padova, Italy and [9]University Hospital Udine, Pediatric Division

Background and Aims:

An increasing number of patients are returning to dialysis after kidney allograft failure (KAF). These patients are at higher risk of complications and mortality compared with incident ESKD patients.. In the pediatric population these data are missing and outcomes have never been investigated before in a nationally representative sample. The aim of this study was to describe the characteristics and hard outcomes of children entering dialysis after KAF in a large population of pediatric dialysis patients.

Method:

We retrospectively reviewed the files of patients receiving chronic dialysis at <18 years, recorded from January 1990 to June 2019 by the Italian Registry of Pediatric Chronic Dialysis (IRPCD), a nationwide population-based chronic dialysis network involving all 12 Italian pediatric dialysis centers. We identified 126 patients who had returned to dialysis after KAF. All patients were followed from (re)initiation of dialysis until death, re-transplantation or loss to follow-up. Multivariable regression and survival analysis were used to evaluate factors involved in the choice of dialysis modality and patient outcomes.

Results:

After KAF, 45 (35.7 %) patients were treated with PD and 81 (64,3%) with HD. Prior to kidney transplantation (Ktx), 74 (58.7%) were on PD, 45 (35.7%) on HD, and 7 on conservative care (5.5%). Compared with PD patients, those on HD were older (median age of 14.8 years [IQR 11.4-17.5] vs. 10.8 [IQR 2-6.5] vs.; p=0.002), had a longer transplant vintage ([55.2 months [13.2-100.3]) vs. 33 [5.1-82.2], and reentered dialysis in more recent calendar years (2013 [2007-2017] vs. 2004 [2001-2009]). Significant predictors for being treated with PD after KAF were a younger age at dialysis start (OR 0.83 per year increase [95%CI 0.72-0.94]) and a history of PD use before Ktx (OR 12.74 [2.2-74.6]). Patients returning to dialysis in more recent eras (OR 0.87 per year increase [0.81-0.94]) and those who were treated with more than one dialysis modality before Ktx (OR 0.15 for being treated with PD [0.04-0.63]) were more likely to be initiated on HD.

Over the observation period, 6 PD (13.6%) and 3 HD (4.2%) patients died. After adjustment for several covariates, patients on PD exhibited an increased risk for mortality compared with HD (HR 4.65 [1.12-19.30], while the difference for modality failure and access to renal transplantation did not reach statistical significance (Fig.1)

Conclusion:

Patients returning to dialysis after KAF in more recent years are more likely to be initiated on HD rather than PD. According to our registry data, the use of PD is associated with a lower survival among patients initiating dialysis after KAF.

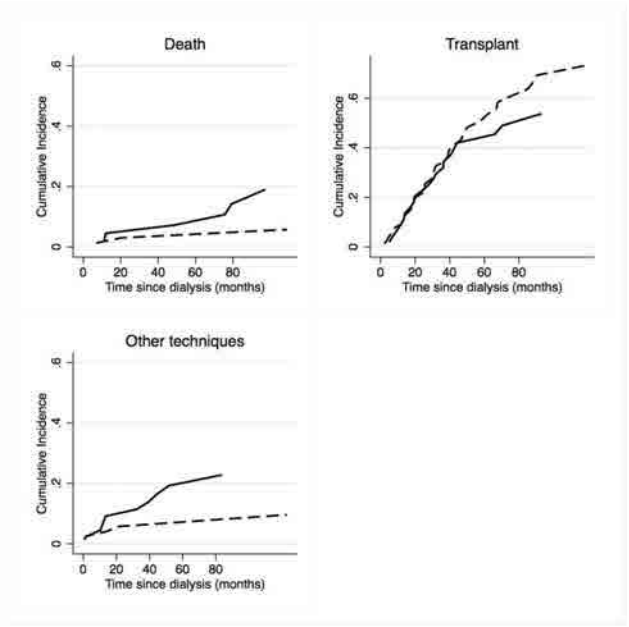


Figure:

Fig.1 Cumulative incidences for the competing events, death, transplant and other techniques (solid line: PD, dash line: HD)

P1805 **UNEXPECTD COMPLEMENT GENES ABNORALITIES IN CHILDREN WITH SECONDARY HEMOLITIC UREMIC SYNDROME**

Luigi Cirillo[1], Francesca Becherucci[1], Francesco Guzzi[1], Carmela Errichiello[1], Elisa Buti[1], Augusto Vaglio[1,2], Marco Materassi[1], Paola Romagnani[1,2], Rosa Maria Roperto[1]

[1]University Hospital Meyer, Nephrology, Firenze, Italy and [2]University of Florence, Firenze, Italy

Background and Aims:

Secondary hemolytic-uremic syndrome (HUS) is currently defined in the absence of genetic defects in complement genes (primary or atypical HUS, aHUS) or Shiga-toxin producing E. Coli infection (STEC-HUS). However, the role of complement genes abnormalities in secondary HUS is still a matter of debate as results coming from studies performed in adults are controversial. Moreover, genetic defects of complement regulation have been recently described in children with STEC-HUS, thus challenging the current HUS classification. The identification of a role of complement genes abnormalities in these patients could have important clinical implications for diagnosis and treatment. In this study, we assessed the presence of complement genes abnormalities in children with secondary HUS.

Method:

We describe a case series of pediatric patients diagnosed with secondary HUS. All patients were screened for the presence of ADAMTS13 auto-antibody and ADAMTS13 deficiency. We performed next-generation sequencing for a panel of complement genes reported in association with aHUS (*CFH, CFI, MCP, C3, FB,* and *THBD*). Copy number variations and hybrid genes assessment were included in the analysis.

Results:

Four patients aged 1-4 years with a diagnosis of sporadic secondary HUS were included in the study. HUS was secondary to glomerulopathy, cobalamin deficiency, bone marrow transplantation, and pneumococcal pneumoniae. Two out of four patients showed hypocomplementaemia (both C3 and C4). Diarrhea was a common clinical feature in all patients at onset, and none of these patients showed neurologic involvement. Renal replacement therapy was required in two patients at onset. Only one patient did not recover kidney function, and subsequently underwent kidney transplantation. Next-generation sequencing showed genetic abnormalities in all the patients (Table 1). All but one genetic variants have already been described in association with atypical HUS. Interestingly, haplotypes in *CHF* and *MCP* were present in three patients, all of Caucasian ethnicity.

Conclusion:

According to the current HUS classification, complement abnormalities are diagnostic of aHUS. However, results coming from pediatric cohorts of STEC-HUS patients already claimed a role for genetic background also outside the aHUS spectrum, suggesting that the current terminology lacks both specificity and suggestion of cause. In this case series, complement genes abnormalities were present in all patients. Whether confirmed in larger cohorts, these findings would support the role of genetic background even in secondary HUS, suggesting the need for a revision of the current HUS classification, in agreement with the pathogenic mechanisms, in order to tailor the optimal treatment.

Tab. 1

	gene	Variant	Haplotype	h/H
ST-HUS	CFH	c.332C>T c.2808G>T c.2016A>G	CFH-H3	h
	MCP	c.897T>C	MCP ggaac	h
Pneumococcal HUS	CFH	c.332C>T		h
	MCP	c897T>C	MCP ggaac	h
cblC HUS	CFH	c.2909T>C *		h
	THBD	c.1418A>T		h
HSCT HUS	CFH	c.332C>T c.2808G>T c.2016A>G	CFH-H3	h
	MCP	c.897T>C	MCP ggaac	h
HUS in glomerulopathy	CFH	c.332C>T c.2808G>T c.2016A>G	CFH-H3	H
	MCP	c897T>C	MCP ggaac	h

*new variant

Figure:

P1806 OUTCOMES OF PEDIATRIC RENOVASCULAR HYPERTENSON: A SINGLE-CENTER EXPERIENCE

Jiwon Jung[1], Joo Hoon Lee[1], Kun suk Kim[2], Young Seo Park[1]

[1]Asan Medical Center, Department of pediatrics, Seoul, Korea, Rep. of South and [2]Asan Medical Center, Department of pediatric urology, Seoul, Korea, Rep. of South

Background and Aims: Renovascular disease is rare but important treatable cause of secondary hypertension in children. We aimed to evaluate the clinical presentations and long-term outcomes of pediatric patients with renovascular hypertension (RVH).

Method: We retrospectively reviewed medical records of patients with renovascular disease at our center between 1994 and 2019. Clinical courses including status of hypertension control with preservation of renal function during follow up were evaluated.

Results: 20 patients were diagnosed with RVH. 50 % (n = 10) were male, and median age at diagnosis was 10.1 (range 1.3 – 17.2) years, and median follow up period was 8.7 (range 0.1 – 24.6) years. 50 % (n = 10) presented with incidently detected high blood pressure (8 patients without symptoms, one with headache, and the other one with proteinuria), 25 % (n = 5) first admitted due to heart failure symptoms, and the rest (25 %, n = 5) presented with neurologic symptoms including seizure or paraplegia. Majority had no underlying disease except for 3 patients with Moyamoya disease. 80 % (n = 16) had unilateral renovascular stenosis. All patients showed elevated basal random renin activity (median 20.0, range 2.5 – 62.1 ng/ml/hr), and 45 % (n = 9) patients showed elevated basal random aldosterone level (median 822, range 266 – 2440 pg/ml). All patients needed antihypertensive medications for blood pressure control; 35 % (n = 7) of patients gained good control of blood pressure only with antihypertensive agents including angiotensin converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB), 40 % (n = 8) of patients who underwent percutaneous transluminal angioplasty all still needed antihypertensive agents including ACEI for blood pressure control. 20 % (n = 4) of the patients initially showed profoundly low relative function of involved kidney on diuretic scan, leading to nephrectomy. Three of these patients with nephrectomy successfully discontinued all antihypertensive agent gaining good control of blood pressure. The remaining one patient showed progressive deterioration of relative function on the involved side of kidney during 13 years, ended up with nephrectomy, but couldn't discontinue ACEI. Glomerular filtration rate (GFR) was within normal range for all patients at diagnosis. For patients without nephrectomy, mean relative function of the involved kidney on diuretic scan was 33.5 ± 11.4 % at diagnosis. There was no significant change or deterioration of relative renal function during a mean follow up period of 10 ± 8 (median 11.5, range 0 – 19.5) years, although they all used ACEI/ARB.

All patients including patients with nephrectomy showed normal GFR with a mean of 114.1 ± 19.5 ml/min/1.73 m^2 at the last follow up.

Conclusion: Antihypertensive medications including ACEI and ARB were safely used with no further deterioration of the renal function of the involved side with or without angioplasty. Pediatric RVH is well managed with preserved renal function in long-term follow up.

P1807

COMPARISON BETWEEN INFERIOR VENA CAVA DIAMETER, BIOIMPEDANCE SPECTROSCOPY AND CLINICAL CRITERION FOR DRY WEIGHT ESTIMATION IN HEMODIALYZED CHILDREN

Varvara Askiti[1], Georgia Malakasioti[1], George Servos[2], Georgia Grigoriadou[2], Andromachi Mitsioni[1]

[1]Aglaia Kyriakou Children's Hospital, Pediatric Nephrology, Athens, Greece and [2]Aglaia Kyriakou Children's Hospital, Pediatric Cardiology, Athens, Greece

Background and Aims: The determination of dry weight (DW) in children on chronic hemodialysis (HD) remains problematic. No method has been shown superior for DW assessment in the few pediatric studies exploring the utility of inferior vena cava expiratory and inspiratory diameter diameter (IVCDe, IVCDi) and BIS against clinical criteria. We aimed to compare the performance of IVCD, BIS and clinical judgement in DW prediction in hemodialyzed children.

Method: IVCD and BIS were measured serially pre and post the midweek HD session. IVCDi, IVCDe and IVC contractility index (IVCCI) associations with: (1) BIS estimated (BIS-relOH) and (2) clinically assessed hydration status (OHc) based on deviation from DW were explored. The interpretation of IVC measurements was based on previously published pediatric reference values. The level of agreement between the three tools in fluid overload recognition was studied.

Results: Fifty-two sets of measurements were undertaken in 13 patients (median age 11 years). OHc and BIS-relOH were positively associated to each other ($r=0,5$, $p<0,05$) and to IVCDi ($r=0,4$, $r=0,5$, $p<0,05$) and IVCDe ($r=0,4$, $r=0,6$, $p<0,05$). A negative association between IVCCI and relOH-BIS was observed ($r= -0,4$, $p<0,05$). There was a poor agreement between the three methods in identification of fluid overload; out of 28 clinically overloaded patients, BIS identified only 7 whereas IVCD none (Cohen's $k<0$).

Conclusion: IVCD measurements alone are not reliable for accurate fluid status prediction in hemodialyzed children as they seem to underestimate fluid overload compared to BIS and clinical criteria. Further studies are warranted to explore the applicability of new technologies for DW assessment of dialysis patients.

P1808

INHIBITION OF MIR-155 IMPROVES PROGNOSIS IN AN EXPERIMENTAL FSGS MOUSE MODEL BY REGULATING AUTOPHAGY

Yu Zhang[1], Jie Wang[1], Jianhua Zhou[1]

[1]*Tongji Hospital of Huazhong University of Science and Technology, Pediatrics, Wuhan, P.R. China*

Background and Aims:

Focal segmental glomerulosclerosis (FSGS), a podocytopathy, is one of the most common primary glomerular diseases causing end-stage renal disease in children. Its mechanisms remain unclear and the effective treatment lacks. MiR-155 is a typical multifunctional miRNA, which serves a crucial role in the regulation of numerous vessel cells. The present study aimed to investigate the role of miR-155 in the pathogenesis of FSGS.

Method:

A FSGS model was establishe by injection of adriamycin in miR-155 knockout mice. Renal pathological changes were observed by Periodic Schiff-Methenamine Silver staining and Masson trichrome staining. Podocyte morphology and autophagosomes were examined with electron microscopy. Podocyte density was estimated by the Weibel-Gomez method. Expression of autophagy markers and apoptosis-associated proteins were analyzed by Western blotting analysis.

Results:

Silencing of miR-155 significantly decreased urinary protein excretion and ameliorated glomerulosclerosis in adriamycin-induced FSGS mice. We found that adriamycin treatment led to fusion of podocyte foot processes, swelling of the podocyte body, dilated mitochondria, and podocyte loss. Inhibition of miR-155 improved podocyte depletion and the above cytopathies induced by adriamycin. In addition, the results also demonstrated that in miR-155 KO mice, the expression of LC3 and ATG5 was increased and the expression of P62 was decreased.

Conclusion:

These suggest that modulated miR-155 can prevent podocyte damage, by regulating the level of autophagy. The present study provides a novel insight into microRNAs as potential therapeutics for the treatment of podocytopathy.

P1809 EARLY URINARY SYSTEM COMPLICATIONS IN CHILDREN WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION

Anar Gurbanov[1], Bora Gülhan[2], Barış Kuşkonmaz[3], Fatma Visal Okur[3], Duygu Uçkan Çetinkaya[3], Gulsah Ozdemir[2], Nesrin Taş[2], Kübra Çelegen[2], Fatih Ozaltin[2], Ali Duzova[2], Rezan Topaloglu[2]

[1]Hacettepe University School of Medicine, Pediatrics, Ankara, Turkey, [2]Hacettepe University School of Medicine, Pediatric Nephrology, Ankara, Turkey and [3]Hacettepe University School of Medicine, Pediatric Hematology, Ankara, Turkey

Background and Aims: Urinary system complications after hematopoietic stem cell transplantation (HSCT) cause severe morbidity and mortality. The aim of the study is to investigate the incidence and risk factors of urinary system complications in patients who had HSCT during their childhood.

Method: Patients who had HSCT between January 2010-2019 with a minimum follow-up period of 6 months were included in the study. Data regarding urinary system complications were collected from the medical records of the patients. pRIFLE and KDIGO classification systems were used for the definition of acute kidney injury (AKI).

Results: 167 patients (108 males and 59 females) with allogeneic (n=165) and autologous (n=2) HSCT were investigated for renal complications. In cohort, HSCT was performed in 41 patients (%24.6) secondary to malignant diseases and in 126 patients secondary to non-malignant diseases. Hemorrhagic cystitis (HC) developed in 28 patients (16.8%) after HSCT. The mean age of the patients with and without HC was 14.6±5.6 years and 10.5±6 years, respectively (p=0.044). Among patients with HC, 17 had concomitant viral infection. Presence of viral infection, gender, disease group, history conditioning regime, total body irradiation, acute graft-versus-host disease and veno-occlusive disease (VOD) did not have any effect on the development of HC in logistic regression analysis. In cohort, 126 patients (75.4%) developed AKI according to KDIGO classification (stage 1; 55 patients, stage 2; 36 patients, stage 3; 35 patients). The mean period of development of AKI after HSCT was 34±22 days. The risk of AKI (according to KDIGO) was higher in patients who had HSCT secondary to malignant diseases and/or who developed viral infections after HSCT (p=0.034 and p=0.013, respectively). Among patients, 71 patients (%42.5) developed AKI according to pRIFLE classification. The risk of AKI (according to pRIFLE) was higher in patients who had HSCT secondary to malignant diseases, who developed viral infections and/or who developed VOD during follow-up (p=0.043, p=0.001 and p=0.006, respectively). One patient developed thrombotic microangiopathy after HSCT. None of the patients had nephrotic syndrome during follow-up period.

Conclusion: Patients who had HSCT secondary to malignant disease, history of viral infections and/or VOD had higher risk of AKI and should be closely monitored.

P1810 **INFECTION TRIGGERS AS A COMPLEMENT-ACTIVATING STATE IN ATYPICAL HEMOLYTIC-UREMIC SYNDROME IN CHILDREN**

Khadizha Emirova[1], Evgeniya Tolstova[1], Olga Orlova[1], Alexandr Muzurov[2], Tatiana Pankratenko[3], Tatiana Abaseeva[3], Galina Generalova[3], Sofya Mstislavskaya[1]

[1]Moscow, Pediatrics, Moscow, Russia, [2]Russian Medical Academy of Postgraduate Education, Children's Anesthesiology and Intensive Care, Moscow, Russia and [3]Snt Vladimir Children's Hospital, Dialysis, Moscow, Russia

Background and Aims: Atypical hemolytic-uremic syndrome (aHUS) is a rare life-threatening disease, which is based on the dysregulation of the complement system. Different complement-activating factors is known for aHUS, including infections, vaccination, concomitant diseases, pregnancy, surgical interventions, transplantation, etc. In 24% of cases, a connection with diarrheal prodrome is revealed, in 18% - with acute respiratory infections. The diagnosis of aHUS is established if other forms of thrombotic microangiopathy (TMA) are rejected: HUS associated with Stx-producing strains of E. Coli and Shigella dysenteriae (STEC / Stx - HUS), TTP. We analyze the etiology of trigger events in children with aHUS.

Method: An analysis of 165 case histories of children with aHUS was carried out for the period from 2000 to 2019. Of these, 70 are boys and 95 are girls. The average age was 4.83 ± 3.84 years (from 2.5 months to 17.8 years). The diagnosis of aHUS was established on the basis of microangiopathic hemolysis, thrombocytopenia, organ dysfunction and recurrent TMA activity. 66 patients were genetically screened, among which mutations in genes encoding complement proteins were detected in 23 (34.9%) children.

Results: The prodromal period of patients with aHUS was characterized by fever (53.9%), weakness (42.4%), decreased appetite (27.3%), catarrhal symptoms (20.6%), nausea (17.6%), and vomiting (63%), abdominal syndrome (26.7%), diarrhea (38.8%), hemocolitis (12.1%). Among the trigger events, acute intestinal infections accounted for 44.2% of cases, acute viral infections - 26.0% (with catarrhal syndrome - 20.6%, intestinal - 5.4%), herpetic infection (CMV, VEB, HSV 1 type) was found in 3% of cases. In 10.3% of children, the TMA symptom complex developed after vaccination with mainly live attenuated vaccines, in 4.2% against other rare conditions (trauma, taking an unknown drug, tonsillitis, etc.). In 12.1% of cases, the disease manifested itself without a complement-activating state. E.coli was confirmed in 16 observations (EHEC - 12, EagEC - 2, EPEC - 2), shigellosis (Shigella Flexner 6) was detected in 1 case. The nature of viral diarrhea was identified in 8 patients: rotovirus RNA - 4, adenovirus DNA - 2, norovirus RNA - 2, type 5 Coxsackie RNA - 1. In the case of TMA after E.coli and shigella, the initial diagnosis was STEC / STx - HUS, which was subsequently transformed into aHUS due to the recurrent TMA activity with persistent dialysis-dependent AKI, and the addition of extrarenal symptoms not associated with volume overload.

Conclusion: Infectious diseases are the most common complement-activating condition for the implementation of aHUS in children. Among them, in most cases, diarrheal prodrome is associated with acute intestinal infections, which differs from population data (44.2% vs 24%). With the development of TMA in children with escherichiosis/shigellosis, repeated episodes of hemolysis, platelet consumption, the appearance of extrarenal symptoms with normalization of hematological parameters, the detection of pathogenic mutations in complement genes and the positive effect of complement blocking therapy (eculizumab) confirms the diagnosis of aHUS in this category of patients. To exclude or confirm aHUS in these cases, monitoring of clinical and laboratory data is necessary.

P1811 GENETIC POLYMORPHISMS IN STAT4, VEGF2578 AND PTPN22 GENES IN CHILDREN WITH GLOMERULOPATHIES

Ina Kazyra[1], Alexandr Sukala[1], Hanna Bialkevich[1], Anna Krylova-Alefirenko[1], Natalia Tur[2], Yulia Shynkarenka[2], Roza Goncharova[3], Natallia Nikitchenko[3], Elisaveta Siniauskaya[3], Nataliya Savina[3]

[1]Belarus State Medical University, 1st Department of Pediatrics, Minsk, Belarus, [2]National Center for Pediatric Nephrology, Nephrology, Minsk, Belarus and [3]Institute of Genetics and Cytology of the National Academy of Sciences of Belarus, Laboratory of molecular bases for genome stability, Minsk, Belarus

Background and Aims: Glomerular diseases (GD) often have genetic predisposition, especially those autoimmune or immune complex-mediated. Our aim was to assess an impact of genetic polymorphism in STAT4 rs7574865 and rs3821236, VEGF rs699947 and PTPN22 rs2476601 on the risk of development of primary (PG) and secondary (SG) glomerulopathies in children.

Method: We enrolled 81 child with GD (m:f 33/48) and 335 healthy controls (m:f 184/151). Patients of the study group were arranged into two groups: 1st - with PG (38 children aged 3-17 yrs, 13±3,45, m:f 22/16) and 2nd - with SG (43 children aged 7-17 yrs, 13±3,59, m:f 11/32).

1st group included 35 patients with hereditary nephritis, 2 with IgA nephropathy, 1 – FSGS. 2nd group included 10 patients with ANCA associated vasculitis, 11 with IgA vasculitis, 22 with systemic lupus erythematosus (SLE). These patients were identified and monitored at the National Center for Pediatric Nephrology. Control group (CG) was matched with the study groups for age and sex and included 335 healthy children (m:f 184/151, age 2-17 yrs, 14,28±2,56). We analyzed DNA by polymerase chain reaction for identification of genotypes.

Results: The frequency of genotypes and allels for STAT4 rs 7574865 was found to be GG 55,26% in 1st, 46,51% in 2nd versus (vs) 62,09% in CG; GT 39,47%, 41,86% vs 32,24%; TT 5,26%, 11,63% vs 5,67%; for minor allele T 25,00%, 32,60% vs 21,79%, respectively. For STAT4 rs3821236: GG found in 65,79% in 1st, 55,81% in 2nd vs 65,07% in CG; GA genotype in 26,32%, 41,86% and 30,15%; AA genotype in 7,89%, 2,33% and 4,78%; minor allele A in 21,05%, 23,26% and 19,85%, respectively. For VEGF2578 rs 699947: AA 28,95% in 1st, 30,23% in 2nd vs 20,30% in CG; AC 44,74% and 51,16% vs 57,31%; CC 26,32% and 18,60% vs 22,39%; minor allele C 48,68%, 44,19% vs 51,04% in 1st and 2nd vs CG, respectively. For PTPN22: CC 68,42% in 1st, 59,46% in 2nd vs 72,95% in CG; CT 28,95%, 35,14%, 24,59%; TT 2,63%, 5,41% and 2,46%; minor allele T in 17,11%, 22,97% vs 14,75% in 1st,2nd and CG, respectively.

The distribution of genotypes observed was tested with the Hardy-Weinberg Equilibrium. There were no differences found in rates of polymorphic genotypes in CG and patients with GD.

For PTPN22 rs 2476601 and VEGF2578 rs6999467 no statistically significant difference between children of 1st, 2nd and CG was observed. We found the difference between patients with GD and healthy children (HC) for minor allele T of STAT4 rs7574865 (OR [95%CI]=1,73 [1,06-2,82], p=0,03), which was most prominent for female patients with SG (OR [95%CI]=2,31 [1,3-4,12], p=0,005). The development of SG was associated with the presence of GT+TT genotype (vs GG genotype) of STAT4 rs7574865 (OR=4,92; 95% CI [2,62-9,23]; p<0,001).

Statistical testing showed significant differences between healthy female controls and SLE females for minor allele T of STAT4 rs7574865 (OR [95%CI]=2,14 [1,07-4,27], p=0,04) and GT+TT genotypes vs GG genotype of STAT4 rs7574865 (OR=2,54; 95%CI[1,00-6,42]; p<0,05).

The analysis of genotypes/alleles for polymorphic locus rs3821236 of STAT4 revealed significant association of GA genotype (OR[95%CI]=2,55 [1,17-5,55], p=0,021), as well as of the sum of genotypes with at least one minor allele (GA+AA) (OR[95%CI]=3,51 [1,59-7,76], p=0,002) with the development of SG in girls. An association of the presence of the minor allele A of STAT4 rs3822136 with the likelihood of SG development in females was observed (OR[95%CI]=2,69 [1,5-4,83], p=0,001).

Conclusion: Minor allele T and GT+TT genotypes of STAT4 rs7574865 is associated with the risk of SG development in children and especially with the risk of SLE development in girls. Minor allele A and GA+AA genotypes of the STAT4 rs3822136 are associated with the predisposition to SG in girls. Minor allele T and GT+TT genotypes of the PTPN22 rs 2476601 are observed to be more frequent in both groups of GD and especially in girls, though failed to be statistically significant (p>0,05).

P1812 DOES THE TOTAL KIDNEY VOLUME REFLECT ALPORT SYNDROME PROGRESSION?

MARINA AKSENOVA[1], Natalia Konkova[1], Tatjana Lepaeva[1], Tatjana Nikishina[1], Oxana Piruzeeva[1], Marina Dobrynina[2], Olga Chumak[2]

[1]Y.Veltischev Research and Clinical Institute for Pediatrics at N.Pirogov Russian Research Medical University, Nephrology department, Moscow, Russia and [2]Y.Veltischev Research and Clinical Institute for Pediatrics at N.Pirogov Russian Research Medical University, Diagnostic department, Moscow, Russia

Background and Aims: The kidney volume can reflect kidney function and predict renal disease progression. The aim of the study was to define the clinical significance of kidney volume in children with Alport syndrome (AS).

Method: The medical records were obtained from 86 children (age Me 8(5;11) years; 50M/36F) with genetically (n=78) and morphologically (n=8) confirmed AS; follow-up Me 4(2;6) years. Albuminuria (Alb), proteinuria (Pr), nephrotic proteinuria (nPr) and decreased eGFR were defined as urine Alb>30 mg/gr Cr, Pr≥100 mg/m^2/day, Pr≥960 mg/m^2/day and eGFR<90 ml/min/1,73m^2, respectively. The Body Superficial Area Related Total Kidney Volume (BSARTKV) was calculated as relation of US kidney volume to BSA: BSARTKV[ml/m^2]=(L*W*D*π/6)/BSA and compared with normal volume range (Th.Scholbach, D.Weitzel, 2012).

Results: The renal volume ≥95 was revealed in $^1/_2$ and $^3/_4$ of children at initial and last evaluation, respectively (0.51 vs 0.76, p>0.05); two boys (q=0.02) with CKD stage 4 had a BSARTKV ≤10 at the last presentation. BSARTKV correlated with age (r=0.3, p<0.05), mean blood pressure percentile (r=-0,22, p<0,05), Alb (r=0.25, p<0.05), Pr (r=0.4, p<0,001) and eGFR (r=0.23, p<0.05). No correlation was found between BSARTKV and birth weight and gender. Each 1SD (23.5 ml/m^2) increase in BSARTKV was related with higher eGFR: OR=6.7 (95%CI 3.51;8.69, p<0,001). The children with nPr and eGFR>35 ml/min/1,73m^2 had enlarged kidneys: OR=30.75(95%CI 2.56;369, p<0,001); the patients with eGFR≤35 ml/min/1,73m^2 had small BSARTKV: OR=167 (95%CI 10.4;2681.3, p<0,0001).

Conclusion: The kidney volume reflects the progression of nephropathy in AS. Probably, an increased renal mass compensates decreased glomerular function, whereas small kidney volume represents the loss of function of most nephrons.

P1813 CLINICAL CHARACTERIZATION OF CONGENITAL SOLITARY FUNCTIONING KIDNEY IN CHILDREN

Francesca Becherucci[1], Francesca Guzzi[1], Luigi Cirillo[1], Alessandra Bettiol[2], Arianna Zuccato[2], Tommaso Mazzierli[2], Elisa Buti[1], Carmela Errichiello[1], Augusto Vaglio[1,2], Lorenzo Masieri[2,3], Catia Olianti[4], Marco Materassi[1], Rosa Maria Roperto[1], Paola Romagnani[1,2]

[1]Meyer Children's Hospital, Nephrology and Dialysis, Florence, Italy, [2]University of Florence, Florence, Italy, [3]Meyer Children's Hospital, Urology, Florence, Italy and [4]Careggi Hospital, Nuclear medicine, Florence, Italy

Background and Aims:

Congenital anomalies of the kidney and urinary tract (CAKUT) are the major cause of chronic kidney disease and end-stage kidney disease in childhood. Solitary functioning kidney (SFK) is part of the spectrum of CAKUT. Congenital SFK is mainly due to unilateral renal agenesis (URA) and multi-cystic dysplastic kidney (MCDK). With the implementation of routine fetal ultrasound screening, SFK is increasingly recognized before birth, significantly raising the number of patients referred to paediatric nephrology units for clinical monitoring during childhood.

Understanding the pathophysiology of SFK is pivotal for guiding the clinical management and informing long-term outcome. However, observational studies performed in children with SFK are controversial, especially about the need, methodology and timing of functional assessment. This may be at least in part due to the fact that different models of SFK, including congenital and acquired after unilateral nephrectomy, are often grouped together.

The aim of this study was to assess the clinical, laboratory and functional features of congenital SFK caused by URA and MCDK in children, with a particular focus on the role of renal scintigraphy in estimating kidney function during childhood and adolescence.

Method:

We retrospectively collected clinical, laboratory and instrumental records of all consecutive pediatric patients (aged 0-18 years) affected by congenital SFK caused by URA or MCDK referred to the Nephrology and Dialysis Unit of Meyer Children's Hospital of Florence (Italy) from 1992 to 2019. Patients with unilateral kidney hypodysplasia were excluded. In particular, we reviewed data from ultrasound scanning and sequential renal scintigraphy over time. URA and MCDK were compared for clinical features, long-term course and outcome.

Results:

A total of 155 patients with congenital SFK were included in the study and divided in two groups according to the cause of SFK (URA, n=100; MCDK, n=55). The median length of follow-up was 47 and 45 months, respectively. Male sex and ethnicity were equally distributed in the two groups. Prenatal diagnosis was more frequent in MCDK group. We did not observe either preterm birth or low birth weight in patients enrolled. Overall, the clinical features were not statistically different between the two groups. In particular, SFK associated CAKUT, including vesicoureteral reflux, occurred at a comparable frequency. Also, measurement of kidney length by ultrasound scanning, which is often considered suggestive of compensatory hypertrophy, did not differ between groups. Although renal clearance from sequential renal scintigraphy appeared not statistically different between URA and MCDK, the latter seems to reach complete functional adaptation more rapidly and earlier in the first two years of life.

Conclusion:

The clinical course and long-term outcome of SFK has been a topic of extensive debate. Due to poor-quality of data (unclear inclusion/exclusion criteria, lack of uniformity in data collection and outcome definition), generalization of findings from observational studies to all patients with SFK could be inappropriate. Congenital SFK could represent the most unbiased group to analyze and this study provides a thorough clinical characterization of a large and strictly selected cohort. Insights from sequential renal scintigraphy suggest a different trend in reaching single kidney complete functional adaptation in URA and MCDK. These results could potentially reveal significant differences in the pathophysiologic mechanisms of reaching compensatory hypertrophy and functional adaptation by the solitary kidney in the two models. Whether confirmed in larger cohorts, these findings could provide important implications for follow-up planning, informing the need, methodology and timing for function assessment, tailoring the clinical management and understanding long-term prognosis.

P1814 ATYPICAL FEATURES IN A TYPICAL DISEASE: ONE THOUSANDS FACES OF IGA NEPHROPATHY IN PAEDIATRIC PATIENTS

Deianira Pedoto[1], Adele Corcione[1], Diletta Apuzzo[1], Francesca Nuzzi[2], Luigi Annicchiarico Petruzzelli[2], Giuseppina Barra[3], Gabriele Malgieri[2], Carmine Pecoraro[2]

[1]Federico II University, Department of Medical Translational Sciences, Naples, Italy, [2]Santobono-Pausilipon Children's Hospital, Paediatric Nephrology Unit, Naples, Italy and [3]University of Salerno, Unit of Pediatrics, Salerno, Italy

Background and Aims: Immunoglobulin A Nephropathy (IgAN) is the most common cause of idiopathic glomerulonephritis in paediatric patients.

The typical presentation is characterized by recurrent episodes of macroscopic haematuria or persistent microhaematuria with mild or overt proteinuria. Renal function is normally preserved, though a slow progression to chronic kidney disease (CKD) may occur.

However, in rare cases IgAN may assume atypical features, presenting with nephrotic syndrome (NS), acute kidney injury (AKI) or assuming the characteristic of a rapidly progressive glomerulonephritis, leading to significant difficulties in management and critical impact on prognosis.

Method: Of total 756 renal biopsies performed in our centre from 2000 till 2019, 174 (23%) diagnosis of IgA nephropathy were made: 123 (70,6%) of 174 with a milder histological stage (I or II according to Lee's) and 51 (29,3%) with severe stages (III-IV).

Clinical onset of these 51 patients was mostly characterized by a nephritic syndrome with micro-macrohaematuria, though in 7 of them it assumed atypical features (table 1).

Results: Patients 1, 2, 3 and 4 showed a rapidly progressive IgAN with extensive crescentic lesions at histological evaluation.

In all of the four patients the onset of the disease was characterised by a compromised renal function, thought, according to the medical history, in patients 2 and 4 clinical signs of nephropathy had started some months before the first medical evaluation.

This detail, considering the poorer clinical outcome of patients 2 and 4 (table 1), strongly highlights the need of promptness in the treatment of these conditions.

Patient 1 achieved a complete remission after steroid pulse therapy (Pozzi scheme), while for patients 2,3,4 an additional immunosuppressive treatment was required.

The nephropathy of patient 5 was, instead, characterized by AKI with consistent macrohaematuria. Interestingly, the severity of the clinical presentation was not related to the glomerular lesion (the histology showed a minimal change disease), rather to the intratubular haemorrhage, causing an obstructive acute kidney injury. Patient 5 achieved a complete remission after steroid treatment.

The onset of IgAN in patients 6 and 7 was characterized by a nephrotic syndrome, which is a very uncommon feature (<2% of all IgAN).

Patient 6, who showed a massive proteinuria (till 11 grams/24 hours) was promptly treated with steroid and tacrolimus, achieving a complete remission in 6 moths.

Patient 7, a sri-lankan girl, was diagnosed in 2008 in Sri-Lanka.

She underwent treatment with steroid and Mycophenolate and successively, for the persistence of proteinuria, with Cyclosporine A.

From 2014 she has been followed by our centre. Despite a second cycle with Cyclosporine she has shown a persistence of proteinuria and a slow progression to CKD.

Conclusion: This study highlights that a typical disease like IgAN may hide behind an atypical and severe presentation.

Moreover, the blackboard of the atypical forms is extremely heterogeneous, stretching from NS to crescentic and progressive diseases.

As a consequence, the treatment of these conditions is not codified and represents an important challenge for the clinician.

This calls for multicentric studies which could provide shared recommendation for the management of these atypical forms of IgAN.

PATIENT	AGE ONSET	DATE DIAGNOSIS	CLINICAL PRESENTATION		BIOPSY	TREATMENT	OUTCOME (December 2019)
1	13	27/03/15	Macrohematuria	x	III-IV stage (crescent)	Steroid (Pozzi scheme)	Complete remission
			Hypertension	x			
			AKI	x			
			NS				
2	10	16/12/13	Macrohematuria		III-IV stage (crescent)	Steroid (Pozzi scheme) Cyclophosphamide	Persistence of proteinuria Preserved renal function
			Hypertension				
			AKI	x			
			NS				
3	14	24/09/15	Macrohematuria	x	III-IV stage (crescent)	Steroid (Pozzi scheme) Cyclophosphamide	Transplanted for end stage renal disease
			Hypertension				
			AKI	x			
			NS				
4	17	10/10/19	Macrohematuria		IV stage (crescent)	Steroid (Pozzi scheme) Mycophenolate	Persistence of proteinuria CKD (III stage)
			Hypertension	x			
			AKI	x			
			NS				
5	14	15/11/19	Macrohematuria	x	I stage (minimal change)	Steroid	Complete remission
			Hypertension				
			AKI	x			
			NS				
6	15	06/02/19	Macrohematuria		III stage	Steroid Tacrolimus	Complete remission
			Hypertension				
			AKI				
			NS	x			
7	6	30/06/08	Macrohematuria	x	II-III stage	Steroid Mycophenolate Cyclosporine	Persistence of proteinuria CKD (III stage)
			Hypertension				
			AKI				
			NS	x			

Figure: Table 1

P1815 **LONG-TERM OUTCOME OF BLADDER DYSFUNCTION IN CHILDREN**

Jameela Kari[1], Mai Banakhar,[2], Khalid Khashoggi[3], Sherif El-Desoky[1]

[1]King Abdulaziz University, Faculty of Medicine, 2Paediatric Nephrology unit, Department of Pediatrics,, Jeddah, Saudi Arabia, [2]King Abdulaziz University, Department of Urology, Jeddah, Saudi Arabia and [3]King Abdulaziz University, Radiology departemt, Jeddah, Saudi Arabia

Background and Aims: Bladder dysfunction is an important cause of chronic kidney disease (CKD) due to neurogenic causes such as a spinal lesion (SL), Hinman's syndrome, or non-neurogenic neurogenic bladder (NNNB), and valve bladder syndrome (VBS). In this study, we evaluated the outcomes of neurogenic bladder caused by different etiologies.

Method: Single-center retrospective study of children with neurogenic bladder (NB) over 13 years (2005-2017).

Results: Totally, 199 children (134 boys, 67.3%) were included and divided into three groups: Group 1 (75, NNNB), Group 2 (64, SL), and Group 3 (60, VBS). Urodynamic examination revealed impaired bladder capacity in 49 children (57.6%), atonic bladder in 1 child (1.1%), and normal bladder compliance in 35 children (41.1%). Additionally, 113 children (56.8%) experienced clean intermittent catheterization (CIC). A significant improvement in the mean estimated glomerular filtration rate and CKD stages was observed among the three studied groups, but the NNNB group showed the least improvement. Children diagnosed and treated during their first year of life had better outcomes than those who presented at a later age. CIC without the need for surgical intervention was associated with improved renal function. Pyelonephritis and hydronephrosis had significant negative impacts on kidney function

Conclusion: Early diagnosis and management of NB in infancy are associated with better outcome and preservation of renal function. CIC is associated with better preservation of kidney function, while vesicostomy is associated with a worse outcome. Children with NB caused by SL experienced the best kidney function preservation, while those with VBS experienced the worst.

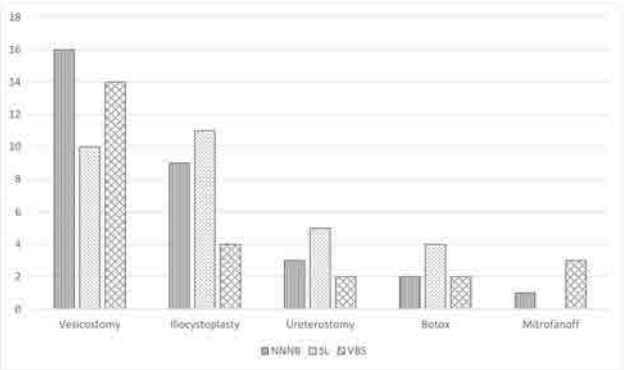


Fig. 1 Types and frequencies of surgical operations conducted for the studied groups

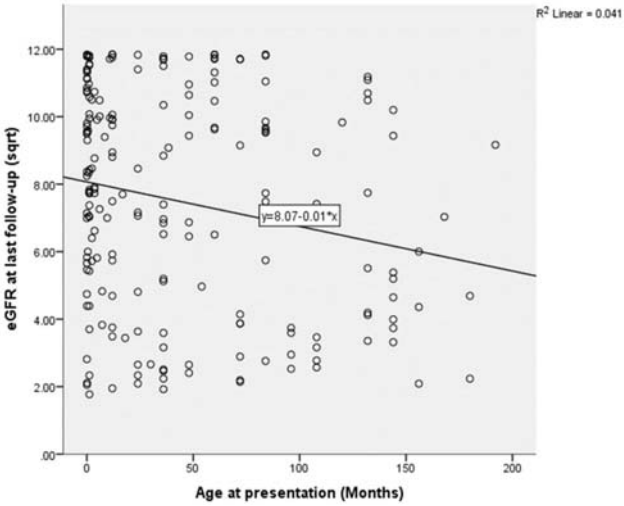


Fig. 2 Correlation between age at presentation and final sqrt eGFR.

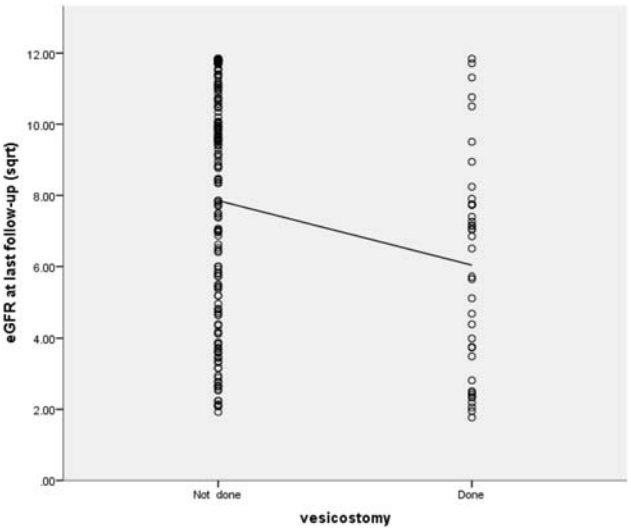


Figure- 3 Correlation between vesicostomy and final sqrt eGFR. and final sqrt eGFR. F3 Correlation between vesicostomy and final sqrt eGFR.

P1816 KIDNEY DAMAGE IN NECROTIZING ENTEROCOLITIS OF PREMATURE BORN INFANTS

Iuliia Kyslova[1], Nataliia Chornopyshchuk[1], Olga Yablon[1], Anastasiia Konoplitska[1], Roman Chornopyshchuk[2]

[1]National Pirogov Memorial Medical University, Pediatrics #1, Vinnytsya, Ukraine and [2]National Pirogov Memorial Medical University, General surgery, Vinnytsya, Ukraine

Background and Aims: Neonatal kidney damage can be the result of hypoxic-ischemic events or nephrotoxic drugs. The long-term effects of hypoxia on the kidneys are still unclear. Unlike full-term infants, premature infants of less than 36 weeks of gestational age exhibit persistent nephrogenesis According to literature database, ischemia as well as reperfusion and infection (hypoxia, acidosis, hypotension, the action of free oxygen radicals) are also major risk factors for necrotizing enterocolitis (NEC). The **aim** is to establish the peculiarities of kidney damage in necrotizing enterocolitis of premature infants who died from it and infants with NEC surviving.

Method: The study involved 54 of premature infants: 21 infants with NEC stage II and III who died (group A), 43 infants who survived with similar stages of NEC (group B). Statistical processing of the data obtained was carried out on a personal computer using STATISTICA 6.1 and IBM SPSS.

Results: Infants in group A had significantly higher body weight - (1371.2±70.5) g than infants in group B - (1163.9±51.6) g ($p<0.05$). Gender peculiarities were established: boys (66.7%) were significantly more prevalent in group A, i.e. there were twice more boys among the dead ($\chi 2 = 7.679$; $p = 0.006$). In 85.7% children with NEC stage II and III who died was diagnosed perinatal hypoxia and 90.5% infants of this group have perinatal infections, $p<0.01$. The level of serum urea and creatinine in children with NEC who died was significantly higher (21.2±2.9 mmol/l and 175.8±23.7 μmol/l respectively) than in premature infants who survived with NEC (6.8±0.6 mmol/l and 76.0±6.9 μmol/l, respectively), ($p<0.01$). Odds ratio (OR) of lethal outcome in premature infants with NEC and elevated levels of urea (OR = 12.364; 95% CI: 3.415–44.768) and creatinine (OR = 8.267; 95 % CI: 2.447-27.589). In premature infants who died, one of the most frequent causes of death was acute kidney damage - in 8 (38.1%) infants, among other causes one of the most common causes was endogenous intoxication in 8 (38.1%) infants, rarely other causes.

Conclusion: Hypoxia and infections during pregnancy and during the birth of premature infants played a significant role in develop of kidney damage. Elevated levels of urea and creatinine in premature infants with NEC one of the factors that associated with mortality.

P1817 **DOES EPIGENETIC FACTORS LIKE HDAC2 PLAYS ROLE IN STEROID RESISTANCE VIA REGULATION OF P-GP AND MRP-1 IN CHILDHOOD IDIOPATHIC NEPHROTIC SYNDROME?**

HARSHIT SINGH[1], Narayan Prasad[2], Vikas Agarwal[3], Akhilesh Kumar Jaiswal[4]

[1]Sanjay Gandhi Post Graduate institute of medical Sciences, Department of Nephrology and Renal transplant, Lucknow, India, [2]Sanjay Gandhi Post Graduate institute of medical Sciences, Department of Nephrology and Renal Transplant, Lucknow, , [3]Sanjay Gandhi Post Graduate institute of medical Sciences, Department of Clinical Immunology, Lucknow, India and [4]Sanjay Gandhi Post Graduate institute of medical Sciences, department of Nephrology and renal transplant, Lucknow, India

Background and Aims: The action of glucocorticoids is to switch off activated inflammatory genes. The activated glucocorticoid receptors (GR) interact with co-repressor molecules to impair NFκB-associated co-activator activity, reducing histone acetylation, chromatin remodelling. Reduction in histone acetylation occurs via recruitment of histone deacetylase (HDAC) 2 to the activated inflammatory gene complex by activated GR, resulting in efficacious suppression of activated inflammatory genes within the nucleus.

To evaluate the effect HDAC 2 on P-gp and MRP-1 expression and function.

Method: Total of 78 subjects were considered in the study out of which 50 were steroid sensitive nephrotic syndrome (SSNS), and 28 were steroid resistant nephrotic syndrome (SRNS) patients. mRNA expression was analyzed on peripheral blood mononuclear cells (PBMCs) in SRNS patients (mean age 8.43±3.8 years), SSNS patients (mean age 7.54±3.5 years). PBMCs were treated with 1μM of Theophylline (HDAC2 stimulator) and 0.8μM of Trichostatin A (HDAC2 inhibitor) for a period of 48 hours. Quantitative PCR was performed using light cycler LC480 using SYBR green PCR technology with SYBR premix relative gene expression levels were calculated and normalized to the corresponding levels of the housekeeping gene (GAPDH).

Results: Expression of P-gp (4.79±0.970 v/s 2.13±0.72, $p<0.0001$) and MRP-1 (3.99 ±0.8 v/s 1.99 ±0.91, $p<0.0001$) on PBMCs was increased in SRNS as compared to that of SSNS. HDAC2 mRNA levels were significantly decreased in SRNS patients as compared to that of SSNS patients (2.97 ± 0.95 v/s 6.02 ± 1.13, $p<0.0001$).

Theophylline(HDAC stimulator) for a period of 48 hours decreased mRNA levels of P-gp and MRP-1 in PBMCs of SRNS with maximal induction at 1μM (fold change 2.65 and 2.21, *$p<0.0001$) However HDAC2 mRNA expression increased significantly (fold change5.67, *$p<0.0001$). In SSNS patients P-gp and MRP-1 mRNA expression decreased at1μM (fold change 1.25, 1.24, *$p<0.0001$) while the mRNA expression was increased (fold change 6.93, *$p<0.0001$).

TSA(HDAC inhibitor) for a period of 48 hours increased mRNA levels of P-gp and MRP-1 in PBMCs of SRNS with maximal induction at 0.8μM (fold change 7.51, 7.31, *$p<0.0001$) and significantly decreased the level of HDAC2 (fold change1.50, *$p<0.0001$) similarly in SSNS patients P-gp and MRP-1 mRNA expression increased at 0.8μM (fold change 3.49, 3.35, *$p<0.0001$) and HDAC2 decreased (fold change2.53, *$p<0.0001$) at 0.8μM.

The functional activity of P-gp and MRP-1 was significantly higher in SRNS group as compared to SSNS group ($p<0.001$), whereas enzymatic activity of HDAC2 was increased in SSNS group as compared to SRNS group ($p<0.001$)

Conclusion: As we observed that HDAC2 regulates P-gp and MRP-1 efflux pumps, Inducer of HDAC2 may be a probable treatment stratergy for patients of Idiopathic Nephrotic Syndrome.

P1818 **CLINICAL AND MOLECULAR CHARACTERISTICS OF CHILDREN WITH WT-1-ASSOCIATED STEROID-RESISTANT NEPHROTIC SYNDROME**

Larisa Prikhodina[1], Zilya Bashirova[1], Tatjana Lepaeva[1], Inna Povolotskaya[1], Natalia Sherbakova[1]

[1]*Research & Clinical Institute for Pediatrics, Russian National Research Medical University, Moscow, RUSSIAN FEDERATION, Inherited & Acquired Kidney Diseases, Moscow, Russia*

Background and Aims: The Wilms tumor suppressor gene 1 (*WT1*) (MIM 607102) has an important role in renal and gonadal development. *WT1* mutations was found to be associated with a large spectrum of phenotypes with autosomal-dominant inheritance, including Wilms tumor, Denys-Drash syndrome (DDS), Frasier syndrome (FS), and isolated steroid-resistant nephrotic syndrome (SRNS). The aim of the study was to investigate clinical and molecular characteristics in children with *WT1*-associated SRNS.

Method: Retrospective analysis of phenotype and genotype of six children (3M/3F) with SRNS and heterozygous *WT1* mutations was performed. Karyotypes were available in all patients. Data on renal histology had three subjects with FS. The median follow-up period was 35.5 (IQR: 20.0; 57.5) months. *WT1* mutations identified by direct Sanger sequencing (n=3) and next generation sequencing (n=3).

Results: The median age at onset of *WT1*-associated SRNS was 10.0 (IQR: 5.5; 22.5) months. 4/6 (66.7%) patients presented with infantile nephrotic syndrome and 2/6 (33.3%) with SRNS. Arterial hypertension was determined in 4/6 (66.7%) of individuals. Among children with *WT1*-associated SRNS 3/6 (50%) patients had DDS (2M/1F) and 3/6 (50%) subjects had FS (1M/2F). Children with DDS had Wilms tumor in 2/3 (66.7%) of cases and gonadal dysgenesis with hypospadias in 1/3 (33.3%) of children. Causative mutations were identified in all three patients with DDS, including 2 earlier described c.1384C>T in exon 9 and c.1098 + 1G>A in intron 6 in *WT1* gene, and one novel mutation c.1378T>G in exon 9. All DDS children had decreased eGFR to CKD stage 2-3 in two patients aged 7 and 11 years and ESKD in one child at the age of 2 years. All 3 patients with FS had focal segmental glomerulosclerosis on biopsy. Two phenotypic girls with FS had karyotype 46, XY and presented with pseudohermaphroditism. The same earlier described splice site mutation c.1432 + 5G>A in intron 9 in *WT1* gene was identified in both cases. One boy with FS had typical male chromosome pattern (46, XY) and gonadal dysgenesis. Splice site mutation c.1432 + 4C>T in intron 9 in *WT1* gene was found in the child. Nobody of patients with FS developed gonadoblastoma. Progression to CKD was found in all three cases with FS, including CKD stage 2-3 in two subjects aged 5 and 15 years and ESKD in one phenotypically girl with sex reversal developed at the age of 8 years.

Conclusion: We found that children with *WT1*-associated SRNS had a wide spectrum of renal and extrarenal phenotypes concerning the development of urogenital system and Wilms tumor with high risk of progression to CKD during childhood. Their phenotypes are clearly associated with the type and location of *WT1* mutations led to DDS or FS. Genetic *WT1* diagnostics is important in all children with SRNS for early detection, optimal treatment, tumor prevention and prognosis.

P1819 PEDIATRIC KIDNEY TRANSPLANTATION IN INDIA :IMPROVING OUTCOMES

Sanjeev Gulati[1], Rajiv Sinha[2], Vishal Saxena[3], Alok Jain[4], Amit Sharma[5], Deepak Kalra[6], Harinder Singh Gill[7]

[1]Fortis Hospital, Nephrology and Kidney Transplantation, Mohali, India, [2]Fortis Hospital, Kolkata, Pedaitric Nephrology, kolkata, India, [3]Fortis Memorial research Institute, GURGAON, India, [4]Fortis Hospital, Nephrology and Kidney Transplantation, Shalimar Bagh, India, [5]Fortis Hospital, Mohali, India, [6]Fortis Hospital, Nephrology and aKidney Transplant, Delhi, India and [7]Fortis Hospital, NBephrology and Kidney Transplanatation, MOhali, India

Background and Aims:

Renal transplantation is the modality of the choice for the management of children with end stage renal disease. It offers better quality of life, though associated with risk of rejection and infection. This study was conducted

1. to study the outcome of Pediatric renal transplant at Fortis group of hospitals over the last 12 years,
2. To evaluate incidence of infection and rejection in these patients.

Method:

This is a retrospective review of patients <= 18 years of age who underwent renal transplant at Fortis hospitals, India from 2006 to 2019.The choice of induction agent was based on the discretion of the treating team and the socioeconomic tests of the patient, All these children were treated with Tacrolimus, MMF and prednisone, At each visit they were subjected to standard haematological and biochemical tests Data on age, sex, use of immunosuppression, incidence of infection and rejection was collected. Percentage, range and median were used to represent the data.

Results:

The study group comprised of a total 120 pediatric patients underwent renal transplant between 2006-2018 at Fortis hospitals. Median age was 14 years (3-18 years) and 85 were boys and 35 were girls. The immunosuppression protocol consisted of induction by either basiliximab or ATG, followed by maintenance immunosuppression with tacrolimus, mycophenolate and steroids. 17 patients received no induction. Median creatinine at the time of discharge was 0.74 mg/dl (0.3-1.6 mg/dl). The median duration of follow up was 60 months (1-156 months). In our cohort, patient survival rate was 97.9 % and graft survival rate was 94.6 %. 18 patients had infections - UTI (8), CMV infections (7), BK virus infection (2), tuberculosis (1), varicella (1), cryptosporidium diarrhea (1) and fungal infection (1). Rate of rejection was 13.3%. Two patients had graft loss in the early post operative period, one secondary to renal vein thrombosis and other due to BK virus infection/acute tubular necrosis. Five patients lost the graft over the next 12 years due to non compliance with medications (4) and recurrence of FSGS (1). 2 patients died with functioning graft, one due to severe pancreatitis and other due to severe sepsis. One died after return to dialysis.

Conclusion:

With advances in immunosuppression, rejection rate and graft survival have improved dramatically over the last decade. Compliance with medications and regular follow up are the major contributors for satisfactory long-term outcome.

P1820

THE DEVELOPMENT OF TRANSITION SERVICES IN RENAL CARE IN SYNERGY WITH YOUNG PATIENTS, PARENTS AND PEDIATRIC AND ADULT HEALTH CARE PROVIDERS: A CO-CREATION APPROACH

Holvoet Els[1], Wim Van Biesen[1], Liesbeth Van Humbeeck[1]

[1]*UZ Ghent, Nephrology, Ghent, Belgium*

Background and Aims: Healthcare transition to adulthood is recognised as challenging for adolescents and young adults (AYA's) diagnosed with chronic kidney disease. Therefore the implementation of a transition programme adjusted to the needs of this patient population is of great importance. However, rarely are the views of young people or their families sought about the process or relevant outcome of their transition process. The aim of this study was to co-develop a transition programme that (1) enables health care providers to facilitate improving transition outcomes from the perspective of all stakeholders, and (2) enhances self-management by young people with chronic kidney disease.

Method: The development of this programme involved (1) an extensive review of currently existing best-practices (published and unpublished), and (2) understanding the current state of transition practice at our centre by means of semi-structured interviews and focus groups with patients, parents and health care providers of both pediatric and adult side.

Results: A working group was established incorporating a reflective process designed to develop a community of practice. During the process, participants' experiences, lessons learned from the review of current state of evidence and practice, and appreciation of the (changing) context within which participants were working were incorporated. Analysis revealed 6 core elements as the foundation of the transition program: the AYA as the main focus, involvement of the parents, holistic approach, flexibility, forward-looking approach, continuity in guidance and follow-up. We also identified the need to distinguish the difference between *transitioning* from child to teenager to young adult and the actual *transfer* between paediatric and adult care. The actual final proposed transition programme can be divided in 4 phases: (1) introduction of the transition process to parents and patients, (2) guiding the patient to become more independent and to gain insight in the disease and related themes, (3) managing the transfer to adult health care and (4) finalizing the transition care plan. Adequate on-going communication and collaboration between paediatric and adult care seems essential for achieving a successful program.

Conclusion: This study addressed the development of a transition programme as a multi-actor process wherein patients, parents and health care providers significantly contribute to the *transition* to adulthood and *transfer* to adult care.

P1821

25 YEARS OF GROWTH HORMONE TREATMENT IN CHILDREN WITH CHRONIC KIDNEY DISEASE IN POLAND - RESULTS OF NATIONAL MULTICENTER STUDY

Beata Leszczyńska[1], Maria Daniel[1], Anna Majcher[2], Beata Pyrzak[2], Maria Szczepanska[3], Ilona Zagozdzon[4], Anna Jander[5], Marcin Tkaczyk[5], Przemysław Sikora[6], Anna Wasilewska[7], Katarzyna Zachwieja[8], Monika Miklaszewska[8], Roman Stankiewicz[9], Wioletta Jarmuzek[10], Jacek Rubik[10], Irena Makulska[11], Małgorzata Pańczyk-Tomaszewska[1]

[1]Medical University of Warsaw, Dep of Pediatrics Nephrology, Poland, [2]Medical University of Warsaw, Dep of Pediatrics Endocrinology, Poland, [3]Medical University of Silesia, Dep of Pediatrics Nephrology, Poland, [4]Medical University of Gdańsk, Dep of Pediatrics Nephrology and Hypertension, Poland, [5]Polish Mather"s Memorial Hospital Research Institute, Dep of Pediatrics and Immunology with Nephrology Unit, Poland, [6]Medical University of Lublin, Dep of Pediatrics Nephrology, Poland, [7]Medical University of Białystok, Dep of Pediatrics Nephrology, Poland, [8]Jagiellonian University Medical Collage, Dep of Pediatrics Nephrology, Poland, [9]Provincial Polyclinic Hospital in Torun, Dep of Pediatrics Nephrology, Poland, [10]Children"s Memorial Health Institute, Dep of Pediatrics Nephrology, Kidney Transplantation and Hypertension, Poland and [11]Medical University of Wroclaw, Dep of Pediatrics Nephrology, Poland

Background and Aims: Growth retardation is one of considerable problems in children with chronic kidney disease (CKD) with a great impact on life activity and quality of life. Recombinant human growth hormone (rhGH) treatment has been used for more than 30 years to improve growth velocity and final growth in children with CKD. In Poland rhGH therapy in children with CKD is available since 1994.

The aim of the study was to assess growth velocity in all children with CKD treated with rhGH in Poland since 1994.

Method: We retrospectively analyzed 321 polish children with CKD (mean age: 10.2±7.60, 210 ♂ (65%) qualified to the rhGH therapy between 1994 and 2019. Among 321 children, 180 (56.1%) were on conservative treatment (CT), 118 (36.7%) on chronic dialysis (RRT) and 23 (7.2%) after kidney transplantation (KTx). In 240 (75%) patients who were treated continuously for at least 12 months we have evaluated: growth velocity and mean annual values of selected biochemical parameters.

Results: Mean height SDS at the beginning of the treatment was -2.73±1.04 SD, among children on CT -2.22±1.20, on RRT -2.9±1.11, after KTx -3.07±1.30. Mean time of rhGH treatment was 23±10.7 months. During one-year rhGH treatment mean growth velocity in 240 children was: 8.5 ± 2.7 cm (ΔSDS 0.78±1.02) and mean height SDS increased significantly

(-2,73±1.04 vs. -1.92±1.11, $p<0.0001$). Children on CT did not differ significantly in age vs. children on RRT (10.66±3.40 vs. 10.26±3.61 years, $p=0.972$), and growth velocity was slower in RRT group expressed in cm (7.52±2.59 vs. 9.2±2.30, $p<0.0001$) and in ΔSDS (0.4±0.83 vs. 0.72±1.15, $p=0.045$). Growth velocity (ΔSDS) correlated negatively with age of rhGH initiation in children on CT ($r=-0.40$, $p=0.008$) and on RRT ($r=-0.28$, $p=0.03$). We found no significant relation between growth velocity and sex, cause of CKD, hemoglobin, total protein, albumin, urea, creatinine, calcium, phosphorus, Ca x P, PTH and alkaline phosphatase.

Conclusion: 1. Growth hormone treatment is highly effective in children with CKD especially those who are treated consevatively. 2. Early initiation of rhGH therapy is the crucial factor determining response to the treatment in children with CKD.

P1822

CLINICAL AND BIOCHEMICAL DIFFERENCES IN PATIENTS WITH CORTICODEPENDENT, CORTICORRESISTENT NEPHROTIC SYNDROME AND FRECUENT RECAIDS THAT DEVELOPED DISEASE CHRONIC RENAL DISEASE

Alan David Belzu Rodriguez[1]

[1]*Bolivia, La Paz, La Paz, Bolivia*

Background and Aims: Nephrotic syndrome not responding to steroids (corticodependent, corticorresistant, frequent relapses) in children is a disease with significant morbidity and mortality. The evolution to chronic kidney disease has a relationship with time to histopathological diagnosis, the treatment performed, its duration, the early identification of risk factors being of utmost importance.

Method: An observational-retrospective study was carried out with transverse temporality, the universe of study was patients with a diagnosis of nephrotic syndrome from 2007 to 2017 with outcome to chronic kidney disease, information was obtained from the clinical files and their subsequent Bivariate analysis of qualitative variables with linear Chi and quantitative variables of normal distribution with ANOVA and abnormal distribution with Kruskas Wails.

Results: The clinical and biochemical differences of 121 patients with a diagnosis of non-steroidal nephrotic syndrome were determined. The clinical presentation of corticorresistant was the most frequent in 89 (73.6%), corticodependents 16 (13.2%) and frequent relapses 16 (13.2%), being the association with the major histopathological type of corticorresistant with GEFS 60 (83.3%), mesangial proliferation 13 (61.9%) and minimum changes 9 (60%) with a p 0.05. The sex that was determined most frequently were men 83 (68.6%), women 38 (31.4%) p 0.8. The age at diagnosis had a frequency of 60 (49.6%) between 2.1 to 10 years of age and 60 (49.6%) in those over 10.1 years of age p 0.7. The evolution to chronic kidney disease was determined in 27 (22.3%), being greater its relationship with GEFS 21 (29.2%), diffuse mesangial proliferation 2 (9.5%), minimum changes 1 (6.7%) p 0.05. The time of evolution to chronic kidney disease between 0 and 3 years was 20 (16.5%), between 4 and 7 years was 4 (3.3%), and greater than 7 years 3 (2.5%), finding a greater relationship with GEFS between the 0 to 3 years that were 15 (20.8%) p 0.1. It was determined that the type of treatment most commonly used were anticalcineurinics (Cyclosporine-Tacrolimus), cyclosporine in 51 (42.1%), tacrolimus in 54 (44.6%), mycophenolate 10 (8.3%), and without treatment 6 (5%) with a higher GEFS ratio of the use of cyclosporine 32 (44.4%) and tacrolimus 32 (44.4%) p.0.017. The use of ACEI and ARA II as antiproteinurics determined only ACEI in 8 (6.6%), ARA II 9 (7.4%) and IECA + ARA II in 52 (43%), none in 52 (43%), with a ratio of use of ACEI + ARA II in patients with GEFS in 35 (48.6%) p 0.5.

Conclusion: In this study, similar results were found in frequency of age, sex, progression to chronic kidney disease, histopathological type, treatment with anticalcineurinics and use of antiproteinurics in patients with nephrotic syndrome not responding to steroids to those reported in the literature, being the first in Mexico should be the beginning of different cohorts (response, duration of treatment, complications of the disease) in this type of patients.

P1823 THE ROLE OF FGF-23 IN CKD PROGRESSION IN CHILDREN

Altynay Balmukhanova[1], Kairat Kabulbayev[1], Assiya Kanatbayeva[1], Harika Alpay[2], Aigul Balmukhanova[3], Abay Shepetov[1]

[1]Asfendiyarov Kazakh National Medical University, Nephrology, Almaty, Kazakhstan, [2]Marmara University, Pediatric Nephrology, Istanbul, Turkey and [3]Asfendiyarov Kazakh National Medical University, Science and research, Almaty, Kazakhstan

Background and Aims: Chronic kidney disease (CKD) is considered a global medical and public health issue. CKD takes a special place among non-infectious diseases because of its prevalence (6-20% according to different surveys and studies) and is associated with a poor life quality, complications and high risk of mortality. In recent years, there have been new biomarkers requiring more research in this area. One of these biomarkers is Fibroblast growth factor-23 (FGF-23) which is found as a bone derived hormone and might be a predictor of progression. However, the role of FGF-23 in CKD progression in children has not been adequately studied, especially on the early stages. Nowadays, the study of FGF-23 in children and the question of the clinical importance of this marker are relevant. Therefore, **the aim of our study** was to establish the role of FGF-23 in CKD progression in children.

Method: A prospective study was conducted on 73 children with different stages of CKD and 14 healthy individuals (control group) matched by age and gender. There were approximately equal numbers of patients in study groups. An average age was 9.61±1.05 years. Exclusion criteria: active inflammatory, bone, infectious, oncological, immunological diseases, taking steroids and vitamin D supplements. Laboratory measurements included all common clinical and biochemical indicators. Serum concentration of intact FGF-23 was assessed by using the ELISA method (Biomedica Medizinprodukte GmbH, Austria). Statistical analysis was conducted in MS Excel 2016 and SPSS 18.0.

Results: The normal range of FGF-23 for this kit was 0.1-1.5 pmol/l. The average value of FGF-23 in the control group was 0.69±0.12 pmol/l. Further studies in the groups with different stages of CKD revealed that FGF-23 concentration gradually rose in parallel with stages of CKD, and it reached the maximum on the last stage. It should be noticed that the level of FGF-23 concentration on the first stage of CKD was normal (0.73±0.14 pmol/l) and the comparison with healthy individuals revealed no significant differences. What is remarkable, despite the fact that the average value of the second stage patients was normal (1.36±0.2 pmol/l), there was a statistically significant difference with the control group (p=0.008). The levels of FGF-23 on the next stages were 2.52±0.52 pmol/l, 5.42±1.61 pmol/l, and 12.16±1.55 pmol/l, respectively. The differences were considerable and proved by statistical analysis ($p<0.01$).

Conclusion: Our study showed that there is an upward trend of FGF-23 as CKD progresses from early to advanced stages. The results on the second and third stages indicate that FGF-23 should be considered as one of early biomarkers of CKD progression in children. Thus, there is a need for more studies in this area.

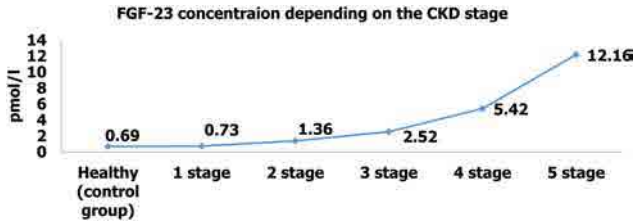


Figure:

P1824 **RETROSPECTIVE STUDY FOR THE ANALYSIS AND EVOLUTION OF RENAL FUNCTION IN A COHORT OF PATIENTS AFFECTED BY THE NEPHRONOPHTHISIS COMPLEX**

Pedro Arango Sancho[1], Víctor López Baez[1], Elena Codina Sampera[1], Yolanda Calzada Baños[1], Ana Vinuesa Jaca[1], Lina Hernández Zúñiga[1], Álvaro Madrid Aris[1]

[1]*Hospital Sant Joan de Déu, Nefrología Pediátrica, Esplugues de Lobregat, Spain*

Background and Aims: Determine evolution of renal function in nephronophthisis patient cohort, prognosis and variability of clinical presentation.

Method: Retrospective observational study to determine evolution of renal function in our cohort(n=13) between 4.5-20 years affected by different syndromes associated with nephronophthisis complex in last 20 years. We compared clinical-analytical parameters to diagnosis with current ones, including needs for kidney transplantation and results of genetics.

Results: Chronic-Kidney-Disease (CKD) prevalence at diagnosis was between 0.9-8.5 years (mean 5.3 years), staging of CKD was: 30.7% stage 2, 15.38% stage 3a and 1 patient stage 3b. 23.07% in stages 4 and 5. 69.23% needs first kidney transplantation and even a second one 15.38%. The average age at first transplantation was 6.04 years(2-11.67 years). The mean age to enter in renal replacement therapy program was 1.3 years(0.1-3.67 years). Among non-transplant, from diagnosis to present its being 0.5-7.25 years(median, 4.24 years). Most frequent symptom at the onset of the disease was delay in weight gain and height(84.61%) and also in cognitive development(53.84%), followed by polyuria-polydipsia(46.15%) and other signs/symptoms such as ataxia, pigmentary retinitis, hepatic insufficiency or skeletal alterations. In fact, in up to 54% of cases, renal involvement was a casual finding. Even with this, the most frequent form of presentation was purely renal(38.46%), followed by Joubert's Syndrome(30.77%), RHYNS(15.38%), Senior-Loken(7.7%) and Maizner-Saldino(7.7%). Currently, calculated glomerular filtration rate ranges between30.2-90.21 ml/min/1.73 m^2 among recipient, with majority in the CKD stages: 3a(56%) and in between 30-128 ml/min/1.73 m^2 among non-transplant patients, with predominance CKD 2 (50%).

Conclusion: The prognosis of renal function in the short-medium term in nephronophthisis is unfortunate. The possible initial symptomatic renal silence, the need (>50%) of multidisciplinary management and the frequency of CKD advanced to the diagnosis make necessary the knowledge of the disease and its possible associations, as well as its active search.

Presentation Forms	
Nephronophthisis	38,46% (5/13)
Joubert Syndrome	30,77% (4/13)
RHYNS Syndrome	15,38% (2/13)
Senior-Loken Syndrome	7,7% (1/13)
Maizner-Saldino Syndrome	7,7% (1/13)

	Numbers	Mean Age	Time since diagnosis	Current CKD grade
Kidney transplant				CKD IIIa 56%
First	69,23% (9/13)	6,04 years (2-11,67 years)	1,3 years (0,1-3,67 years)	–
Second or more	15,38% (2/13)	–	–	–
Not transplanted				CKD II 50%
	30,77% (4/13)	–	4,25 years (0,5-7,25)	–

Figure:

P1825 **ANALYSIS OF LATE RENAL COMPLICATIONS AND RISK FACTORS IN CHILDREN WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION**

Anar Gurbanov[1], Bora Gülhan[2], Barış Kuşkonmaz[3], Fatma Visal Okur[3], Duygu Uçkan Çetinkaya[3], Gulsah Ozdemir[2], Nesrin Taş[2], Kübra Çelegen[2], Fatih Ozaltin[2], Ali Duzova[2], Rezan Topaloglu[2]

[1]Hacettepe University School of Medicine, Pediatrics, Ankara, Turkey, [2]Hacettepe University School of Medicine, Pediatric Nephrology, Ankara, Turkey and [3]Hacettepe University School of Medicine, Pediatric Hematology, Ankara, Turkey

Background and Aims: The aim of the study is to investigate the incidence and risk factors of hypertension (HT) and chronic kidney disease (CKD) in patients who had *hematopoietic stem cell transplantation* (HSCT) during their childhood.

Method: Patients who had HSCT between January 2010-2019 with a minimum follow-up period of 6 months were included in the study. Data regarding renal complications were collected from the medical records of the patients. Guidelines of European Society of Hypertension (ESH) and American Academy of Pediatrics (APA) were used for the evaluation of hypertension. 24-hr ambulatory blood pressure monitoring (ABPM) was performed in children older than 5 years of age (68 patients). Ambulatory hypertension is diagnosed when systolic and/or diastolic blood pressure (BP) load is higher than 25%. Ambulatory prehypertension is diagnosed when mean systolic and/or diastolic BP is less than 95th percentile with systolic and/or diastolic BP load higher than 25%.

Results: A total of 72 patients (41 males and 31 females) were included in the study. The mean age of the patients at last visit was 10.8±4 years. ABPM revealed ambulatory HT in 6 patients (8.8%) and ambulatory prehypertension in 12 patients (17.6%). Office BP revealed HT in 3 patients (4.2%) and increased BP in four patients (5.6%) according to APA guideline (2017). In cohort, 12 patients with normal office BP (according to APA guideline) had ambulatory prehypertension or hypertension with ABPM. Office BP revealed HT in 1 patient (1.4%) and high-normal BP in 3 patients (4.2%) according to ESH guideline. In cohort, 15 patients with normal office BP (according to ESH guideline) had ambulatory prehypertension or hypertension with ABPM (Table 1). After a mean follow-up period of 4.4±2.5 years, CKD developed in 8 patients (11.1%). Patients with chronic graft-versus-host disease, with HLA-mismatched HSCT and/or transplantation of peripheric or cord blood hematopoietic stem cells had increased risk of CKD (p=0.041, p=0.033 and p=0.002, respectively).

Conclusion: Patients with HSCT should be regularly followed for the development of HT and ABPM should be used on regular basis. Patients with risk factors should be closely monitored for the development of CKD.

Table 1. Distribution of the patients according to the ABPM and office BP.

Office BP (APA)	**ABPM**			
	Normal (n)	Prehypertension (n)	Hypertension (n)	Total (n)
Normal (%)	49 (80.3%)	8 (13..1%)	4 (6,6%)	61 (100%)
Increased (%)	0	3 (75%)	1 (25%)	4 (100%)
Hypertension (%)	1 (33.3%)	1 (33.3%)	1 (33,3%)	3 (100%)
Total (%)	50 (73.5%)	12 (17.6%)	6 (8.8%)	68 (100%)
Of˚ce BP (ESH)				
Normal (%)	49 (76.6%)	10 (15.6%)	5 (7.8%)	64 (100%)
High-normal (%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	3 (100%)
Hypertension (%)	0	1 (100%)	0	1 (100%)
Total (%)	50 (73.5%)	12 (17.6%)	6 (8.8%)	68 (100%)

P1826

ASSESSMENT OF GROWTH PARAMETERS OF CHILDREN IN LONG TERM FOLLOW UP WITH DIFFERENT RELAPSING COURSE OF NEPHROTIC SYNDROME

Sonia Sharma[1]

[1]*Consultant Pediatric nephrology, Max Super Speciality Hospital, Shalimar Bagh, Pediatric/Pediatric nephrology, New Delhi, India*

Background and Aims: Childhood Nephrotic syndrome has its peak onset in the age group 2-4 years, and that is also a period of significant height growth. Corticosteroids and chronic diseases are known to have long term effects on growth parameters of these children. Hence we assessed and compared the growth of children with Infrequent relapsing (IFRNS) and remission (R) as group 1, Frequent -relapsing (FR), and steroid - dependent (SD) as group 2 and steroid -resistant (SR) as group 3.

Method: This retrospective single center study collected data from medical records of children presented in a pediatric nephrology clinic in a tertiary care center in New Delhi. Nephrotic children, aged 1-18 years with regular follow up in the period of 2014 to 2019 were included. Basic demographic details including age at onset and age at last follow up in clinic, sex, anthropometry details at last follow up were recorded. We traced initial height at nephrotic syndrome onset to assess growth velocity but were unavailable at the moment so excluded from analysis. Also, children completed less than 1 year follow up, and compliance issues were excluded. Z scores (standard deviation score) for weight, height and BMI were calculated. Initial comparison of three groups as FR/SDNS, IFRNS/R and SRNS was done. But in the second comparison, we combined FR/SD and SR children in one group as Difficult nephrotic syndrome (DNS) group. Anova Kruskal-Wallis test was used to find significance in three groups in table 1. Subsequent analysis was done by the non-parametric statistic method Mann-Whitney Test to assess significance in subgroups of boys and girls.

Results: : 27 IFR/R nephrotic children, 36 FR/SD, and 15 SRNS were compared as in Table1. D-NS and IFRNS-R for boys and girls ratio (11; 16) & (18; 32) followed for a median period of 18 (max 46; 12), 24.6 (57.6; 12), and 32 (50;12) months respectively.

Table 1. All patients

Parameters	FRNS median (max;min)	IFR/SR NS median (max;min)	SRNS	P value
Numbers	36	27	15	
Age of Onset (years)	3.5 (7; 1)	3.7 (11.2; 2)	3.5 (13.5;1.5)	0.69
Present age (years)	7.3 (19.1; 3.7)	5.2 (16.1; 2.8)	7.05 (16.7; 2)	0.03
Sex (Male ;Female)	26;10	16;11	5;10	
Weight SDS	-0.38 (2.2;-3.5)	-0.3 (2.9; -2.9)	0.18 (2.7;-3.1)	0.71
Height SDS	**-0.38 (1.6; -2.3)**	**0.06 (2.4; -2.2)**	**-0.65 (2.2;-3.6)**	**0.03**
BMI SDS	0.15(1.9; -3.0)	-0.3(3.1;-3.4)	0.33(2.5;-1.8)	0.33

Table 2. Boys

	D-NS	IFR/R	P value
Numbers	31	16	
Median Age (max;min)	7.6 (19.1; 2.8)	5.5 (15; 3)	
Median Weight SDS	-0.41	-0.31	0.50
Height SDS	-0.34	-0.07	0.18
BMI SDS	0.22	-0.10	0.74

Table 3. Girls

	D-NS	IR/FR	P value
Numbers	20	11	
Median Age (max;min)	7.5 (16.7;2.8)	4.3 (16.1; 2.8)	
Weight SDS	-0.14	-0.34	0.79
Height SDS	**-0.64**	**1.07**	**0.03**
BMI SDS	0.125	-0.90	0.26

Conclusion: Linear growth (height) is the most affected parameters in children in SRNS and FR/SD nephrotic syndrome. Effect is more significant in girls then in boys as they showed improvement in . No difference in weight and BMI is seen on applied statistics in two groups.

P1827 SIMPLE METHOD OF RENAL BIOPSY WITHOUT ADMISSIN IN CHILDREN

Byoung-Soo Cho[1], Hyaejin Yun[2], Sungmin Jung[3], Hyun-soon Lee[4]

[1]Dr. Cho's Kidney center, Pediatric, Seoul, Korea, Rep. of South, [2]NUR hospital, Internal medicine, Seoul, Korea, Rep. of South, [3]Dr. Cho's Kidney center, Internal medicine, Seoul, Korea, Rep. of South and [4]Korea pathology lab, Pathology, Seoul, Korea, Rep. of South

Background and Aims: Renal biopsy is an essential procedure for diagnosis and prognosis of the glomerular diseases, however needs a lot of skill and experience to do and usually requires admission for a couple of days, unless sometimes needs an embolization, transfusion, nephrectomy etc. We have an experience of more than 3,000 cases of renal biopsy without major complications such as bleeding, embolization, nephrectomy etc.. Recently we performed 309 cases of renal biopsies, whose age is under 20 year old, at the OPD level without admission.

Method: Before renal biopsy we checked bleeding tendencies and blood thinning agents were hold for more than 1 week. Kidney biopsy was done under local lidocain anesthetic at biopsy site and IV ketamine in uncooperative children. Biopsy needle was inserted under the ultrasound guide(GE LogiQ E9) at the lower pole of the kidney. We checked renal hematoma, AV-fistula formation etc. by ultrasound 3 times every one hour until go home. Biopsy materials were sent to H.S.Lee's pathology lab. All patients went home in 6 hours after procedure. As far as we know, our clinic is the world's first time try doing kidney biopsy at OPD plus pathology together, although some kidney pathology reading centers are available in some place.

IF results were reported by on-line on the day of kidney biopsy after 5 hours and LM and EM were reported by on-line within two days. All cases went home after 6 hours of procedure.

Results: We performed 309 cases of renal biopsy at OPD level without any major complications, of which 43 cases were follow up renal biopsies. No major complications were noted such as bleeding, AV fistular, embolization, nephrectomy etc.. Male to female ratio was 1.24. Age distribution was from 2 to 20 year-old.

Biopsy results were as follows; mesangial proliferative glomerulonephritis 82 cases(26.51%), IgA nephropathy 81 cases(26.2%), mild focal nonspecific glomerulonephritis 45 cases(14.6%), HSP 23 cases(7.4%), focal segmental glomerulosclerosis 17 cases(5.5%), podocyte disease 13 cases (4.2%), Alport's syndrome 10 cases(3.2%), minor glomerular change 10 cases (3.2%), MPGN 8 cases (2.6%), membranous nephropathy 6 cases(1.9%), and Lupus nephritis, C1q nephropathy, C3 nephropathy, obesity related nephropathy were 11 cases respectively and others include acute PSGN, chronic tubulointerstitial nephritis.

Conclusion: OPD level percutaneous renal biopsy in children is no more a dangerous procedure if performed exactly at lower pole of the kidney, with close follow up for 6 hours by ultrasound examination.

P1828 A PANEL OF URINE BIOMARKERS FOR EARLY KIDNEY INJURY DETECTION IN NEWBORNS

Irina Pevzner[1,2], Kirill Goryunov[2], Valentina Vtorushina[2], Vasily Popkov[1,2], Denis Silachev[1,2], Egor Plotnikov[1,2], Yulia Podurovskaya[2], Artem Burov[2], Dmitry Zorov[1,2], Gennadiy Sukhikh[2]

[1]A.N. Belozersky Institute of Physico-Chemical Biology, M.V. Lomonosov Moscow State University, Moscow, Russia and [2]V.I. Kulakov National medical research center for obstetrics, gynecology and perinatology, Moscow, Russia

Background and Aims: Neonatal kidney damage is a wide spread pathology, especially among preterm infants. Acute kidney injury (AKI) in newborns remains one of the most important problems because the features of neonatal nephrogenesis and physiology. The current clinical criteria for the diagnosis of AKI, including pediatric scales pRIFLE and nRIFLE, rely on glomerulal filtration rate (GFR), blood urea nitrogen (BUN), and serum creatinine (SCr), which are the late biomarkers detectable only within days or weeks after kidney damage occurred, and therefore have limitations when used within the first days after birth. Therefore, sensitive and specific tests for early diagnostics of kidney injury are extremely needed in neonatology. Urine biomarkers appear to be promising for early diagnosis of AKI. Quite often renal pathologies result in markedly increased (or decreased) urinary excretion of a number of protein biomarkers, indicating subclinical tubular injury while conventional AKI signs are not manifested yet.

The aim of this study was to determine clinical value of urine molecular biomarkers for the prediction of acute kidney injury in newborns.

Method: Urine samples from newborns with congenital malformation were collected on the 1st day after born, and then once a week until the 21th postnatal day. Urine samples were centrifuged, aliquoted and stored at –80°C until testing. The next urinary biomarkers were analyzed: calbindin 1, clusterin, IL-18, KIM-1, GST-π, MCP-1 and NGAL. Quantitative determination was performed with immunoassay kit Bio-Plex Pro™ RBM Human Kidney Toxicity Panel 1 (Bio-Rad Inc., USA) and Human NGAL ELISA kit (Invitrogen, Germany). Control group included five age-matched healthy infants.

Results: 8 of 20 patients showed a direct correlation of increased NGAL levels in urine (50-fold compared to control group) with high levels of C-reactive protein in the blood (3-10-fold rise above the reference level). NGAL is the most sensitive marker for assessing AKI or tubular damage. These 8 patients were further investigated for other urine biomarkers.

The IL-18 level in urine was slightly increased in 4 patients. IL-18 is proposed to be a predictor for AKI severity and mortality in children with critical illness.

KIM-1 has low basal expression in the normal kidney but its appearance is highly specific and sensitive sign for nephrotoxicity in proximal tubules. We observed the increase of KIM-1 urinary excretion for 7 patients. However, we discover the equal occurrence of decrease or increase of urine MCP-1 through studied patients. Elevated levels of urine MCP-1 were earlier observed in experimental maleate induced azotemia, LPS injection and in model of unilateral ureteral obstruction (UUO). An increase of KIM-1 and/or MCP-1 urinary excretion is known to be associated with some risk of AKI development.

We found 3-fold growth of urine clusterin in 7 children. It is noticed, that clusterin increased in damaged tubular cells during polycystic kidney disease and renal carcinoma.

Additionally, we revealed 7-fold decrease of calbindin 1 in urine of 7 patients. Calbindin 1 exclusively localized in the kidney distal nephron segment, and its decrease was discribed for models of UUO, glomerulonephritis and cisplatin nephropathy.

GST-π protein is found in cells lining the lumen of the distal tubules and is elevated in the urine of patients with sepsis, independently of accompanied AKI. We also observed 10- to 20-fold rising of urine GST-π for all 8 NGAL-positive newborns.

Conclusion: The specificity, rate of increase, and non-invasive detection of urine markers studied in this work, make them indispensable in clinical practice. However, their use in neonatology is still experimental. We showed potential applicability of wide biomarker panel for early detection and prediction of AKI in newborns.

P1829 CARDIOVASCULAR DISORDERS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

Aigul Nugmanova[1], Nuriya Meriken[1], Saule Dikanbayeva[1], Zeinep Zhumagulova[1], Zhuldyz Baidauletova[1], Khursanbek Eshankulov[1], Aigerim Kuandykova[1], Bakyt Auyezkhanov[1]

[1]*KRMU, Pediatrics, Almaty, Kazakhstan*

Background and Aims: Pathology of the cardiovascular system is the leading cause of death in patients with CKD, while determining the causes of the formation of cardiac events is often difficult.

Method: We conducted an analysis of echocardiography data performed by 50 children with CKD. On the echoCG, the final systolic and diastolic sizes of the left ventricle (FSS and FDS), the final systolic and diastolic volumes of the left ventricle (FSV and FDV) were determined; measured the thickness of the interventricular septum (IVS) and the posterior wall of the left ventricle (PWLV). Left ventricular myocardial mass (LVMM) was determined by the formula proposed by R. Devereux and N. Reichek: LVMM = 1.04x (/ IVS+PWLV+FDS/^{3}-FDS^3) - 13.6where, IVS - thickness of IVS in diastole,PWLV-thickness of PWLV in diastole, FDS-final diastolic size of the left ventricle.

Results: We conducted an analysis of echocardiography data performed by 50 children with CKD. On the echoCG, the final systolic and diastolic sizes of the left ventricle (FSS and FDS), the final systolic and diastolic volumes of the left ventricle (FSV and FDV) were determined; measured the thickness of the interventricular septum (IVS) and the posterior wall of the left ventricle (PWLV). Left ventricular myocardial mass (LVMM) was determined by the formula proposed by R. Devereux and N. Reichek: LVMM = 1.04x (/ IVS+PWLV+FDS/^{3}-FDS^3) - 13.6where, IVS - thickness of IVS in diastole,PWLV-thickness of PWLV in diastole, FDS-final diastolic size of the left ventricle.

Conclusion: The mechanisms of damage to the heart and blood vessels in patients with CKD begin to function already in the initial stage of renal failure and increase as it progresses. The need to know the data of clinical, laboratory and instrumental examination methods at the terminal stage of CKD is dictated, first of all, by the possibility of exposure to them. An important stimulus for conducting an echocardiographic examination is the early detection and correction of cardiovascular disorders, in connection with the prospect of increasing the survival of patients after kidney transplantation.

P1830 HEMODIALYSIS IN CHILDREN:NINE YEARS OF EXPERIENCE OF ALBANIAN CHILDREN HEMODIALYSIS CENTER

Ornela Xhango[1], Rezar Xhepa[1], Diamant Shtiza[1]

[1]*University Hospital Center "Mother Theresa" Tirana, Pediatrics, Tirana, Albania*

Background and Aims: Hemodialysis is one of the modalities of renal replacement therapies, which is required for patients with serious acute or chronic renal dysfunction, in consequence, with uremic toxicity and derangement of electrolytes and acid-base balance.

We started provided an hemodyalisis treatment for children in Albania, for the first time about nine years ago. We want to show you our modest experience and some statistical data about the only centre of the hemodialysis for children in Albania.

Method: All patients who received hemodyalisis treatment between September 2010 and September 2019, were enrolled in the study.

Results: 55 children with acute or chronic injury received hemodyalisis treatment over 9 years; 28 females and 27 males, aged from 6 months to 17 years old. 29 cases had acute kidney injury (14 of them due to HUS). 23 of AKI cases are completely recovered. 5 cases had fatal outcome, one left with renal sequelae. Of 26 children with chronic kidney disease, 13 of them underwent live-related renal transplantation, 3 children are left to continue their treatments abroad, one child actually is in CAPD, 2children died, the others continue the dialysis treatments. 14 children came from Kosovo.

Conclusion: Despite the limited experience, our hemodialysis center has successfully handled cases not only from Albania, but also from Kosovo.

P1831 **ABPM DIFFERENCE BETWEEN OBESE AND NON OVERWEIGHT HYPERTENSIVE CHILDREN**

Adele Corcione[1], Diletta Apuzzo[1], Deianira Pedoto[1], Giuseppina Barra[1], Luigi Annicchiarico Petruzzelli[1], Carmine Pecoraro[1], Gabriele Malgieri[1], Serena Ascione[1], Pasquale Barra[1], Annamaria Pagano[1], Lorenza Lepore[1]

[1]*A.O.R.N. Santobono-Pausilipon - Ospedale Santobono, Pediatric Nephrology, Napoli, Italy*

Background and Aims: The goal of our study was to analyze the difference in ABPM pattern in overweight and non overweight hypertensive children

Method: The ABPM were performed using Spacelab 90207 and recorded over 24h.Readings were taken every 15 minutes while awake,and every 20 minutes while asleep. In both groups were evaluated the 24h MAP,daytime MAP,nocturnal MAP, systolic and diastolic load,mean 24h SBP and DBP.

A total of 108 pts were enrolled. Pts were divided in two groups.In the first group 54 pts non overweight with primary hypertension:33 male and 21 female with mean age of 10.4 y. In the second group the obese hypertensive children, with mean age of 10.5 y, were divided into two subgroups according to BMI Z-scores:subgroup 1 BMI Z-score >2<3 n 40 pts (17 f;21m); subgroup 2 BMI Z-score >3 n (4f;10m).

Results: Systolic load was significantly higher in obese group (p 0,0409).In obese group n.12 were dipper (22,2%).Obese with BMI zscore >3 was all non dipper (n14 ;100%). In the lean group n 26 was dipper (48.1%),and 28 (51.8%) non dipper. 24 h MAP, Systolic and Diastolic load were significantly higher (p 0,0001) in the obese with BMI z score >3 compared to the lean group.

Conclusion: The statistically significant pathological pattern among obese is the increase inmean PAS and systolic load, as well as the absence of night dipping in severe obese. The increase in systolic load is already evident in obese mild.This gives a significant predictive value of cardiovascular damage to ABPM which increases with the severity of obesity worse.

P1832

IGG4 RELATED DISEASE: NEPHROPATHY AND BONE MARROW FAILURE IN A 2 YEAR-OLD CHILD

Edoardo La Porta[1,2], Filomena Pierri[3], Isabella Pisani[4], Francesco Paolo Pilato[5], Edoardo Lanino[3], Luca Lanino[6], Angela Rita Sementa[7], Enrico Eugenio Verrina[1]

[1]I.R.C.C.S. Giannina Gaslini, Nephrology Dialysis and Transplantation, Genova, Italy, [2]ICLAS - Istituto Clinico Ligure di Alta Specialità, Nephrocardiology, Rapallo, Italy, [3]Istituto Giannina Gaslini, Bone Marrow Transplantation Unit, Genova, Italy, [4]Azienda Ospedaliero-Universitaria di Parma, Nephrology Dept., Parma, Italy, [5]Azienda Ospedaliero-Universitaria di Parma, Pathology Unit, Parma, Italy, [6]Di.M.I. - Dipartimento di Medicina Interna e Specialità Mediche, Genova, Italy and [7]I.R.C.C.S. Giannina Gaslini, Pathology Unit, Genova, Italy

Background and Aims:

IgG4 related disease (IgG4 RD) is a recently recognized systemic immune-mediated disorder. Pathophysiology of the disease is still unclear. It is characterized by fibro-inflammatory damage of the tissues, IgG-4 positive plasma-cells and often by elevated serum IgG4. This systemic disease can potentially affect every organ. Renal involvement can include tubulo-interstitial nephritis (TIN), membranous glomerulopathy (MGP) and retroperitoneal fibrosis.

The epidemiology is still poorly described, but the disease seems more frequent in men over 50 years of age. Only few cases of IgG4 RD are reported in pediatric patients.

Method:

We describe the first case of IgG4 related kidney disease (IgG4 RKD) in a child with concomitant bone marrow failure.

Results:

M.C., a 2 year-old child, was diagnosed in 2017 with a trilinear bone marrow failure (HB 7.2 g/dL; PLT 6.000/mmc; PMC 923/mmc). Bone marrow biopsy showed poor and dyshomogeneous cellularity (20%) and lymphoplasmacytic infiltrate organized in two follicular structures. All investigations performed to rule out inherited bone marrow failure were negative (DEB test, telomere lenght measurement, c-Mpl mutation analysis, mithocondrial DNA analysis)

IgG subclass analysis showed elevated serum levels of IgG4 subclass (353 mg/dL- normal level $<$ 120 mg/dL).

During the hospitalization, kidney failure with tubular acidosis was also found (creatinine 1.3 mg/dL, eGFR 28.5 mL/min/1.73 mq, bicarbonate 8.3 mEq/L). Urine analysis showed microematuria, proteinuria (1.07 g/L) and granular casts. Renal ultrasound did not demonstrate abnormal findings.

A renal biopsy was performed and a kidney sample with up to 40 glomeruli was obtained. Light microscopy (H&E, JSM, PAS and Masson's trichrome stains) showed tubule-interstitial inflammatory infiltrate (mainly composed of lymphoplasmacytic cells), irregular thickening of the glomerular basement membranes. IHC stains for C4D showed subepithelial deposits (++).

IF was negative for IgA, IgM, C4 and C1q while showed subepithelial glomerular membrane IgG deposits (+++) with granular pattern and tubular wall deposits; glomerular deposits (+) and focal tubular deposits (+++) of C3.

A diagnosis of MGP associated with TIN was made. IHC staining for IgG4 was also performed, which demonstrated plasmacells with overlapping positivity for IgG and IgG4.

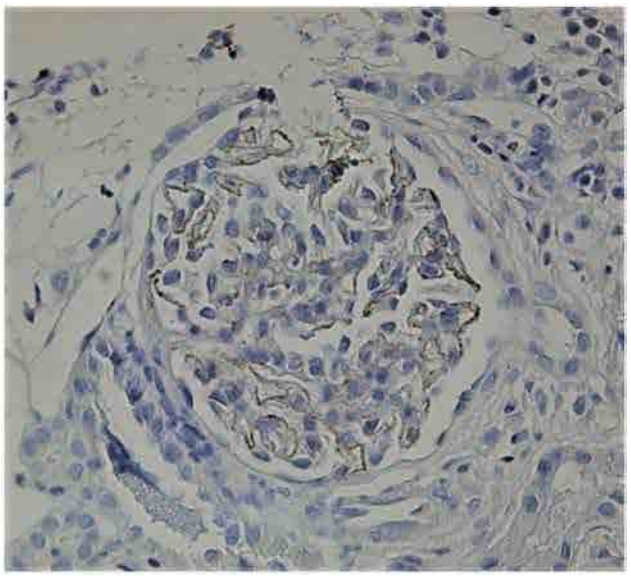


Fig 1. C4d granular deposits in the sub-endothelial GBM. *C4d IHC X 600*

After the diagnosis of IgG4 RKD, an immune-suppressive therapy with steroids (1 mg/kg/die)– targeting both the haematological disorder and glomerulopathy - was started, without clinical response. Thereafter the patient underwent bone marrow transplant from HLA-identical family donor.

Conclusion:

GMP indeed is a very uncommon disease in childhood. Moreover, the association of GMP with TIN is reported in few cases in the literature. Only in the last decade some case of TIN and GMP have been recognized as IgG4 RD and few cases have been reported in adults of IgG4 RKD with simultaneous TIN and GMP. To exclude primary GMP we will perform also the research of antiPLA2r1 antibodies in kidney biopsy. However, the specificity of antiPLA2r in children is lower than in adults and the association of primary GMP with IgG4 TIN is unlikely. IgG4 RD is an emerging systemic disease and it should be taken into account in differential diagnosis in systemic autoimmune diseases, also in the pediatric age. IgG4 RKD and bone marrow failure IgG4 RD are very rare in children but its real incidence among pediatric patients could be still underestimated.

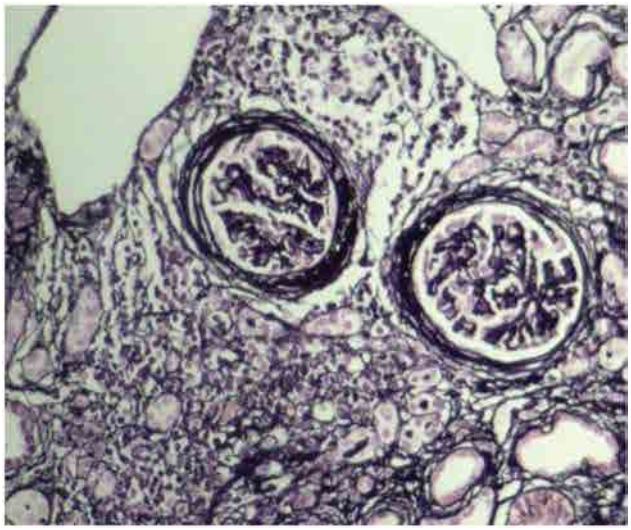


Fig 2. Thickening of the capillary wall and GBM. Bowman capsule enlargement and reduplication. *JSM X200*

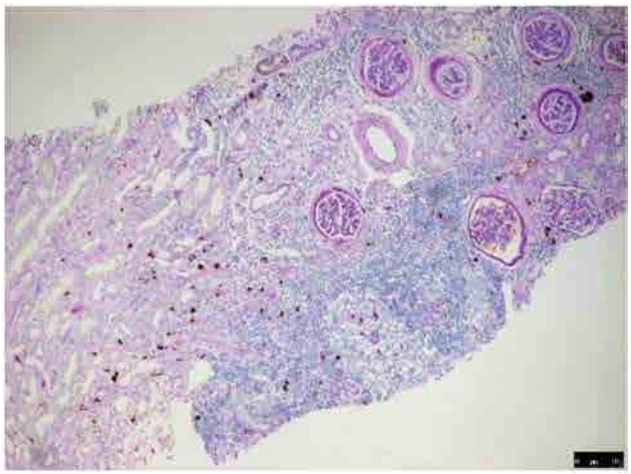


Fig 3. Interstitial and peri-tubular IgG4 deposits. Tubular atrophy and interstitial fibrosis. Focal and periglomerular lympho-plasmacytic infiltrate. *PAS+ IgG4 IHC. X100*

P1833 **HOW DO WE DEFINE HYPERCALCIURIA IN 24 HR URINE?**

Hyowon Choi[1], Mee Kyung Namgoong[1]

[1]*Yonsei University Wonju Severance Christian Hospital, pediatrics, Weonju, Korea, Rep. of South*

Background and Aims:

Hypercalciuria can clinically present itself as gross hematuria, microscopic hematuria, dysuria or abdominal pain without urinary lithiasis. It is also one of main metabolic causes of urinary lithiasis in children. In Nelson pediatrics, hypercalciuria is defined by a 24 -hour urine for calcium excretion>4mg/kg/day. A spot urine calcium creatinine ratio of >0.2, is considered abnormal in older children and adolescents. Both of them are not a standardized detect in children. Fasting and postprandial spot urinary calcium creatinine ratios may not detect hypercalciuria so accurately, that a 24-hour urine is preferred. In addition, 24hr urine collection is frequently under- or over-collected, which leads to an inadequate sampling hard to pick up which one the more accurate calculating methodology for the hypercalciuria detection with 24hr urine is. In this study, we evaluated the comparisons of 24 hr urine calcium creatinine ratio(Ca/Cr), 24hr urine calcium excretion(mg/kg)(Ca/Kg) and CCCR in school aged children.

24-hour urine for calcium excretion>4mg/kg/day

24-hour urine calcium creatinine ratio of >0.2

Calcium creatinine clearance ratio(CCCR); (24-hour U-calcium/P-total calcium) / (24-hour U-creatinine/P-creatinine), as known as fractional excretion of calcium(FeCa)

Method:

We enrolled 250 normal kidney function patients who's age is 7 to 18 year, was able to collect 24 hr urine in a single hospital unit. We conducted 24 hr urine collection, serum calcium creatinine levels on the same day from January 2007 to December 2019. We analyze of each values. We used SPSS. 25.0

Results:

Table 1. Mean(+2SD) values according to calculating method

age	7-9 yr		10-12 yr		13-15yr		16-18yr		Total
sex	M(n53)	F(n34)	M(n33)	F(n25)	M(n48)	F(n28)	M(n14)	F(n15)	(n250)
Ca/kg	1.81(5.47)	1.81(4.70)	2.4(8.67)	2.12(6.06)	1.74(8.73	1.83(5.53)	1.48(3.69)	1.06(2.48)	1.84(6.50)
Uca/Cr	0.10(0.28)	0.15(0.49)	0.16(0.6)	0.14(0.39)	0.10(0.50)	0.13(0.36)	0.08(0.23)	0.15(0.72)	0.13(0.46)
CCCR	0.005(0.014)	0.006(0.018)	0.009(0.033)	0.007(0.018)	0.007(0.046)	0.007(0.014)	0.006(0.017)	0.009(0.039)	0.007(0.028)

The mean and 95% values were shown in table 1. Also frequencies of hypercalciuria which met each criteria were shown in table 2. Based on kappa statistics, Ca/Kg and Ca/Cr, Ca/Kg and CCCR, CCCR and Ca/Cr were relevant with each other. (P=0.01)(P=0.01)(P=0.01) In case of CCCR > 1% and Ca/Cr > 0.2mg/mg, kappa value was 0.807(+/- 0.050), which is almost perfect agreement. But in case of CCCR > 1% and Ca/Kg, Ca/Cr and Ca/Kg, each kappa value was 0.541(+/-0.077), 0.499(+/- 0.076), which is moderate agreement. But when we use CCCR > 2% criteria, agreement with Ca/Cr was fair. (kappa value=0.281 +/-0.080) Also agreement with Ca/Kg was fair too(Kappa value=0.370 +/- 0.113).

Table 2. Frequency of hypercalciuria according to calculating method

	7-9 yr	10-12 yr	13-15yr	16-18yr	Total	**Satisfied both criteria**		**Satisfied all criteria**
Ca/Cr	15(17.2%)	16(27.6%)	9(11.8%)	2(6.9%)	42(16.7%)	13(5.2%)		6(2.4%%)
Ca/Kg	10(11.5%)	8(13.8%)	3(3.9%)	1(3.4%)	22(8.8%)		2(0.8%)	18(7.2%)
CCCR 2%	2(2.3%)	3(5.2%)	1(1.3%)	2(6.9%)	8(3.2%)		37(14.8%)	
CCCR 1%	16(18.4%)	15(25.9%)	11(14.5%)	4(13.8%)	46(18.4%)			

Conclusion:

24hr urine calcium / Kg shows less agreement with other values.

P1834 MONITORING ANTICOAGULATION IN PEDIATRIC PATIENTS ON REGULAR HEMODIALYSIS: CAN A DREAM COME TRUE?

Ihab Elhakim[1], M.Said Ragia[2], Ahmed Baranek[3]

[1]Ain Shams University, Pediatrics, Pediatric Nephrology, Cairo, Egypt and [3]Minstry of Health and Population, pediatrics, Cairo, Egypt

Background and Aims: Anticoagulation in hemodialysis aims at preventing the activation of coagulation cascade during the procedure. Appropriate anticoagulation for hemodialysis (HD) requires a precise balance between under- and over-heparinization to prevent extracorporeal circuit (ECC) clotting and bleeding, respectively. This type of balance is practiced in hemodialysis centers, on daily basis, depending on each center's experience and tailored to every patient, rather than in accordance to a clear guideline. Our aim was to objectively evaluate the adequacy of heparin therapy used for anticoagulation in pediatric patients on regular hemodialysis.

Method: A follow up observational study for 12 months including 44 pediatric end stage renal disease patients on regular hemodialysis through an A-V fistula or an A-V graft. We excluded patients with a known bleeding disorder, chronic liver disease, thrombophilia, vasculitis or receiving anticoagulation for any condition. All patients were subjected to thorough history taking including dialysis history, assessment of dialysis adequacy by calculating Kt/V and blood pressure monitoring before, during and after session. Clinical evaluation of anticoagulation was done through visual inspection of extra-corporeal circuit, observing transmembrane pressure and recording the duration of compression over the puncture site at the end of the hemodialysis session. Biological monitoring was done by Bedside Activated clotting time (ACT) test.

Results: On initial evaluation of patients, 11 cases had either clotting or bleeding clinically (only 4 had abnormal ACT values), being on either hemodialysis (HD) or hemodiafilteration (HDF) and receiving unfractionated heparin (UFH) either as a bolus or through a pump. They were further evaluated after being put; on HDF and a heparin pump and showed neither clotting nor bleeding though 2 cases had prolonged predialysis ACT values. On HDF and heparin bolus, no bleeding or clotting were detected though 3 cases had abnormal predialysis ACT values. On HD and heparin pump no bleeding or clotting were detected, 2 cases had low kt/V, a case had abnormal ACT values (5 minutes, 1 hour and at the end ACT values).

Conclusion: Hemodialysis mode, rather than method of heparin delivery, had a bigger impact on correcting clinical defects of anticoagulation in our patients. ACT as a bedside test of anticoagulation adequacy during HD sessions did not offer extra benefit over clinical evaluation, which is still considered a more accurate method.

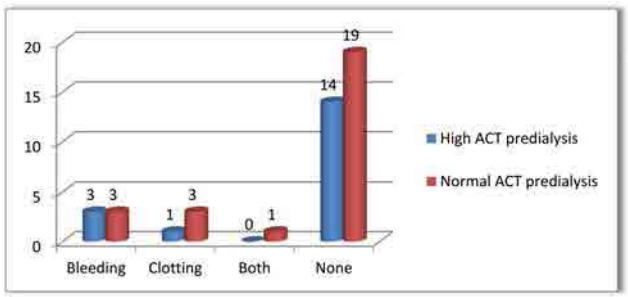


Figure: *Figure (1): ACT monitoring of cases*

P1835 PREDICTION OF CHRONIC OF KIDNEY FAILURE BASED ON ARTIFICIAL INTELLIGENCE SYSTEM USING THE FUZZY DECISION TREE ALGORITHM

Rifaldy Fajar[1], Prihantini Jupri[1]

[1]*Universitas Negeri Yogyakarta, Computational Biology, Sleman, Indonesia*

Background and Aims:

Chronic kidney disease is one type of disease that can cause death. Until now, chronic kidney failure has no antidote, so this disease cannot be cured but can be slowed down or stopped its development. Early diagnosis of this disease will help to prevent these fatal consequences. To diagnose this disease, several laboratory tests are needed in which the results of these tests will be calculated and concluded the results by a doctor or medical practitioner. The development of science and technology, especially in the field of computers will help the work of doctors to analyze the results of laboratory tests become easier and faster. In this study, a prediction attempt is made using the Fuzzy Decision Tree classification algorithm, which is expected to obtain high accuracy results.

Method:

This study uses the Chronic Kidney Disease (CKD) dataset taken from the UCI Machine Learning Repository. Data was collected from the hospital for approximately two months. This dataset covers a total of 400 samples with numerical attributes totaling 11 columns and nominal totaling 14 columns. Data samples were provided as many as 400 rows with 250 samples being the ckd group (positive for chronic kidney failure) and 150 samples for the notckd group (chronic kidney failure). But after going through the preprocessing stage, data that can be used amounted to 158 rows with 43 samples are the ckd group (positive chronic kidney failure) and 115 samples of the notckd group (negative chronic kidney failure).

Results:

The trial was conducted using several predetermined thresholds and the most optimal accuracy was 98.3%, which showed a fairly high degree of accuracy.

Conclusion:

Thus, it can be concluded that the Fuzzy Decision Tree algorithm can be said to be able to predict chronic kidney failure with a very good results.

HISTORY OF NEPHROLOGY

P1840 EVOLUTION OF FACTORS ASSOCIATED WITH THE DEVELOPMENT OF CALCIPHYLAXIS AFTER KIDNEY TRANSPLANTATION

Elena Guillen Olmos[1], Jose-Vicente Torregrosa[1], Fritz Diekmann[1], David Cucchiari[1]

[1]*Hospital Clínic, Renal Transplant Unit, Barcelona, Spain*

Background and Aims: Calciphylaxis, also known as calcific uremic arteriolopathy (CUA), is a rare and underdiagnosed condition usually associated with end-stage renal disease (ESRD), with a poor prognosis once established. Although typically related with ESRD vintage, there are some reports of CUA after kidney transplantation (KT). The development of CUA in patients with KT is uncommon, and the underlying factors for its development remain unclear.

Method: Revision of the factors associated with the development of CUA after KT in 37 cases, of which 8 cases were extrapolated from our local registry and 29 cases reported by the literature from 1969 to 2019. Differences between groups were analyzed with Student's T-test and Fisher's exact test, according to the studied variable (continuous/dichotomous).

Results: Demographic and baseline characteristics are displayed in Table 1. In the whole population, 52.8% of patients were men and mean age was of 46.95 ± 18.72 years. Diabetes mellitus was present in 36.4% of patients while only 5.3% were reported to be obese. Vitamin K inhibitors were used in almost half of the population (45.5%). Creatinine at diagnosis was 3.14 ± 3.63 mg/dl. Dialysis and transplant vintage were respectively 76.97 ± 141.90 and 29.54 ± 56.11 months. Mean PTH was 631.15 ± 502.64 and previous parathyroidectomy was performed in 21.6% of patients. It has to be highlighted that 28.0% of total population had PTH levels < 100 pg/ml at diagnosis. Total calcium was 9.69 ± 1.04 mg/dl and phosphorus 4.16 ± 1.51 mg/dl. Many of these factors differed greatly depending on the time period of the diagnosis (before or after 1990). Patients diagnosed before 1990 were younger than those diagnosed after 1990 (31.57 ± 10.19 years vs. 56.30 ± 16.44 years; $p < 0.001$). Creatinine at diagnosis was much lower in patients diagnosed before 1990 (1.44 ± 0.58 vs. 3.68 ± 4.03). Dialysis and transplant vintage were greater in cases diagnosed after 1990 (dialysis plus transplant vintage 19.87 ± 12.65 vs. 115.04 ± 174.14, p=0.02). Patients diagnosed after 1990 had higher phosphorus and lower calcium compared to the other group. The employed immunosuppression changed considerably during time, being based on azathioprine (90.9%) and prednisone (100.0%) before 1990 and on calcineurin inhibitors (76.5%), mycophenolic acid (41.2%) and/or mTOR inhibitors (41.2%) and steroids (82.4%) after 1990. The CUA treatment demonstrated great variability too. Before 1990, 76.9% of patients were submitted to therapeutic parathyroidectomy, while after 1990 it was only performed in 10.5% of patients (P<0.01). Tiosulphate was administered in 31.6% and biphosphonates in 36.8% of cases. Mortality was similar in both groups (57.1% and 52.2% for patients diagnosed before and after 1990 respectively).

Conclusion: Factors associated with the development of CUA after KT varied greatly during time. Patients diagnosed before 1990 were younger, with better renal function, shorter dialysis and transplant vintage, higher calcium and lower phosphorus. Parathyroidectomy was the main therapeutic option before 1990 while after 1990 treatment was multimodal.

	Whole population 1969-2019 (n=37)	**Before 1990 (n=14)**	**After 1990 (n=23)**	**P-value**
Age (years)	46.95 ± 18.72	31.57 ± 10.19	56.30 ± 16.44	<0.001
Sex (%male)	52.8%	42.9%	59.1%	0.495
Obesity (%yes)	5.3%	N/A	5.3%	N/A
Diabetes mellitus (%yes)	36.4%	N/A	36.4%	N/A
Use of Vitamin K inhibitors (%yes)	45.5%	N/A	45.5%	N/A
Transplant life (months)	29.54 ± 56.11	10.80 ± 8.67	40.94 ± 68.91	0.050
Dialysis vintage (months)	76.97 ± 141.90	11.60 ± 8.69	93.81 ± 158.02	0.055
Creatinine (mg/dl)	3.14 ± 3.63	1.44 ± 0.58	3.68 ± 4.03	0.194
Total Calcium (mg/dl)	9.69 ± 1.04	10.11 ± 0.87	9.41 ± 1.07	0.050
Phosphorus (mg/dl)	4.16 ± 1.51	3.50 ± 0.86	4.55 ± 1.69	0.056
Previous parathyroidectomy (%yes)	21.6%	14.3%	26.1%	0.683
PTH (pg/ml) mean ±DS	631.15 ± 502.64	785.00 ± 510.60	601.85 ± 508.36	0.516
0-100	28.0%	25.0%	28.6%	
101-500	24.0%	0.0%	28.6%	
>500	48.0%	75.0%	42.9%	

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P1841 **THE JOURNEY OF KIDNEY TRANSPLANTATION IN EGYPT: STILL EXTRA-MILES TO GO**

Mohamed Elrggal[1], Mohamed Gendia[2], Rowan Saad Zyada[1,3], Ali Moustafa Shendi Mohamed[2]

[1]Kidney and Urology Center, Department of Nephrology, Alexandria, Egypt, [2]Faculty of Medicine, Zagazig University, Nephrology Unit, Egypt and [3]Alexandria Main University Hospital, Department of Nephrology, Alexandria, Egypt

Background and Aims: Kidney transplantation is the renal replacement therapy of choice for patients with end-stage kidney disease. Egypt is a developing country with social, religious and demographic characteristics having enormous impact on the development and progress of its own national transplant program.

Method: A web-based review of relevant bibliography: articles and textbooks, reporting the progress in the transplant practice in Egypt and its legislations was conducted.

Results: Kidney transplantation started in Egypt about 43 years ago when the first transplant was performed at Mansoura Urology and Nephrology Center (UNC) in March 1976. The practice of kidney transplantation in Egypt has then evolved over the years. While about ten thousand transplants were performed from 1976 to 2011, the annual mean number of kidney transplantation between 2011 and 2016 increased to 1100 cases/year. The number of transplant centers has also grown from 12 in 1997 to 35 currently licensed centers. However, Egypt is still lacking a national transplant registry data.

The legal framework developed over the last decade towards establishing a national transplant program. Until 2010, organ transplantation was only regulated by the professional code of ethics and conduct of the Egyptian Medical Syndicate. Representatives of the Istanbul Declaration met with the Egyptian Minister of Health and Egyptian Society of Nephrology leaders in Cairo in October 2008; since then, Egypt has been working to terminate illegal practices associated with organ transplantation, organ trafficking and transplant tourism. The first legislation for a national organ transplant program "The executive list for law number 5 of the year 2010 regarding regulating human organ transplants" was then issued after approval by the parliament. The law established "The Higher Committee for Organ Transplants" which includes 7 - 11 experts and is responsible for regulating and supervising all organ and tissue transplant procedures in the country. The new law criminalizes organ trafficking and set strict penalties for physicians, hospitals and medical facilities performing illegal organ transplant procedures. In 2017, the legislation has been further modified to make the penalties even harsher "Law number 142 of the year 2017 modification of some articles in law number 5 of the year 2010 regarding regulating human organ transplants".

Transplantation practice is still limited to live transplants. The cadaveric transplant program has not yet been put into action despite the new 2010 legislation has set the legal framework, yet lacking a clear definition of the legal death. Cadaveric transplantation was performed twice in Egypt in 1992 at Cairo (kasr El Aini hospital) from 2 criminals after execution in Alexandria. This was faced with social anger and rejection which led to legal restrictions for non-living organ procurement at that time. Barriers to establishment of a national transplant program in Egypt include cultural and religious rejection of deceased donation, organ shortage, and long waiting time in national transplant centers.

Conclusion: Despite the recent ameliorations in the current Egyptian transplant practice, the overall progress has been slow. This can be attributed to a complex interaction between social, religious and financial factors. Further advances are vital to reduce the burden implied by the state-funded dialysis therapy and to demolish organ trafficking and transplant tourism. As such, state efforts would continue to further improve the living donor and to implement the deceased donor transplantation programs.

P1842 THE HISTORY OF VETERINARY RENAL PHYSIOLOGY AND NOSOLOGY IN ANCIENT AND MIDDLE AGES GREEK TEXTS

Athanasios Diamandopoulos[1]

[1]*Louros Foundation for the History of Medicine, Board, Athens, Greece*

ackground and Aims: Background and Aims: To present the ideas of Ancient and Byzantine Greek authors about the renal anatomy, physiology and nosology of mammals, birds, insects and fishes.

Method: Method: We searched for the appropriate passages in the works of Aristotle, Aristophanes Byzantius, Galen, Cladius Aelianus, Alexander Aphrodisiensis, Basilius Caesariensis, Gregorius Nyssensus, Nemesius Emesenus, Hippiatrica Berolinensia, Hippiatrica Parisiana, Hippiatrica Cantabergiensia, Michael Ephesius and Michael Glycas. These texts extended from the 4th cent. BC until the 12th cent. AD.

Results: Aristotle elaborates on the varied number of kidneys in several animals and on the abundance of perirenal fat. The last tissue is essential for protecting and warming the animal but, in excess, it may be lethal, as in the case of sheep. He then describes the multilubular kidneys of some animals and the supposed lack of a bladder in birds and marine animals, with the exception of the sea turtle. Aristophanes adds the issue of the deer's ectopic kidneys and their number in canines. Basilius and Gregorius elaborate on the minute details of some animals' organs, like the kidneys and feathers of flying ants and the moral rationale of all these. Nemesius discusses the possibility of some animals surviving without kidneys. The monumental work "Hippiatrica" deals exclusively with horse health and refers, inter alia, to kidney afflictions. It describes the clinical signs of what it calls "nephritis", with oedema and predominating neurological symptoms. For treatment it recommends several methods of causing renal hyperaemia, like massaging, ointments, warm rooms, heated irons, but also bloodletting. Michael Ephesius returns on the absence of proper kidneys in birds and their substitution with kidney-like organs called "nephroids". Glycas "justifies" the lack of bladder and kidneys in birds as useless because they secrete their excess water via the feathers, a long flying time and watery stools.

Conclusion: The Ancient and Byzantine Greek authors had understood well several topics of the anatomy, physiology and nosology of the veterinary renal system but they also made some very great mistakes. We will present the above conclusions in length.

P1843 NEPHROLOGICAL THEMATOLOGY IN PUBLICATIONS DIACHRONICALLY APPEARING IN THE PUBMED BIBLIOGRAPHICAL DATABASE

Ioannis Stefanidis[1], Athanasios Diamandopoulos[2]

[1]University of Thessaly, Nephrology, Larissa, Greece and [2]Louros Foundation, Athens, Greece

Background and Aims:

Nephrology is a medical specialty, which in the last 50 years experienced very important scientific developments, which formally revolutionized clinical practice, namely renal biopsy, renal replacement therapy and transplantation. In addition understanding pathogenesis and clinic of renal disease also improves steadily, resulting in renewal of definitions, classifications and therapeutics in nephrology. In this context publications with nephrological content are also expanding. The aim of this bibliography-study was to analyze the publications, related to nephrology specific keywords, as they appear in the PubMed database.

Method:

Certain nephrology related keywords were applied: "nephrology", "acute renal failure", "renal biopsy", "hemodialysis", "peritoneal dialysis" and "renal transplantation" were applied as terms in PubMed. Instead of renal kidney was used as an alternative term.

Results:

Nephrology as a term appears 141573 times in the database and beginning from 1946 its appearance is expanding in the last three decades. The term "acute renal failure" is found for the time in 1932 in one publication and in a total number 92278 of publications. Renal biopsy appears from 1943 in a total number of 15506 publications. Hemodialysis appears in 182730 citations for the first time in 1915 in human application. Peritoneal dialysis appears in 32266 citations for the first time in 1901 and 1946 in human application. One publication on renal transplantation appears in 1946 and the total number of publications related to renal transplantation is 106075.

Conclusion:

According to the above findings there is a clear expansion of nephrological publications in the last decades. In addition, hemodialysis remains still the most frequent term used in nephrology related publications. Historical analysis the PubMed database is very useful as a tool to understand the research and publication trends in nephrology, as we approach to the new era of precision medicine.

P1844 **QUOTATIONS FROM AHRUN AL-QASS RELATED TO THE GENITOURINARY SYSTEM DISEASES IN RHAZES'S LIBER CONTINENS**

Ahmet ACIDUMAN[1], Çağatay AŞKİT[2]

[1]Ankara University, Faculty of Medicine, Department of History of Medicine and Ethics, Ankara, Turkey and [2]Ankara University, Faculty of Languages, History and Geography, Department of Ancient Languages and Cultures, Sub-Department of Latin Language and Literature, Ankara, Turkey

Background and Aims: Ahrun al-Qass "the priest", one of the last Alexandrian physicians before the Islamic era and probably a contemporary of Paul of Aegina, composed an enormous *Medical Pandect* (*Kunnāsh fī al-Tibb*) containing 30 books. This work is considered to have been originally written in Greek and later to have translated into Syriac. It became one of the important sources of medicine throughout the Islamic world after having been translated from Syriac into Arabic by Māsarjawayh. Some fragments of this lost work have survived in *Kitāb al-Hāwī*/*Liber Continens*. The purpose of this study is to present the Ahrun's fragments related to the genitourinary system diseases existing in Rhazes's abovementioned work and to introduce them to the history of medicine in the English language.

Method: The quotations from Ahrun related to the genitourinary system diseases in the 10th book of *Kitāb al-Hāwī*, entitled as "fī amrāḍ al-kulā wa majārī al-bawl wa ghayrihā" are identified via the Arabic and Latin text. Consequently, they are compared to each other and translated into English.

Results: The quotations, in which Rhazes mentioned Ahrun's name, are related to the genitourinary system diseases such as kidney ulcers, kidney and bladder stones and their treatment, urinary retention, diabetes, involuntarily flow of sperm and its treatment. Some of these quotations also have Rhazes's comments.

Conclusion: In this study, fragments of Ahrun al-Qass related to the genitourinary system diseases and Rhazes's comments on them in *Liber Continens* are discussed and registered to the literature in the field of history of medicine in the English language.

P1845 **HISTORY AND FUTURE PERSPECTIVES OF PAROXYSMAL NOCTURNAL HEMOGLOBINURIA**

Guido Gembillo[1], Guido Bellinghieri[1], Vincenzo Savica[2], Ersilia Satta[3], Rossella Siligato[1], Antonino Salvo[1], Domenico Santoro[1]

[1]Policlinic G. Martino, Department of Clinical and Experimental Medicine, Unit of Nephrology and Dialysis, Italy, [2]A. Monroy Institute of Biomedicine and Molecular Immunology, National Research Council, Palermo, Italy. and [3]Nefrocenter Research Network

Background and Aims: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal disorder that affects about 1-1,5 cases per million individuals, characterized by hemolysis, peripheral blood cytopenia, bone marrow dysfunction, thrombosis, renal impairment and arterial and pulmonary hypertension.

The first case of PNH was probably described in 1793 by a surgeon, Dr Charles Stewart, in the medical commentaries "Account of a singular periodical discharge of blood from the urethra". In the following decades several cases have been reported by the most eminent physicians and scientists of the time.

Method: In 1882 Paul Strübing was the first to identify PNH as a new disease entity. Hijmans in 1911 considered the possibility that the complement system mediated the hemolysis of PNH erythrocytes and in the same year, Italian scientists Ettore Marchiafava and Nazari scrupulously described the pathogenesis of the affection.

In the 1925 Enneking introduced for the first time the name "paroxysmal nocturnal hemoglobinuria", to define this pathology.

Results: Despite the increased knowledge of this syndrome, therapies for PNH were still only experimental and symptomatic, with the use of antimicrobial agents, corticosteroids and blood transfusions. The natural history of PNH changed remarkably only in the 2007, with the introduction of Eculizumab complement blockade agent. The Ravulizumab, a long-acting C5 complement inhibitor approved on December 2018 by the U.S. food and drug Administration (FDA), and on July 2019 by the European Commission, represent a new promising instrument for PNH treatment.

Conclusion: Second generation of anti-complement agents are currently under investigation, representing future promising instruments for the treatment of PNH.

P1846 HISTORY OF ARTIFICIAL INTELLIGENCE AND ITS APPLICATION IN NEPHROLOGY

Danijela Tasic[1], Milos Milovancevic[2], Katarina Djordjevic[3], Slobodanka Galovic[4], Zorica Dimitrijevic[5], Branka Mitic[6], Stevan Glogovac[7]

[1]Univeristy of Nis, faculty of medicine, CC Nis, Clinic of nephrology, Nis, Serbia, [2]Univeristy of Nis, Faculty of Mechanical Engineering, Nis, Serbia, [3]University of Belgrade, Faculty of Physics, Belgrade, Serbia, [4]Institute of Nuclear Sciences "Vinca", University of Belgrade, Belgrade, Serbia, [5]University of Nis CC Nis faculty of Medicine, Clinic of nephrology, Nis, Serbia, [6]Univeristy of Nis Facultty of medicine, CC Nis Clinic of nephrology, Nis, Serbia and [7]Clinical center Nis, Clinic of nephrology, Nis, Serbia

Background and Aims: The application of artificial intelligence and neural networks in medicine is used to help solve problems that cannot be handled by the classical approach. The common name "cybernetics" encompassed the fields of management, information technology and biomedicine, but these disciplines continued to evolve independently due to the explosion of new knowledge. Over time, the development of neural networks has been turbulent and is now widely used in various fields of medicine and even in nephrology.

The aim of the paper is to analyze the history of the development of artificial intelligence and its application in nephrology.

Method: Data were collected from books, magazines, encyclopedias and databases.

Results: Basic research on cybernetics and medicine was done by Golgi and Kelley doctors after Isaak Newton and Hermann von Helmholtz. The first theoretical mathematical models were derived in 1943 by Warren Mc Culloch and Walter Pitts. A few years later, a more contemporary contribution to the development of neural networks was given by Norbert Wiener and John von Neumann because they thought that research into biomedicine based on human brain function would be very interesting. In addition, in 1948 Norbert Wiener was the first to publish a work explaining the term cybernetics. At that time, the first experiments were made and new theories in the field of artificial intelligence were put forward by Marvin Misnki. The first training of neurons and the basis of all methods for training neurons was described by the Canadian Donald O Hebb. After the first successful neurocomputer in 1957, on which Rosenblatt worked, scientists have perfected various models of neural networks to this day. So far, mostly retrospective studies have been done in clinical nephrology, transplantation and dialysis with the help of algorithms used in neural networks.

Particularly complex nephrologic patient relationships as well as assistance with timely implementation of new good clinical practice guidelines, patient prediction in at least the next month, and patient selection for palliative care are just some segments in nephrology that require the introduction of such tools into daily clinical practice with the aim of sensitive patient populations have better treatment outcomes, with physicians having more comprehensive insight and control over the mass of data.

Conclusion: Today's application of artificial intelligence in nephrology is based on retrospective research. The dizzying rise in technological development so far will allow the use of cybernetics and available tools based on neural network algorithms to enable and improve the nephrologists' dedication and effectiveness.

PATIENT EDUCATION RESEARCH AND TRAINING IN NEPHROLOGY

P1847 **IMPROVING SHARED DECISION MAKING FOR END-STAGE RENAL DISEASE PATIENTS IN THE NETHERLANDS**

Anita Van Eck van der Sluijs[1], Aase Riemann[1], Karen Prantl[2], Anna Bonenkamp[3], Brigit Van Jaarsveld[3,4], A Abrahams[1]

[1]UMC Utrecht, Nephrology and Hypertension, Utrecht, Netherlands, [2]Nierpatiënten Vereniging Nederland, Bussum, Netherlands, [3]Amsterdam UMC, locatie VUmc, Nephrology, Amsterdam, Netherlands and [4]Diapriva - Dialyse Centrum Amsterdam, Amsterdam, Netherlands

Background and Aims:

Annually, more than 2.000 end-stage renal disease (ESRD) patients in the Netherlands receive education regarding renal replacement therapies (RRT). The choice for RRT has major impact on a patient's life. Ideally, this choice is made during a process of Shared Decision Making (SDM), since this improves satisfaction of patients and quality of care. Since 2017, three decision aids for SDM are available in the Netherlands: the 3 Good Questions, Option Grids and Dutch Kidney Guide (www.nierwijzer.nl). However, it is unknown whether these decision aids are sufficiently implemented in daily practice. Therefore, we evaluated SDM and developed an SDM workshop to train centres how to implement these decision aids.

Method:

Twelve centres in the Netherlands were randomly selected and invited to participate. In these centres, the degree of SDM experienced by patients, who recently received RRT information, was measured using the SDM-Q-9 and collaboRATE questionnaires. Furthermore, SDM awareness and use of the decision aids by health care professionals was explored. Finally, we provided a 2-hour workshop for professionals with information regarding SDM and the three decision aids.

Results:

In the twelve participating centres (two academic, ten non-academic), 176 patients completed the questionnaires; 73% found the general impression of the received information (very) good, 84% found the total number of consults good, and 86% found the received amount of information good.

On a scale from 0 – 100, with a higher score indicating better SDM, the mean SDM-Q-9 score was 75±22 and the collaboRATE score 86±14. Overall, no significant difference between centres in the SDM-Q-9 and collaboRATE scores was found.

When centres with the worst SDM-Q-9 score (< 70) were compared to centres with the best score (> 77), a difference was noticed in the use of kidney-specific decision aids, i.e. Option Grids and Dutch Kidney Guide, and the eGFR level at which the information was given. Only 50% of the worst scoring centres used the decision aids compared to 100% of the best scoring centres. The majority of the worst scoring centres started at an eGFR between 20 and 30 ml/min/1.73 m^2, while the best scoring centres all started at an eGFR between 15 and 20 ml/min/1.73 m^2. In addition, best scoring centres provided information about all treatment modalities, including nocturnal haemodialysis and conservative treatment (100% of the best vs. 50% of the worst scoring centres), and more often provided information at home (67% of the best vs. 25% of the worst scoring centres).

A total of 117 health care professionals (27% physicians, 8% physician assistants, 38% nurses, 14% social workers, 13% other) completed the questionnaire; 81% found the general impression of the education process (very) good, 80% found the total number of consults good, and 56% found the amount of provided information good, while 28% found the amount too much.

Fifty-six percent of the professionals believed SDM was applied, however only 28% used the 3 Good Questions and 31 – 33% the Option Grids. The Dutch Kidney Guide was used by 51%.

Subsequently, ten of the twelve centres participated in the SDM workshop which was appreciated with a 7.5±0.4 on a scale from 0 – 10.

Conclusion:

Although patients and health care professionals are fairly satisfied with the RRT information and degree of SDM, the use of SDM decision aids by health care professionals is limited. An SDM workshop introducing the decision aids was developed to train centres how to implement them. When optimizing SDM for ESRD patients in the Netherlands, attention should be paid to providing information about all treatment options, including nocturnal haemodialysis and conservative treatment, and providing information at home, to patients with an eGFR between 15 and 20 ml/min/1.73 m^2.

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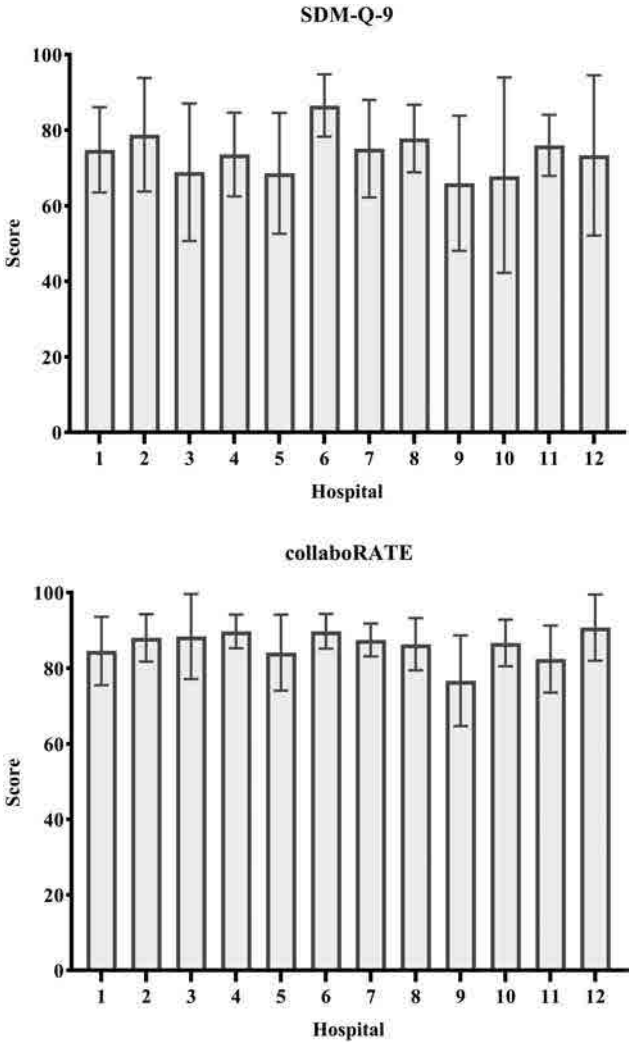


Figure:

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P1848

SUSTAINABILITY OF ACTIVE LIFESTYLE INTERVENTION BENEFITS FOR KIDNEY TRANSPLANT RECIPIENTS AFTER STUDY COMPLETION: POST-HOC ANALYSIS OF THE CAVIAR RANDOMISED CONTROLLED TRIAL

Joanne Driscoll[1], Kulli Kuningas[1], Mary Dutton[1], Edward Day[2], Adnan Sharif[1,2]

[1]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom and [2]University of Birmingham, Birmingham, United Kingdom

Background and Aims. CAVIAR (Comparing glycaemic benefits of Active Versus passive lifestyle Intervention in kidney Allograft Recipients) was a single-centre, randomised, controlled trial that recruited stable kidney transplant recipients without diabetes between 3-24 months' post-transplantation. Participants were randomly assigned to active (personalised renal dietetic-led sessions using evidence-based behaviour change techniques) versus passive lifestyle intervention (current standard of care) for a six-month intervention period. Our findings showed encouraging clinical improvements including reduction in weight (mean difference -2.47kg [-.401 to -0.92], p=0.002), fat mass (-1.537 [-2.947 to -0.127], p=0.033) and rates of post-transplantation diabetes (7.6% versus 15.6% respectively, p=0.123). However, evidence from the general population suggests lifestyle intervention behaviour change techniques must be sustained to achieve the greatest benefit. It is unclear whether the same is true for kidney transplant recipients. Therefore, the aim of this study was to conduct a post-hoc analysis of the CAVIAR study to explore 1-year study outcomes (6-months after completion of the study interventions) to explore how clinical outcomes have evolved.

Methods. The methodology of the CAVIAR study has already been summarised above and main findings published (*Kuningas et al. Transplantation 2019; early online*). Assessment of 1-year study outcomes was prespecified in the CAVIAR trial protocol to understand post-intervention outcomes. Between August 2015 and December 2017, 130 individuals were recruited to the trial and final study visits were conducted in February 2018. Electronic patient records were analysed for all study participants and 1-year outcome data (up to August 2019) were extracted in relation to cardio-metabolic risk outcomes where available. The trial is registered on clinicaltrials.org (identifier: NCT02233491).

Results. While CAVIAR participants randomised to active versus passive lifestyle intervention demonstrated beneficial weight change in the six-month study period with a negative mean difference, in the six-month period *after* study completion we observed the opposite effect with a positive mean difference (+1.23 kg [-0.05 to 2.51], p=0.060). Two participants from both active and passive intervention arms subsequently developed post-transplantation diabetes in the six-months after study closure, although difference in post-transplantation diabetes rates remained clinically significant at 1-year (10.6% versus 18.8% respectively, p=0.143). There was no significant correlation between study baseline Situational Motivation Score components (intrinsic motivation, intrinsic regulation, extrinsic regulation or amotivation) and weight change either during or after CAVIAR study completion

Conclusion. Our post-hoc analysis of the CAVIAR study suggest active lifestyle intervention using renal dietitian-led behaviour change techniques must be a continuous rather than a one-off strategy to sustain long-term clinical benefits and is unrelated to baseline motivation. This has implications for service delivery and workforce planning for established kidney transplant programs across Europe.

P1849 ANALYSIS OF ASSOCIATION BETWEEN URBANIZATION AND REDUCED RENAL FUNCTION IN INDIAN POPULATION

Rahul Kumar[1]

[1]*Sardar Bhagwan Singh PG Institute of Bio-medical Science & Research, Pharmaceutical sciences, Dehradun, India*

Background and Aims: While chronic kidney disease (CKD) is a growing public health concern in low- and middle-income countries, such as India, few studies have investigated the association between urbanization and the occurrence of CKD in those countries.

METHODS: We investigated the association between urbanization and estimated glomerular filtration rate (eGFR), an important CKD risk marker. Data came from the India Health and Nutrition Survey wave 2017, in which we collected fasting serum, individual and household data along with community level urbanization data, which was used to derive a study-specific urbanization measure, in 218 communities across fifteen states. A total of 8754 men and 8566 women participants aged 18 years or older were included in the analysis. Reduced renal function was defined as eGFR of less than 60 mL/min/1.73 m2 measured using serum creatinine concentration (mg/dL).

RESULTS: After adjusting for socio-demographic (e.g., age, education and household income), a sex-stratified multilevel logistic model revealed that living in a more urbanized community was associated with higher odds of reduced eGFR (odds ratio [OR] = 1.38 per one-standard deviation [SD] increase in the CHNS specific urbanization index, 95% confidence interval [CI] = 1.11-1.73 for men; OR = 1.35, 95% CI = 1.11-1.62 for women). After adjusting for behavioral variables (i.e., alcohol consumption, smoking, physical activity and diet), as well as obesity and cardiometabolic risk factors, the association was attenuated in men (OR = 1.25, 95% CI = 0.98-1.59), but remained statistically significant in women (OR = 1.24, 95% CI = 1.01-1.52).

CONCLUSION: Our findings suggest that living in an urban environment is linked with higher odds of reduced renal function independently of behavioral and cardiometabolic risk factors, which have been shown to increase along with urbanization.

P1850

INCREASING UPTAKE OF PERITONEAL DIALYSIS IN THE EAST OF ENGLAND: AN INDIVIDUALISED RENAL REPLACEMENT EDUCATION PROGRAMME DELIVERED IN THE HOME SETTING

Annika Wallis[1], Hsu Pheen Chong[1], Vivian Yiu[1,2], Nicola Moncrieff[2], William Petchey[1,2]

[1]*West Suffolk Hospital, Nephrology, Bury St Edmunds, United Kingdom and* [2]*Addenbrooke's Hospital, Nephrology, Cambridge, United Kingdom*

Background and Aims:

Survival on Peritoneal Dialysis (PD) is comparable to or better than in-centre haemodialysis (HD), but with the added benefit of enhanced patient autonomy, improved quality of life, and preservation of residual renal function. Despite this, only a minority of patients choose this as their first choice renal replacement therapy (RRT).

In the West Suffolk (East of England) catchment, patient preparation for RRT has historically been the remit of the tertiary referral centre (Cambridge University Hospitals NHS Trust; CUHT), who employ lecture-based group education to supplement Low Clearance Clinic (LCC) visits. Due to the growing population exceeding clinic capacity, a new LCC service was established at the West Suffolk Hospital (WSH) in December 2018. The clinic utilises a multidisciplinary team (MDT) approach involving a Consultant Nephrologist, Clinical Nurse Specialist (CNS), Dietician, Palliative Care Consultant, and a Counsellor.

To enhance uptake of PD and address the perceived barrier of lack of individualised education, the MDT agreed a 'home-first' dialysis ethos, and designed a bespoke programme to address this, with home-based 1:1 training, follow-up group meetings, and peer-networking opportunities.

Aims:

1. To assess whether an individualized approach to patient education impacts upon uptake of PD as first-choice RRT.
2. To evaluate patient satisfaction with this approach to renal replacement therapy education.

Method:

On first attendance at the WSH LCC, a 1:1 home visit is offered to discuss RRT education. All appropriate modalities of RRT are discussed, including conservative management. The CNS simultaneously assesses the environment for home therapy suitability. Regular group 'RRT Roadshows' are also offered, where the LCC MDT are available for informal question and answer sessions regarding RRT options. This helps reinforce patient education, and peer-to-peer support is offered by current dialysis patients.

Anonymised patient questionnaires have been given out prospectively following both home education/group sessions. Data regarding patient outcomes and incident RRT modality is collected as part of UK Renal Registry (UKRR) returns, with national data (90-day incident RRT modality) taken from the 21st UKRR Report 2017.

Results were analysed using Microsoft Excel and R software.

Results:

Since December 2018 WSH LCC has had 127 incident patients (Age 76 $\pm$ 13 years, 70% male); 18 have started RRT; 13 initiated HD (72%), 4 started PD (22%, none of whom were eligible for transplant), and 1 (6%) received a transplant. The PD rate is almost twice that seen in the same area previously, and above the national average (Table 1).

Table 1. RRT modality on instigation of Dialysis (% Incident population)

Initial RRT Choice	CUHT (2016-19)	UK average (2016/17)	WSH (2018/19)
HD	69	73	72
PD	13	19	22
Pre-emptive transplant	18	8	6

With regards to RRT education, 93% of patients found the home visit useful/extremely useful, compared to 76% finding the RRT Roadshow useful/extremely useful. Prior to the home visit, patient preference for RRT modality was as follows (multiple choices allowed): 27% HD, 13% PD, 13% pre-emptive transplant, 27% conservative management, and 20% were unsure. Following education, this changed to 33% for HD, 33% for PD (60% of whom had not considered PD beforehand), 13% pre-emptive Tx, 13% for conservative management, and 7% remained unsure.

Conclusion:

Initial data would suggest a personalised RRT education programme delivered at home enhances uptake and access to PD as first choice modality, over group-based education. The vast majority of patients found home-based education beneficial for shared decision making with regards to planning RRT.

Whilst the numbers are small and there are a number of confounders that need to be acknowledged, this is promising pilot data which if sustained in the coming months may suggest a strategy to increase PD numbers for other units.

P1851

INCREASING CO-MORBIDITY REDUCES A PATIENT'S ABILITY TO SELF-MANAGE: AN OBSERVATIONAL STUDY IN NON-DIALYSIS CKD PATIENTS

Katherine Memory[1], Thomas Wilkinson[1], Jared Palmer[2], Alice Smith[1]

[1]*University of Leicester, Department of Health Sciences, Leicester, United Kingdom and* [2]*University Hospitals of Leicester, United Kingdom*

Background and Aims: Co-morbidity is high in CKD patients and associated with greater mortality and disease burden. Increased burden from other health conditions, as well as CKD, may impact the successful self-management of a patient's health. A patient's perceived ability to self-manage their condition can be assessed through the concept of 'Patient Activation (PA)' which encompasses a patient's knowledge, skills, and confidence to undertake self-management tasks. Low PA is associated with poor self-reported health, greater renal impairment, and increased hospitalisation rates. Understanding PA may help the development and initiation of self-management interventions (e.g., low 'activated' individuals may require further education on their condition(s) whilst high 'activated' patients may require better support in maintaining their current lifestyle). This study aimed to assess how co-morbidity may influence PA and sought to identify which conditions, in exception to CKD, impact PA the most. This may help identify how co-morbidities affect patient's ability self-manage successfully and aid the development of individualised intervention.

Method: The Patient Activation Measure (PAM), a validated 13 item questionnaire, assessed patient activation by measuring patients perceived ability to self-manage their condition. Results categorise participants into four activation categories (1 to 4; low to high). 152 non-dialysis CKD patients (52.6% female, age 67.9 (SD:12.7) years, eGFR 42.2 (SD:18.6) ml/min) provided self-reported information about their co-morbidities, and completed the PAM. Data was analysed by general linear modelling adjusting for age, sex and eGFR.

Results: 134/152 (88.2%) of patients were multi-morbid, defined as 2 or more conditions including CKD, with a mean of 2.1 (SD:1.4) comorbidities. Increasing co-morbidities were associated with reduced PAM score (p=0.009). PAM scores decreased from 67.96 (SE:3.68) in patients with no other co-morbidities to 55.57 (SE:2.81) with 4+ co-morbidities; a reduction from PA level 4 (high) to 2 (low) respectively. The co-morbidities which explained the largest variance in PAM score were diabetes (β=-.193, p=.021), respiratory conditions (β=-.184, p=.37), and MSK conditions (β=-.154, p=.081). No other conditions were predictive of PAM score.

Conclusion: Co-morbidity in non-dialysis CKD patients is high and is associated with reduced PA (i.e. the perceived ability of patients to self-manage their condition(s)). We identified that CKD patients with diabetes, respiratory, and musculoskeletal conditions found it more difficult to self-manage their co-existing conditions. Individuals with musculoskeletal or respiratory conditions may perceive poor self-management ability due to this conditions impact on function (e.g. physical activity limitations) and/or quality of life (e.g. symptoms or sleep). Diabetes could challenge perceived self-management ability due to its chronicity, management complexity (e.g. medication regimens and side effects) and demoralising health sequelae (e.g. cardiovascular risk).

Variable	Co-morbidity count by mean (standard deviation)					P value
	0	1	2	3	4+	
PAM Score (N=144)	68.0 (SE: 3.7)	62.6 (SE: 2.4)	57.7 (SE: 2.4)	56.9 (SE: 2.4)	55.6 (SE: 2.8)	p=0.009*

P1852 REGISTRATION WITH PATIENT-FACING ONLINE HEALTH RECORDS IN CHRONIC KIDNEY DISEASE IS ASSOCIATED WITH A LOWER INCIDENCE OF HYPERKALAEMIA

Kaitlin Mayne[1], Alastair Rankin[1,2], Jennifer Lees[1,2], Jamie Traynor[1], Patrick Mark[1,2], Keith Gillis[1]

[1]Queen Elizabeth University Hospital, Glasgow Renal and Transplant Unit, Glasgow, United Kingdom and [2]University of Glasgow, British Heart Foundation Glasgow Cardiovascular Research Centre, Glasgow, United Kingdom

Background and Aims:

PatientView (https://patientview.org) is a web-based health record available throughout the United Kingdom which allows patients to review blood results and clinical communication from renal services. PatientView registration may differ across demographic groups and may be associated with improved clinical end points. We investigated the demographic factors associated with PatientView registration, and the association with incidence of severe hyperkalaemia.

Method:

A retrospective analysis was performed of a prospectively-acquired database of adults with chronic kidney disease (CKD) stages 3 – 5 in a single Scottish health board attending 2006–2017. Individual start date was point of first clinic attendance; end date was date of death, commencement of renal replacement therapy or point of data extraction. Covariates included age, sex, biochemistry, socioeconomic status and co-morbidity. The Scottish Index of Multiple Deprivation (SIMD) was used as a measure of socioeconomic status, where quintile 1 is most deprived. A survival analysis of time to severe hyperkalaemia (>6.5mmol/L) was performed with PatientView registration as a time dependent covariate.

Results:

Of 9935 patients, 967 (9.7%) were registered users of PatientView. The PatientView group had lower age in years (54.7 [42.7-65.6] vs 71.5 [62.1-78.4], $p<0.001$), estimated glomerular filtration rate (eGFR) (27.1 [18.6-38.8] vs 38.5 [28.3-51.8] ml/min/1.73m^2, $p<0.001$), and higher SIMD (indicating lower levels of deprivation) (23 vs 13% in least deprived quintile, 25 vs 37% in most deprived quintile, $p<0.001$); fewer patients were female in the PatientView group (46 vs 51%, $p<0.001$).

PatientView users had lower body mass index (29.1 $\pm$ 7.6 vs 29.8 $\pm$ 7.3 kg/m^2, $p<0.001$), and lower prevalence of diabetes (28 vs 33%, $p<0.001$), heart failure (5 vs 7%, $p<0.001$), myocardial infarction (13 vs 22%, $p<0.001$) and stroke (3 vs 6%, $p<0.001$).

On Cox regression, PatientView was associated with reduced risk of hyperkalaemia (HR 0.43, 95% CI 0.32,0.58) after adjustment for baseline eGFR, baseline serum potassium, SIMD, sex, diabetes and heart failure.

Conclusion:

PatientView use is more prevalent amongst male, middle-aged patients with higher socioeconomic status. Registration with PatientView is associated with reduced likelihood of adverse clinical events including hyperkalaemia. Limitations include lack of ethnicity data, retrospective design and drug therapy.

PatientView usage may associate with concordance to a low potassium diet, reflecting general health literacy. However, it is plausible that a causal relationship exists between Patientview usage and hyperkalaemia, by facilitating feedback on, and engagement with, lifestyle changes encouraged by healthcare providers.

Whilst there remains a lack of PatientView registration in certain demographic groups, these should be targeted via quality improvement initiatives to enhance renal outcomes in underserved groups.

P1853

FIVE YEARS PROSPECTIVE, OBSERVATIONAL, INTERNATIONAL STUDY ON THE IMPACT OF DECISION-MAKING TOOLS FOR CHOICE OF RENAL REPLACEMENT THERAPY MODALITY

Belén Marrón[1], Suzanne Pearce[2], Janusz Ostrowski[3], Dan Munteanu[4], Marietta Torok[5], Michael Roesch[6], Claudia Martín[7], Pawel Kochman[3], Attila Orosz[8], Jaime García Marrón[9], Fernando Macário[10]

[1]Diaverum Renal Services, Corporate Home Therapies & Patients Safety Director. Medical Office, Malmö, Sweden, [2]Diaverum Renal Services, Corporate Nursing Director. Medical Office, Malmö, Sweden, [3]Diaverum Renal Services, Wloclawek Clinic, Wloclawek, Poland, [4]Diaverum Renal Services, Fundeni Clinic, Bucharest, Romania, [5]Diaverum Renal Services, Rokus Clinic, Budapest, Hungary, [6]Diaverum Renal Services, Schlankreye Clinic, Hamburg, Germany, [7]Diaverum Renal Services, Barracas Clinic, Buenos Aires, Argentina, [8]Diaverum Renal Services, Bajcsy Clinic, Budapest, Hungary, [9]ESIC, Big Data Fellowship, Madrid, Spain and [10]Diaverum Renal Services, VP Medical Office, Mälmo, Sweden

Background and Aims: Decision-Making Tools (DMTs) are still not widely used but are considered the Gold Standard to ensure patients are well informed to choose renal replacement therapy (RRT) modality.

To analyze the impact of a structured modality information program (via DMTs) on RRT modality choice and start.

Method: All 2014-2017 predialysis patients (pts) with CKD G4-G5 and those starting unplanned dialysis without a prior information process underwent a DMTs process for RRT choice and were followed up to Dec.31st, 2018. DMTs included values evaluation, RRT information with different tools, staff deliberation support and patient modality choice. Results shown as percentage of pts who reached a certain stage over the total number of pts under evaluation.

Results: 2012 pts (mean age 61 y.) from 48 clinics (cl.) in Poland (PL, 19 cl., 980 pts), Romania (RO, 12 cl., 351 pts), Hungary (HU, 10 cl., 341 pts), Germany (DE, 6 cl., 292 pts) and Argentina (AR, 1 cl., 48 pts) underwent DMTs. Staff considered PD contraindicated in 29% of pts, hence optimal candidates for HD/PD were 1408 pts. (mean age 60y. and 46% prone for a home therapy). Early referral ($\geq$3 m. in clinic before DMT started): 51%. Aids used included written information (97% of pts), DVD in 27% and HD/PD utility visits in 49%. Relatives' participation in the process was 82%. Most pts (91%) considered the program useful whilst 64% of staff felt that this program was better than the prior one. PD choice (35%) varied among countries: 15% (RO), 30% (PL), 36% (HU), 62% (DE) and 98% (AR). For pts who had started dialysis by study closure (n=948), PD as chronic RRT was 31% (9% after an unplanned HD start); 13% (RO), 27% (PL), 34% (HU), 54% (GE) and 83% (AR).

Conclusion: Use of DMTs at the time of RRT modality choice complies with patient empowerment and decision sharing (patients-relatives-staff). PD choice and take-on varied among countries. Most patients who chose PD were chronically ascribed to PD representing at least one third of the suitable patients for both dialysis modalities.

P1854 SOCIAL NETWORK AS A SOURCE OF HEALTH EDUCATION IN NEPHROLOGY: THE CASE OF RENAL HEALTH INSTAGRAM

Geraldo Bezerra da Silva Junior[1], Marjan Askari[2], Diovana Dourado[1], Thiago Praça Brasil[1], Barbara Carneiro de Holanda[1], Juliana Gomes Ramalho de Oliveira[1], Elizabeth De Francesco Daher[3], Jose Eurico Vasconcelos Filho[1], Maria Andreia Formico Rodrigues[1]

[1]UNIFOR - Universidade de Fortaleza, Public Health, Medical Sciences and Applied Informatics Graduate Programs, Fortaleza, Brazil, [2]Erasmus University Rotterdam, School of Health Policy & Management, Rotterdam, Netherlands and [3]Federal University of Ceará, School of Medicine, Fortaleza, Brazil

Background and Aims: Chronic kidney disease (CKD) have been affecting a large number of patients worldwide and presents increasing numbers. Beyond professional intervention, it is extremely necessary to have patients' involvement in treatment. One useful way to disseminate CKD knowledge is the social network, through which we can not only reach a large public interested on the posts, but also influence the routine quality of a CKD patient. The aim of this study is to present the creation of an Instagram profile named "Renal Health", which focuses on providing specific information for patients with CKD to help them improve the quality of treatment results and maintain a healthy lifestyle, as well as to analyze the spontaneous comments and feedbacks received from its followers.

Method: The Renal Health project started in 2015, in Fortaleza, Brazil, aiming to create technological tools to help CKD patients cope with the disease and increase adherence to treatment. The research team has a multi-professional background, from Health, Information Technology, Computer Science and Communication fields, and also aims to create educational tools to increase health literacy focusing on kidney disease and its prevention. An Instagram profile (https://www.youtube.com/channel/UC3-GHeHAndcrRmbE4I_qE_w) have been created to provide people with access to these specialized contents. Within that context, we collected spontaneous comments and feedbacks from 4,229 followers from the Renal Health Instagram posts from June 2018 (when the profile was created) to December 2019.

Results: We have reached a total of 4,229 followers. There were 505 posts, 16 (3.16%) about medication, 65 (12.87%) about nutrition, 12 (2.3%) about physical exercise, 132 (26.13%) about kidney disease and comorbidities, 82 (16.23%) about CKD treatment, 61 (12.07%) about kidney transplant and organ donation, and 137 (27.12 %) about other subjects, including motivational messages. Of a total of 1,560 comments, we have identified 543 profiles, of these 88 (16.2%) were men, and 412 (75.8%) women, noting the prevalence of women among the comments made. Among those comments, 223 were regarding congratulations on the profile. We have identified 99 patients with kidney diseases, mainly CKD; 81 (81.81%) spontaneously reported their illnesses in their comments, being 46 (56.8%) on dialysis, 13 (16.4%) transplanted patients, 5 (6.7%) glomerulonephritis, 4 (4.9%) kidney stones and 4 (4.9%) renal cysts. In the group of 46 patients on dialysis, we have identified 105 comments, of which 14 were regarding the value of the information on the posts, followed by 71 comments on personal experiences on the subject and 20 comments containing questions about the topic, which we had prompt answered. Among the group of 13 renal transplanted patients, 12 comments demonstrated their happiness after the transplant and their experiences on the subject, and 1 comment containing a question about kidney transplant. We have also identified other health professionals interacting with the profile, declaring that it was helpful to guide their patients. Furthermore, this platform had crossed the borders, being identified comments by people from around the world, such as other South American countries, the Middle East and Europe. The most recent posts can be seen in Figure 1.

Conclusion: Through the analysis of the comments we noticed the possibility of better knowing the followers of the project, enabling the development of personalized information for each patient. Social networks, such as the Instagram, seem to be great tools for health education and interaction between health care team and patients. In addition, the use of digital platforms to share trusted health information can reach a broad audience.



Figure 1. The Renal Health Instagram profile, January 2020.

P1855

ONLINE PATIENT/CAREGIVER EDUCATION ON HYPERKALEMIA CAN IMPROVE KNOWLEDGE AND COMPETENCE AS WELL AS PROMPT REAL LIFE CHANGES

Amy Larkin[1], Don Blatherwick[1]

[1]*Medscape Education*

Background and Aims: Managing hyperkalemia with a strict diet is limiting and difficult for patients. We sought to measure the impact of online education for patients/caregivers on knowledge and confidence as well as prompting change in daily life.

Method: The patient/caregiver education was designed as 2 online, interactive activities. Both were comprised of text and integrated visuals; the second also included a patient commentary video. Demographic questions were asked prior to starting the education. A knowledge question was asked both before and after the activity to assess learning gains, as well as intent to change and confidence questions at the end. Absolute improvements were calculated for pre/post questions. The activities launched in April and May of 2019, and data collected through October 2019.

Results: To date, 98,462 learners have participated in the patient/caregiver activity.

Activity 1: High Potassium: Causes and reasons to Treat

Participants: 60,060

Completers of all questions (included in outcomes analysis): 7,262

Demographics: 59% female; 49% white, non-Hispanic; 66% over the age of 54; 16% have hyperkalemia, 75% were interested in learning more about the condition

Knowledge changes: 13% improvement in understanding what causes hyperkalemia (46% pre to 59% post)

Intent-to-act: 66% plan to talk to an HCP about next steps for treating hyperkalemia

Confidence changes: 82% reported increased confidence understanding why it's important to treat hyperkalemia

Activity 2: It's Complicated: How to Manage High Potassium and Heart Failure

Participants: 38,402

Completers of all questions (included in outcomes analysis): 3,816

Demographics: 60% female; 63% white, non-Hispanic; 69% over the age of 54; 58% were interested in learning more about the condition and 25% have this condition

Knowledge changes: 13% improvement in recognizing how potassium levels effect the heart (76% pre to 89% post)

Intent-to-act: 64% plan to talk to their healthcare provider about a plan to manage my hyperkalemia

Confidence changes: 82% reported increased confidence understanding how important is it to manage my heart failure and hyperkalemia

Conclusion: The metrics and outcomes gathered in this assessment are a strong indicator that these patient/caregiver-focused online educational activities improved knowledge and confidence, and prompted intent to act by patients/caregivers related to hyperkalemia.

P1856 KIDNEY CRISES: USING IN SITU SIMULATION TEACHING TO FACILITATE MULTIDISCIPLINARY TEAM WORKING IN RENAL EMERGENCIES

Ailish Nimmo[1], Katie Adams[1]

[1]*North Bristol NHS Trust, Richard Bright Renal Service, Bristol, United Kingdom*

Background and Aims: The haemodialysis unit is a unique clinical environment. Specialist nursing staff look after patients, frequently without on-site medical cover, and need to manage medical issues until help arrives. Junior doctors often have limited experience managing renal patients and may not be aware of specialty-specific issues when dealing with medical emergencies. The different skill sets in these groups creates an opportunity for shared learning. Simulation teaching provides a safe environment for individuals to develop communication, team working and clinical skills and helps facilitate discussion and reflection on clinical scenarios. We describe a programme of renal *in situ* simulation sessions for nurses and junior doctors to allow them to practise their roles in an emergency and evaluate feedback on their perception of the programme.

Method: Seventeen hour-long simulation sessions were delivered between June 2017 and January 2020 within the renal ward in 2 hospitals and in a satellite outpatient dialysis unit. They utilised a high-fidelity SimMan® mannequin. Scenarios were based on common or rare-but-serious medical emergencies (hyperkalaemic cardiac arrest, arrhythmia on dialysis, air embolism, major haemorrhage post-renal biopsy, line sepsis, hypertensive seizure, pulmonary oedema and drug-induced anaphylaxis). Sessions comprised an orientation to the mannequin, a clinical scenario and a debrief discussion. Doctors and nurses completed post-tutorial feedback exploring their thoughts on the programme.

Results: 59 healthcare professionals (40 doctors and 19 nurses) participated and completed post-event feedback. All attendees felt that sessions improved their knowledge and increased their confidence in managing similar scenarios in the future. They all felt they would be able to apply their learning to their day job. 86% of participants strongly agreed that the programme helped them develop stronger relationships with colleagues. In white-space boxes, individuals described the sessions as being helpful in developing communication, teamwork, leadership and delegation skills in addition to specific learning points for the individual scenarios. Sessions also identified practical issues, such as where to source medications or monitoring equipment, and led to the creation of an updated protocol folder and distribution of Advanced Life Support algorithms throughout the ward.

Conclusion: Nurses and junior doctors report increased confidence in managing medical emergencies in renal patients and improved relationships with colleagues following a simulation training programme. The programme promotes a learning culture within the unit. It provides an opportunity to discuss potentially serious situations and allows reflection on similar scenarios encountered within the ward and dialysis unit. Further work is needed to determine if *in situ* simulation teaching has an impact on patient outcome measures.

P1857 SALT CONSUMPTION, LIFESTYLE AND PROTEINURIA IN A HETEROGENEOUS YOUNG POPULATION

Claudia Zullo[1], Lorenzo Dallari[1], Alfredo Bagalà[1], Chiara Somma[1], Giuseppe Ferro[1], Lorenzo Burgio[1], Pietro Dattolo[1]

[1]*S. M. Annunziata Hospital, Internal Medicine, Nephrology, Firenze, Italy*

Background and Aims: Obesity, hypertension, smoke, high dietary salt intake and physical inactivity are the main modifiable risk factors for chronic kidney disease, that affects about 9-10% of Italian people. About daily salt intake, the World Health Organization recommends a maximum consumption of 5 grams of salt per day. In Italy, most people consume too much salt – on average 8-10 grams per day or around twice the recommended maximum level of intake. Aim of this study was to investigate dietary habits and lifestyle of the heterogeneous students population of "Scuola Carabinieri di Firenze" (attended by people coming from all Italian regions) and their relations with urinary abnormalities.

Method: from November 2018 to March 2019 we collected anamnestic and anthropometric data, blood pressure measurements and body cellular mass (BCM) of 257 young subjects (152 males, 105 females; mean age 32 + 11 yy).

We determinated sodium, chlorine and protein excretion on a spot urine sample in addition to plasma creatinine levels. Statistical analyses were performed using SPSS.

Results: We analyzed preliminary data of urinary sodium excretion (U_{Na}), proteinuria (U_p) and hematuria (U_{rbc}) of all the subjects. Fifty-five percent of them had a U_{Na} higher than 100 mmol/L (approximately equivalent to a dietary salt intake of 6 grams/day). In these subjects with higher salt consumption, U_p and U_{rbc}, measured by urine dipstick, were detectable in 32% and 21% respectively. In subjects with lower salt intake (less than 6 grams/day), U_p and U_{rbc} were 0% and 5% respectively.

To determine if there was an association between our variables, we used Pearson correlation coefficient. We found that U_{Na} was directly related to U_p (r 0.26, p 0.002), age (r 0.22 p 0.011) and diastolic blood pressure (DBP, r 0.22, p 0.012). We also found that poor exercise (r -0.15, p 0.7) and low lean body mass percentage (r -0.15, p 0.7) were inversely related to U_{Na}.

Conclusion: high dietary salt intake is associated with elevated blood pressure and proteinuria in a young and "healthy" population. Hypertension and proteinuria are both known risk factors for the development of chronic kidney disease. Wrong dietary habits and lifestyles must be detected and corrected in order to prevent nephropathy onset.

Correlations

		Age	uPr	uNa	DBP	LTM%	Exercise
Age	Pearson	1	.336**	.215*	.289**	-.483	-.417**
	Sig (2-tailed)		.000	.011	.001	.000	.000
	N	241	241	241	230	236	238
uPr	Pearson	.335**	1	.255**	.247**	-.128	-.119
	Sig (2-tailed)	.000		.002	.005	.136	.165
	N	241	241	241	230	236	238
uNa	Pearson	.215*	.255**	1	.220*	-.151	-.150
	Sig (2-tailed)	.011	.002		.012	.079	.079
	N	241	241	241	230	236	238
DBP	Pearson	.289**	.247**	.220*	1	-.157	-.126
	Sig (2-tailed)	.001	.005	.012		.073	.154
	N	241	230	230	232	232	229
LTM%	Pearson	-.483**	-.128	-.151	-.157	1	.350**
	Sig (2-tailed)	.000	.136	.079	.073		.000
	N	236	236	236	232	239	235
Exercise	Pearson	-.417**	-0119	-.150	-.126	.350**	1
	Sig (2-tailed)	.000	.165	.079	.154	.000	
	N	238	238	238	229	235	239

** Correlation is significant at the .01 level (2-tailed)

* Correlation is significant at the .05 level (2-tailed)

Figure:

P1858 PSYCOEDUCATIONAL TEAM IN PRE- HEMODIALYSIS FOR PATIENTS AND CAREGIVERS

Marica Mulè[1], Paola Gaggia[1], Ezio Movilli[1], Chiara Manenti[1], Miriam Appiani[1], Orietta Zani[1], Anna Bertoni[2], Francesco Scolari[1]

[1]ASST Spedali Civili, U.O. Nephrology, Brescia, Italy and [2]Catholic University of the Sacred Heart, Psychology, Milano, Italy

Background and Aims: The aim of this work is to explain the training to create a multidisciplinary team that in the future will activate the psychoeducational groups in nephrology. These groups will be support to patients and caregivers already in the waiting period from the intervention of the fistula at the beginning hemodialysis.

Method: The training of five meetings was realized from March 2019 to May 2019. The training for a team composed by 3 nephrologist, 4 nurses, 1 dietician, 1 nursing coordinator was conducted of a psychologist to established modalities and aims of a psychoeducational pathway for patients that will begin hemodialysis and their caregivers. In the first meeting, through a focus group, the participants discussed the word "to cure". In the second meeting participants defined patient and caregiver's needs after the diagnosis of Chronic Kidney Disease. In the third meeting the team work defined the objectives and methods of conducting future groups psychoeducational. In the fourth meeting participants decided the duration and modalities of the psychoeducational pathway for patient and caregiver. Finally, in the fifth meeting, the team reviewed the objectives, recipients and thematic areas of the meetings for patients and caregivers. In addition, an evaluation questionnaire was administered to verify the benefit and satisfaction of the training. All the contents of the training were transcribed in a diary and analyzed with a pencil and paper mode.

Results: In the first meeting the team discussed the need to accompany and educate patients even before the onset of haemodialysis. In the second meeting team decided that the therapeutic education is not only for patients waiting to start haemodialysis but also on their caregivers often uninformed and not involved by doctors and nurses. In this focus the caregiver appears an important figure that support the patient at home and if not properly informed it can become an obstacle in patient care. In the fourth and fifth meetings have been defined a possible psychoeducational training in three total meetings so named:

1. *Knowing each other differently:* to get to know both the patient and the caregiver in an active listening setting.
2. *Knowing dialysis concretely*: to know better the treatment and pay attention to the care of your psychological well-being too.
3. *Knowing the diet actively:* to inform and support the patient and caregiver of future and current changes in eating habits.

The participants in the satisfaction questionnaire to the question "how much did this training respond to the needs of your job?" on nine answers collected, the outcome it was M = 4.7 on Likert scale 1(few)-5 (much).

Conclusion: The training has managed to build a multidisciplinary team ready to care patients and caregivers that will begin haemodialysis in a more informed and aware way. Currently, two psychoeducational groups have been created for patient and caregiver. As shared in the multidisciplinary team's training these psychoeducational groups are activated to help the patient to accept dialysis at the same time help the family member to take on the role of caregiver. This project has made it possible to improve not only teamwork but overall patient and caregiver care.

P1859

"HEADING AWARDS 3.0 PATIENTS" IMPACT OF AN ONLINE HEALTH WORKSHOP ON INTERNET SEARCH OF HEALTH-RELATED ISSUES BY PERITONEAL DIALYSIS UNITS PATIENTS, FROM THE NEPHROLOGY SERVICE.

Francisco Javier Centellas Pérez[1], Ricardo Martínez Reolid[2], Pablo Alejandro Sarduy Coronado[1], Sara Piqueras Sánchez[1], Consuelo Martínez Antolinos[1], Aitana Aparicio Simón[1], Cristina Ruiz González[1], Jesús Masiá Mondéjar[1], Juan Pérez Martínez[1], Agustin Ortega Cerrato[1]

[1]Hospital General Universitario de Albacete, Nephrology, Albacete, Spain and [2]Hospital General Universitario de Albacete, Emergency, Albacete, Spain

Background and Aims: New technologies have advanced diagnostic techniques and enabled patient self-information, nonetheless, they can become a weapon of misinformation if not used appropriately.

Online health resources utilization, gamification and the appearance of new specialized Apps are becoming a challenge in the quest for correct use of new technologies in the Nephrological field and in the patient empowerment process.

Aims:

1st Phase: Determine how frequent medical information is searched for online, the main topics and the different sources of information used by PD patients in our Service of Nephrology.

Method: Observational prospective study using a cohort of patients from PD Unit (pre dialysis and on dialysis). First, an online survey was used in order to obtain demographic variables and to determine the use of different sources of information and their quality. Secondly, patients were instructed in ICTs via virtual desktop as well as in two live workshops.

Results: 52 patients (37 men, 15 women). Mean age: 61.7 years. Academic level (elementary school: 20). Place of residence (urban: 65.4%). **48% never uses the internet**. From the rest: 68% searches in a regular manner for health-related issues, with "Google" being the main search engine (77.8%). **100% have searched for their own illnesses**, 72.2% consider the information found not completely reliable. **61% looks for information before and after the clinical encounter. 72.2% have asked other patients about nephrological health related issues**, while 27.8% have given counsel of said issues to others. 86.5% doesn't use health related Apps and only 5.8% use blogs. Among the variables analysed, differences where found in being **older age and less use of internet** (ANOVA test $p<0.001$) and with **lower cultural level and less use of new technologies** (Chi-squared test $p<0.001$).

Conclusion:

The analysed data show that nowadays we face two main problems in our PD unit:

- **Generational digital divide**: we have patients who have not incorporated into their lives the use of new technologies, in contraposition to others who use them in regular bases.
- **Guarantee** that those who use digital resources can access them in a **simple and trustworthy manner**.

Therefore, we believe that the second phase of this project, both the workshops and the virtual desktop, are tools that can help fix these problems.

P1860

PERIOPERATIVE CHANGES IN PHYSICAL FUNCTION AND ACCELEROMETER-MEASURED PHYSICAL ACTIVITY IN PRE-EMPTIVE OR POST-DIALYSIS KIDNEY TRANSPLANT RECEIPIENTS

Takafumi Ichikawa[1], Ryota Matsuzawa[2], Daisuke Ishii[3], Fumino Noguchi[4], Yuki Imura[5], Shohei Yamamoto[6], Atsuhiko Matsunaga[6], Kazunari Yoshida[7]

[1]kitasato university hospital, rehabilitation, sagamihara, Japan, [2]Hyogo University of Health Sciences, rehabilitation, Hyogo, Japan, [3] Kitasato University School of Medicine, Urology, sagamihara, Japan, [4]kitasato university hospital, transplant support center, sagamihara, Japan, [5]kitasato university hospital, nursing, sagamihara, Japan, [6]Kitasato University Graduate School of medical Sciences, Rehabilitation Sciences, sagamihara, Japan and [7] Kitasato University School of Medicine, Organ Transplant Medicine, sagamihara, Japan

Background and Aims:

Pre-emptive kidney transplant (PEKT) is known to have better graft survival, and thereby well established as the optimal treatment for end-stage renal disease patients. On the other hand, the delayed recovery of physical function and physical activity after KT reportedly occurs in approximately 20% of KT recipients, which leads to poor prognosis. However, it is less clear whether PEKT delays recovery of them after KT. We aimed to investigate any differences in perioperative changes in physical function and physical activity for PEKT versus non-PEKT.

Method:

Consecutive 34 recipients who had received a living-donor KT from January 2016 to January 2019 were enrolled in this prospective cohort study. Patient characteristics including age, sex, body mass index, primary cause of kidney disease, smoking habits, and comorbidities were collected at baseline. Six-minute walk distance (6MWD), gait speed, isometric leg strength, accelerometer-measured physical activity (number of steps and moderate to vigorous activity time) and kidney function (eGFR) were assessed at before and 2 months after KT. We divided the recipients into 2 groups: PEKT (n=11) and non-PEKT (n=23), and compared outcomes between the 2 groups using ANCOVA adjusted for baseline patient characteristics. This study was approved by institute ethical committee.

Results:

KT successfully improved eGFR of all the study participants from 6.1±4.6 to 35.4±15.3. PEKT group showed significant shorter dialysis duration as compared with non-PEKT group (mean duration: 0 months in PEKT vs 64.8±95.5 months in non-PEKT, $P < 0.001$). The 6MWD significantly improved after KT in the PEKT group, but not in the non-PEKT group as compared with that of baseline (adjusted mean change [95% confidence interval]: 44.7 [8.2 to 81.2] vs. 8.80 [-32.8 to 15.2], P=0.025). We found a tendency toward improvement of gait speed (0.11 [-0.11 to 0.32] vs. -0.15 [-0.29 to -0.01], P=0.065), and moderate-to-vigorous activity time per day (7.19 [-2.84 to 17.23] vs. -5.60 [-12.97 to 1.77], P=0.057) in the PEKT group.

Conclusion:

PEKT recipients showed higher perioperative changes in physical function and physical activity compared to non-PEKT. Our findings suggest that PEKT may have benefits on early recovery of physical function and physical activity after KT.

P1861 ARTIFICIAL PHOSPHATE- HOW DIFFICULT IS IT TO AVOID IT?

Oonagh Smith[1], Sarah Kiernan[2]

[1]Tallaght University Hospital, Nutrition and Dietetics, Dublin, Ireland and [2]University College Dublin,, Human Nutrition Undergraduate

Background and Aims: Hyperphosphataemia has been independently associated with increased morbidity and mortality across the lifecycle of chronic kidney disease. Dietary phosphate restriction is the corner stone of hyperphosphataemia management. Traditionally the focus was on limiting foods that are naturally high in phosphate such as meats, dairy, wholegrain and nut products. However, phosphate-containing additives are a growing concern. Artificial phosphates are thought to be readily absorbed by the body and are increasingly being added to processed foods, at a time when there is an increased desire and reliance on convenience foods. It has been shown that educating patients with end stage renal disease to avoid phosphate-containing food additives can result in a modest but clinically significant improvement in serum phosphorus levels. 1 The aim of this study was to evaluate how feasible it is for a patient to source convenience packaged cooked meats/poultry that are free from artificial phosphate and if such products are a suitable option for the renal patient in relation to salt and protein content.

Method: Data was manually collected in a branch of the five leading supermarket chains. The ingredient list of each product food label was checked for artificial phosphate (phos), artificial potassium (K) or the corresponding E numbers and the nutrition table examined for salt and protein content (per 100g / 25g portion or slice). The price was checked in store and manually calculated per 7g protein exchange.

Results:

Products (n= 172)s	Beef	Chicken	Turkey	Ham
Number containing phosphate	4	40	15	65
Number free of artificial phos	6	12	4	26
Number free of artificial phos & K	6 (60%)	12 (23%)	4 (21%)	7 (8%)

Table 1: Number of packaged products which contained or were free of artificial phosphate and potassium.

Products	Brand Name	Store A own brand	Store B own brand	Store C own brand	Store D own brand	Store E own brand
Total	32	30	17	25	31	37
No. free of artificial phos & K	11 (34%)	10 (33%)	5 (29%)	2 (8%)	1 (3%)	1 (3%)

Table 2: Number of branded & store own brands free of artificial phosphate and potassium.**Table 3:** Median Salt & Protein content per 100g and Price per 7g protein exchange.

In total, when compared to the products containing artificial phosphate, items free of artificial phosphate and potassium were statistically:Lower in salt per 100g, t-test, p value <0.05Higher in protein per 100g, t test, p value <0.001More expensive per 7g protein exchange, t-test, p value <0.001.

P1862

USE OF NOVEL E-HEALTH TECHNOLOGIES AND ITS ACCEPTABILITY BY KIDNEY TRANSPLANTED PATIENTS: FIRST EXPERIENCE IN NORTHEAST BRAZIL

Juliana Gomes Ramalho de Oliveira[1], Marjan Askari[2], Daniele Cabral Dias[1], Helady Sanders-Pinheiro[3], Elizabeth De Francesco Daher[4], Jose Eurico Vasconcelos Filho[1], Maria Andreia Formico Rodrigues[1], Geraldo Bezerra da Silva Junior[1]

[1]UNIFOR - Universidade de Fortaleza, Public Health, Medical Sciences and Applied Informatics Graduate Programs, Fortaleza, Brazil, [2]Erasmus University Rotterdam, School of Health Policy & Management, Rotterdam, Netherlands, [3]Universidade Federal de Juiz de Fora, School of Medicine, Juiz de Fora, Brazil and [4]Federal University of Ceará, School of Medicine, Fortaleza, Brazil

Background and Aims: The World Health Organization defines eHealth as the use of information and communication technologies for health purposes. One of its 4 components, mHealth or mobile health, refers more specifically to the provision of health information and services through mobile and wireless technologies. With approximately 7 billion mobile subscriptions worldwide, in many places people are more likely to have access to a smartphone than to drinking water. The aim of this study was to investigate the acceptability of renal transplanted patients to the use of eHealth technologies for their treatment.

Method: This is a cross-sectional study, performed in a reference hospital located in northeastern Brazil, from January to March 2019, including renal transplant patients older than 18 years old. Data collection was performed through interviews at the post-transplant outpatient clinic in the period preceding the follow-up appointments. The following variables were studied: sociodemographic (gender, age, marital status, race, religion, origin, education, occupation and income), use of technologies (communication devices ownership and / or internet access mobile or at home), purpose and frequency of use, reasons for non-use, and interest in using eHealth tools to assist in post-transplant treatment. We have also interviewed physicians and nurses from the renal transplantation unit regarding this subject.

Results: A total of 147 patients were interviewed, 63.2% were male, age varied from 13 to 45.1 $\pm$ 13 years old, 41.5% were single, with 4 to 10 years of schooling, family income of 2 to 3 minimum wages in Brazil (approximately 400 to 700 US dollars). The patients had had been transplanted around 5 to 6 years ago. As for handset ownership, 90.5% had a smartphone, 39.5% a notebook, 36% a home computer and 12.2% a tablet. As for use, 13% used only for calls. Among the other purposes, 85% used for messaging, 72.1% for internet searches and 74.8% for social networks. Regarding frequency of use, 61.2% used these technologies many times a day. Concerning their interest in using eHealth tools, 93.2% pointed that they would like the tool to be developed for smartphones, and 96.6% said they would use eHealth tools to help them cope with their treatment. The health professionals (10 physicians and 3 nurses) pointed as the main barriers that difficult treatment post-renal transplantation were: patient's adherence to treatment (76.9%) and low health literacy (53.8%). These professionals pointed that the eHealth technologies can help to increase patients' adherence, and 23% of them had doubts about effective acceptability by patients.

Conclusion: To our knowledge, this is the first study in Brazil that addresses the acceptability of eHealth tools among kidney transplanted patients. Transplant recipients were found to already use information technology and are interested in using eHealth tools to help them with the treatment. Health professionals support this initiative and believe these technological tools can increase patient compliance. The next steps of this study are to develop and test eHealth technologies directed for kidney transplanted patients.

P1863

KNOWLEDGE ABOUT CHRONIC KIDNEY DISEASE AND THE WAYS OF PREVENTION: A POPULATION-BASED STUDY IN NORTHEAST BRAZIL

Geraldo Bezerra da Silva Junior[1,2], Michelle Jacintha Cavalcante Oliveira[3,4], Alyne Suellen Silva Pedrosa[4], Gabriel Araújo Pereira[1], Isis Holanda Pinheiro Vilela[4], Felipe Camilo Santiago Veloso[5], Leticia Lima de Oliveira[4], Fernanda Melo Oliveira[4], Diandra Alcântara Jordão[4], Ana Beatriz Arrais Lima Costa[1], Sarah Maria Brito de Aguiar Castro[1], Clarissa Sanders Costa[1], Juliana Gomes Ramalho de Oliveira[1], Marjan Askari[6], Elizabeth De Francesco Daher[2]

[1]Universidade de Fortaleza, Public Health and Medical Sciences Graduate Programs, Fortaleza, Brazil, [2]Federal University of Ceará, School of Medicine, Fortaleza, Brazil, [3]Federal University of Alagoas, School of Medicine, Maceio, Brazil, [4]University Center Tiradentes, School of Medicine, Maceio, Brazil, [5]State University Of Health Sciences Of Alagoas, School of Medicine, Maceio, Brazil and [6]Erasmus University Rotterdam, School of Health Policy & Management, Rotterdam, Netherlands

Background and Aims: The incidence and prevalence of chronic kidney disease (CKD) is increasing worldwide, and health literacy is an important goal of any program of health care. The aim of this study is to investigate the knowledge of the population in Brazil about CKD and the ways of prevention, as well as the use of novel technologies to achieve knowledge and get awareness on CKD.

Method: This is a population-based study conducted in two large urban centers in Northeast Brazil (Fortaleza city, Ceara, and Maceio city, Alagoas). We have applied a questionnaire with questions regarding the knowledge about CKD, its preventive measures, causes, and ways of diagnose (for example, what is "creatinine"?). We have also investigated the use of novel technologies, focused on applications (apps) to achieve information related to health (if the interviewed) already uses to get health information through apps and if they would like to. Sociodemographic information was also collected. Exclusion criteria were: people from the healthcare sector (because they would already have specialized knowledge about CKD, and we aimed to know what the general population know about CKD), people with CKD, other kidney diseases or medical conditions that could lead to the knowledge about CKD.

Results: A total of 1,147 individuals were interviewed, with a mean age of 38.7±16.0 years, and 621 (54.1%) were female. Regarding the questions about the knowledge about CKD ("Do you know what is chronic kidney disease?"), 442 (38.5%) was found to answer yes. When asked if they know what is creatinine, only 176 (15.3%) said yes. In relation to the risk factors for CKD, 466 (40.6%) answered to know which factors were associated with increased risk for CKD, and 587 (51.1%) said to know how to prevent CKD. Another question was about the use of applications (app) to healthcare, and 358 individuals (31.2%) said to use some type of app to take care of their health. We have also questioned if the interviewed would use applications to get information regarding CKD, and 773 (67.3%) said yes, they would like to.

Conclusion: CKD is a Public Health problem in Brazil, with huge costs to the health system. Prevention is the key determinant to decrease the disease burden to everyone, people, society and healthcare players. Awareness of CKD seem to be slowly increasing in our country, once a significant percentage of interviewed said to know the ways of prevention, but it is still far from ideal. Technology seem to be an interesting solution to achieve our goals in terms of prevention and treatment of CKD.

P1864 RENAL HEALTH MOBILE APPLICATION: AN ANALYSIS OF ITS USE IN BRAZIL

Erica Maria Rodrigues de Araújo[1], Geraldo Bezerra da Silva Junior[1], Ronaldo Almeida de Freitas Filho[1], Juliana Gomes Ramalho de Oliveira[1], Ana Carolina Albuquerque[1], Ricardo De Sousa Lucas[1], Marjan Askari[2], Elizabeth De Francesco Daher[3], Jose Eurico Vasconcelos Filho[1], Maria Andreia Formico Rodrigues[1]

[1]Universidade de Fortaleza, Public Health, Medical Sciences and Applied Informatics Graduate Programs, Fortaleza, Brazil, [2]Erasmus University, School of Health Policy & Management, Rotterdam, Netherlands and [3]Federal University of Ceará, School of Medicine, Fortaleza, Brazil

Background and Aims: Chronic kidney disease (CKD) have been considered, worldwide, an important public health problem due to its increasing prevalence and its potential consequence in reducing the time and quality of life of affected patients. In addition, the number of individuals with CKD will continue to increase if no strategies are adopted for preventing and delaying the progression of CKD. Thus, corroborating this strategic thinking and the spread of the internet around the world, we developed the Renal Health mobile app (Oliveira et al. Kidney Int Rep. 2019 Jan 28;4(4):609-613). Because it is easily accessible, free of charge and has essential tools for the promotion of renal health, such as diet therapy guidelines, it has conquered users throughout Brazil, connecting patients and health professionals. From this perspective, the objective of this study was to statistically analyze Renal Health application downloads in 16 Brazilian states, where the app was found to be in use.

Method: Using the Power BI tools and Dashboards it was possible to extract statistical data from the Renal Health application, since its last updated version, last year, to January 2020. Power BI software is a set of analysis and data sharing tools where the main purpose is to generate reports along with Dashboards which is a kind of graphical interface that provides visualizations of key metrics and performance indicators of a mobile application. This way, from this toolkit, it was possible to obtain a real-time and transparent progress report on the number of Renal Health application downloads, with no personal identification of users.

Results: The 16 Brazilian states under analysis make up a total of 526 Renal Health application downloads by January 2020. Among these states, São Paulo obtained a total of 129 downloads (24.53%), being the place with the largest number of Renal Health users. The second largest state in number of downloads was Ceara, with a total of 111 (21.10%). The states of Rio de Janeiro, Acre and Minas Gerais also obtained a significant number of downloads of the Renal Health application, totaling 53 (10.08%), 48 (9.13%) and 45 (8.56%), respectively (Figure 1). Comparing the results of this study with the last Brazilian Dialysis Survey, which is coordinated by the Brazilian Society of Nephrology, we can observe the coherence of these results, since the states of São Paulo, Minas Gerais and Rio de Janeiro were cited by this survey as the states with the largest prevalence rates of patients undergoing dialysis, evidencing a possible correlation between the use of this type of technological tool (Renal Health) and the highest prevalence of dialytic CKD, once the Renal Health application is a good way to improve patients' adherence to treatment and help them cope with the disease.

Conclusion: The Renal Health application is becoming better known by CKD patients in Brazil, and, based on the number of users currently presented in this study, we conclude that there is a growing search for CKD patients for knowledge about kidney disease on mobile platforms. Therefore, there is a challenge to improve new tools with increasingly interactive content and accessible language, as our team intend to do in the next versions of this app.

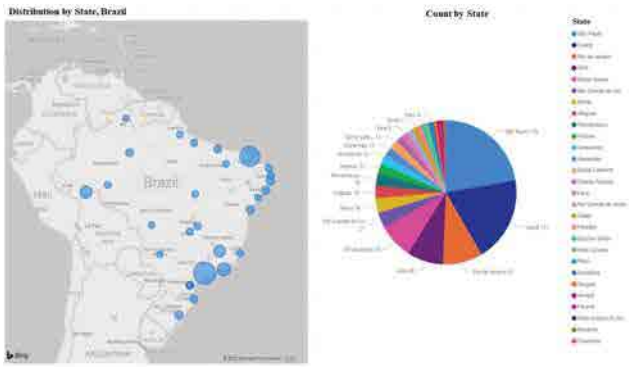


Figure 1. Renal Health application downloads in Brazil, November 2018 – January 2020.

P1866

TO INVESTIGATE THE EFFICACY AND SAFETY OF MOLIDUSTAT IN NON-DIALYSIS PATIENTS WITH RENAL ANEMIA WHO ARE NOT TREATED WITH ERYTHROPOIESIS-STIMULATING AGENTS: MIYABI ND-C

Hiroyasu Yamamoto[1], Megumi Taguchi[2], Kiyoshi Nobori[3], Yoshimi Matsuda[3], Kazuma Iekushi[2], Tadao Akizawa[4]

[1]The Jikei University School of Medicine, Tokyo, Japan, [2]Bayer Yakuhin Ltd, Medical Affairs & Pharmacovigilance, Osaka, Japan, [3]Bayer Yakuhin Ltd, Research & development Japan, Osaka, Japan and [4]Showa University, Tokyo, Japan

Background and Aims: Anemia is a common complication of chronic kidney disease (CKD). A hypoxia-inducible factor prolyl-hydroxylase (HF-PH) inhibitor is developing as a new treatment option of renal anemia. Molidustat, an oral HIF-PH inhibitor, stimulated endogenous production of erythropoietin and was well tolerated in phase IIb clinical trials. The phase III program entitled **M**ol**I**dustat once dail**Y** improves renal **A**nemia **B**y **I**nducing EPO (MIYABI) was conducted in Japan.

Method: MIYABI Non-Dialysis-Correction (ND-C) of Hb study (up to 52 weeks, randomized, darbepoetin-controlled, open-label) was conducted to investigate the efficacy and safety of molidustat (MO) in non-dialysis patients with renal anemia who are not treated with erythropoiesis-stimulating agents. Study drug doses were titrated regularly with the aim of correcting and maintaining the patients' Hb values between the target range (11.0-13.0 g/dL). The primary efficacy variables were the mean Hb values during the evaluation period (30-36 weeks) and its change from baseline to demonstrate the non-inferiority of MO to darbepoetin alfa (DA) using a non-inferiority margin of 1.0g/dL. Safety variables included adverse events (AE). Prespecified primary analysis results up to 36 weeks are presented here.

Results: 82 patients were treated with a starting dose of 25mg of MO and 79 patients were treated with a starting dose of 30μg/2weeks of DA. The mean of baseline Hb values were 9.84 g/dL and 10.00 g/dL in the MO and DA group, respectively. MO increased the mean Hb values (rate of rise from baseline in Hb values at the first dose change up to 8 weeks: mean: 0.086 g/dL/week (95%CI; 0.047, 0.126)) and achieved the lower limit of target range at 12 weeks. MO maintained Hb values after 12 weeks, and for the mean Hb values during the evaluation period, the mean was 11.28 g/dL (95%CI; 11.07, 11.50). As the primary efficacy variables (the changes from baseline of mean Hb values during the evaluation period), the means were 1.45 g/dL (95%CI; 1.21, 1.68) and 1.70 g/dL (95%CI; 1.47, 1.92) in the MO and DA group, respectively. The LS mean difference was -0.38 (95%CI; -0.67, -0.08), therefore the non-inferiority of MO to DA was established. The mean (SD) doses during the study period were 45.33 (28.88) mg/day of MO and 17.87 (12.49) μg/week of DA. The most common maximum dose of MO was 25 mg (26 patients, 31.7%) followed by 75 mg (16 patients, 19.5%) and 50mg (14 patients, 17.1%). AEs were experienced in 84.1% of patients in the MO group and in 91.1% of patients in the DA group up to 36 weeks. The most common AEs occurred $\geq$ 5% of patients in any group were nasopharyngitis (20.7% and 25.3%, respectively) and worsening of chronic kidney disease (13.4% and 6.3%, respectively).

Conclusion: Correction and Maintenance effect of MO on the Hb values was investigated and the non-inferiority of MO to DA was established in non-dialysis patients with untreated anemia. The MO showed no new safety concern but further longitudinal investigation will be needed.

P1868

TO INVESTIGATE THE EFFICACY AND SAFETY OF MOLIDUSTAT IN NON-DIALYSIS PATIENTS WITH RENAL ANEMIA WHO ARE TREATED WITH ERYTHROPOIESIS-STIMULATING AGENTS: MIYABI ND-M

Hiroyasu Yamamoto[1], Megumi Taguchi[2], Kiyoshi Nobori[3], Yoshimi Matsuda[3], Kazuma Iekushi[2], Tadao Akizawa[4]

[1]The Jikei University School of Medicine, Tokyo, Japan, [2]Bayer Yakuhin Ltd, Medical Affairs & Pharmacovigilance, Osaka, Japan, [3]Bayer Yakuhin Ltd, Research & development Japan, Osaka, Japan and [4]Showa University, Tokyo, Japan

Background and Aims: Treatment with subcutaneous erythropoiesis-stimulating agent (ESA) is the standard of care for renal anemia in non-dialysis patients. A hypoxia-inducible factor prolyl-hydroxylase (HF-PH) inhibitor is an oral medication and might be a new treatment option of renal anemia. Molidustat mimics the physiological response to hypoxia, thereby stimulating endogenous EPO production by the kidneys. The phase III program entitled **M**ol**I**dustat once dail**Y** improves renal **A**nemia **B**y **I**nducing EPO (MIYABI) was conducted in Japan.

Method: MIYABI Non-Dialysis- Maintenance (ND-M) of Hb study (up to 52 weeks, randomized, darbepoetin-controlled, open-label) was conducted to investigate the efficacy and safety of molidustat (MO) in non-dialysis patients with renal anemia who are treated with ESAs. A starting dose was in accordance with previous ESA dose and study drug doses were titrated regularly with the aim of maintaining the patients' Hb values between the target range (11.0-13.0 g/dL). The primary efficacy variables were the mean Hb values during the evaluation period (30-36 weeks) and its change from baseline to demonstrate the non-inferiority of MO to darbepoetin alfa (DA) using a non-inferiority margin of 1.0 g/dL. Safety variables included adverse events. Prespecified primary analysis results up to 36 weeks are presented here.

Results: 82 patients were treated with MO, starting doses were 25 mg for 27 patients and 50 mg in 55 patients. 82 patients were treated with DA, starting doses were in accordance with previous ESA dose and interval. The mean of baseline Hb values were 11.31 g/dL and 11.27 g/dL in the MO and DA group, respectively. For the mean Hb values during the evaluation period in MO, the mean was 11.67 g/dL (95%CI; 11.48, 11.85) and the mean Hb values of 66 patients (80.5%) were within the target range. As the primary efficacy variables (the changes from baseline of mean Hb values during the evaluation period), the means were 0.35 g/dL (95%CI; 0.12, 0.58) and 0.26 g/dL (95%CI; 0.04, 0.48) in the MO and DA group, respectively. The LS mean difference was 0.13 (95%CI; -0.15, 0.40), therefore the non-inferiority of MO to DA was established. The mean (SD) doses during the study period were 52.16 (32.58) mg/day of MO and 21.33 (12.33) μg/week of DA. AEs were experienced in 87.8% of patients in the MO group and 89.0% of patients in the DA group up to 36 weeks. The most common AEs occurred $\geq$ 5% of patients in any group were nasopharyngitis (29.3% and 30.5%, respectively) and worsening of chronic kidney disease (12.2% and 7.3%, respectively).

Conclusion: Maintenance effect of MO on the Hb values was investigated and the non-inferiority of MO to DA was established in non-dialysis patients with anemia treated with ESAs. The MO showed no new safety concern but further longitudinal investigation will be needed.

P1869

COFFEE INTAKE AND HEADACHE IN HAEMODIALYSIS (COFFEEHD TRIAL): A RANDOMIZED DOUBLE BLIND MULTICENTER CLINICAL TRIAL

Mabel Aoun[1,2], Najla Hilal[3], Beaini Chadia[4], Ghassan Sleilaty[5], Joseph Hajal[1,6], Celine Boueri[3], Dania Nehme Chelala[1,6]

[1]School of Medicine, Saint-Joseph University, Nephrology, Lebanon, [2]Saint-George Hospital, Nephrology, Ajaltoun, Lebanon, [3]Saint-George Hospital, Ajaltoun, Lebanon, [4]Bellevue Medical Center, Lebanon, [5]School of Medicine, Saint-Joseph University, Lebanon and [6]Hotel-Dieu de France, Nephrology, Lebanon

Background and Aims: Coffee with its major component caffeine can enhance alertness and decrease tiredness and headache. Headache was reported in 40 to 75 % of hemodialysis patients. Caffeine circulates unbound in the blood and passes the dialysis membrane. Some authors suggested that headache can result from caffeine withdrawal. This study aims to compare the incidence of headache and hypotension between patients taking or not coffee during dialysis.

Method: This is a randomized double-blind multicenter trial. Patients of three hemodialysis units were included. Patients with atrial fibrillation were excluded. 156 patients were randomized to two groups, group A was given 80 cc of coffee and group B 80 cc of decaffeinated coffee in the middle of the session for 12 consecutive sessions. Ultrafiltration rate was fixed to a maximum of 13 ml/kg/h. The primary outcome was the incidence of headache and the secondary incidence of hypotension. This clinical trial received the approval of the ethics committee of Saint-Joseph University (HDF-1463) and was registered on ClinicalTrials.Gov (NCT04057313).

Results: A total of 139 patients completed the trial (6.4% vs 15.4 % of withdrawal in groups A and B respectively). Baseline characteristics are summarized in Table 1. The number of sessions with headache was not significantly different between group A and B (34% vs 37% respectively, p=0.522), nor the number of sessions with hypotension (27% vs 26% respectively, p= 0.539). In a subgroup analysis, headache was higher in group B (p=0.06) in two categories of patients: those with the highest potassium dialysate (K=2) and the non-hypertensive patients.

Conclusion: Headache occurred in 34 to 37% of dialysis sessions. There was no difference in headache or hypotensive episodes between patients in the coffee versus decaffeinated group.

Table 1. Baseline characteristics: comparison of group A and B.

		A	B	P-value
Age		64.3 ± 13	69 ± 11.4	0.016*
Sex	M	56(71.8%)	46(59%)	0.092**
	F	22(28.2%)	32(41%)	
Dialysis Vintage		39[17 - 84]	27[14 - 55]	0.086***
Smoking	N	51(65.4%)	60(76.9%)	0.112**
	Y	27(34.6%)	18(23.1%)	
Alcohol	N	75(96.2%)	75(96.2%)	1.000****
	Y	3(3.8%)	3(3.8%)	
Hypertension	N	7(9%)	12(15.4%)	0.221**
	Y	71(91%)	66(84.6%)	
Coffee cups per day		2.4 ± 1.4	2.3 ± 1.5	0.783*
Coffee intake before session	N	36(46.2%)	37(47.4%)	0.873**
	Y	42(53.8%)	41(52.6%)	
Coffee during dialysis	N	51(65.4%)	47(60.3%)	0.508**
	Y	27(34.6%)	31(39.7%)	
Diabetes	N	45(57.7%)	36(46.2%)	0.149**
	Y	33(42.3%)	42(53.8%)	
Coronary artery disease	N	49(62.8%)	42(53.8%)	0.256**
	Y	29(37.2%)	36(46.2%)	
Headache usually	N	64(82.1%)	67(85.9%)	0.513**
	Y	14(17.9%)	11(14.1%)	
Beta-blockers	N	18(23.1%)	17(21.8%)	0.848**
	Y	60(76.9%)	61(78.2%)	
Antidepressant/benzodiazepin	N	58(74.4%)	58(74.4%)	1.000**
	Y	20(25.6%)	20(25.6%)	
Urea Reduction Ratio		75.6 ± 5.3	76.5 ± 4.9	0.274*
Dialysate potassium	0	4(5.1%)	6(7.7%)	0.468**
	1	33(42.3%)	26(33.3%)	
	2	41(52.6%)	46(59%)	
Pre HD systolic pressure (averaged)		146.5 ± 21.7	140.4 ± 21.1	0.076*
Pre HD diastolic pressure (averaged)		76.7 ± 12.8	72.6 ± 11.9	0.036*
Pre HD heart rate (averaged)		71.6 ± 10	68.8 ± 10	0.077*

*Independent Samples Test; **Pearson Chi-Square; ***Mann-Whitney U;****Fischer's Exact Test

N, No; Y; Yes

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LATE BREAKING CLINICAL TRIALS

LB001

EFFICACY AND SAFETY OF BELIMUMAB IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS: A PHASE 3, RANDOMISED, PLACEBO-CONTROLLED TRIAL

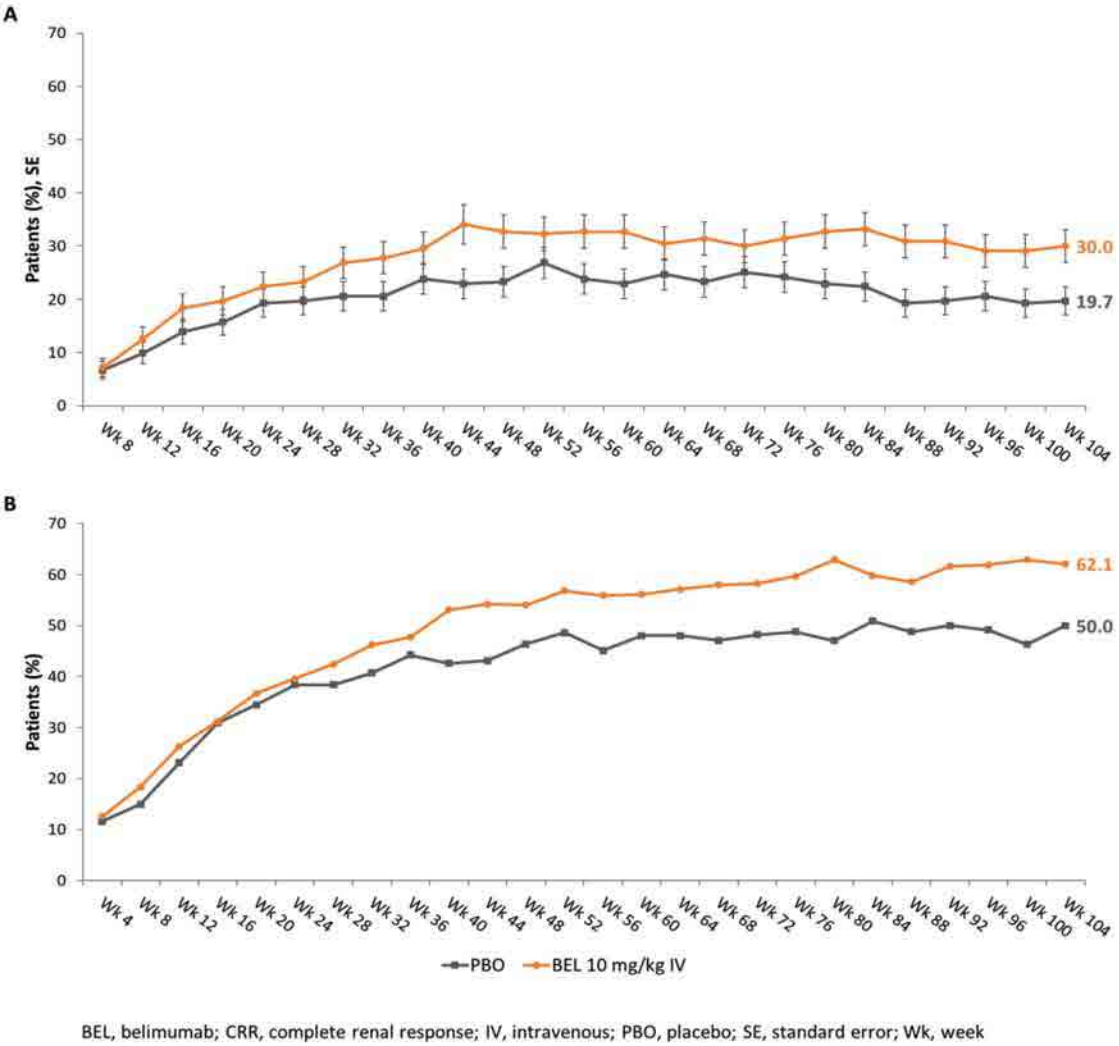
Brad Rovin[1], Frédéric A. Houssiau[2], Richard Furie[3], Ana Malvar[4], Y.K.O. Teng[5], Chi Chiu Mok[6], Gabriel Contreras[7], Xueqing Yu[8], Sebastian Dolff[9], Beulah Ji[10], David Roth[11], Christi Kleoudis[12], Damon Bass[11], Anuradha Madan[11], Amanda Wright[11], Carly Barnett[10], Yulia Green[10]

[1]The Ohio State University, Division of Nephrology, Columbus, United States of America, [2]Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain and Service de Rhumatologie, Cliniques Universitaires Saint-Luc, Pôle de Pathologies Rhumatismales Inflammatoires et Systémiques, Brussels, Belgium, [3]Northwell Health, Division of Rheumatology, Great Neck, United States of America, [4]Organizacion Medica de Investigacion, Buenos Aires, Argentina, [5]Leiden University Medical Center, Expert Center for Lupus-, Vasculitis- and Complement-mediated Systemic diseases, Department of Internal Medicine – section Nephrology, Leiden, Netherlands, [6]Tuen Mun Hospital, Department of Medicine, Hong Kong SAR, P.R. China, [7]University of Miami Miller School of Medicine, Division of Nephrology, Division of Hypertension, Department of Medicine, Miami, United States of America, [8]Guangdong Provincial People's Hospital, Department of Nephrology, Guangzhou, P.R. China, [9]University Hospital Essen, University of Duisburg-Essen, Department of Infectious Diseases, Essen, Germany, [10]GlaxoSmithKline, Uxbridge, United Kingdom, [11]GlaxoSmithKline, Collegeville, United States of America and [12]Parexel, Durham, United States of America

Background and Aims: Belimumab (BEL), an anti-B-cell-activating factor (BAFF) monoclonal antibody, is approved in patients (pts) ≥5 years of age with active systemic lupus erythematosus (SLE). *Post hoc* analyses of pooled renal outcomes data from two Phase 3 SLE studies showed favourable trends of greater reduction in proteinuria, haematuria, pyuria and lower renal flare rates in BEL-treated pts vs placebo (PBO).[1] This is the largest study in acute lupus nephritis (LN) to date that evaluated efficacy and safety of intravenous (IV) BEL plus standard therapy (ST) in pts with active LN.

Method: BLISS-LN is a Phase 3, randomised, double-blind, placebo-controlled, 104-week study (GSK study BEL114054, NCT01639339); eligible pts (≥18 years) with autoantibody-positive SLE and active, biopsy-proven LN (classes III, IV and/or V) were randomised (1:1) to monthly BEL 10 mg/kg IV or PBO, plus ST. Randomisation was stratified by induction regimen: high dose corticosteroids [HDCS] plus either

Figure 1. (A) CRR response by visit and (B) proteinuria shift from ≥0.5 at baseline to <0.5 while on study



BEL, belimumab; CRR, complete renal response; IV, intravenous; PBO, placebo; SE, standard error; Wk, week

Figure:

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cyclophosphamide (CyC), followed by azathioprine + low dose corticosteroids (LDCS), or mycophenolate mofetil (MMF), followed by MMF + LDCS. Primary endpoint: primary efficacy renal response (PERR; defined as urine protein creatinine ratio [uPCR] $\leq$0.7; estimated glomerular filtration rate [eGFR] no more than 20% below pre-flare value or $\geq$60 ml/min/1.73m^2; no rescue therapy) at Week (Wk) 104. Key secondary endpoints: complete renal response (CRR; defined as uPCR $<$0.5; eGFR no more than 10% below pre-flare value or $\geq$90 ml/min/1.73m^2; no rescue therapy) at Wk 104; PERR at Wk 52; risk of renal-related event (defined as end-stage renal disease/doubling of serum creatinine/renal worsening/renal disease-related treatment failure) or death at any time up to Wk 104. Other endpoints: PERR and CRR at Wk 104 by induction regimen; proportions of pts with baseline uPCR $\geq$0.5 with uPCR shift to $<$0.5 while on study.

Results: Overall, 448 pts were randomised (efficacy: 223/treatment group; safety: 224/treatment group); 118 pts received CyC induction and 328 MMF induction; 278 (62.3%) completed the treatment.

At Wk 104, 43.0% BEL and 32.3% PBO pts achieved PERR (OR [95% CI] vs PBO 1.55 [1.04, 2.32], p=0.0311); 30.0% BEL and 19.7% PBO pts achieved CRR (OR [95% CI] vs PBO 1.74 [1.11, 2.74], p=0.0167). Over 104 weeks, more BEL than PBO pts achieved CRR at each visit (**Figure 1A**). PERR at Wk 52 was achieved by 46.6% BEL and 35.4% PBO pts (OR [95% CI] vs PBO 1.59 [1.06, 2.38], p=0.0245).

The risk of a renal-related event or death was 49% lower with BEL than PBO (HR [95%CI] 0.51 [0.34, 0.77]; p=0.0014) at any time point during the study. Overall, 15.7% of BEL and 28.3% of PBO pts experienced a renal-related event or death.

When analysed by induction regimen, PERR at Wk 104 was achieved by 33.9% BEL and 27.1% PBO CyC-induced pts (OR [95% CI] vs PBO 1.52 [0.66, 3.49], p=0.3272), and by 46.3% BEL and 34.1% PBO MMF-induced pts (OR [95% CI] vs PBO 1.58 [1.00, 2.51], p=0.0501). CRR at Wk 104 was achieved by 18.6% BEL and 18.6% PBO CyC-induced pts (OR [95% CI] vs PBO 1.07 [0.41, 2.78], p=0.8843), and by 34.1% BEL and 20.1% PBO MMF-induced pts (OR [95% CI] vs PBO 2.01 [1.19, 3.38], p=0.0085).

Proportions of pts with uPCR shift from $\geq$0.5 at baseline to $<$0.5 while on study (calculated *post hoc*) are presented in the **Figure 1B**.

Overall, 95.5% BEL and 94.2% PBO pts had $\geq$1 adverse event (AE); 25.9% BEL and 29.9% PBO pts had $\geq$1 serious AE; 13.8% BEL and 17.0% PBO pts had serious infections; 12.9% pts in each group had $\geq$1 AE resulting in study treatment discontinuation; on-treatment fatal AEs were reported in 1.8% BEL and 1.3% PBO pts.

Conclusion: BEL demonstrated improved renal responses vs PBO in pts with active LN, with a safety profile consistent with previous BEL trials.

LB002

ILLUMINATE-A, A PHASE 3 STUDY OF LUMASIRAN, AN INVESTIGATIONAL RNAI THERAPEUTIC, IN CHILDREN AND ADULTS WITH PRIMARY HYPEROXALURIA TYPE 1 (PH1)

Sander Garrelfs[1], Yaacov Frishberg[2], Sally Hulton[3], Michael Koren[4], William O'Riordan[5], Pierre Cochat[6], Georges Deschenes[7], Hadas Shasha-Lavsky[8], Jeffrey Saland[9], William Van't Hoff[10], Daniel Guido Fuster[11], Daniella Magen[12], Shabbir Moochhala[13], Gesa Schalk[14], Eva Simkova[15], Jaap Groothoff[1], David Sas[16], Kristin Meliambro[9], Jiandong Lu[17], Pushkal Garg[17], John Gansner[17], Tracy McGregor[17], John Lieske[16]

[1]Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, , [2]Division of Pediatric Nephrology, Shaare Zedek Medical Center, Israel, [3]Birmingham Children's Hospital, Birmingham, United Kingdom, [4]Jacksonville Center for Clinical Research, Jacksonville, FL, United States of America, [5]eStudySite, San Diego, CA, United States of America, [6]Hospices Civils de Lyon, Université de Lyon, Lyon, France, [7]Hospital Robert Debré, Paris, France, [8]Galilee Medical Center, Nahariya, Israel, [9]Icahn School of Medicine, New York, NY, United States of America, [10]Great Ormond Street Hospital, London, United Kingdom, [11]Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, [12]Pediatric Nephrology Institute, Rambam Health Care Campus, Technion Faculty of Medicine, Haifa, Israel, [13]Royal Free Hospital, London, United Kingdom, [14]University of Bonn, Bonn, Germany, [15]Al Jalila Children's Hospital, Dubai, United Arab Emirates, [16]Mayo Clinic, Rochester, MN, United States of America and [17]Alnylam Pharmaceuticals, Cambridge, MA, United States of America

Background and Aims:

PH1 is a rare genetic disorder characterized by hepatic oxalate overproduction, leading to recurrent kidney stones, nephrocalcinosis, progressive kidney failure, and multiorgan damage from systemic oxalosis. There are no approved pharmacologic therapies for PH1. Lumasiran is a subcutaneously-administered investigational RNAi therapeutic that targets glycolate oxidase to reduce hepatic oxalate production. We report the first results from the six-month, double-blind period of ILLUMINATE-A, a randomized, placebo-controlled Phase 3 study to evaluate lumasiran in patients with PH1.

Method:

Key inclusion criteria: age$\geq$6 years, 24hr urinary oxalate (UOx)$\geq$0.70 mmol/24hr/1.73m^2, confirmed PH1 diagnosis, eGFR$\geq$30 mL/min/1.73m^2. Randomization: 2:1; lumasiran (n=26), placebo (n=13). Dosing: 3 mg/kg monthly$\times$3, then quarterly. Primary endpoint: percent change in 24hr UOx excretion from baseline to month (M) 6. Primary comparison: least square (LS) mean treatment difference in percent change from baseline (average of M3-6).

Results:

Lumasiran led to a statistically significant percent reduction in 24hr UOx excretion compared to placebo: the LS mean change from baseline to M6 (average of M3-6) was -65.4% with lumasiran and -11.8% with placebo (LS mean difference: -53.5%; $p=1.7 \times 10^{-14}$). Subgroup analyses of the primary endpoint showed a consistent effect of lumasiran across age, baseline UOx, eGFR, and concomitant pyridoxine use. Lumasiran led to statistically significant improvements in all hierarchically tested secondary endpoints, including: proportion of lumasiran-treated patients that achieved normalization or near-normalization of 24hr UOx at M6 (84% vs 0% of placebo-treated patients, $p=8.3 \times 10^{-7}$), and percent change in plasma oxalate from baseline to M6 (average of months 3-6) (-39.5%, $p=2.9 \times 10^{-8}$). There were no serious or severe adverse events. The most common adverse events related to lumasiran were mild, transient injection site reactions.

Conclusion:

Lumasiran resulted in clinically meaningful, rapid, sustained, and statistically significant reductions in urinary and plasma oxalate levels compared to placebo during the six-month double-blind period. Lumasiran has a favorable safety profile.

LB003

A RANDOMIZED, DOUBLE-BLIND, ACTIVE CONTROLLED STUDY OF AVACOPAN IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

David Jayne[1], Peter Merkel[2], Huibin Yue[3], Thomas J. Schall[3], Catherine Kelleher[3], Pirow Bekker[3]

[1]University of Cambridge, Medicine, Cambridge, United Kingdom, [2]University of Pennsylvania and [3]ChemoCentryx, Inc., Mountain View, United States of America

Background and Aims:

Complement fragment C5a is strongly linked to the pathogenesis of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). The C5a receptor (C5aR), is a G protein-coupled receptor present on neutrophils. Avacopan (previously CCX168) is an orally-administered selective antagonist of C5aR which blocks C5a-induced cell activation. Two previous Phase 2 clinical trials provided evidence of effectiveness of avacopan in AAV.

This Phase 3 study evaluated the efficacy and safety of avacopan for the treatment of AAV as well as the potential of avacopan to eliminate extensive use of glucocorticoids (GC) and GC-related toxicities.

Method:

Eligible subjects were randomized 1:1 to receive either prednisone or avacopan in combination with either a) cyclophosphamide (oral or IV) followed by azathioprine or b) rituximab (four IV infusions). Randomization was stratified by the treatment regimen (rituximab, IV cyclophosphamide, or oral cyclophosphamide), ANCA serotype, and newly-diagnosed or relapsing disease. Treatment period was 52 weeks; primary efficacy endpoints were the proportion of subjects achieving disease remission at Week 26, and sustained disease remission at Week 52. Remission was defined as a Birmingham Vasculitis Activity Score (BVAS) of zero and not taking glucocorticoids for AAV within 4 weeks prior to Week 26. Sustained remission was defined as being in remission at Week 26 and sustained through Week 52 without relapse. Change in estimated glomerular filtration rate (eGFR) from baseline to week 52 was a pre-specified secondary endpoint.

Results:

330 subjects were randomized and dosed: 166 in the avacopan and 164 in the prednisone groups. At Week 26, 72.3% subjects achieved remission in the avacopan compared to 70.1% in the prednisone group ($p<0.0001$ for non-inferiority). At Week 52, 65.7% subjects achieved sustained remission in the avacopan compared to 54.9% in the prednisone group achieving both non-inferiority and superiority to prednisone group ($p=0.0066$ for superiority of avacopan).

The avacopan arm had a significant reduction in glucocorticoid-related toxicity compared to the prednisone arm as measured by the Glucocorticoid Toxicity Index of Cumulative Worsening Score ($p=0.0002$) and Aggregate Improvement Score ($p=0.0082$).

In subjects with renal disease at baseline, the avacopan group (n=134) showed a mean increase in eGFR of 7.3 mL/min/1.73 m^2 from baseline to week 52 as compared to 4.1 mL/min/1.73 m^2 increase in the prednisone group (n=132) ($p=0.029$). A pre-specified sub-group analysis showed a greater difference in the avacopan sub-group with a baseline eGFR <30 (13.7 mL/min/1.73 m^2 vs. 8.2 mL/min/1.73 m^2; $p<.005$).

Conclusion:

Treatment with avacopan resulted in remission in patients with AAV receiving rituximab or cyclophosphamide/azathioprine at a rate that was non-inferior to the active comparator prednisone at Week 26 and superior to prednisone in sustained remission at Week 52. A significant reduction in glucocorticoid-related toxicity was observed in the avacopan vs. prednisone arms. The increase in eGFR seen with avacopan was marked among subjects with more severe renal disease. The safety profile of avacopan was acceptable for use in patients with AAV. The ADVOCATE trial demonstrated avacopan is an effective treatment for patients with AAV.

LB004

A RANDOMIZED, CONTROLLED TRIAL OF RITUXIMAB VERSUS AZATHIOPRINE AFTER INDUCTION OF REMISSION WITH RITUXIMAB FOR PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND RELAPSING DISEASE

Rona Smith[1], David Jayne[1], Peter Merkel[2]

[1]University of Cambridge, Cambridge, United Kingdom and [2]University of Pennsylvania, United States of America

Background and Aims: Rituximab is an effective therapy for induction of remission in ANCA-associated vasculitis (AAV). However, the effect of rituximab is not sustained, and subsequent relapse rates are high, especially in patients with a history of relapse. The RITAZAREM trial (ClinicalTrials.gov identifier: NCT01697267) is an international, multi-center, open-labelled, randomized, controlled trial of patients with AAV with relapsing disease comparing the efficacy, after induction of remission with rituximab, of two relapse-prevention strategies: repeat dosing of rituximab or daily oral azathioprine.

Method: Patients with AAV were recruited at the time of relapse and received induction therapy with rituximab and glucocorticoids. If remission was achieved by month 4, patients were randomized in a 1:1 ratio to receive either rituximab (1000 mg every 4 months for 5 doses) or azathioprine (2 mg/kg/day) as maintenance therapy. Patients were followed for a minimum of 36 months, with the primary outcome being time to disease relapse. The formal hypothesis testing plan initially considers the hazard ratio for relapse across all time periods. If, and only if this global test is significant at a 5% level then the hazard ratios during the treatment period and the follow-up periods are considered separately.

Results: 190 patients were enrolled and 170 randomized at 4 months (85 to rituximab; 85 to azathioprine). The data are complete on all patients up to at least month 24. Median age was 59 years (range 19-89), with a prior disease duration of 5.3 years (0.4-38.5). 123/170 (72%) patients had a history of testing positive for anti-proteinase 3 ANCA; 47/170 (28%) for myeloperoxidase ANCA; 104/170 (61%) were enrolled having suffered a major relapse, and 48/170 (28%) received a pre-specified higher dose glucocorticoid induction regimen.

Rituximab was superior to azathioprine in preventing disease relapse with a preliminary overall hazard ratio (HR) estimate of 0.36 (95% CI 0.23-0.57, p <0.001) and a during-treatment HR estimate of 0.30 (95% CI 0.15-0.60, p<0.001) (**Figure 1**). After adjustment, none of the randomization stratification covariates (ANCA type, glucocorticoid induction regimen, or relapse severity) had a significant differential effect on the primary outcome. By 24 months after entry, 20 months after randomization, 11/85 (13%) patients in the rituximab group had experienced a relapse compared to 32/85 (38%) patients in the azathioprine group. In the rituximab group 2/11 (18%) relapses were classified as major, compared to 12/32 (38%) in the azathioprine group. 19/85 (22%) patients in the rituximab group and 31/85 (36%) patients in the azathioprine group experienced at least one severe adverse event (SAE). 25/85 (29%) and 42/85 (49%) patients in the rituximab group developed hypogammaglobulinaemia (IgG <5g/l) and non-severe infections respectively, compared to 21/85 (25%) and 41/85 (48%) in the azathioprine group.

Conclusion: In the RITAZAREM trial, following induction of remission with rituximab, rituximab was superior to azathioprine for preventing disease relapse in patients with AAV with a prior history of relapse. There were no new major safety signals for use of these medications in this population.

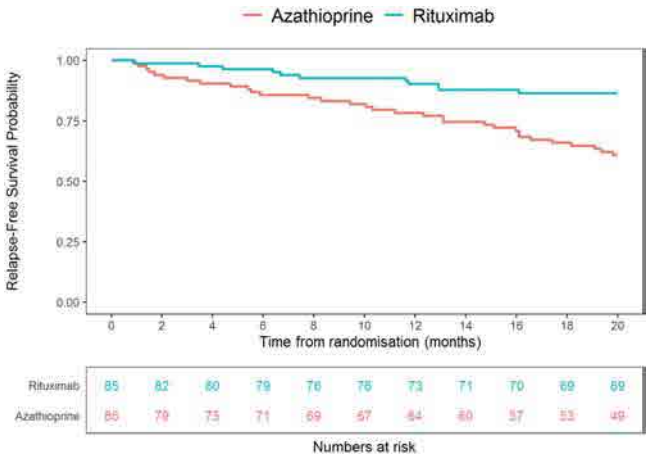


Figure 1: **Relapse-free survival in RITAZAREM trial: rituximab versus azathioprine**

LB005

KIDNEY IMPLICATIONS OF THE INITIAL EGFR RESPONSE TO SGLT2 INHIBITION WITH EMPAGLIFLOZIN: THE 'EGFR DIP' IN EMPA-REG OUTCOME

Bettina J. Kraus[1,2], Matthew Weir[3], George Bakris[4], Michaela Mattheus[5], David Cherney[6], Naveed Sattar[7], Hiddo Lambers Heerspink[8], Ivana Ritter[9], Maximilian Von Eynatten[9], Bernard Zinman[10], Silvio Inzucchi[11], Christoph Wanner[1], Audrey Koitka-Weber[1,9,12]

[1]University Hospital Würzburg, Department of Internal Medicine I, Würzburg, Germany, [2]University Hospital Würzburg, Comprehensive Heart Failure Centre, Würzburg, Germany, [3]University of Maryland School of Medicine, Division of Nephrology, Department of Medicine, Baltimore, United States of America, [4]University of Chicago Medicine, Department of Medicine, Am. Heart Assoc. Comprehensive Hypertension Center, Chicago, United States of America, [5]Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany, [6]University Health Network, Department of Medicine and Department of Physiology, Division of Nephrology, Toronto, Canada, [7]University of Glasgow, Institute of Cardiovascular and Medical Sciences, United Kingdom, [8]University of Groningen, University Medical Center Groningen, Department of Clinical Pharmacy and Pharmacology, Groningen, Netherlands, [9]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany, [10]Mount Sinai Hospital, and University of Toronto, Lunenfeld-Tanenbaum Research Institute, Toronto, Canada, [11]Yale University School of Medicine, 11Section of Endocrinology, New Haven, United States of America and [12]Monash University, Department of Diabetes, Central Clinical School, Melbourne, Australia

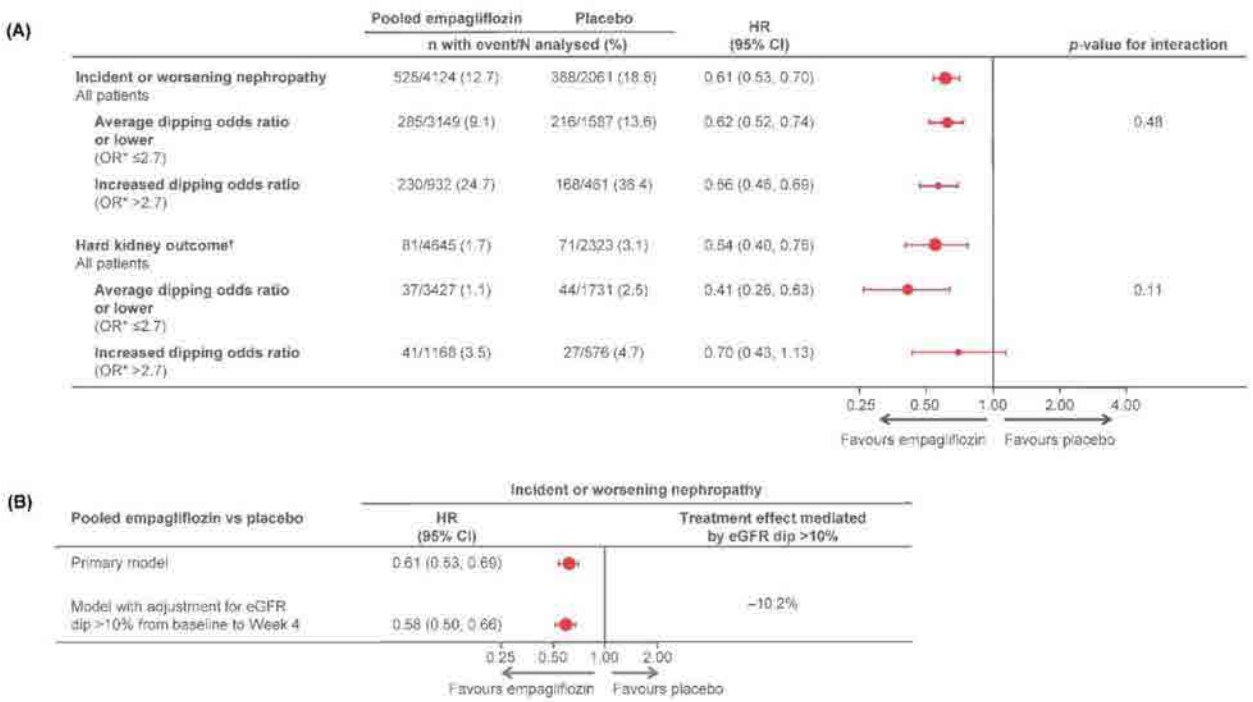
Background and Aims: Empagliflozin (EMPA) reduces cardiovascular and renal risk in patients with type 2 diabetes (T2D) and established cardiovascular disease (CVD). EMPA induces an initial 'dip' in estimated glomerular filtration rate (eGFR). Although considered to be of haemodynamic origin and largely reversible, this needs to be better understood. We investigated whether the initial eGFR dip after EMPA initiation was influenced by baseline characteristics and/or might have an impact on the EMPA-induced risk reduction in kidney outcomes.

Method: In the EMPA-REG OUTCOME trial, patients with T2D and established CVD were treated (1:1:1) with EMPA 10 mg, 25 mg or placebo (PBO), in addition to standard of care. In this post hoc analysis, 6,668 participants who received at least one dose of study drug and had an available eGFR value at both baseline and Week 4 were categorised by initial percentage eGFR change from baseline. A multivariate logistic regression model was used to identify which baseline characteristics are predictive of an initial eGFR dip >10% in EMPA-treated participants versus PBO. Across these predictive baseline factors, we investigated the occurrence of incident or worsening nephropathy, hard kidney outcomes (defined as doubling of serum creatinine with eGFR [MDRD] ≤45 ml/min/1.73 m2 or initiation of renal replacement therapy or death from renal disease), and kidney safety (narrow standardized MedDRA query acute renal failure). The impact of an eGFR dip >10% on the risk reduction with EMPA for incident or worsening nephropathy was assessed using Cox regression analysis adjusting for such eGFR dip.

Results: In the EMPA-REG OUTCOME trial cohort, an initial eGFR dip of >10% from baseline at Week 4 occurred in more than twice as many participants on EMPA (28.3%) compared to PBO (13.4%). However, a more pronounced eGFR dip of >30% was uncommon, occurring in only 1.4% and 0.9%, respectively. Within the EMPA group, participants with an eGFR dip >10% were significantly older, had longer diabetes duration and showed a higher KDIGO (Kidney Disease: Improving Global Outcomes) risk category. Diuretic use and/or higher KDIGO risk category at baseline were predictive of an initial eGFR dip of >10% in EMPA vs. PBO. The average odds ratio [OR; 95% CI] for an eGFR dip >10% with EMPA was 2.7 [2.3–3.0]. In subgroups with a dipping odds ratio below vs. above that average, beneficial treatment effects with EMPA on incident or worsening nephropathy and the hard kidney outcome were consistent (panel A). Also, an eGFR dip >10% did not affect risk reduction for the primary kidney outcome (panel B). Acute renal failure rates were generally lower or similar in EMPA vs. PBO, regardless of baseline predictive factors for an eGFR dip.

Conclusion: T2D patients with more advanced kidney disease and/or on diuretic therapy at baseline were more likely to have an initial eGFR dip >10% with EMPA. However, EMPA treatment appeared to be safe and was associated with improved kidney outcomes, regardless of these baseline predictive factors or an initial eGFR dip >10%.

Kidney outcomes overall and in subgroups by predicted odds ratio for an eGFR dip >10% in empagliflozin-treated patients versus placebo (A) and percentage of risk reduction on incident or worsening nephropathy mediated by an eGFR dip >10% (B)



Participants treated with ≥1 dose of study drug who have an eGFR value available at baseline and Week 4.
(A) Risk reduction for kidney outcomes overall and by baseline diuretic use/KDIGO category subgroups categorised according to their risk (OR) below and above average (≤2.7 and >2.7) for an initial eGFR dip >10% from baseline with empagliflozin vs placebo. OR (95% CI) for eGFR dip >10% in empagliflozin vs placebo in the overall population: 2.7 (2.3–3.0).
*For an initial eGFR dip >10% from baseline with empagliflozin vs placebo. Average dipping OR or lower: participants with no diuretic use at baseline and any KDIGO risk or diuretic use at baseline and low KDIGO risk. Increased dipping OR: participants with baseline diuretic use and KDIGO risk moderate to high.
†Doubling of serum creatinine with eGFR (MDRD) ≤45 ml/min/1.73 m² or initiation of renal replacement therapy or death from renal disease.
Results based on Cox regression with factors for treatment, age, sex, baseline BMI, baseline HbA1c, region, subgroup, and interaction of subgroup by treatment.
(B) Percentage of empagliflozin treatment effect mediated by an eGFR dip >10% including from comparison of treatment effect from primary model with treatment effect adjusted for eGFR dip >10% based on landmark analyses following Week 4.
Cox proportional hazards model with adjustment for treatment group, age, sex, baseline BMI, baseline HbA1c, baseline eGFR and region without/with factor for eGFR dip >10%.
BMI: body mass index; CI: confidence interval; eGFR: estimated glomerular filtration rate; HR: hazard ratio; KDIGO: Kidney Disease: Improving Global Outcomes; MDRD: Modification of Diet in Renal Disease; OR: odds ratio.

Figure: